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STRATEGIC ANALYSIS,  
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Department of Global Health | University of Washington

## VACCINE DELIVERY RESEARCH DIGEST

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UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH, & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

NOVEMBER 15, 2016

PRODUCED BY: LEVINE, GA; SLYKER, J.



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## **1. Real-Time Monitoring of Vaccination Campaign Performance Using Mobile Phones - Nepal, 2016.**

Oh DH, Dabbagh A, Goodson JL, Strebel PM, Thapa S, Giri JN, et al.

MMWR Morb Mortal Wkly Rep. 2016 Oct 7;65(39):1072-1076.

PMID:27711034

### **ABSTRACT**

In 2012, the Global Vaccine Action Plan established a goal to achieve measles and rubella elimination in five of the six World Health Organization (WHO) regions (194 countries) by 2020. Measles elimination strategies aim to achieve  $\geq 95\%$  coverage with 2 routine doses of measles-containing vaccine, and implement supplementary immunization activities (SIAs) in settings where routine coverage is low or where there are subpopulations at high risk. To ensure SIA quality and to achieve  $\geq 95\%$  SIA coverage nationally, rapid convenience monitoring (RCM) is used during or immediately after SIAs. The objective of RCM is to find unvaccinated children and to identify reasons for nonvaccination in areas with persons at high risk, to enable immediate implementation of corrective actions (e.g., reassigning teams to poorly vaccinated areas, modifying the timing of vaccination, or conducting mop-up vaccination activities). This report describes pilot testing of RCM using mobile phones (RCM-MP) during the second phase of an SIA in Nepal in 2016. Use of RCM-MP resulted in 87% timeliness and 94% completeness of data reporting and found that, although 95% of children were vaccinated, 42% of areas required corrective vaccination activities. RCM-MP challenges included connecting to mobile networks, small phone screen size, and capturing Global Positioning System (GPS) coordinates. Nonetheless, use of RCM-MP led to faster data transmission, analysis, and decision-making and to increased accountability among levels of the health system.

**WEB:** <http://www.dx.doi.org/10.15585/mmwr.mm6539a5>

**IMPACT FACTOR:** 3.12

**CITED HALF-LIFE:** 0.00

**START SCIENTIFIC COMMENT:** The RCM-MP used Android phones to electronically collect the information in the standard RCM data collection tool. The platform provides real-time data visualization of key performance indicators of campaign performance, presented in “dashboards” of either “action”-specific outputs or “monitoring”-specific outputs (Table 2).

An example of the RCM-MP dashboard which displays key real-time outputs for use in guiding campaign activities, is provided in Figure 1.

Monitors reported the following challenges in using RCM-MP: Finding and connecting to older third generation (3G) or Wi-Fi networks, mistakenly striking incorrect keys (potentially due to small screen size), and recording GPS location. About two-thirds of monitors found the mobile technology easy or somewhat easy to use, and about half found it easier than paper data collection. Most monitors believed the data accuracy was better with RCM-MP, and the vast majority recommended its use. All of the district and national supervisors reported that RCM-MP technology was helpful.

The impact of RCM-MP on SIA coverage was not assessed in this study.



## 2. Improving hepatitis B birth dose in rural Lao People's Democratic Republic through the use of mobile phones to facilitate communication.

Xeuatvongsa A, Datta SS, Moturi E, Wannemuehler K, Philakong P, Vongxay V, et al.

Vaccine. 2016 Oct 11.

PMID: 27742222

### ABSTRACT

**BACKGROUND:** Hepatitis B vaccine birth dose (HepB-BD) was introduced in Lao People's Democratic Republic to prevent perinatal hepatitis B virus transmission in 2008; high coverage is challenging since only 38% of births occur in a health facility. Healthcare workers report being unaware of home births and thus unable to conduct timely postnatal care (PNC) home visits. A quasi-experimental pilot study was conducted wherein mobile phones and phone credits were provided to village health volunteers (VHV) and healthcare workers (HCWs) to assess whether this could improve HepB-BD administration, as well as birth notification and increase home visits.

**METHODS:** From April to September 2014, VHVs and HCWs in four selected intervention districts were trained, supervised, received outreach per diem for conducting home visits, and received mobile phones and phone credits. In three comparison districts, VHVs and HCWs were trained, supervised, and received outreach per diem for conducting home visits. A post-study survey compared HepB-BD coverage among children born during the study and children born one year before. HCWs and VHVs were interviewed about the study.

**FINDINGS:** Among intervention districts, 463 study children and 406 pre-study children were enrolled in the survey; in comparison districts, 347 study children and 309 pre-study children were enrolled. In both arms, there was a significant improvement in the proportion of children reportedly receiving a PNC home visit (intervention  $p < 0.0001$ , comparison  $p = 0.04$ ). The median difference in village level HepB-BD coverage (study cohort minus pre-study cohort), was 57% (interquartile range [IQR] 32-88%,  $p < 0.0001$ ) in intervention districts, compared with 20% (IQR 0-50%,  $p < 0.0001$ ) in comparison districts. The improvement in the intervention districts was greater than in the comparison districts ( $p = 0.0009$ ).

**CONCLUSION:** Our findings suggest that the provision of phones and phone credits might be one important factor for increasing coverage. However, reasons for improvement in both arms are multifactorial and discussed.

**WEB:** <http://dx.doi.org/10.1016/j.vaccine.2016.09.056>

**IMPACT FACTOR:** 3.62

**CITED HALF-LIFE:** 5.50

**START SCIENTIFIC COMMENT:** The study was limited to villages that already had village health worker. It should be noted that while villages were excluded in the intervention arm if the village lacked network coverage or the village health worker lacked an available method to charge the phone, such exclusions were not made in the control villages, which could lead to baseline differences between the intervention and control group on factors that might also influence vaccination coverage, and thus could have introduced bias into the study.

Although authors report that mobile phone use is common in the study population, even without the provision of phones and credit from the study, village health workers in the intervention arm reported less problems with mobile phones or problems with lack of phone credit than did control-arm workers.

Measures that evaluated the behavior of village health workers, such as how often they informed the health care workers of deliveries and when they informed health care workers about deliveries, were self-reported in a post-intervention survey, and could potentially be subject to measurement error and recall bias.

In intervention and control districts health workers were trained in appropriate perinatal care and were provided with a per diem for each household visit conducted, which could partially explain the improvement in home-visit and vaccination coverage observed in both intervention and control districts from baseline.



### [3. Assessing the Potential Cost-Effectiveness of Microneedle Patches in Childhood Measles Vaccination Programs: The Case for Further Research and Development.](#)

Adhikari BB, Goodson JL, Chu SY, Rota PA, Meltzer MI.

Drugs R & D. 2016 Oct 1.

PMID:27696306

#### **ABSTRACT**

**OBJECTIVE:** Currently available measles vaccines are administered by subcutaneous injections and require reconstitution with a diluent and a cold chain, which is resource intensive and challenging to maintain. To overcome these challenges and potentially increase vaccination coverage, microneedle patches are being developed to deliver the measles vaccine. This study compares the cost-effectiveness of using microneedle patches with traditional vaccine delivery by syringe-and-needle (subcutaneous vaccination) in children's measles vaccination programs.

**METHODS:** We built a simple spreadsheet model to compute the vaccination costs for using microneedle patch and syringe-and-needle technologies. We assumed that microneedle vaccines will be, compared with current vaccines, more heat stable and require less expensive cool chains when used in the field. We used historical data on the incidence of measles among communities with low measles vaccination rates.

**RESULTS:** The cost of microneedle vaccination was estimated at US\$0.95 (range US\$0.71-US\$1.18) for the first dose, compared with US\$1.65 (range US\$1.24-US\$2.06) for the first dose delivered by subcutaneous vaccination. At 95 % vaccination coverage, microneedle patch vaccination was estimated to cost US\$1.66 per measles case averted (range US\$1.24-US\$2.07) compared with an estimated cost of US\$2.64 per case averted (range US\$1.98-US\$3.30) using subcutaneous vaccination.

**CONCLUSIONS:** Use of microneedle patches may reduce costs; however, the cost-effectiveness of patches would depend on the vaccine recipients' acceptability and vaccine effectiveness of the patches relative to the existing conventional vaccine-delivery method. This study emphasizes the need to continue research and development of this vaccine-delivery method that could boost measles elimination efforts through improved access to vaccines and increased vaccination coverage.

**WEB:** <http://dx.doi.org/10.1007/s40268-016-0144-x>

**IMPACT FACTOR:** 1.23

**CITED HALF-LIFE:** 2.40

**START SCIENTIFIC COMMENT:** Cost-effectiveness estimates for the delivery approaches will be sensitive to the model assumptions. In modeling cost-effectiveness, authors assumed: a) the target vaccination coverage was 95 %, b) vaccine effectiveness was 85 % for microneedle patches and subcutaneous vaccination, c) 100% compliance with subcutaneous injection and 90 % for microneedle patches, d) 7.7 % drop out for the second dose of measles-containing vaccine (MCV) for both groups. Figure 3 shows the average cost-effectiveness ratio of microneedle (MN) patches compared with subcutaneous (SC) injection at different levels of compliance rate of MN patches.

Cost-savings in micro-needle patches primarily resulted from less vaccine wastage; personnel costs including supervision, planning, and training for microneedle patches due to the relative ease of delivery and lack of need for higher-trained medical staff with patches; the need for only a cool chain versus a cold chain; less vaccine wastage with microneedles due to greater heat stability, lower manufacturing costs.

Authors note that in a setting where incidence is high, estimates would not be accurate if the microneedle patch were to confer less protection than subcutaneous injection.

Figure 1 depicts the measles incidence under different coverage levels with the first dose of measles-containing vaccine for single and two-dose strategies with microneedles and subcutaneous injection. Figure 2 depicts cost per case of measles averted by percentage of the population vaccinated at vaccine effectiveness of 77%, 85%, and 94%, with microneedle patch or subcutaneous injection delivery methods.



#### **4. Improving cold chain systems: Challenges and solutions.**

Ashok A, Brison M, LeTallec Y.

Vaccine. 2016 Sep 23. [Epub ahead of print].

PMID: 27670076

#### **ABSTRACT**

While a number of new vaccines have been rolled out across the developing world (with more vaccines in the pipeline), cold chain systems are struggling to efficiently support national immunization programs in ensuring the availability of safe and potent vaccines. This article reflects on the Clinton Health Access Initiative, Inc. (CHAI) experience working since 2010 with national immunization programs and partners to improve vaccines cold chains in 10 countries-Ethiopia, Nigeria, Kenya, Malawi, Tanzania, Uganda, Cameroon, Mozambique, Lesotho and India - to identify the root causes and solutions for three common issues limiting cold chain performance. Key recommendations include: (1) To address cold chain capacity: developing an accurate picture of cold chain capacity gaps based on current and future needs; resource mobilization, and; effective monitoring during implementation. (2) To encourage upgrade of cold chain with latest technology suitable in country: in-country piloting of new equipment; utilization of tools to better understand equipment trade-offs, and; guide equipment selection and regular engagement with suppliers. (3) To control temperature excursions and equipment breakdowns introduction of temperature monitoring and control (TMC) devices and practices; improve competence and availability of existing and future technicians, and; ensure availability of spare parts. Collectively, the solutions detailed in this article chart a path to substantially improving the performance of the cold chain. Combined with an enabling global and in-country environment, it is possible to eliminate cold chain issues as a substantial barrier to effective and full immunization coverage over the next few years.

**WEB:** <http://dx.doi.org/10.1016/j.vaccine.2016.08.045>

**IMPACT FACTOR:** 3.62

**CITED HALF-LIFE:** 5.50

**START SCIENTIFIC COMMENT:** From their experience working with national immunization programs and partners, authors describe the following three key challenges in immunization cold chains: "1) Insufficient capacity; 2) Unsafe technology and slow adoption of better equipment, and 3) Inadequate temperature control and maintenance systems."

Causes of insufficient capacity include poor visibility/understanding of current cold chain equipment status; insufficient forecasting of future capacity requirements; and inadequate implementation systems. Causes of sufficiency gaps include insufficient awareness and recognition of benefits of the features and benefits of new products; costs associated with switching over technologies; and expensive product offerings. The causes of poor temperature regulation include lack of awareness and lack of ongoing/continuous monitoring; and lack of availability of services and resources. The proposed solutions address each of these causal factors. Authors note that solutions should be considered in partnership, as approaches to address challenges in isolation will likely fail to result in an improved and functioning structure or overall system.



## **5. Re-designing the Mozambique vaccine supply chain to improve access to vaccines.**

Lee BY, Haidari LA, Prosser W, Connor DL, Bechtel R, Dipuve A, et al.

Vaccine. 2016 Sep 22;34(41):4998-5004. Epub 2016 Aug 26.

PMID: 27576077

### **ABSTRACT**

**INTRODUCTION:** Populations and routine childhood vaccine regimens have changed substantially since supply chains were designed in the 1980s, and introducing new vaccines during the "Decade of Vaccine" may exacerbate existing bottlenecks, further inhibiting the flow of all vaccines.

**METHODS:** Working with the Mozambique Ministry of Health, our team implemented a new process that integrated HERMES computational simulation modeling and on-the-ground implementers to evaluate and improve the Mozambique vaccine supply chain using a system-re-design that integrated new supply chain structures, information technology, equipment, personnel, and policies.

**RESULTS:** The alternative system design raised vaccine availability (from 66% to 93% in Gaza; from 76% to 84% in Cabo Delgado) and reduced the logistics cost per dose administered (from \$0.53 to \$0.32 in Gaza; from \$0.38 to \$0.24 in Cabo Delgado) as compared to the multi-tiered system under the current EPI. The alternative system also produced higher availability at lower costs after new vaccine introductions. Since reviewing scenarios modeling deliveries every two months in the north of Gaza, the provincial directorate has decided to pilot this approach diverging from decades of policies dictating monthly deliveries.

**DISCUSSION:** Re-design improved not only supply chain efficacy but also efficiency, important since resources to deliver vaccines are limited. The Mozambique experience and process can serve as a model for other countries during the Decade of Vaccines. For the Decade of Vaccines, getting vaccines at affordable prices to the market is not enough. Vaccines must reach the population to be successful.

**WEB:** <http://dx.doi.org/10.1016/j.vaccine.2016.08.036>

**IMPACT FACTOR:** 3.62

**CITED HALF-LIFE:** 5.50

**START SCIENTIFIC COMMENT:** HERMES, a software platform for generating event simulation models of a vaccine supply chain, was a key component of the approach. The process for the re-design of the supply chain included the following steps: 1) Engage with the Ministry of Health; 2) Conduct training workshops on the HERMES 3) Develop a computational simulation model of the immunization supply chain to determine the supply chain's "vulnerabilities and constraints" and to evaluate the expected impact of different designs of supply chain systems; 4) Engage in discussions to determine how to transition knowledge from the computational modeling to system implementation.

Model scenarios were developed based on models that stakeholders proposed at the training workshops. HERMES was used to compare the current model in use, an alternative model proposed by a stakeholder, and variations of the proposed model, for each province in the country separately. For instance, in Gaza province the current model of a multi-tiered distribution system was compared with an alternative multi-tiered distribution system with transport loops in one region of the province which used less district stores to distribute to the same number of health centers, and a structure in which transport loops were used throughout the province and district stores were eliminated. HERMES was used to model options for both current EPI vaccines, and options for the introduction of additional vaccines including rotavirus, HPV, in-activated polio, and a second dose of measles, using each different proposed structure. The primary indicators used for system comparison/system selection are vaccine availability and cost per dose administered.

In both provinces, the alternative models indicated potential improved availability and reduced cost compared with the current system in place.



## [6. Assessing strategies for increasing urban routine immunization coverage of childhood vaccines in low and middle-income countries: A systematic review of peer-reviewed literature.](#)

Nelson KN, Wallace AS, Sodha SV, Daniels D, Dietz V.

Vaccine. 2016 Sep 28.

PMID: 27692772

### **ABSTRACT**

**INTRODUCTION:** Immunization programs in developing countries increasingly face challenges to ensure equitable delivery of services within cities where rapid urban growth can result in informal settlements, poor living conditions, and heterogeneous populations. A number of strategies have been utilized in developing countries to ensure high community demand and equitable availability of urban immunization services; however, a synthesis of the literature on these strategies has not previously been undertaken.

**METHODS:** We reviewed articles published in English in peer-reviewed journals between 1990 and 2013 that assessed interventions for improving routine immunization coverage in urban areas in low- and middle-income countries. We categorized the intervention in each study into one of three groups: (1) interventions aiming to increase utilization of immunization services; (2) interventions aiming to improve availability of immunization services by healthcare providers, or (3) combined availability and utilization interventions. We summarized the main quantitative outcomes from each study and effective practices from each intervention category.

**RESULTS:** Fifteen studies were identified; 87% from the African, Eastern Mediterranean and Southeast Asian regions of the World Health Organization (WHO). Six studies were randomized controlled trials, eight were pre- and post-intervention evaluations, and one was a cross-sectional study. Four described interventions designed to improve availability of routine immunization services, six studies described interventions that aimed to increase utilization, and five studies aiming to improve both availability and utilization of services. All studies reported positive change in their primary outcome indicator, although seven different primary outcomes indicators were used across studies. Studies varied considerably with respect to the type of intervention assessed, study design, and length of intervention assessment.

**CONCLUSION:** Few studies have assessed interventions designed explicitly for the unique challenges facing immunization programs in urban areas. Further research on sustainability, scalability, and cost-effectiveness of interventions is needed to fill this gap.

**WEB:** <http://dx.doi.org/10.1016/j.vaccine.2016.09.038>

**IMPACT FACTOR:** 3.62

**CITED HALF-LIFE:** 5.50

**START SCIENTIFIC COMMENT:** Authors note that many of the interventions tested and many of the recommendations for strategies to improve coverage were not specific to the urban setting. Rather, interventions that are effective in rural settings may also be appropriate in and provide benefit to populations in urban settings. For example, within the urban setting, the use of community volunteers for health education and health facility referrals for vaccination were effective, even in urban settings where social cohesion is expected to be lower.

Authors note important gaps exist in generalizability of results and in understanding the impact of interventions in the long term, as most studies had relatively short follow-up and were often conducted among only a single population/site. Authors also note specific factors particularly relevant to urban populations which have not yet been addressed, including ways to transfer immunization records or make them transferrable, which is specifically important to urban populations where migration may be high and where care-seeking may occur at multiple facilities.



## **7. Measuring populations to improve vaccination coverage.**

Bharti N, Djibo A, Tatem AJ, Grenfell BT, Ferrari MJ.

Sci Rep. 2016 Oct 5;5:34541.

PMID:27703191

### **ABSTRACT**

In low-income settings, vaccination campaigns supplement routine immunization but often fail to achieve coverage goals due to uncertainty about target population size and distribution. Accurate, updated estimates of target populations are rare but critical; short-term fluctuations can greatly impact population size and susceptibility. We use satellite imagery to quantify population fluctuations and the coverage achieved by a measles outbreak response vaccination campaign in urban Niger and compare campaign estimates to measurements from a post-campaign survey. Vaccine coverage was overestimated because the campaign underestimated resident numbers and seasonal migration further increased the target population. We combine satellite-derived measurements of fluctuations in population distribution with high-resolution measles case reports to develop a dynamic model that illustrates the potential improvement in vaccination campaign coverage if planners account for predictable population fluctuations. Satellite imagery can improve retrospective estimates of vaccination campaign impact and future campaign planning by synchronizing interventions with predictable population fluxes.

**WEB:** <http://dx.doi.org/10.1038/srep34541>

**IMPACT FACTOR:** 3.12

**CITED HALF-LIFE:** 0.00

**START SCIENTIFIC COMMENT:** Size of the population in three urban centers in Niger were estimated using daily, serial satellite images of nighttime lights. Authors used these serial measures to quantify the fluctuations in population in the regions that occurred annually, primarily fueled by seasonal labor-related migration. Authors compared coverage estimates using population estimates from the local Ministry of Health, Medecins Sans Frontiers and the UN, to demonstrate how coverage estimates differed when applying different population denominator estimates, compared with Lot Quality Assurance (LQA) estimates. Without accounting for the seasonal population fluctuations which were indicated on the satellite images, population denominators from all three sources appeared to be inaccurate, resulting in biased coverage estimates, compared with LQA. The population fluctuation patterns identified in the satellite imagery coincided with seasonal trends in infection rates, which authors explain as indicative of the importance of seasonal migration on transmission patterns. Authors recommend using satellite data to identify trends in migration and population flow to inform timing and locations of campaigns to prevent outbreaks.



## **8. Informing rubella vaccination strategies in East Java, Indonesia through transmission modeling.**

Wu Y, Wood J, Khandaker G, Waddington C, Snelling T.

Vaccine. 2016 Sep 23. [Epub ahead of print]

PMID: 27670077

### **ABSTRACT**

An estimated 110,000 babies are born with congenital rubella syndrome (CRS) worldwide annually; a significant proportion of cases occur in Southeast Asia. Rubella vaccine programs have led to successful control of rubella and CRS, and even the elimination of disease in many countries. However, if vaccination is poorly implemented it might increase the number of women reaching childbearing age who remain susceptible to rubella and thereby paradoxically increase CRS. We used an age-structured transmission model to compare seven alternative vaccine strategies for their impact on reducing CRS disease burden in East Java, a setting which is yet to implement a rubella vaccine program. We also investigated the robustness of model predictions to variation in vaccine coverage and other key epidemiological factors. Without rubella vaccination, approximately 700 babies are estimated to be born with CRS in East Java every year at an incidence of 0.77 per 1000 live births. This incidence could be reduced to 0.0045 per 1000 live births associated with 99.9% annual reduction in rubella infections after 20 years if the existing two doses of measles vaccine are substituted with two doses of measles plus rubella combination vaccine with the same coverage (87.8% of 9-month-old infants and 80% of 6-year-old children). By comparison a single dose of rubella vaccine will take longer to reduce the burden of rubella and CRS and will be less robust to lower vaccine coverage. While the findings of this study should be informative for settings similar to East Java, the conclusions are dependent on vaccine coverage which would need consideration before applying to all of Indonesia and elsewhere in Asia.

**WEB:** <http://dx.doi.org/10.1016/j.vaccine.2016.09.010>

**IMPACT FACTOR:** 3.62

**CITED HALF-LIFE:** 5.50

**START SCIENTIFIC COMMENT:** The different vaccination strategies compared included: 1) no rubella vaccination; 2) universal infant vaccination (replacement of measles-rubella (MR) for measles vaccine (MV) at 6 months with only MV given at 9 months); 3) school-based vaccination at 6 years with MR while 9 month olds receive only MV; 4-6) routine MR vaccination at 9 months and 6 years and broad catch-up vaccines for all people in the population younger than 6, 15 or 40 years; and 7) female-only adolescent vaccination with MR at 12 years. Figure 2 depicts the estimated incidence of CRS per 1000 live births under the alternative vaccine strategies over 50 years, and Table 2 provides the quantitative estimates of cases averted and cost-effectiveness for each of the scenarios modeled.



## **9. Impact on Epidemic Measles of Vaccination Campaigns Triggered by Disease Outbreaks or Serosurveys: A Modeling Study.**

Lessler J, Metcalf CJ, Cutts FT, Grenfell BT.

PLoS Med. 2016 Oct 11;13(10):e1002144.

PMID: 27727285

### **ABSTRACT**

**BACKGROUND:** Routine vaccination supplemented by planned campaigns occurring at 2-5 y intervals is the core of current measles control and elimination efforts. Yet, large, unexpected outbreaks still occur, even when control measures appear effective. Supplementing these activities with mass vaccination campaigns triggered when low levels of measles immunity are observed in a sample of the population (i.e., serosurveys) or incident measles cases occur may provide a way to limit the size of outbreaks.

**METHODS AND FINDINGS:** Measles incidence was simulated using stochastic age-structured epidemic models in settings conducive to high or low measles incidence, roughly reflecting demographic contexts and measles vaccination coverage of four heterogeneous countries: Nepal, Niger, Yemen, and Zambia. Uncertainty in underlying vaccination rates was modeled. Scenarios with case- or serosurvey-triggered campaigns reaching 20% of the susceptible population were compared to scenarios without triggered campaigns. The best performing of the tested case-triggered campaigns prevent an average of 28,613 (95% CI 25,722-31,505) cases over 15 y in our highest incidence setting and 599 (95% CI 464-735) cases in the lowest incidence setting. Serosurvey-triggered campaigns can prevent 89,173 (95% CI, 86,768-91,577) and 744 (612-876) cases, respectively, but are triggered yearly in high-incidence settings. Triggered campaigns reduce the highest cumulative incidence seen in simulations by up to 80%. While the scenarios considered in this strategic modeling exercise are reflective of real populations, the exact quantitative interpretation of the results is limited by the simplifications in country structure, vaccination policy, and surveillance system performance. Careful investigation into the cost-effectiveness in different contexts would be essential before moving forward with implementation.

**CONCLUSIONS:** Serologically triggered campaigns could help prevent severe epidemics in the face of epidemiological and vaccination uncertainty. Hence, small-scale serology may serve as the basis for effective adaptive public health strategies, although, in high-incidence settings, case-triggered approaches are likely more efficient.

**WEB:** <http://dx.doi.org/10.1371/journal.pmed.1002144>

**IMPACT FACTOR:** 10.35

**CITED HALF-LIFE:** 5.70

**START SCIENTIFIC COMMENT:** Authors point out that while serologically-triggered campaigns may be less efficient than case-triggered campaigns in regions where measles vaccine coverage is low and measles incidence is high, in both low- and high-coverage (high- and low- incidence settings), triggered campaigns tend to limit the absolute size of large outbreaks; in all settings triggered campaigns limited size of epidemic by approximately 64%. Authors thus emphasize this approach may be beneficial for preventing or mitigating “the worst” epidemics in all settings.

Figure 2 depicts the cumulative case burdens (numbers of cases) in the four country case-studies for a range of different types of vaccination scenarios (case-triggered, serosurvey triggered, no trigger), assuming triggered campaigns are delayed by 3 months relative to the trigger, and assuming triggered campaigns reach 20% of the susceptible population. Figure 4 depicts a range of percentiles of the cumulative measles incidence over 15 years, from simulations assuming a range of vaccination rates, under the different intervention scenarios, and with an additional 20% coverage, in the four different incidence and population case-study countries.



## **10. Systematic Review and Meta-Analysis of Interventions to Improve Access and Coverage of Adolescent Immunizations.**

Das JK, Salam RA, Arshad A, Lassi ZS, Bhutta ZA.

J Adolesc Health. 2016 Oct;59(4S):S40-S48.

PMID:27664595

### **ABSTRACT**

Vaccination strategies are among the most successful and cost-effective public health strategies for preventing disease and death. Until recently, most of the existing immunization programs targeted infants and children younger than 5 years which have successfully resulted in reducing global infant and child mortality. Adolescent immunization has been relatively neglected, leaving a quarter of world's population underimmunized and hence vulnerable to a number of preventable diseases. In recent years, a large number of programs have been launched to increase the uptake of different vaccines in adolescents; however, the recommended vaccination coverage among the adolescent population overall remains very low, especially in low- and middle-income countries. Adolescent vaccination has received significantly more attention since the advent of the human papillomavirus (HPV) vaccine in 2006. However, only half of the adolescent girls in the United States received a single dose of HPV vaccine while merely 43% and 33% received two and three doses, respectively. We systematically reviewed literature published up to December 2014 and included 23 studies on the effectiveness of interventions to improve immunization coverage among adolescents. Moderate-quality evidence suggested an overall increase in vaccination coverage by 78% (relative risk: 1.78; 95% confidence interval: 1.41-2.23). Review findings suggest that interventions including implementing vaccination requirement in school, sending reminders, and national permissive recommendation for adolescent vaccination have the potential to improve immunization uptake. Strategies to improve coverage for HPV vaccines resulted in a significant decrease in the prevalence of HPV by 44% and genital warts by 33%; however, the quality of evidence was low. Analysis from single studies with low- or very low-quality evidence suggested significant decrease in varicella deaths, measles incidence, rubella susceptibility, and incidence of pertussis while the impact was nonsignificant for incidence of mumps with their respective vaccines. Further rigorous evidence is needed to evaluate the effectiveness of strategies to improve immunization uptake among adolescents from low- and middle-income countries.

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**IMPACT FACTOR:** 0.57

**CITED HALF-LIFE:** 7.30

**START SCIENTIFIC COMMENT:** For school-based vaccination requirement interventions and training clinic staff interventions, a substantial proportion of the amount of difference in the effect estimates observed across studies was due to heterogeneity in the effect of the intervention, versus chance alone ( $I^2 = 99\%$  and  $I^2 = 94\%$ , respectively). This indicates these interventions may work differently in different populations, or when implemented differently. Despite this heterogeneity in effect, 5 of the 7 studies of school-based vaccination requirements did find statistically significant beneficial effects, even if the magnitude of the estimate differed across studies. Meta-analysis combined similar intervention approaches, such as school requirements, across different vaccinations including measles, rubella and HPV, but the effect of such interventions may depend on the vaccine for which the intervention was introduced.

Although the search and inclusion criteria would have included studies conducted in low- and middle-income countries, all of the studies which ultimately met criteria and were included in the review were conducted in high-income countries.



## APPENDIX: PUBMED SEARCH TERMS

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(((((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 ("2016/9/15"[PDAT] : "2016/10/14"[PDAT]))

\* On October 22, 2016, this search of English language articles published between September 15, 2016 and October 14, 2016 and indexed by the US National Library of Medicine resulted in 210 unique manuscripts.

