

VACCINE DELIVERY RESEARCH DIGEST

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

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<b>1. Reorganizing Nigeria's Vaccine Supply Chain Reduces Need For Additional Storage Facilities, But More Storage Is Required.</b>	<b>3</b>
○ A modeling study using national program data from the National Primary Health Care Development Agency to simulate how changes in supply and demand effect storage capacity requirements.	
<b>2. Effectiveness of a pay-for-performance intervention to improve maternal and child health services in Afghanistan: a cluster-randomized trial.</b>	<b>4</b>
○ A cluster randomized controlled trial of a pay for performance (P4P) intervention to improve maternal and child services, including childhood pentavalent vaccine, among primary care facilities in Afghanistan.	
<b>3. The composition of demand for newly launched vaccines: results from the pneumococcal and rotavirus vaccine introductions in Ethiopia and Malawi.</b>	<b>5</b>
○ A descriptive epidemiologic study to explore the demand for newly introduced vaccines, and to describe the proportion of demand attributable to new and “backlog” cohorts.	
<b>4. Communication strategies to promote the uptake of childhood vaccination in Nigeria: a systematic map.</b>	<b>6</b>
○ A landscape of current vaccination communication interventions in two states in northern Nigeria from interviews with key stakeholders and document/policy review.	
<b>5. Demand Creation for Polio Vaccine in Persistently Poor-Performing Communities of Northern Nigeria: 2013-2014.</b>	<b>7</b>
○ A quasi-experimental (non-randomized, non-controlled), pre-post evaluation of the effect of a variety of interventions to increase demand for polio vaccine in local government areas (LGAs) in northern Nigeria.	
<b>6. Implementation of a Systematic Accountability Framework in 2014 to Improve the Performance of the Nigerian Polio Program.</b>	<b>8</b>
○ A quasi-experimental (non-randomized, non-controlled) pre-post study to determine the impact of an accountability framework to improve performance of WHO field officers.	
<b>7. Mucosal vaccine delivery: Current state and a pediatric perspective.</b>	<b>9</b>
○ An overview of the current landscape of mucosal vaccine delivery, including description of mechanisms through which they work; currently-approved vaccines; delivery routes; barriers and opportunities.	
<b>8. Publicly Available Online Tool Facilitates Real-Time Monitoring Of Vaccine Conversations And Sentiments.</b>	<b>10</b>
○ A descriptive overview of a publically available platform for monitoring vaccination-related social media and electronic published media content, Vaccine Sentimeter, and exemplar of the use of the tool.	
<b>9. Process development of a new <i>Haemophilus influenzae</i> type <i>b</i> conjugate vaccine and the use of mathematical modeling to identify process optimization possibilities.</b>	<b>11</b>
○ A mathematical modeling analysis using predictive models to inform development and distribution systems, and to improve systems and processes to reduce price. The example of Hib vaccine is used.	
<b>10. Polio vaccine hesitancy in the networks and neighborhoods of Malegaon, India.</b>	<b>12</b>
○ A network analysis of social and spatial clustering of vaccine hesitancy (accepting, reluctance, refusal), from a population-based household survey in a high vaccine-hesitancy region at high risk of polio outbreak.	
<b>Appendix: PubMed Search Terms</b>	<b>13</b>



## 1. **Reorganizing Nigeria's Vaccine Supply Chain Reduces Need For Additional Storage Facilities, But More Storage Is Required.**

Shittu E, Harnly M, Whitaker S, Miller R.  
Health Aff (Millwood). 2016 Feb 1;35(2):293-300.  
PMID: 26858383

### **ABSTRACT**

One of the major problems facing Nigeria's vaccine supply chain is the lack of adequate vaccine storage facilities. Despite the introduction of solar-powered refrigerators and the use of new tools to monitor supply levels, this problem persists. Using data on vaccine supply for 2011–14 from Nigeria's National Primary Health Care Development Agency, we created a simulation model to explore the effects of variance in supply and demand on storage capacity requirements. We focused on the segment of the supply chain that moves vaccines inside Nigeria. Our findings suggest that 55 percent more vaccine storage capacity is needed than is currently available. We found that reorganizing the supply chain as proposed by the National Primary Health Care Development Agency could reduce that need to 30 percent more storage. Storage requirements varied by region of the country and vaccine type. The Nigerian government may want to consider the differences in storage requirements by region and vaccine type in its proposed reorganization efforts.

**WEB:** <http://dx.doi.org/10.1377/hlthaff.2015.1328>

**IMPACT FACTOR:** 3.35

**CITED HALF-LIFE:** 4.80

**UW EDITORIAL COMMENT:** The National Primary Health Care Development Agency plans to redesign the current distribution system (6 zonal vaccination storage hubs) by developing “national vaccine delivery hubs” in Abuja, Lagos and Kano, from which vaccines would be distributed to storage facilities at the state level, in order to expand the current supply chain. Authors used models to estimate requirements for increases in cold storage capacity to meet “100% fill rate” for BCG, OPV, YF, TT, Hep B, using the supply chain system in its current state, and simulated expected requirements with the proposed redesigned system. Exhibit 2 shows the expected increase in vaccine storage capacity needed to improve reliability to meet 100 percent fill rate for each of the 5 vaccines studied, by each of the three hubs in the proposed redesigned system. Exhibit 3 shows the expected increase in vaccine storage capacity needed to improve reliability to meet 100 percent fill rate for each of the 5 vaccines studied, by each of the three hubs in the proposed redesigned system. Exhibit 4 shows expected overall increase in vaccine storage capacity for the current and redesigned system, but vaccine-specific contribution.

This article is part of a special issue of Health Affairs published in Feb, which focuses specifically on global vaccine discovery, production and delivery both in the US and globally. The full issue is available at: [http://measlesrubellainitiative.org/wpcontent/uploads/2016/03/HealthAffairs\\_FEB2016\\_Vx.pdf](http://measlesrubellainitiative.org/wpcontent/uploads/2016/03/HealthAffairs_FEB2016_Vx.pdf)



## 2. Effectiveness of a pay-for-performance intervention to improve maternal and child health services in Afghanistan: a cluster-randomized trial.

Engineer CY, Dale E, Agarwal A, Agarwal A, Alonge O et al.  
Int J Epidemiol. 2016 Feb 13. [Epub ahead of print]  
PMID: 26874927

### ABSTRACT

**BACKGROUND:** A cluster randomized trial of a pay-for-performance (P4P) scheme was implemented in Afghanistan to test whether P4P could improve maternal and child (MCH) services.

**METHODS:** All 442 primary care facilities in 11 provinces were matched by type of facility and outpatient volume, and randomly assigned to the P4P or comparison arm. P4P facilities were given bonus payments based on the MCH services provided. An endline household sample survey was conducted in 72 randomly selected matched pair catchment areas (3421 P4P households; 3427 comparison). The quality of services was assessed in 81 randomly sampled matched pairs of facilities. Data collectors and households were blinded to the intervention assignment. MCH outcomes were assessed at the cluster level.

**RESULTS:** There were no substantial differences in any of the five MCH coverage indicators (P4P vs comparison): modern contraception (10.7% vs 11.2% ( $p = 0.90$ ); antenatal care: 56.2% vs 55.6% ( $p = 0.94$ ); skilled birth attendance (33.9% vs 28.5%,  $p = 0.17$ ); postnatal care (31.2% vs 30.3%,  $p = 0.98$ ); and childhood pentavalent3 vaccination (49.6 vs 52.3%,  $p = 0.41$ ), or in the equity measures. There were substantial increases in the quality of history and physical examinations index ( $p = 0.01$ ); client counselling index ( $p = 0.01$ ); and time spent with patients ( $p = 0.05$ ). Health workers reported limited understanding about the bonuses.

**WEB:** <http://ije.oxfordjournals.org/content/early/2016/02/13/ije.dyv362.full.pdf+html>

**IMPACT FACTOR:** 9.18

**CITED HALF-LIFE:** 8.40

**UW EDITORIAL COMMENT:** Authors speculate that failing to focus on the demand-side factors, and poor communication/challenges in communicating with health workers about the intervention and how the payment scheme worked, may have undermined the program's potential benefit. For example, although nearly 87% of health workers reported their health facility had received incentives, only 37.9% of health workers sampled recognized that they had received any payment from the P4P intervention, and levels of performance were not consistently communicated to staff or clearly linked with the receipt (or failure to receive) payment. Authors also recommend that a more nuanced understanding of the motivations of health worker, and how such motivations influence behavior, is needed to be successful with similar programs in future. Authors also point out that a more complex understanding of the other important drivers of behavior of health services personnel, including "organizational culture, leadership, management and psychology" should be considered when designing and assessing interventions in future. For changes in childhood vaccination coverage in particular, the study period may not have been long or large enough to detect a difference in the proportion of children vaccinated at the population-level, even if in fact a larger proportion of children who sought care at the facilities were getting appropriately vaccinated. Authors also note that changes in population-level measures of vaccination coverage are heavily dependent on demand and care-seeking practices in the target population, and population-level impact may be limited without addressing drivers and constraints on the demand side, such as maternal health-seeking behavior, if care-seeking is low in the overall population.



### 3. **The composition of demand for newly launched vaccines: results from the pneumococcal and rotavirus vaccine introductions in Ethiopia and Malawi.**

Williams BA, Kidane T, Chirwa G, Tesfaye N, Prescott MR, et al.  
Health Policy Plan. 2016 Feb 7. [Epub ahead of print]  
PMID: 26856361

#### **ABSTRACT**

Understanding post-launch demand for new vaccines can help countries maximize the benefits of immunization programmes. In particular, low- and middle-income countries (LMICs) should ensure adequate resource planning with regards to stock consumption and service delivery for new vaccines, whereas global suppliers must produce enough vaccines to meet demand. If a country underestimates the number of children seeking vaccination, a stock-out of commodities will create missed opportunities for saving lives. We describe the post-launch demand for the first dose of pneumococcal conjugate vaccine (PCV1) in Ethiopia and Malawi and the first dose of rotavirus vaccine (Rota1) in Malawi, with focus on the new birth cohort and the 'backlog cohort', comprised of older children who are still eligible for vaccination at the time of launch. PCV1 and Rota1 uptake were compared with the demand for the first dose of pentavalent vaccine (Penta1), a routine immunization that targets the same age group and immunization schedule. In the first year, the total demand for PCV1 was 37% greater than that of Penta1 in Ethiopia and 59% greater in Malawi. In the first 6 months, the demand of Rota1 was only 5.9% greater than Penta1 demand in Malawi. Over the first three post-introduction months, 70.7% of PCV1 demand in Ethiopia and 71.5% of demand in Malawi came from children in the backlog cohort, whereas only 28.0% of Rota1 demand in Malawi was from the backlog cohort. The composition of demand was impacted by time elapsed since vaccine introduction and age restrictions. Evidence suggests that countries' plans should account for the impact of backlog demand, especially in the first 3 months post-introduction. LMICs should request for higher stock volumes when compared with routine needs, plan social mobilization activities to reach the backlog cohort and allocate human resources and cold chain capacity to accommodate high demand following vaccine introduction.

**WEB:** <http://heapol.oxfordjournals.org/content/early/2016/02/07/heapol.czv103.long>

**IMPACT FACTOR:** 3.47

**CITED HALF-LIFE:** 7.20

**UW EDITORIAL COMMENT:** Authors recommend that using a strategy that focuses on vaccinating a large proportion of of the 'backlog cohort,' versus using strict age-specific eligibility criteria for new vaccines, can result in substantial efficiencies in saving lives. Although a large proportion of demand for new vaccines was initially due to the backlog cohort, at later times post-introduction the proportion accounted for by backlog cohort was smaller. By the end of the post-launch period for PCV1 backlog cohort represented only slightly more than 1% of demand in Malawi and Ethiopia. The contributions of the backlog cohort to demand depended on country and differed for the different vaccines. Authors point out that in developed countries there is some indication that introduction of new vaccines can result in deleterious effects on coverage of existing vaccines, perhaps through disruption in system functioning. However, in this study, authors observed that adding a new vaccine (PCV) was followed by higher than average administration of existing vaccines (Penta1). Authors attribute differences in the size of demand from backlog cohort to age restrictions, limiting the potential size of the cohort of qualifying children, rather than differences in care-seeking or vaccine-specific demand, and thus recommend relaxing age restrictions to ensure maximum numbers of children who may potentially benefit are reached.



#### 4. **Communication strategies to promote the uptake of childhood vaccination in Nigeria: a systematic map.**

Oku A, Oyo-Ita A, Glenton C, Fretheim A, Ames H, et al.  
Glob Health Action. 2016;9:30337.  
PMID: 26880154

##### **ABSTRACT**

**BACKGROUND:** Effective communication is a critical component in ensuring that children are fully vaccinated. Although numerous communication interventions have been proposed and implemented in various parts of Nigeria, the range of communication strategies used has not yet been mapped systematically. This study forms part of the 'Communicate to vaccinate' (COMMVAC) project, an initiative aimed at building research evidence for improving communication with parents and communities about childhood vaccinations in low- and middle income countries.

**OBJECTIVE:** This study aims to: 1) identify the communication strategies used in two states in Nigeria; 2) map these strategies against the existing COMMVAC taxonomy, a global taxonomy of vaccination communication interventions; 3) create a specific Nigerian country map of interventions organised by purpose and target; and 4) analyse gaps between the COMMVAC taxonomy and the Nigerian map.

**DESIGN:** We conducted the study in two Nigerian states: Bauchi State in Northern Nigeria and Cross River State in Southern Nigeria. We identified vaccination communication interventions through interviews carried out among purposively selected stakeholders in the health services and relevant agencies involved in vaccination information delivery; through observations and through relevant documents. We used the COMMVAC taxonomy to organise the interventions we identified based on the intended purpose of the communication and the group to which the intervention was targeted.

**RESULTS:** The Nigerian map revealed that most of the communication strategies identified aimed to inform and educate and remind or recall. Few aimed to teach skills, enhance community ownership, and enable communication. We did not identify any intervention that aimed to provide support or facilitate decision-making. Many interventions had more than one purpose. The main targets for most interventions were caregivers and community members, with few interventions directed at health workers. Most interventions identified were used in the context of campaigns rather than routine immunisation programmes.

**CONCLUSIONS:** The identification and development of the Nigerian vaccination communication interventions map could assist programme managers to identify gaps in vaccination communication. The map may be a useful tool as part of efforts to address vaccine hesitancy and improve vaccination coverage in Nigeria and similar settings.

**WEB:** <http://dx.doi.org/10.3402/gha.v9.30337>

**IMPACT FACTOR:** 1.93

**CITED HALF-LIFE:** 2.40

**UW EDITORIAL COMMENT:** This study is part of a larger initiative to inform the evidence of how to improve communication about childhood vaccination in low resource settings, the 'Communicate to vaccinate' (COMMVAC) project. Authors categorized interventions as: 1) Inform or educate; 2) Remind or recall; 3) Teaching skills; 4) Providing support; 5) Facilitating decision making; 6) Enabling communication; 7) Enhancing community ownership. Examples of communication interventions in Bauchi and Cross River states in each category is provided in Table 3.



## 5. Demand Creation for Polio Vaccine in Persistently Poor-Performing Communities of Northern Nigeria: 2013-2014.

Warigon C, Mkanda P, Muhammed A, Estano A, Korir C, et al.  
J Infect Dis. 2016 Feb 3. [Epub ahead of print]  
PMID: 26908717

### ABSTRACT

**INTRODUCTION:** Poliomyelitis remains a global threat despite availability of oral polio vaccine (OPV), proven to reduce the burden of the paralyzing disease. In Nigeria, children continue to miss the opportunity to be fully vaccinated, owing to factors such as unmet health needs and low uptake in security-compromised and underserved communities. We describe the implementation and evaluation of several activities to create demand for polio vaccination in persistently poor-performing local government areas (LGAs).

**METHODS:** We assessed the impact of various polio-related interventions, to measure the contribution of demand creation activities in 77 LGAs at very high risk for polio, located across 10 states in northern Nigeria. Interventions included provision of commodities along with the polio vaccine.

**RESULTS:** There was an increasing trend in the number of children reached by different demand creation interventions. A total of 4,819,847 children were vaccinated at health camps alone. There was a reduction in the number of wards in which >10% of children were missed by supplementary immunization activities due to noncompliance with vaccination recommendations, a rise in the proportion of children who received  $\geq 4$  OPV doses, and a decrease in the proportion of children who were underimmunized or unimmunized.

**CONCLUSIONS:** Demand creation interventions increased the uptake of polio vaccines in persistently poor-performing high-risk communities in northern Nigeria during September 2013–November 2014.

**WEB:** <http://jid.oxfordjournals.org/content/early/2016/02/03/infdis.jiv511.full.pdf+html>

**IMPACT FACTOR:** 6.00

**CITED HALF-LIFE:** 8.70

**UW EDITORIAL COMMENT:** Demand creation interventions included training packages for Qur’anic teachers, “dramatic road shows” to increase visibility; “attractive pluses” or add-ons/gifts distributed to children and caregivers who received vaccines (soap, sugar detergent, etc.); health camps; state-level interventions; and use of local leaders/religious leaders and *Ardo* leaders in security-challenged areas and Nomadic *Ardo* underserved communities. Authors report changes in the number of children vaccinated in the local government areas (LGAs) that received the interventions, from vaccination team tally sheets, immunization registers, and treatment records in clinics, and changes in acute flaccid paralysis (AFP) from surveillance data. Changes in vaccination frequency and proportion of children vaccinated were attributed to the effect of the interventions, but note that this pragmatic evaluation wasn’t able to compare changes over time in other similar regions not receiving interventions. It is possible that other factors, in addition to the interventions, may also have changed over time in the regions, and could partially explain changes in vaccination frequency. It is also possible that improvements or changes in field-based program documentation (which was a focus of some interventions) could account for some of the differences observed over time.



## 6. Implementation of a Systematic Accountability Framework in 2014 to Improve the Performance of the Nigerian Polio Program.

Teegne SG, MKanda P, Yehualashet YG, Erbetto TB, Touray K et al.  
J Infect Dis. 2016 Jan 27. [Epub ahead of print]  
PMID: 26823334

### ABSTRACT

**BACKGROUND:** An accountability framework is a central feature of managing human and financial resources. One of its primary goals is to improve program performance through close monitoring of selected priority activities. The principal objective of this study was to determine the contribution of a systematic accountability framework to improving the performance of the World Health Organization (WHO)-Nigeria polio program staff, as well as the program itself.

**METHODS:** The effect of implementation of the accountability framework was evaluated using data on administrative actions and select process indicators associated with acute flaccid paralysis (AFP) surveillance, routine immunization, and polio supplemental immunization activities. Data were collected in 2014 during supportive supervision, using Magpi software (a company that provides service to collect data using mobile phones). A total of 2500 staff were studied.

**RESULTS:** Data on administrative actions and process indicators from quarters 2-4 in 2014 were compared. With respect to administrative actions, 1631 personnel (74%) received positive feedback (written or verbal commendation) in quarter 4 through the accountability framework, compared with 1569 (73%) and 1152 (61%) during quarters 3 and 2, respectively. These findings accorded with data on process indicators associated with AFP surveillance and routine immunization, showing statistically significant improvements in staff performance at the end of quarter 4, compared with other quarters.

**Conclusions:** Improvements in staff performance and process indicators were observed for the WHO-Nigeria polio program after implementation of a systematic accountability framework.

**WEB:** <http://dx.doi.org/10.1093/infdis/jiv492>

### IMPACT FACTOR:

### CITED HALF-LIFE:

**UW EDITORIAL COMMENT:** WHO field officers assessed included field volunteers, local government area (LGA) facilitators, cluster coordinators (ie, medical officers who monitor and supervise districts in a cluster), and state coordinators. Magpi uses mobile phones and a real-time cloud-based system with global positioning system (GPS) coordinates and time stamping, to record surveillance and immunization activities, and provide real-time feedback to officers. Authors assessed changes in officer performance over time by comparing frequency of “administrative actions” (letters of warning/citations; letters of superb performance; contract extensions etc. for staff); availability of immunization monitoring charts, and proportion of appropriate active case searching for AFP, before and after Magpi introduction. It should be noted that no “comparison group” of staff not utilizing Magpi was available to follow over time, so it is possible that observed changes in administrative actions could be due to other changes in the systems or personnel during the that time, or that using Magpi changed the way staff performance was tracked, documented, and evaluated, resulting in perceptions of better performance, even if actual performance was similar. Nonetheless, the use of Magpi to track important process indicators for vaccination systems, such as proportion of facilities in which active case searching was completed or proportion of facilities in which data quality self-assessments were completed, and to assess for trends over time, is a valuable feature of this tool.





## 7. **Mucosal vaccine delivery: Current state and a pediatric perspective.**

Shakya AK, Chowdhury MY, Tao W, Gill HS.

J Control Release. 2016 Feb 6. [Epub ahead of print]

PMID: 26860287

### **ABSTRACT**

Most childhood infections occur via the mucosal surfaces, however, parenterally delivered vaccines are unable to induce protective immunity at these surfaces. In contrast, delivery of vaccines via the mucosal routes can allow antigens to interact with the mucosa-associated lymphoid tissue (MALT) to induce both mucosal and systemic immunity. The induced mucosal immunity can neutralize the pathogen on the mucosal surface before it can cause infection. In addition to reinforcing the defense at mucosal surfaces, mucosal vaccination is also expected to be needle-free, which can eliminate pain and the fear of vaccination. Thus, mucosal vaccination is highly appealing, especially for the pediatric population. However, vaccine delivery across mucosal surfaces is challenging because of the different barriers that naturally exist at the various mucosal surfaces to keep the pathogens out. There have been significant developments in delivery systems for mucosal vaccination. In this review we provide an introduction to the MALT, highlight barriers to vaccine delivery at different mucosal surfaces, discuss different approaches that have been investigated for vaccine delivery across mucosal surfaces, and conclude with an assessment of perspectives for mucosal vaccination in the context of the pediatric population.

**WEB:** <http://dx.doi.org/10.1016/j.jconrel.2016.02.014>

**IMPACT FACTOR:** 7.71

**CITED HALF-LIFE:** 7.00

**UW EDITORIAL COMMENT:** Figure 4 provides a schematics of the possible mucosal routes of delivery (stomach and intestine; nasal cavity; oral cavity; skin) and summarizes key barriers to delivery for each route.

Authors describe the following delivery systems for mucosal vaccines: live bacteria and viruses; polymeric particles; inorganic particles; liposomes; virus like particles; pollen grain shells; terrestrial plants and algae; microneedles for skin and oral cavity; and other merging systems for skin and oral cavity.

The potential benefits and barriers in the pediatric and infant populations are discussed. Although many of the pathogens that cause mortality in infants enter through the mucosa, currently the only mucosal vaccines recommended for infants are rotavirus and OPV, due to lack of safety data for attenuated strains in other mucosal vaccines, and safety concerns about the potential of vaccine strains to regain virulence. Authors note that non-viral vaccines may be an alternative, but since they don't infect mucosal epithelial cells to produce immune response, delivery is more challenging. Authors dispel concerns about competency of infant mucosal system at birth and describe the systems that ensure it is sufficiently developed to respond to antigen stimulation at birth, and also describe the 'early window' for oral vaccination available during the period of intestinal membrane permeability in the first 48 hours of life.

Authors caution that the cost of development and of conducting clinical trials should be considered along with costs of formulation and development of delivery system platforms when considering the total cost of mucosal vaccines.



## 8. Publicly Available Online Tool Facilitates Real-Time Monitoring Of Vaccine Conversations And Sentiments.

Bahk CY, Cumming M, Paushter L, Madoff LC, Thomson A, Brownstein JS.  
Health Aff (Millwood). 2016 Feb 1;35(2):341-7.  
PMID: 26858390

### ABSTRACT

Real-time monitoring of mainstream and social media can inform public health practitioners and policy makers about vaccine sentiment and hesitancy. We describe a publicly available platform for monitoring vaccination-related content, called the Vaccine Sentimeter. With automated data collection from 100,000 mainstream media sources and Twitter, natural-language processing for automated filtering, and manual curation to ensure accuracy, the Vaccine Sentimeter offers a global real-time view of vaccination conversations online. To assess the system's utility, we followed two events: polio vaccination in Pakistan after a news story about a Central Intelligence Agency vaccination ruse and subsequent attacks on health care workers, and a controversial episode in a television program about adverse events following human papillomavirus vaccination. For both events, increased online activity was detected and characterized. For the first event, Twitter response to the attacks on health care workers decreased drastically after the first attack, in contrast to mainstream media coverage. For the second event, the mainstream and social media response was largely positive about the HPV vaccine, but antivaccine conversations persisted longer than the provaccine reaction. Using the Vaccine Sentimeter could enable public health professionals to detect increased online activity or sudden shifts in sentiment that could affect vaccination uptake.

**WEB:** <http://dx.doi.org/10.1377/hlthaff.2015.1092>

**IMPACT FACTOR:**

**CITED HALF-LIFE:**

**UW EDITORIAL COMMENT:** The Vaccine Sentimeter collects data by conducting hourly searches of online sources for vaccine-specific language in English, Spanish and French using the HealthMap system (also used for disease outbreak monitoring and public health threats). Data has been collected since 2012, but has only been analyzed for public availability through 2014, due to resource constraints. Data are both automatically and manually processed and can be tailored to create interactive visualizations based on specific interest. A dashboard feature is an open access tool that can be used “to detect early signals in shifting conversations” or to “conduct case-studies” of the influence of certain events, such as those conducted by the authors. Using the dashboard, individuals can produce simple visual reports of numbers of articles by location and sentiment, and can create lists of relevant communications filtered by date, article title, vaccine, category, sentiment and location. From the case studies conducted for the article, authors produced charts of trends over time in frequency of mainstream media and Tweets about polio vaccine in Pakistan (Exhibits 1) and HPV vaccination (Exhibit 2), monthly for over two years, overlaid with dates of critical local and international events relevant to the specific vaccines. Exhibits 3 and 4 show mainstream media and Twitter, daily frequencies of communication categorized as “negative sentiment” and “positive sentiment”, in the days surrounding critical HPV vaccine-relevant events.



**9. Process development of a new *Haemophilus influenzae* type b conjugate vaccine and the use of mathematical modeling to identify process optimization possibilities.**

Hamidi A, Kreeftenberg H, V D Pol L, Ghimire S, van der Wielen LA, Ottens M.  
Biotechnol Prog. 2016 Jan 29. [Epub ahead of print]  
PMID: 26821825

**ABSTRACT**

Vaccination is one of the most successful public health interventions being a cost-effective tool in preventing deaths among young children. The earliest vaccines were developed following empirical methods, creating vaccines by trial and error. New process development tools, for example mathematical modeling, as well as new regulatory initiatives requiring better understanding of both the product and the process are being applied to well-characterized biopharmaceuticals (for example recombinant proteins). The vaccine industry is still running behind in comparison to these industries. A production process for a new *Haemophilus influenzae* type b (Hib) conjugate vaccine, including related quality control (QC) tests, was developed and transferred to a number of emerging vaccine manufacturers. This contributed to a sustainable global supply of affordable Hib conjugate vaccines, as illustrated by the market launch of the first Hib vaccine based on this technology in 2007 and concomitant price reduction of Hib vaccines. This paper describes the development approach followed for this Hib conjugate vaccine as well as the mathematical modeling tool applied recently in order to indicate options for further improvements of the initial Hib process. The strategy followed during the process development of this Hib conjugate vaccine was a targeted and integrated approach based on prior knowledge and experience with similar products using multi-disciplinary expertise. Mathematical modeling was used to develop a predictive model for the initial Hib process (the 'baseline' model) as well as an 'optimized' model, by proposing a number of process changes which could lead to further reduction in price.

**WEB:** <http://dx.doi.org/10.1002/btpr.2235>

**IMPACT FACTOR:** 2.15

**CITED HALF-LIFE:** 2.27

**UW EDITORIAL COMMENT:** Key model inputs specific to Hib conjugate vaccine were based on prior knowledge, and related to components of upstream development; downstream development, conjugation process and formulation and filling. Authors considered performance indicators (PI's), key process parameter (KPPs) and key raw materials (KRM)s for each step in the development process. In order to develop the optimization models, "experiments" or simulations were used to develop input data, in the absence of available data on unit operations specific to the vaccine system being modeled.

Table 1 and Figure 1 are heuristic examples of applying this approach to modeling for a specific vaccine, and show Target Product Profile for new *Haemophilus influenzae* type b conjugate vaccine, and the schematic of the associated process flow used in the 'baseline model.' Table 3 lists the specific performance indicators and key process parameters for the development of Hib type b conjugate, throughout the development process.

The 'optimized' process model simulated different scenarios at the upstream, downstream, conjugation, purification and formulation stages, and considered results in terms of both product quality and economic feasibility (process economics). Process changes simulated to assess for possible reductions in price in the "optimized" model include using fed-batch instead of batch, not including inactivation, chromatography instead of precipitation, and factors relating to formulation (liquid instead of freezing) and filling/differences in dose.



## 10. Polio vaccine hesitancy in the networks and neighborhoods of Malegaon, India.

Onnela JP, Landon BE, Kahn AL, Ahmed D, Verma H. et al.  
Soc Sci Med. 2016 Mar;153:99-106. [Epub ahead of print]  
PubMed PMID: 26889952.

### ABSTRACT

**OBJECTIVES:** Eradication and control of childhood diseases through immunization can only work if parents allow their children to be vaccinated. To learn about social network factors associated with polio vaccine hesitancy, we investigated social and spatial clustering of households by their vaccine acceptance status in Malegaon, India, an area known for vaccine refusal and repeated detection of polio cases.

**METHODS:** We interviewed family heads from 2462 households in 25 neighborhoods in July 2012 and constructed social networks based on advice seeking from other households. We restricted our main analyses to surveyed households for which we also had data on whether they accepted the polio vaccine for their eligible children or not.

**RESULTS:** Data from 2452 households was retained and these households made 2012 nominations to 830 households. Vaccine-refusing households had fewer outgoing ties than vaccine-accepting households. After excluding 24 isolated households, vaccine-refusing households had 189% more nominations to other vaccine-refusing households (93% more in the largest component of the network) compared to vaccine-accepting households, revealing that vaccine-refusing households cluster in the social network. Since roughly half of all ties connect households within neighborhoods, vaccine-refusing clusters lie in spatially localized “pockets”.

**CONCLUSIONS:** The social (and spatial) clustering of vaccine-refusing households could be leveraged to tailor communication strategies to improve vaccine acceptance and community perceptions of immunization programs for polio and other vaccine-preventable diseases.

**WEB:** <http://dx.doi.org/10.1016/j.socscimed.2016.01.024>

**IMPACT FACTOR:** 2.89

**CITED HALF-LIFE:** 9.20

**UW EDITORIAL COMMENT:** Households were classified as “accepting” (vaccinated qualifying child on first attempt); “reluctant” (vaccinated child qualifying child on second attempt) or “resistant” (failed to vaccinate qualifying child on  $\leq$  attempts) based on WHO OPV campaign records.

Authors provide the following basic definitions for terminology from the social networking literature. A participant (“node”) is asked to generate the name of another person to participate in the study, and this is referred to as a “nomination,” and indicates a connection between the two individuals. A pair of individuals are called a “dyad.” The person doing the nomination is called the “ego” and the person nominated is called the “alter.” Connections between individuals all called “ties” or “edges.” The number of outgoing-edges refer to “out-degree” and number of in-going edges refer to “in-degree.” A person’s “network neighbors” are all individuals they are tied to (in-degree or out-degree).

One important limitation the authors note is that “clustering” of ideas and characteristic in a network of people can be due to three distinct mechanisms: influence (individuals influence or effect the beliefs/behaviors of others); selection (individuals choose to connect with those who have similar beliefs/behaviors to their own, even if not directly affecting those of others); confounding (some other factor(s) is affecting the beliefs/behaviors of both individuals so that their beliefs/behaviors seem similar even in the absence of influence or selection). Given the design of this study, it isn’t possible to disentangle which of these three mechanisms may be operating, but the impact of interventions aimed at “leveraging” social and spatial clustering to improve vaccine acceptance, such as those recommended by authors, will depend on which of these mechanisms is at play.



#### 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 ("2015/1/15"[PDAT] : "2016/02/14"[PDAT]))

\* On February 26, 2016, this search of English language articles published between January 15, 2015 and February 14, 2016 and indexed by the US National Library of Medicine resulted in 242 unique manuscripts.

