# VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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# Details of Articles

## 1. [Can vaccination coverage be improved by reducing missed opportunities for vaccination? Findings from assessments in Chad and Malawi using the new WHO methodology](#)

Ogbuanu IU, Li AJ, Anya BM, Tamadji M, Chirwa G, Chiwaya KW, et al.

## ABSTRACT

BACKGROUND:

In 2015, the World Health Organization (WHO) updated the global methodology for assessing and reducing missed opportunities for vaccination (MOV), when eligible children have contact with the health system but are not vaccinated. This paper presents the results of two pilot assessments conducted in Chad and Malawi.

METHODS:

Using the ten-step global WHO MOV strategy, we purposively selected districts and health facilities, with non-probabilistic sampling of <24 month old children for exit interviews of caregivers and self-administered knowledge, attitudes, and practices (KAP) surveys of health workers. MOV were calculated based on a child's documented vaccination history (i.e., from a home-based record (HBR) or a health facility vaccination register), including selected vaccines in the national schedule.

RESULTS:

Respondents included caregivers of 353 children in Chad and of 580 children in Malawi. Among those with documented vaccination history, 82% (195/238) were eligible for vaccination in Chad and 47% (225/483) in Malawi. Among eligible children, 51% (99/195) in Chad, and 66% (149/225) in Malawi had one or more MOV on the survey date. During non-vaccination visits, 77% (24/31) of children eligible for vaccination in Chad and 92% (119/129) in Malawi had a MOV compared to 46% (75/164) and 31% (30/96) during vaccination visits, respectively. Among health workers, 92% in Chad and 88% in Malawi were unable to correctly identify valid contraindications for vaccination.

CONCLUSION:

The new MOV tool was able to characterize the type and potential causes of MOV. In both countries, the findings of the assessments point to two major barriers to full vaccination of eligible children-a

lack of coordination between vaccination and curative health services and incomplete vaccination during vaccination visits. National immunization programs should explore tailored efforts to improve health worker practices and to increase vaccine delivery by making better use of existing health service contacts.

## START COMMENTARY

Using a ten-step strategy to limit missed opportunities for vaccination, summarized in Figure 1 and described in more detail in the WHO Planning guide to reduce missed opportunities for vaccination (MOV) and Methodology for the assessment of missed opportunities for vaccination, Ogbuanu et al. conducted a pilot study to assess the strategy in Chad and Malawi. The strategy builds upon previous work conducted by the Pan American Health Organization with a simplifying sampling strategy, inclusion of qualitative data, and emphasis on follow-up and intervention. Ogbuanu et al. sought to answer the following three questions: "(1) how many opportunities are being missed, (2) why are these opportunities being missed, and (3) what can be done to reduce MOVE?" Figure 2 shows a flowchart of determining missed opportunities for vaccination. Limitations of the study included the non-random sampling, limiting representativeness country-wide. Countries may need to refer to other data to understand any changes in overall immunization coverage due to addressing MOV. Authors note, however, that the intention of the study is to "diagnose major program issues and implement actions to reduce MOV." Related, MOV among those not attending health facilities was not captured in this study. Children without recorded vaccination dates were excluded from the study, which authors state would bias their results towards the null. Children not included in the study are more likely to have MOV and therefore the effect of reducing MOV would have been higher. Finally, the cross-sectional study design prevents a causal association to be established. Authors comment on the benefit of the new strategy, which allows for ease of implementation. It also allows for tailoring to fit country-specific needs. The advantage of this study is that it shows how this strategy can feasibly be applied and acted upon. Effectiveness of interventions derived from the results of the assessment phase have yet to be tested, nor the impact on overall vaccination coverage and protection are yet to be seen, but the feasibility and data-driven results show promise.

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# 2. [Developing standardized competencies to strengthen immunization systems and workforce](#)

Traicoff D, Pope A, Bloland P, Lal D, Bahl J, Stewart S, et al.

## ABSTRACT

Despite global support for immunization as a core component of the human right to health and the maturity of immunization programs in low- and middle-income countries throughout the world, there is no comprehensive description of the standardized competencies needed for immunization programs at the national, multiple sub-national, and community levels. The lack of defined and standardized competencies means countries have few guidelines to help them address immunization workforce planning, program management, and performance monitoring. Potential consequences resulting from the lack of defined competencies include inadequate or inefficient distribution of resources to support the required functions and difficulties in adequately managing the health workforce. In 2015, an international multi-agency working group convened to define standardized competencies that national immunization programs could adapt for their own workforce planning needs. The working group used a stepwise approach to ensure that the competencies would align with immunization programs' objectives. The first step defined the attributes of a successful immunization program. The group then defined the work functions needed to achieve those attributes. Based on the work functions, the working group defined specific competencies. This process resulted in three products: (1) Attributes of an immunization program described within eight technical domains at four levels within a health system: National, Provincial, District/Local, and Community; (2) 229 distinct functions within those eight domains at each of the four levels; and (3) 242 competencies, representing eight technical domains and two foundational domains (Management and Leadership and Vaccine Preventable Diseases and Program). Currently available as a working draft and being tested with immunization projects in several countries, the final document will be published by WHO as normative guidelines. Vertical immunization programs as well as integrated systems can customize the framework to suit their needs. Standardized competencies can support immunization program improvements and help strengthen effective health systems.

## START COMMENTARY

The working group comprised of individuals from agencies in global immunization, a health immunization program, and country-specific nongovernmental organizations. Competency modeling was guided by work from Campion et al. and Shippman et al. A description of the variables used for a level of rigor analysis of the competency modeling are provided in Table 1. Data were collected from PubMed and Google Scholar searches, including a review of gray literature from the Bill and Melinda Gates Foundation, Gavi, the Vaccine alliance, the US Centers for Disease Control and Prevention, PATH, UNICEF, WHO, and others. In addition to a literature review, the working group engaged subject matter experts and conducted informant interviews with immunization program staff members from country and WHO regional offices. Figure 2 shows a summary of attributes of a successful EPI in seven domains and four organizational levels. Table 2 summaries the immunization workforce competencies and Tables 3 and 4 provide sample expansions of competencies by each organizational level. Figure 3 shows a schematic of the immunization program as an adaptive system. Authors state limitations to this work include not having "equal geographic representation," potential lack of detail in the competency statements, and potential lack of candor from interviewees. This work was presented at a SAGE meeting in April 2017 and the working group seek to pilot a protocol and management tools.

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## 3. [The impact of supplementary immunization activities on routine vaccination coverage: An instrumental variable analysis in five low-income countries](#)

Chakrabarti A, Grépin KA, Helleringer S.

## ABSTRACT

BACKGROUND:

Countries deliver vaccines either through routine health services or supplementary immunization activities (SIAs), usually community-based or door-to-door immunization campaigns. While SIAs have been successful at increasing coverage of vaccines in low- and middle-income countries, they may disrupt the delivery of routine health services. We examine the impact of SIAs on routine vaccine coverage in five low-income countries.

METHODS:

Data on the number and timing of SIAs conducted in various countries was compiled by WHO and obtained through UNICEF. Information on the coverage of vaccines not targeted by SIAs (e.g., DPT) was extracted from the Demographic and Health Surveys. We focus on SIAs that took place between 1996 and 2013 in Bangladesh, Senegal, Togo, Gambia, and Cote d'Ivoire, and examine outcomes for children aged 12-59 months. To avoid biases resulting from non-random placement and timing of SIAs, we use age of a child at her first SIA as an instrumental variable for total exposure to SIAs.

RESULTS:

We find that SIA exposure reduced the likelihood of receiving routine vaccines in all the countries included in the study; the coefficients of interest are however statistically insignificant for Gambia and Cote d'Ivoire. In countries that witnessed statistically significant SIA-induced declines in the likelihood of obtaining DPT 3, measles as well as BCG, reductions ranged from 1.3 percentage points (Senegal) to 5.5 percentage points (Bangladesh).

CONCLUSION:

SIA exposure reduced routine vaccination rates in study countries. Efforts should be made to limit the detrimental impact of SIAs on the services provided by routine health systems.

**CITED HALF-LIFE:** 2.70

## START COMMENTARY

Chakrabarti et al. use a novel approach to assess the impact of supplementary immunization activities (SIAs) on receipt of routine vaccines. Using an instrumental variable, age of child at first SIA exposure, that is strongly correlated with the covariate of interest, total SIA exposure, but "unrelated to any of the unobserved factors that shape outcome variable." From this study, authors conclude that SIAs have a detrimental impact on receipt of routine vaccines. While an association may be observed, the conclusions may be an overstatement. It is unclear whether the instrumental variable is truly unrelated to the unobserved factors and therefore subject to confounding. Also unclear is the potential feedback of vaccination coverage on the implementation of SIA. Authors also comment on the limitation of excluding countries where SIAs were not national in scope and for which SIAs were sporadic in time (such that age at first SIA exposure would not correlate with total SIA exposure), nor was the mechanism by which the SIA-routine vaccination association observed.

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# 4. District-level health management and health system performance

Fetene N, Canavan ME, Megentta A, Linnander E, Tan AX, Nadew K, et al.

*PLoS One.* 2019 Feb 1;14(2):e0210624.

PubMed ID: 30707704

## ABSTRACT

Strengthening district-level management may be an important lever for improving key public health outcomes in low-income settings; however, previous studies have not established the statistical associations between better management and primary healthcare system performance in such settings. To explore this gap, we conducted a cross-sectional study of 36 rural districts and 226 health centers in Ethiopia, a country which has made ambitious investment in expanding access to primary care over the last decade. We employed quantitative measure of management capacity at both the district health office and health center levels and used multiple regression models, accounting for clustering of health centers within districts, to estimate the statistical association between management capacity and a key performance indicator (KPI) summary score based on antenatal care coverage, contraception use, skilled birth attendance, infant immunization, and availability of essential medications. In districts with above median district management capacity, health center management capacity was strongly associated (p < 0.05) with KPI performance. In districts with below median management capacity, health center management capacity was not associated with KPI performance. Having more staff at the district health office was also associated with better KPI performance (p < 0.05) but only in districts with above median management capacity. The results suggest that district-level management may provide an opportunity for improving health system performance in low-income country settings.

**WEB**: 10.1371/journal.pone.0210624
**IMPACT FACTOR:** 2.77
**CITED HALF-LIFE:** 2.70

## START COMMENTARY

As part of a 3-year interventional study, Fentene et al. conducted a cross-sectional study using baseline measurement of health management metrics and a composite health system performance indicator. Management capacity measures were calculated at both the woreda (i.e., district) health office and health center levels. The woreda measure was based on compliance to the woreda management standards (WMS) which are described in supplementary Tables 1 and 2. The health center level measure was based on compliance to the Ethiopia Health Center Reform

Implementation Guidelines, outlined in supplementary Table 3. Fentene et al. used generalized linear regression models accounting for the cluster sampling design. Furthermore, they tested the model for interaction between the management capacity measures for the woreda and the health center. As the authors stated, this study addresses a gap in quantitatively assessing the impact of health management capacity on healthcare outcomes. However, there are a number of study limitations the readers should consider. The first limitation is the cross-sectional design of the study, which limits any causal inference to be made about health management capacity and healthcare outcomes. Other limitations stem from lack of data, either due to the small sample size preventing authors to tease apart sub-components of the composite measures, or lack of data on potential confounders, such as sociodemographic and economic factors of the woredas. Authors also expressed concern about the quality of data collected, citing potential misclassification bias. However, authors expect non-differential misclassification, biasing their results to the null. Related, some of the management capacity measures are vague and may be subject to ambiguity on whether compliance was achieved. Despite these limitations, further study using longitudinal data to show changes over time would provide insights on the impact of management capacity on health outcomes.

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# 5. POLICI: A web application for visualising and extracting yellow fever vaccination coverage in Africa

Hamlet A, Jean K, Yactayo S, Benzler J, Cibrelus L, Ferguson N, et al.

## ABSTRACT

Recent yellow fever (YF) outbreaks have highlighted the increasing global risk of urban spread of the disease. In context of recurrent vaccine shortages, preventive vaccination activities require accurate estimates of existing population-level immunity. We present POLICI (POpulation-Level Immunization Coverage - Imperial), an interactive online tool for visualising and extracting YF vaccination coverage estimates in Africa. We calculated single year age-disaggregated sub-national population-level vaccination coverage for 1950-2050 across the African endemic zone by collating vaccination information and inputting it into a demographic model. This was then implemented on an open interactive web platform. POLICI interactively displays age-disaggregated, population-level vaccination coverages at the first subnational administrative level, through numerous downloadable and customisable visualisations. POLICI is available at https://polici.shinyapps.io/yellow_fever_africa/. POLICI offers an accessible platform for relevant stakeholders in global health to access and explore vaccination coverages. These estimates have already been used to inform the WHO strategy to Eliminate Yellow fever Epidemics (EYE).

**WEB**: 10.1016/j.vaccine.2019.01.074
**IMPACT FACTOR:** 3.29
**CITED HALF-LIFE:** 5.50

## START COMMENTARY

Data sources that inform the POLICI tool include the UN World Population Prospects, LandScan 2015, historical large-scale vaccination activities, WHO Weekly Epidemiological Record and WHO Disease Outbreak News, WHO/UNICEF Estimates of National Immunization Coverage, and WUENIC. Data were analyzed and visualized through R packages, Shiny, Leaflet and Plotly. Hamlet et al. noted several assumptions and limitations including within-country age structures were assumed to be homogenous, population migration was not considered, quantification for uncertainty of coverage estimates were not provided, and missed vaccination activities and wasted dosages may underestimate true coverage. Despite these limitations, the POLICI tool serves as an

accessible, visual resource for policymakers to use immunization data to inform Yellow Fever elimination strategies.

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# 6. [Global certification of wild poliovirus eradication: insights from modelling hard-to-reach subpopulations and confidence about the absence of transmission](#)

Duintjer Tebbens RJ, Kalkowska DA, Thompson KM.

## ABSTRACT

OBJECTIVE:

To explore the extent to which undervaccinated subpopulations may influence the confidence about no circulation of wild poliovirus (WPV) after the last detected case.

DESIGN AND PARTICIPANTS:

We used a hypothetical model to examine the extent to which the existence of an undervaccinated subpopulation influences the confidence about no WPV circulation after the last detected case as a function of different characteristics of the subpopulation (eg, size, extent of isolation). We also used the hypothetical population model to inform the bounds on the maximum possible time required to reach high confidence about no circulation in a completely isolated and unvaccinated subpopulation starting either at the endemic equilibrium or with a single infection in an entirely susceptible population.

RESULTS:

It may take over 3 years to reach 95% confidence about no circulation for this hypothetical population despite high surveillance sensitivity and high vaccination coverage in the surrounding general population if: (1) ability to detect cases in the undervaccinated subpopulation remains exceedingly small, (2) the undervaccinated subpopulation remains small and highly isolated from the general population and (3) the coverage in the undervaccinated subpopulation remains very close to the minimum needed to eradicate. Fully-isolated hypothetical populations of 4000 people or less cannot sustain endemic transmission for more than 5 years, with at least 20 000 people required for a 50% chance of at least 5 years of sustained transmission in a population without seasonality that starts at the endemic equilibrium. Notably, however, the population size required for persistent transmission increases significantly for realistic populations that include some vaccination and seasonality and/or that do not begin at the endemic equilibrium.

CONCLUSIONS:

Significant trade-offs remain inherent in global polio certification decisions, which underscore the need for making and valuing investments to maximise population immunity and surveillance quality in all remaining possible WPV reservoirs.

## START COMMENTARY

Table 1 provides the parameters of the differential equation-based model used to estimate poliovirus transmission among hard-to-reach populations and a stochastic approach developed by Eichner and Dietz to estimate the confidence of no circulation. Further details of the model can be found in the online supplementary appendix. Figure 5 depicts a conceptual diagram of the impact of the timing of certification of poliovirus eradication on financial and societal costs, which highlights the desire to achieve a level of confidence of no circulation that would minimize total costs. Authors comment on the need for high quality surveillance of subpopulations to increase confidence of no circulation after last detection of poliovirus, as well as better vaccination coverage to ensure high immunity. The model makes simplifying assumptions that may not fully capture the stochastic nature of the population.

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# 7. [Achieving the end game: employing "vaccine diplomacy" to eradicate polio in Pakistan](#)

Shakeel SI, Brown M, Sethi S, Mackey TK.

## ABSTRACT

BACKGROUND:

On April 28, 2014, the World Health Organization (WHO) declared polio a "Public Health Emergency of International Concern" (PHIC) under the authority of the International Health Regulations. Although polio has been eradicated from nearly every nation on earth, Pakistan is one of three countries where wild polio and vaccine-derived polio strains remain, thwarting global eradication efforts.

AIMS:

Polio eradication progress is complicated by security and conflict issues at the border area between Pakistan and Afghanistan. In addition to security issues, other critical challenges, such as maintaining cold supply chain for vaccines, active and sentinel surveillance, false beliefs about vaccines, distrust of healthcare workers, and accessibility to conflict areas due to terrorist activities, all play a role in the continued persistence of Polio. In response to these challenges, we assess the local and international policy environment and its impact on polio eradication in Pakistan.

FINDINGS:

Based on our analysis of existing barriers and challenges associated with polio eradication in Pakistan, this study discusses why employing "vaccine diplomacy" represents a key policy and advocacy strategic approach to achieve the overall end game of polio eradication. Specifically, we identify a set of concrete public health, international development, and diplomatic and policy recommendations that can act synergistically under the umbrella of health and vaccine diplomacy to finally put an end to polio.

## START COMMENTARY

Shakeel et al. highlight the importance of continued funding for immunization efforts as well as achieving bilateral support from Pakistan and Afghanistan to ensure access to immunizations, healthcare, and water and sanitation in the conflict-area that borders the two countries and where

individuals are at high risk of poliovirus. Table 1 provides a summary of global health diplomacy recommendations, which include the challenges and potential solutions for each recommendation. The recommendations touch on increased access to vaccines, improving water and sanitation in affected areas, enhancing environmental surveillance, mobilizing community and religious leaders, assisting internally displaced persons, and effective health promotion communication.

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## 8. [Health care worker vaccination against Ebola: Vaccine acceptance and employment duration in Sierra Leone](#)

Jendrossek M, Edmunds WJ, Rohan H, Clifford S, Mooney TA, Eggo RM.

## ABSTRACT

Health care workers (HCW) are at high risk of Ebola virus disease (EVD) infection during epidemics and may contribute to onward transmission, and therefore HCW-targeted prophylactic vaccination strategies are being considered as interventions. To assess the feasibility of preventive HCW vaccination, we conducted a pilot survey on staff turnover and vaccine acceptance amongst 305 HCW in Freetown and Kambia districts of Sierra Leone. Multivariable logistic regression demonstrated which demographic and behavioural factors were associated with acceptance of a hypothetical new vaccine. We quantified the duration of employment of HCW, and used multivariable gamma regression to detect associations with duration of employment in current or any health care position. Finally, we simulated populations of HCW, to determine the likely future immunisation coverage amongst HCW based on our estimates of vaccine acceptance and employment duration. Most HCW we surveyed had a positive opinion of EVD vaccination (76.3%). We found that being a volunteer HCW (vs being on the government payroll) was associated with increased vaccine acceptance. We found that HCW have stable employment, with a mean duration of employment in the health sector of 10.9 years (median 8.0 years). Older age and being on the government payroll (vs volunteer HCW) were associated with a longer duration of employment in the health sector. Assuming a single vaccine campaign, with 76.3% vaccine acceptance, 100% vaccine efficacy and no waning of vaccine-induced protection, immunisation coverage was sustained over 50% until 6 years after a vaccination campaign. If vaccine-induced immunity wanes at 10% per year, then the immunisation coverage among HCW would fall below 50% after 3 years. Vaccinating HCW against EVD could be feasible as employment appeared stable and vaccine acceptance high. However, even with high vaccine efficacy and long-lasting immunity, repeated campaigns or vaccination at employment start may be necessary to maintain high coverage.

## START COMMENTARY

A limitation of the study was the cross-sectional design, which could be subject to length time bias; the likelihood of being included in the study is higher for those with longer employment, thus overestimating the length of employment time. The study also obtained a convenience sample, which limits the representativeness of the study results. However, authors state that the sample is representative in terms of age and gender, and some health facility types and professions were oversampled. Related, authors also note the effect of payroll and volunteer status may only be applicable to Sierra Leone as other countries may have a different experience of government payroll employees and volunteers. Another consideration authors pose is the impact of the EBOVAC project (a study to evaluation the immunogenicity of the prime-boost EVD vaccine) on health worker vaccine acceptance.

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# 9. Carriage of penicillin non-susceptible pneumococci among children in northern Tanzania in the 13-valent pneumococcal vaccine era

Emgård M, Msuya SE, Nyombi BM, Mosha D, Gonzales-Siles L, Nordén R, et al.

## ABSTRACT

OBJECTIVES:

To determine antibiotic susceptibility and serotype distribution of colonizing *Streptococcus pneumoniae* in Tanzanian children, we performed serial cross-sectional surveys following national introduction of the 13-valent pneumococcal conjugate vaccine PCV13 in December 2012.

METHODS:

775 children below 2 years of age were recruited and sampled from nasopharynx at primary health centres in Moshi, Tanzania between 2013 and 2015. S. pneumoniae were isolated by culture and tested for antibiotic susceptibility by disc-diffusion and E-tests; molecular testing was used to determine serotype/group.

RESULTS:

Penicillin non-susceptibility in the isolated pneumococci increased significantly from 31% (36/116) in 2013, to 47% (30/64) in 2014 and 53% (32/60) in 2015. Non-susceptibility to amoxicillin/ampicillin and ceftriaxone was low (n=8 and n=9, respectively), while 97% (236/244) of the isolates were non-susceptible to trimethoprim-sulfamethoxazole. The majority of the children (54%, n=418) had been treated with antibiotics in the past 3 months and amoxicillin/ampicillin was overall the most commonly used antibiotics. Carriage of penicillin non-susceptible pneumococci was more common in children with many siblings. The prevalence of PCV13 serotypes among the detected serotypes/groups decreased from 56% (40/71) in 2013 to 23% (13/56) in 2015.

CONCLUSIONS:

Penicillin non-susceptibility in *S. pneumoniae* colonizing Tanzanian children increased during an observation period shortly after the PCV13 introduction. Measures to ensure rational use of antibiotics and more effective systems for surveillance of antibiotic resistance and serotype distribution are needed to assure continued effectual treatment of pneumococcal disease.

**WEB**: 10.1016/j.ijid.2019.01.035
**IMPACT FACTOR:** 3.20

**CITED HALF-LIFE:** 4.70

## START COMMENTARY

Figure 1 shows a flowchart of samples tested and found positive for *Streptococcus pneumoniae*. Samples from 2013 and 2015 came from children residing in Bondeni, Njoro, and Pasua. Samples from 2014 came from children residing in Majengo, Rau, and Shirimatunda (see Table 1). Figure 2 shows the percent non-susceptible to various antibiotics by sample year, with non-susceptibility to penicillin G showing significant increase between 2013 and 2014 ($p=0.042$) and between 2013 and 2015 ($p=0.033$). Serotype distributions, including penicillin-susceptibility by serotype, are displayed in Figures 3 and 4. Authors note a high prevalence of serotype 19B, which has not been reported in recent African studies. This study also identified high use of antibiotics, with 87% of children receiving antibiotics the week of sampling and only one-third with symptoms indicating the need for antibiotics. Authors call for continued monitoring of antibiotic non-susceptibility as well as efforts to more appropriately use antibiotics.

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# 10. Impact of the introduction of the *Haemophilus influenzae* type b conjugate vaccine in an urban setting in southern India

Fitzwater SP, Ramachandran P, Kahn GD, Nedunchelian K, Suresh S, Santosham M, et al.

## ABSTRACT

INTRODUCTION:

*Haemophilus influenzae* type b was the leading cause of bacterial meningitis in infants and children below the age of two years prior to the introduction of *H. influenzae* type b conjugate vaccines. In December 2011, the Indian government introduced *H. influenzae* b vaccine in the state of Tamilnadu. A prospective surveillance for bacterial meningitis was established at the Institute of Child Health in Chennai to evaluate the etiology of meningitis and impact of the vaccine.

MATERIAL AND METHODS:

Infants aged one to 23 months who were admitted to the hospital with symptoms of suspected bacterial meningitis were enrolled and lumbar puncture was performed. Cerebrospinal fluid samples were analyzed for white blood cells, protein, and glucose. Bacterial culture and a latex agglutination test for common bacterial pathogens were performed.

RESULTS:

Between January 2009 and March 2014, 4,770 children with suspected bacterial meningitis were enrolled. Prior to the introduction of the vaccine, an average of 11.7 cases of *H. influenzae* b meningitis and 31.1 cases of probable meningitis with no etiology were identified each year. After introduction, the number of cases were reduced by 79% and 44% respectively. The average *H. influenzae* b vaccine coverage after introduction was 69% among all children with clinically suspected meningitis. In contrast, the mean number of aseptic meningitis and pneumococcal meningitis cases remained stable throughout the pre and post vaccination period; 28.2 and 4.8 per year, respectively.

CONCLUSIONS:

*H. influenzae* b conjugate vaccine reduced the number of cases of *H. influenzae* b meningitis and probable meningitis within the first two years of its introduction. The impact against meningitis was higher than the vaccination rate, indicating indirect effects of the vaccine. India has recently scaled up the use of Hib conjugate vaccine throughout the country which should substantially reduce childhood meningitis rates further in the country.

**WEB**: 10.1016/j.vaccine.2019.01.080

## START COMMENTARY

Fitzwater et al. evaluated the impact of *Haemophilus influenzae* type b conjugate vaccine in Chennai, Tamilnadu. Table 1 summarizes the results of the meningitis surveillance system. Of the 4,770 children with suspected bacterial meningitis, 148 were aseptic, 136 were probable bacterial, and 87 were confirmed bacterial, with 43 Hib. Authors note limitations of the study included differences in demographic characteristics between pre- and post-Hib introduction, though authors reason that differences observed would arguably result in an increase in Hib detection, with the exception of an increase in antibiotic use prior to lumbar puncture. One challenge of this population is the wide use of antibiotics prior to lumbar puncture (77%), resulting in sterilization of cerebrospinal fluid and low culture yield. It is for this reason that authors prioritized latex agglutination assay to determine the etiology of bacterial meningitis, rather than grow culture. However, latex agglutination is subject to false positives. Despite these limitations, one would not expect differential detection of Hib pre- and post-introduction of vaccine. This study shows promising impact of Hib vaccine introduction in reducing cases of bacterial meningitis, with potential for reductions in pneumonia caused by Hib.

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# Appendix

The literature search for the March 2019 Vaccine Delivery Research Digest was conducted on February 19, 2019. We searched English language articles indexed by the US National Library of Medicine and published between January 15, 2019 and February 15, 2019. The search resulted in 226 items.

## 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]) ("2019/01/15"[PDAT] : "2019/02/14"[PDAT]))