VACCINE DELIVERY RESEARCH DIGEST

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

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1. 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 et al.

Lancet. 2015 July 8. pii: S0140-6736(15)61140-0. [Epub ahead of print].

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 wholecell 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: 9.10

UW EDITORIAL COMMENT: Figure 3 shows the Kaplan-Meier assessment of overall vaccine effectiveness. This study is important from a vaccine delivery standpoint for two reasons: 1) the inclusion of an intervention arm with both behavioral change and vaccination showed no significant difference in protection from the vaccination-only arm, and 2) the vaccine was delivered through routine government immunization services.



2. 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, Brulé A, Lasala-Blanco N, Coleman M et al.

Lancet Infect Dis. 2015 July 10. pii: S1473-3099(15)00178-4. [Epub ahead of print].

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: 19.45 CITED HALF-LIFE: 4.80

UW EDITORIAL COMMENT: Table 1 shows reported vaccination coverage from Nigeria and Pakistan in both high- and low-conflict areas. Table 4 shows caregiver attitudes about polio disease and vaccine. Table 6 shows community priorities. Implications for vaccine delivery are numerous: trust, increased caregiver knowledge, and community priorities are all important considerations when designing delivery strategies.



3. PAID MATERNITY LEAVE AND CHILDHOOD VACCINATION UPTAKE: LONGITUDINAL EVIDENCE FROM 20 LOW-AND-MIDDLE-INCOME COUNTRIES.

Hajizadeh M, Heymann J, Strumpf E, Harper S, Nandi A.

Soc Sci Med. 2015 Jul 11;140:104-117. [Epub ahead of print].

PMID: 26210658

ABSTRACT

The availability of maternity leave might remove barriers to improved vaccination coverage by increasing the likelihood that parents are available to bring a child to the clinic for immunizations. Using information from 20 low-and-middle-income countries (LMICs) we estimated the effect of paid maternity leave policies on childhood vaccination uptake. We used birth history data collected via Demographic and Health Surveys (DHS) to assemble a multilevel panel of 258,769 live births in 20 countries from 2001 to 2008; these data were merged with longitudinal information on the number of full-time equivalent (FTE) weeks of paid maternity leave guaranteed by each country. We used Logistic regression models that included country and year fixed effects to estimate the impact of increases in FTE paid maternity leave policies in the prior year on the receipt of the following vaccines: Bacillus Calmette-Guérin (BCG) commonly given at birth, diphtheria, tetanus, and pertussis (DTP, 3 doses) commonly given in clinic visits and Polio (3 doses) given in clinic visits or as part of campaigns. We found that extending the duration of paid maternity leave had a positive effect on immunization rates for all three doses of the DTP vaccine; each additional FTE week of paid maternity leave increased DTP1, 2 and 3 coverage by 1.38 (95% CI = 1.18, 1.57), 1.62 (CI = 1.34, 1.91) and 2.17 (CI = 1.76, 2.58) percentage points, respectively. Estimates were robust to adjustment for birth characteristics, household-level covariates, attendance of skilled health personnel at birth and time-varying country-level covariates. We found no evidence for an effect of maternity leave on the probability of receiving vaccinations for BCG or Polio after adjustment for the above-mentioned covariates. Our findings were consistent with the hypothesis that more generous paid leave policies have the potential to improve DTP immunization coverage. Further work is needed to understand the health effects of paid leave policies in LMICs.

WEB: http://dx.doi.org/10.1016/j.socscimed.2015.07.008

IMPACT FACTOR: 2.56
CITED HALF-LIFE: 8.50

UW EDITORIAL COMMENT: Figure 1 shows trends in vaccination rates for BCG, DTP, and polio in countries that changed their maternal leave policies (treated countries) and control countries during the study period. While a limitation of this study is the lack of formal employment in many included countries that precipitates paid maternal leave, this study highlights the importance of identifying immunization barriers at all levels, from individual to country-wide, and the ways in which policies that affect parental employment can affect child health.



4. EVALUATING THE VALUE PROPOSITION FOR IMPROVING VACCINE THERMOSTABILITY TO INCREASE VACCINE IMPACT IN LOW AND MIDDLE-INCOME COUNTRIES.

Karp CL, Lans D, Esparza J, Edson EB, Owen KE, Wilson CB et al.

Vaccine. 2015 Jul 9;33(30):3471-9. Epub 2015 Jun 6.

PMID: 26055297

ABSTRACT

The need to keep vaccines cold in the face of high ambient temperatures and unreliable access to electricity is a challenge that limits vaccine coverage in low and middle-income countries (LMICs). Greater vaccine thermostability is generally touted as the obvious solution. Despite conventional wisdom, comprehensive analysis of the value proposition for increasing vaccine thermostability has been lacking. Further, while significant investments have been made in increasing vaccine thermostability in recent years, no vaccine products have been commercialized as a result. We analyzed the value proposition for increasing vaccine thermostability, grounding the analysis in specific vaccine use cases (e.g., use in routine immunization [RI] programs, or in campaigns) and in the broader context of cold chain technology and country level supply chain system design. The results were often surprising. For example, cold chain costs actually represent a relatively small fraction of total vaccine delivery system costs. Further, there are critical, vaccine use casespecific temporal thresholds that need to be overcome for significant benefits to be reaped from increasing vaccine thermostability. We present a number of recommendations deriving from this analysis that suggest a rational path toward unlocking the value (maximizing coverage, minimizing total system costs) of increased vaccine thermostability, including: (1) the full range of thermostability of existing vaccines should be defined and included in their labels; (2) for new vaccines, thermostability goals should be addressed up-front at the level of the target product profile; (3) improving cold chain infrastructure and supply chain system design is likely to have the largest impact on total system costs and coverage in the short term-and will influence the degree of thermostability required in the future; (4) in the long term, there remains value in monitoring the emergence of disruptive technologies that could remove the entire RI portfolio out of the cold chain.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.05.071

IMPACT FACTOR: 3.49
CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 3 shows a breakdown of costs for each step of the vaccine delivery system, from national program management to healthcare worker time. Because this evaluation found cold chain costs to be surprisingly low and few breakthroughs have been achieved in efforts to improve vaccine thermostability, the authors recommend improving cold chain infrastructure and overall vaccine delivery systems as the best means to lower total systems costs and increase coverage.



5. FIELD EVALUATION OF MEASLES VACCINE EFFECTIVENESS AMONG CHILDREN IN THE DEMOCRATIC REPUBLIC OF CONGO.

Doshi RH, Mukadi P, Shidi C, Mulumba A, Hoff NA, Gerber S et al.

Vaccine. 2015 Jun 26;33(29):3407-14. Epub 2015 Apr 30.

PMID: 25937449

ABSTRACT

BACKGROUND: Large-scale measles outbreaks in areas with high administrative vaccine coverage rates suggest the need to re-evaluate measles prevention and control in the Democratic Republic of Congo (DRC). Monitoring of measles Vaccine Effectiveness (VE) is a useful measure of quality control in immunization programs. We estimated measles VE among children aged 12-59 months in the Democratic Republic of Congo (DRC) using laboratory surveillance data from 2010-2012.

METHODS: We used the case-based surveillance system with laboratory confirmation to conduct a case-control study using the test negative design. Cases and controls were selected based on presence (n=1044) or absence (n=1335) of measles specific antibody IgM or epidemiologic linkage. Risk factors for measles were assessed using unconditional logistic regression, stratified by age.

RESULTS: Among children 12-59 months, measles vaccination was protective against measles [aOR (95%C)], 0.20 (0.15-0.26) and estimated VE was 80% (95% CI 74-85%). Year of diagnosis, 2011: 6.02 (4.16-8.72) and 2012; 8.31 (5.57-12.40) was a risk factor for measles when compared to 2010. Compared to Kinshasa, children in Bas-Congo, Kasai-Oriental, Maniema and South Kivu provinces all had higher odds of developing measles. Measles VE was similar for children 12-23 months and 24-59 months (80% and 81% respectively).

CONCLUSIONS: Repeated occurrences of measles outbreaks and lower than expected VE estimates suggest the need to further evaluate measles vaccine efficacy and improve vaccine delivery strategies in DRC.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.04.067

IMPACT FACTOR: 3.49 CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 2 outlines the study population selection; cases were people presenting with measles-like illness (MLI) who were confirmed with lab tests or epidemiologic linkage; controls had MLI but were not confirmed to have measles. Table 2 shows the characteristics associated with measles in children, stratified by age. Because of poor overall vaccine delivery systems and the failure of both routine and supplementary immunization activities in the DRC, the authors suggest new interventions such as remote temperature monitoring systems, computerized immunization information systems, using solar freezers and community-level clinics, and creating new supply chain models.



6. COMPARING THE HEALTH AND SOCIAL PROTECTION EFFECTS OF MEASLES VACCINATION STRATEGIES IN ETHIOPIA: AN EXTENDED COST-EFFECTIVENESS ANALYSIS.

Driessen J, Olson ZD, Jamison DT, Verguet S.

Soc Sci Med. 2015 Aug;139:115-22. Epub 2015 Jun 16.

PMID: 26189009

ABSTRACT

Vaccination coverage rates often mask wide variation in access, uptake, and cost of providing vaccination. Financial incentives have been effective at creating demand for social services in a variety of settings. Using methods of extended cost-effectiveness analysis, we compare the health and economic implications of three different vaccine delivery strategies for measles vaccination in Ethiopia: i) routine immunization, ii) routine immunization with financial incentives, and iii) mass campaigns, known as supplemental immunization activities (SIAs). We examine annual birth cohorts of almost 3,000,000 births over a ten year period, exploring variation in these outcomes based on economic status to understand how various options may improve equity. SIAs naturally achieve higher levels of vaccine coverage, but at higher costs. Routine immunization combined with financial incentives bolsters demand among more economically vulnerable households. The relative appeal of routine immunization with financial incentives and SIAs will depend on the policy environment, including short-term financial limitations, time horizons, and the types of outcomes that are desired. While the impact of financial incentives has been more thoroughly studied in other policy arenas, such as education, consideration of this approach alongside standard vaccination models such as SIAs is timely given the dialog around measles eradication.

WEB: http://dx.doi.org/10.1016/j.socscimed.2015.06.018

IMPACT FACTOR: 2.56 CITED HALF-LIFE: 8.50

UW EDITORIAL COMMENT: Figure 1 shows the extended cost-effectiveness analysis results for each immunization program, per income quintile. Figure 2 shows the effect of varying costs on outcomes across vaccination strategies. The value of this study for vaccine delivery is the exploration of different delivery strategies given different time and financial parameters (focusing on economically vulnerable households).



7. APPLYING LESSONS LEARNED FROM THE USAID FAMILY PLANNING GRADUATION EXPERIENCE TO THE GAVI GRADUATION PROCESS.

Shen AK, Farrell MM, Vandenbroucke MF, Fox E, Pablos-Mendez A.

Health Policy Plan. 2015 Jul;30(6):687-95. Epub 2014 Jun 28.

PMID: 24974106

ABSTRACT

As low income countries experience economic transition, characterized by rapid economic growth and increased government spending potential in health, they have increased fiscal space to support and sustain more of their own health programmes, decreasing need for donor development assistance. Phase out of external funds should be systematic and efforts towards this end should concentrate on government commitments towards country ownership and self-sustainability. The 2006 US Agency for International Development (USAID) family planning (FP) graduation strategy is one such example of a systematic phaseout approach. Triggers for graduation were based on pre-determined criteria and programme indicators. In 2011 the GAVI Alliance (formerly the Global Alliance for Vaccines and Immunizations) which primarily supports financing of new vaccines, established a graduation policy process. Countries whose gross national income per capita exceeds \$1570 incrementally increase their co-financing of new vaccines over a 5-year period until they are no longer eligible to apply for new GAVI funding, although previously awarded support will continue. This article compares and contrasts the USAID and GAVI processes to apply lessons learned from the USAID FP graduation experience to the GAVI process. The findings of the review are 3fold: (1) FP graduation plans served an important purpose by focusing on strategic needs across six graduation plan foci, facilitating graduation with pre-determined financial and technical benchmarks, (2) USAID sought to assure contraceptive security prior to graduation, phasing out of contraceptive donations first before phasing out from technical assistance in other programme areas and (3) USAID sought to sustain political support to assure financing of products and programmes continue after graduation. Improving sustainability more broadly beyond vaccine financing provides a more comprehensive approach to graduation. The USAID FP experience provides a window into understanding one approach to graduation from donor assistance. The process itself-involving transparent country-level partners well in advance of graduation-appears a valuable lesson towards success.

WEB: http://dx.doi.org/10.1093/heapol/czu045

IMPACT FACTOR: 3.00 CITED HALF-LIFE: 7.20

UW EDITORIAL COMMENT: Lessons from the USAID family planning graduation strategy vary in relevance to GAVI graduation, but some are particularly useful. Contraceptive commodity security and the appropriate supply chain and logistics systems were a requirement for the USAID graduation, and should be for the GAVI process as well. Building political commitment is also important.



8. HBV IMMUNIZATION AND VACCINE COVERAGE AMONG HOSPITALIZED CHILDREN IN CAMEROON, CENTRAL AFRICAN REPUBLIC AND SENEGAL: A CROSS-SECTIONAL STUDY.

Bekondi C, Zanchi R, Seck A, Garin B, Giles-Vernick T, Gody JC et al.

BMC Infect Dis. 2015 Jul 12;15:267.

PMID: 26164361

ABSTRACT

BACKGROUND: Hepatitis B is a major health concern in Africa. The vaccine against hepatitis B virus (HBV) was introduced into the Expanded Programme on Immunization (EPI) of Cameroon and Senegal in 2005, and of CAR (Central African Republic) in 2008. A cross-sectional study was conducted to assess HBV immunization coverage following the vaccine's introduction into the EPI and factors associated with having been vaccinated.

METHODS: All hospitalized children, regardless of the reasons for their hospitalization, between 3 months and 6 years of age, for whom a blood test was scheduled during their stay and whose condition allowed for an additional 2 mL blood sample to be taken, and who provided the parent's written consent were included. All children anti-HBs- and anti-HBc + were tested for HBsAg. Vaccination coverage was assessed in three different ways: immunization card, maternal recall and serologic anti-HBs profile.

RESULTS: 1783 children were enrolled between April 2009 and May 2010. An immunization card was only available for 24 % of the children. The median age was 21 months. Overall HBV immunization coverage based on immunization cards was 99 %, 49 % and 100 % in Cameroon, CAR and Senegal, respectively (p < 0,001). The immunization rate based on maternal recall was 91 %, 17 % and 88 % in Cameroon, CAR and Senegal, respectively (p < 0,001). According to serology (anti-HBs titer \geq 10 mUI/mL and anti-HBc-), the coverage rate was 68 %, 13 % and 46 % in Cameroon, CAR and Senegal, respectively (p < 0,001). In Senegal and Cameroon, factors associated with having been vaccinated were: mother's higher education (OR = 2.2; 95 % CI [1.5-3.2]), no malnutrition (OR = 1.6; 95 % CI [1.1-2.2]), access to flushing toilets (OR = 1.6; 95 % CI [1.1-2.3]), and < 24 months old (OR = 2.1; 95 % CI [1.3-3.4] between 12 and 23 months and OR = 2.7; 95 % CI [1.6-4.4] < 12 months). The prevalence of HBV-infected children (HBsAg+) were 0.7 %, 5.1 %, and 0.2 % in Cameroon, CAR and Senegal, respectively (p < 0.001).

CONCLUSIONS: Assessing immunization coverage based on immunization cards, maternal recall or administrative data could be usefully reinforced by epidemiological data combined with immunological profiles. Serology-based studies should be implemented regularly in African countries, as recommended by the WHO. Malnutrition, lack of maternal education and poverty are factors associated with vaccine noncompliance. The countries' vaccination programs should actively address these problems.

WEB: http://dx.doi.org/10.1186/s12879-015-1000-2

IMPACT FACTOR: 2.61
CITED HALF-LIFE: 3.40

UW EDITORIAL COMMENT: Figure 1: Serologic measures of HBV immune protection by year of birth and country show variable (and generally lower) levels compared to WHO coverage estimates.



9. THE GLOBAL CONTEXT OF VACCINE REFUSAL: INSIGHTS FROM A SYSTEMATIC COMPARATIVE ETHNOGRAPHY OF THE GLOBAL POLIO ERADICATION INITIATIVE.

Closser S, Rosenthal A, Maes K, Justice J, Cox K, Omidian PA et al.

Med Anthropol Q. 2015 Jun 18. [Epub ahead of print].

PMID: 26084915

ABSTRACT

Many of medical anthropology's most pressing research questions require an understanding how infections, money and ideas move around the globe. The Global Polio Eradication Initiative (GPEI) is a \$9 billion project that has delivered 20 billion doses of oral polio vaccine in campaigns across the world. With its array of global activities, it cannot be comprehensively explored by the traditional anthropological method of research at one field site. This paper describes an ethnographic study of the GPEI, a collaborative effort between researchers at eight sites in seven countries. We developed a methodology grounded in nuanced understandings of local context but structured to allow analysis of global trends. Here, we examine polio vaccine acceptance and refusal to understand how global phenomena-in this case, policy decisions by donors and global health organizations to support vaccination campaigns rather than building health systems-shape local behavior.

WEB: http://dx.doi.org/10.1111/maq.12229

IMPACT FACTOR: 1.30 CITED HALF-LIFE: 0.00

UW EDITORIAL COMMENT: The literature in anthropology tends to frame vaccine refusal in four different but interrelated ways: religion, history and politics, health system context, and service delivery of immunizations. This article suggests that the Global Polio Eradication Initiative tends to frame refusals in terms of ignorance or the political dynamics of Islam, which may not be an accurate representation of the complexity of the issue. Figure 1 shows the eight countries in which qualitative case studies were conducted. Table 1 shows data on number of polio campaigns, year of last polio case, level of routine vaccine service provision, and polio vaccine refusals.



10. COST-EFFECTIVENESS OF NOROVIRUS VACCINATION IN CHILDREN IN PERU.

Mirelman AJ, Ballard SB, Saito M, Kosek MN, Gilman RH.

Vaccine. 2015 Jun 17;33(27):3084-91. Epub 2015 May 15.

PMID: 25980428

ABSTRACT

BACKGROUND: With candidate norovirus (NV) vaccines in a rapid phase of development, assessment of the potential economic value of vaccine implementation will be necessary to aid health officials in vaccine implementation decisions. To date, no evaluations have been performed to evaluate the benefit of adopting NV vaccines for use in the childhood immunization programs of low- and middle-income countries.

METHODS: We used a Markov decision model to evaluate the cost-effectiveness of adding a two-dose NV vaccine to Peru's routine childhood immunization schedule using two recent estimates of NV incidence, one for a peri-urban region and one for a jungle region of the country.

RESULTS: Using the peri-urban NV incidence estimate, the annual cost of vaccination would be \$13.0 million, offset by \$2.6 million in treatment savings. Overall, this would result in 473 total DALYs averted; 526,245 diarrhea cases averted;153,735 outpatient visits averted; and 414 hospitalizations averted between birth and the fifth year of life. The incremental cost-effectiveness ratio would be \$21,415 per DALY averted; \$19.86 per diarrhea case; \$68.23 per outpatient visit; and \$26,298 per hospitalization. Using the higher jungle NV incidence rates provided a lower cost per DALY of \$10,135. The incremental cost per DALY with per-urban NV incidence is greater than three times the 2012 GDP per capita of Peru but the estimate drops below this threshold using the incidence from the jungle setting. In addition to the impact of incidence, sensitivity analysis showed that vaccine price and efficacy play a strong role in determining the level of cost-effectiveness.

CONCLUSIONS: The introduction of a NV vaccine would prevent many healthcare outcomes in the Peru and potentially be cost-effective in scenarios with high NV incidence. The vaccine cost-effectiveness model could also be applied to the evaluation of NV vaccine cost-effectiveness in other countries in resource-poor settings, where NV incidence rates are expected to be higher.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.05.004

IMPACT FACTOR: 3.49 CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 2 shows total vaccine costs, treatment savings, averted outcomes, and cost-effectiveness. Figure 2 shows one-way sensitivity of cost per disability-adjusted life year averted versus vaccine cost and vaccine effectiveness and shows greater cost effectiveness for jungle areas, associated with higher incidence in jungle vs. peri-urban areas.



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 ("2015/06/15"[PDAT] : "2015/07/14"[PDAT]))

*On July 27, 2015, this search of English language articles published between June 15, 2015 and July 14, 2015 and indexed by the US National Library of Medicine resulted in 214 unique manuscripts.

