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VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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LIST OF ARTICLES

1. **Understanding threats to polio vaccine commitment among caregivers in high-priority areas in Afghanistan: a polling study.** {Abstract & UW comment} {Full article}
    - Survey of caregivers of children < 5 years of age in Afghanistan assessed commitment to polio vaccination and associated knowledge, attitudes, or experiences that could influence commitment to vaccination. Lack of trust and knowledge of polio's ability to spread via contaminated water were both indicators for lack of commitment to vaccination among caretakers.

2. **Progress Toward Measles Elimination - Bangladesh, 2000-2016.** {Abstract & UW comment} {Full article}
    - Measles elimination efforts in Bangladesh from 2000-2016 resulted in increased first measles-containing vaccine dose, introduction of second MCV, increased coverage of second MCV, and decreased measles incidence.

3. **The complexity and cost of vaccine manufacturing - An overview** {Abstract & UW comment} {Full article}
    - Authors summarize process and cost-drivers of childhood vaccine manufacturing for dissemination to decision makers in LMICs

4. **The Typhoid Vaccine Acceleration Consortium (TyVAC): Vaccine effectiveness study designs: Accelerating the introduction of typhoid conjugate vaccines and reducing the global burden of enteric fever. Report from a meeting held on 26-27 October 2016, Oxford, UK.** {Abstract & UW comment} {Full article}
    - This report summarizes discussions informing typhoid conjugate vaccines (TCV) introduction and planned next steps for effectiveness studies.

5. **Summary of workshop "global burden of diarrheal diseases among children in developing countries: Incidence, etiology, and insights from new molecular diagnostic techniques".** {Abstract & UW comment} {Full article}
    - This review summarized findings from the Global Enteric Multicenter Study (GEMS), including diagnostics and identification of relevant components of vaccines for Shigella and enterotoxigenic E. coli.

6. **Feasibility of using global system for mobile communication (GSM)-based tracking for vaccinators to improve oral poliomyelitis vaccine campaign coverage in rural Pakistan.** {Abstract & UW comment} {Full article}
    - Pilot study in rural Pakistan utilizing real-time mobile tracking of vaccinators to identify if all target areas are reached and workforce attendance was accurate.

7. **Who pays for cooperation in global health? A comparative analysis of WHO, the World Bank, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria, and Gavi, the Vaccine Alliance.** {Abstract & UW comment} {Full article}
    - Financial flow analysis across four case study institutions demonstrates disproportionate funding from US, UK, and the BMGF for three of the four institutions.

8. **Digital immunization registry: evidence for the impact of mHealth on enhancing the immunization system and improving immunization coverage for children under one year old in Vietnam.** {Abstract & UW comment} {Full article}
    - Digital immunization registry, which included SMS reminders, was implemented in Vietnam in 2012 by PATH and the Vietnam National Expanded Program on Immunization. Evaluation of the program demonstrated increased immunization rate, decreased dropout rate, improved timeliness of vaccination after implementation of the intervention (compared to pre-intervention period) and willingness from parents to pay for SMS reminders.

9. **Impact of rotavirus vaccines in low and middle-income countries.** {Abstract & UW comment} {Full article}
    - Authors assessed the impact and cost-effectiveness of rotavirus vaccine for children < 5 years old in LMICs and found decreases in morbidity in SSA and an impact on hospitalizations and economic burden.

10. **Using Cluster Analysis to Group Countries for Cost-Effectiveness Analysis: An Application to Sub-Saharan Africa.** {Abstract & UW comment} {Full article}
    - The authors describe the utility of cluster analysis for cost-effectiveness of a maternal immunization intervention based on economic and health measures in Sub-Saharan African countries.

1. Understanding threats to polio vaccine commitment among caregivers in high-priority areas of Afghanistan: a polling study
   SteelFisher GK, Blendon RJ, Guirguis S, Lodge II W, Caporello H, Petit V, et al.
   The Lancet Infectious diseases. 2017 Aug 14. [Epub ahead of print]
   PubMed ID: 28818541

ABSTRACT
BACKGROUND: Eradication of poliovirus from endemic countries relies on vaccination of children with oral polio vaccine (OPV) many times a year until the age of 5 years. We aimed to determine caregivers' commitment to OPV in districts of Afghanistan at high risk for polio transmission and to examine what knowledge, attitudes, or experiences could threaten commitment.
METHODS: We designed and analysed a poll using face-to-face interviews among caregivers of children under 5 years of age. The sample was drawn via a stratified multistage cluster design with random route household selection. We calculated the percentage of committed and uncommitted caregivers. All percentages were weighted. We then compared percentages of uncommitted caregivers among those with varying knowledge, attitudes, and experiences, using logistic regression to control for possible demographic confounders.
FINDINGS: Between Dec 19, 2014, and Jan 5, 2015, we interviewed 1980 caregivers, 21% of whom were "uncommitted" to accepting OPV. Multiple measures of knowledge, attitudes, and experiences are associated with lack of commitment. For example, compared with their relevant counterparts, caregivers are more likely to be uncommitted if they did not trust vaccinators "a great deal" (54% vs 9%), if they do not know that polio spreads through contaminated water (41% vs 14%), or if they believe rumours that OPV is not halal (50% vs 21%).
INTERPRETATION: To enhance OPV commitment, it might be useful to consider a multifactorial approach that highlights building trust in vaccinators, providing facts about transmission, sharing positive messages to overcome key rumours, and strengthening community support for vaccination.

WEB: 10.1016/S1473-3099(17)30397-3
IMPACT FACTOR: 5.82
CITED HALF-LIFE: 4.70

START SCIENTIFIC COMMENT: This is the first quantitative study in Afghanistan to describe the relationship between caregivers' perceptions of oral polio vaccine (OPV) and vaccination practices for children. Thirty three of 47 low-performing districts, as determined by the Global Polio Eradication Initiative partners, in Afghanistan were surveyed with a 55-question questionnaire. Among caregivers surveyed, 98% were aware of polio, and were the focus for the subsequent analyses. There was little variation in lack of commitment across demographic categories, with statistical differences seen between respondents age 25 – 34 compared to respondents ages ≥ 35 (25% vs. 18%, p-value = 0.0002) and between respondents with 3-4 children in household compared to ≥ 5 children in household (25% vs. 17%, p-value = 0.0445; Table 2). Lack of concern about a child getting sick with polio was associated with lack of commitment (15% vs. 33%, p-value=<0.0001; Table 3). Lack of religious leader support and negative perceptions from neighbors were also associated with lack of polio vaccination commitment (Table 4). There is an opportunity to leverage "factual knowledge" to motivate vaccine commitment to this population, such as increased information regarding transmission. Additionally, engagement with community and religious leaders can create a support system for improving vaccine commitment. A limitations of this study is the cross-sectional study design which prevents establishing a causal relationship. Also, "social desirability bias" may cause the future vaccine uptake data to not align with recorded vaccine commitment due to people overstating their commitment.

2. Progress Toward Measles Elimination - Bangladesh, 2000-2016.
Khanal S, Bohara R, Chacko S, Sharifuzzaman M, Shamsuzzaman M, Goodson JL, et al.
MMWR Morb Mortal Wkly Rep. 2017 Jul 21. 66(28):753-757. [Epub ahead of print]
Pubmed ID: 28727678

ABSTRACT
In 2013, at the 66th session of the Regional Committee of the World Health Organization (WHO) South-East Asia Region (SEAR), a regional goal was established to eliminate measles and control rubella and congenital rubella syndrome* by 2020 (1). WHO-recommended measles elimination strategies in SEAR countries include 1) achieving and maintaining >/=95% coverage with 2 doses of measles-containing vaccine (MCV) in every district, delivered through the routine immunization program or through supplementary immunization activities (SIAs)dagger; 2) developing and sustaining a sensitive and timely measles case-based surveillance system that meets targets for recommended performance indicators; and 3) developing and maintaining an accredited measles laboratory network (2). In 2014, Bangladesh, one of 11 countries in SEAR, adopted a national goal for measles elimination by 2018 (2,3). This report describes progress and challenges toward measles elimination in Bangladesh during 2000-2016. Estimated coverage with the first MCV dose (MCV1) increased from 74% in 2000 to 94% in 2016. The second MCV dose (MCV2) was introduced in 2012, and MCV2 coverage increased from 35% in 2013 to 93% in 2016. During 2000-2016, approximately 108.9 million children received MCV during three nationwide SIAs conducted in phases. During 2000-2016, reported confirmed measles incidence decreased 82%, from 34.2 to 6.1 per million population. However, in 2016, 56% of districts did not meet the surveillance performance target of >/=2 discarded nonmeasles, nonrubella cases section sign per 100,000 population. Additional measures that include increasing MCV1 and MCV2 coverage to >/=95% in all districts with additional strategies for hard-to-reach populations, increasing sensitivity of measles case-based surveillance, and ensuring timely transport of specimens to the national laboratory will help achieve measles elimination.

WEB: 10.15585/mmwr.mm6628a3
IMPACT FACTOR: 7.82
CITED HALF-LIFE: N/A

START Scientific Comment: SIAs helped continue the increasing trend in MCV1 coverage, starting in 2005 (Figure). A challenge to accurate vaccine coverage estimates occur with the presence of routine immunization (RI) in each district alongside nationwide SIA; therefore, the administrative coverage rates were overestimated due to the inclusion of SIA doses and doses for children outside of target age groups. An outbreak in 2016 revealed inefficiencies in the RI and SIA coverage and lack of implementation of isolation procedures for measles cases in health care facilities. Areas identified for improvement include improved social engagement and communication to remind and encourage caretakers when to obtain/return for vaccination, expansion of surveillance sites (beyond acute flaccid paralysis reporting units) to all health facilities across the country, increased genotyping to better track transmission pathways, and better infection prevention and control practices within health care facilities. A main limitation to the surveillance data is that it likely is an underestimate due to imperfect reporting of cases and not all who are diseased seek care.

3. The complexity and cost of vaccine manufacturing - An overview.
   Plotkin S, Robinson JM, Cunningham G, Iqbal R, Larsen S.
   Vaccine. 2017 Jul 24. 35(33):4064-4071. [Epub ahead of print]
   Pubmed ID: 28647170

ABSTRACT
As companies, countries, and governments consider investments in vaccine production for routine immunization and outbreak response, understanding the complexity and cost drivers associated with vaccine production will help to inform business decisions. Leading multinational corporations have good understanding of the complex manufacturing processes, high technological and R&D barriers to entry, and the costs associated with vaccine production. However, decision makers in developing countries, donors and investors may not be aware of the factors that continue to limit the number of new manufacturers and have caused attrition and consolidation among existing manufacturers. This paper describes the processes and cost drivers in acquiring and maintaining licensure of childhood vaccines. In addition, when export is the goal, we describe the requirements to supply those vaccines at affordable prices to low-resource markets, including the process of World Health Organization (WHO) prequalification and supporting policy recommendation. By providing a generalized and consolidated view of these requirements we seek to build awareness in the global community of the benefits and costs associated with vaccine manufacturing and the challenges associated with maintaining consistent supply. We show that while vaccine manufacture may prima facie seem an economic growth opportunity, the complexity and high fixed costs of vaccine manufacturing limit potential profit. Further, for most lower and middle income countries a large majority of the equipment, personnel and consumables will need to be imported for years, further limiting benefits to the local economy.

WEB: 10.1016/j.vaccine.2017.06.003
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START SCIENTIFIC COMMENT: Vaccine manufacturing is challenging due to the combined risk of "biological and physical variability". Figure 1 provides a range of production complexities across viral and bacterial vaccines. For manufacturers, it is most advantageous to develop a vaccine portfolio to minimize high fixed costs, however this is difficult due to lengthy research phases, balancing multiple products, and avoiding production short falls.

Table 1 outlines major costs, their impact on Cost of Goods Sold (COGS), and describes options to minimize COGS. Labor requires highly skilled and technical workforce, which in turn must have accessible training and education systems. Labor costs vary depending on locally available versus supplemental expatriate workforce. Raw materials can have limited supply, require extensive testing if of animal origin, and when in short supply can be expensive. Consumables offer an opportunity for local production for low-resource countries, with prices 15% that of high-resource countries.

Local producers versus large manufacturers have opposing perspectives to identifying the right size facility and reduction of fixed costs. Local producers are more in tune with the in-country population trends, however small lot production sizes result in higher unit prices for manufactured goods. Large manufacturers can minimize costs due to their large volumes but base their supply on multiple markets, which can be difficult to anticipate due to the influence of competitors on available market share.

4. The Typhoid Vaccine Acceleration Consortium (TyVAC): Vaccine effectiveness study designs: Accelerating the introduction of typhoid conjugate vaccines and reducing the global burden of enteric fever.
   Meiring JE, Gibani M.
   Vaccine. 2017 Aug 09. [Epub ahead of print]
   Pubmed ID: 28802757

ABSTRACT
Typhoid fever is estimated to cause between 11.9-26.9 million infections globally each year with 129,000-216,510 deaths. Access to improved water sources have reduced disease incidence in parts of the world but the use of efficacious vaccines is seen as an important public health tool for countries with a high disease burden. A new generation of Vi typhoid conjugate vaccines (TCVs), licensed for use in young children and expected to provide longer lasting protection than previous vaccines, are now available. The WHO Strategic Advisory Group of Experts on Immunization (SAGE) has convened a working group to review the evidence on TCVs and produce an updated WHO position paper for all typhoid vaccines in 2018 that will inform Gavi, the Vaccine Alliance's future vaccine investment strategies for TCVs. The Typhoid Vaccine Acceleration Consortium (TyVAC) has been formed through a $36.9 million funding program from the Bill & Melinda Gates Foundation to accelerate the introduction of TCVs into Gavi-eligible countries. In October 2016, a meeting was held to initiate planning of TCV effectiveness studies that will provide the data required by policy makers and stakeholders to support decisions on TCV use in countries with a high typhoid burden. Discussion topics included (1) the latest evidence and data gaps in typhoid epidemiology; (2) WHO and Gavi methods and data requirements; (3) data on TCV efficacy; (4) cost effectiveness analysis for TCVs from mathematical models; (5) TCV delivery and effectiveness study design. Specifically, participants were asked to comment on study design in 3 sites for which population-based typhoid surveillance is underway. The conclusion of the meeting was that country-level decision making would best be informed by the respective selected sites in Africa and Asia vaccinating children aged from 9-months to 15-years-old, employing either an individual or cluster randomized design with design influenced by population characteristics, transmission dynamics, and statistical considerations.

WEB: 10.1016/j.vaccine.2017.08.001
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START Scientific Comment: Typhoid fever disease burden is unknown, and in regions where it is defined there is inter and intra-country variability, with most of the surveillance in urban centers. An effectiveness trial is needed that is generalizable to different contexts, robust enough to provide accurate data, and capable of providing estimates of cost-effectiveness and overall cases/death averted to policy makers.

Table 1 outlines data gaps needed to guide TCV policy and use, outlining the WHO's perspective. "Tybar-TCV is the first TCV to be submitted for prequalification by WHO," have higher anti-Vi IgG responses than Vi-polysaccharide, and immunogenic for children < 2 years.

Trial design currently needs to focus on effectiveness studies to inform policy makers of the protection and factors for implementation consideration. Consensus on a cluster randomized trial (CRT) to evaluate total and overall effects of TCV for routine immunization, alongside a nested immunogenicity study for <2 age group.

5. Summary of workshop "global burden of diarrheal diseases among children in developing countries: Incidence, etiology, and insights from new molecular diagnostic techniques"
   Kotloff KL, Platts-Mills JA, Nasrin D, Roose A, Blackwelder WC, Levine MM.
   Vaccine. 2017 Jul 29. [Epub ahead of print]
   Pubmed ID: 28765005

ABSTRACT
The Global Enteric Multicenter Study (GEMS) demonstrated that *Shigella* and enterotoxigenic *Escherichia coli* (ETEC) producing heat stable toxin (ST) (either alone or in combination with heat labile toxin) are among the most important pathogens associated with moderate-to-severe diarrhea (MSD) in children younger than 5 years of age living in developing countries. To inform the design of vaccines and other interventions, we reviewed published data and new results from GEMS characterizing the burden of *Shigella* and ST-ETEC infections. Clinical parameters were assessed to examine the value of various case definitions as indicators of MSD associated with *Shigella* and ST-ETEC for use in clinical trials. We discussed advantages and disadvantages of culture-based and culture-independent molecular diagnostics for detecting clinically and epidemiologically relevant disease. *Shigella* serotyping data from GEMS were examined to identify desirable components of *Shigella* and ETEC vaccines likely to confer broad protection. These findings can inform the development and implementation of vaccines to prevent these important infections among infants and children in developing countries.

WEB: 10.1016/j.vaccine.2017.07.036
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START SCIENTIFIC COMMENT: There are limited effective therapies for *Shigella* and ST-ETEC infections and no recommended antibiotics for children with associated watery diarrhea. Table 1 provides Shigella and ST-ETEC disease burden for 7 study sites, stratified by age. The prevalence of Shigella among age-stratified episodes of watery diarrhea and dysentery is presented in Table 3, and an area of further research to understand the expected impact of the Shigella vaccine.

A modified Vesikari scale was used to assess the GEMS clinical data; however, this scale is typically used for enteric infections that cause vomiting and dehydration and authors concluded it was not optimal for assessing vaccine infection prevention. Tables 5 and 6 present the performance of the parameters, which lowered the likelihood of ST-ETEC and Shigella children to achieve scores in the moderate to severe range as compared to rotavirus.

A re-analysis of GEMS molecular diagnostics identified useful diagnostic techniques for identification of Shigella and ST-ETEC. Quantitative PCR (qPCR) may provide a better diagnostic for Shigella and ST-ETEC and improve comparability of clinical trials across different settings. The attributable incidence nearly doubled for Shigella and increased by 50% for ST-ETEC.

ETEC vaccine designs are focused on neutralizing anti-ST and anti- heat liable toxin (LT) antibodies, targeting common surface proteins across ETECs, and simulating natural protection via “secretory IgA anti-colonization factor intestinal antibodies.“ Shigella has 51 separate serotypes and sub-types. There are 4 GEMS case isolates which account for 75% of the isolates and an opportunity for an economical and feasible vaccine. Similar GEMS analyses to identify colonization factor antigens are underway for ETEC associated with MSD, with the goal of developing a combined multivalent Shigella-ETEC vaccine.

6. Feasibility of using global system for mobile communication (GSM)-based tracking for vaccinators to improve oral poliomyelitis vaccine campaign coverage in rural Pakistan
   Chandir S, Dharma VK, Siddiqi DA, Khan AJ
   Vaccine. 2017 Aug 09. [Epub ahead of print]
   Pubmed ID: 28802756

ABSTRACT
Despite multiple rounds of immunization campaigns, it has not been possible to achieve optimum immunization coverage for poliovirus in Pakistan. Supplementary activities to improve coverage of immunization, such as door-to-door campaigns are constrained by several factors including inaccurate hand-drawn maps and a lack of means to objectively monitor field teams in real time, resulting in suboptimal vaccine coverage during campaigns. Global System for Mobile Communications (GSM) - based tracking of mobile subscriber identity modules (SIMs) of vaccinators provides a low-cost solution to identify missed areas and ensure effective immunization coverage. We conducted a pilot study to investigate the feasibility of using GSM technology to track vaccinators through observing indicators including acceptability, ease of implementation, costs and scalability as well as the likelihood of ownership by District Health Officials. The real-time location of the field teams was displayed on a GSM tracking web dashboard accessible by supervisors and managers for effective monitoring of workforce attendance including 'time in-time out', and discerning if all target areas - specifically remote and high-risk locations - had been reached. Direct access to this information by supervisors eliminated the possibility of data fudging and inaccurate reporting by workers regarding their mobility. The tracking cost per vaccinator was USD 0.26/month. Our study shows that GSM-based tracking is potentially a cost-efficient approach, results in better monitoring and accountability, is scalable and provides the potential for improved geographic coverage of health services.

WEB: 10.1016/j.vaccine.2017.07.026
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START Scientific Comment: This pilot study was awarded the Innovation for Uptake, Scale, and Equity in Immunisation (INFUSE) award by Gavi. The initial performance deficiencies among 20 individuals tracked included: 3 started work 2-3 hours late, 1 was out of town and visited the area for an afternoon for < 30 minutes, and 8 failed to visit their assigned area during the supplemental immunization activity. The District Health Officer shared this information during the polio evening meeting and attendance approved in the 2nd and 3rd days of the campaigns. The addition of GSM tracking for SIA would be <2% increase in Pakistan's annual district cost and potentially decrease with wider use across the country (Table 1). A limitation of this study is the potential lack of generalizability due to the convenience-sampled individuals who participated. Also, the results may not transfer to dense urban settings due to informal squatter settlements that may not be detectable on Google Maps and the inability to identify households with GSM tracking precision varying from 50 to 100m. The INFUSE team plans a scale-up and coordination with other mobile network operators (MNO) to develop a universal platform that can track vaccinators across various MNO subscriptions.

7. Who pays for cooperation in global health? A comparative analysis of WHO, the World Bank, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria, and Gavi, the Vaccine Alliance
   Clinton C, Sridhar D
   Lancet. 2017 Jul 15. 390(10091):324-332. [Epub ahead of print]
   Pubmed ID: 28139255

ABSTRACT
In this report we assess who pays for cooperation in global health through an analysis of the financial flows of WHO, the World Bank, the Global Fund to Fight HIV/AIDS, TB and Malaria, and Gavi, the Vaccine Alliance. The past few decades have seen the consolidation of influence in the disproportionate roles the USA, UK, and the Bill & Melinda Gates Foundation have had in financing three of these four institutions. Current financing flows in all four case study institutions allow donors to finance and deliver assistance in ways that they can more closely control and monitor at every stage. We highlight three major trends in global health governance more broadly that relate to this development: towards more discretionary funding and away from core or longer-term funding; towards defined multi-stakeholder governance and away from traditional government-centered representation and decision-making; and towards narrower mandates or problem-focused vertical initiatives and away from broader systemic goals.

WEB: 10.1016/S0140-6736(16)32402-3
IMPACT FACTOR: 8.04
CITED HALF-LIFE: 9.20

START Scientific Comment: Funding for "new" partnerships, such as the Global Fund and Gavi, and increased voluntary contributions to "old institutions", the WHO and the World Bank, demonstrate donor's motivations to provide voluntary contributions that can be earmarked and closely monitored. The WHO is made up of two pools of funding: the contributions from member states (based on the country's gross national product) and voluntary contributions from member states and other organizations/individuals. There is no enforcement of member state payment, which was at 86% in 2014. The proportion of the WHO's overall budget is nearly 80% voluntary contributions. This increasing financial trend reflects alignment of donor influence on WHO focus. In 2012, the top three contributors to the WHO were The Gates Foundation, the USA, and the UK (Figure 2). The primary donors for the World Bank's International Development Association (IDA) are similar to those at the WHO (Figure 3). The Global Fund has "focused mandates" and relies entirely on voluntary contributions at specific intervals. Figure 4 shows USA, UK, and Japan as the top three Global Fund donors from 2000- 2013. Gavi, despite having similar sources of funding, was initially funded by ad-hoc donor contributions and innovative mechanisms, prior to its first pledging conference in 2011. The Gates Foundation, the UK and the USA were the three top contributors from 2000 to 2013. Unlike the other organizations/partnerships, the influence of Gavi's highest donors is not clear or publicized.

Donors are more likely to achieve goals via new partnerships due to structurally aligned objectives with global agencies, utilizing incentives, reduced knowledge gap, and close agency monitoring. There are risks of shifting financial flows away from "old" institutions, such as: priorities of powerful donor countries are imposed on poorer countries; inefficiency due to focus on short-term priorities; and, poorly integrated global health knowledge and information. WHO governance: focus on unique global health areas; define membership; improve transparency; and, provide an opportunity for input from non-state actors.

8. Digital immunization registry: evidence for the impact of mHealth on enhancing the immunization system and improving immunization coverage for children under one year old in Vietnam
   Nguyen NT, Vu HM, Dao SD, Tran HT, Nguyen TXC
   mHealth. 2017 Jul 19. 3(26):[Epub ahead of print]
   Pubmed ID: 28828373

ABSTRACT
BACKGROUND: The Vietnam National Expanded Program on Immunization (NEPI) has been successfully implementing a nationwide immunization system since 1985. From the start, the program has increased the immunization coverage rate; however, data on immunization coverage in Vietnam are gathered and aggregated from commune health centers in routine, paper-based reports, which have shortcomings. Also, calculations of coverage are inconsistent at subnational levels, which lead to uncertainty about the size of the target population used as the denominator in coverage calculations. The growth of mobile networks in Vietnam provides an opportunity to apply mHealth to improve the immunization program. In 2012, PATH and the Vietnam NEPI developed and piloted a digital immunization registry, ImmReg, to overcome the challenges of the paper system. A final evaluation was conducted in 2015 to assess the impact of ImmReg, including its use of SMS reminders, on improving the immunization program.
METHODS: The study population comprised all children born in Ben Tre province in September and October of 2013, 2014, and 2015, representing pre-intervention, post-intervention, and one year post-intervention, respectively. Data exported from ImmReg were used to compare the immunization rate, dropout rate, and timeliness of vaccination before and after the intervention. Additionally, a rapid survey was conducted to understand the willingness of parents with children due for vaccination to pay for SMS reminder messages on the immunization schedule.
RESULTS: Timely administration of oral polio vaccine, Quinvaxem, and measles 1 vaccine significantly increased over time from baseline to post-intervention to one year post-intervention. In particular, the timeliness of vaccination with the third dose of Quinvaxem increased from 53.6% to 65.8% to 77.2%. For measles 1 vaccine, the rate increased from 70.4% to 76.2% to 92.3%. In addition, the dropout rate from Quinvaxem 1 to Quinvaxem 3 declined from 4.2% in 2013 to 0% in 2015, and the dropout rate from Bacillus Calmette-Guerin (BCG) to measles 1 fell from 12.8% in 2013 to 0% in 2015. Full immunization coverage of children under one year old increased significantly from 75.4% in 2013 to 81.7% in 2014 to 99.2% in 2015. Also, survey results indicated that 93.3% of interviewees were willing to pay for SMS reminders for immunization.
CONCLUSIONS: A digital immunization registry that includes SMS reminders can improve immunization coverage and timeliness of vaccination, thereby strengthening the quality and effectiveness of immunization programs. Integrating this system into the national health information system and leveraging it for other health programs, such as maternal and child health and nutrition as well as infectious disease control, can bring more benefits to the health care system in Vietnam.

WEB: 10.21037/mhealth.2017.06.03
IMPACT FACTOR: N/A
CITED HALF-LIFE: N/A

START Scientific Comment: Since at least 2009, there was an increasing trend of full vaccine coverage in Ben Tre province; therefore, in the absence of the intervention, vaccine coverage would likely continue increasing. The selection of the survey sample for willingness to pay was not explained and the 120 parents who participated may not be generalizable.

9. Impact of rotavirus vaccines in low and middle-income countries
   Chella Sindhu KN, Babji S, Ganesan SK
   Curr Opin Infect Dis. 2017 Jul 15. [Epub ahead of print]
   Pubmed ID: 28719399

ABSTRACT
PURPOSE OF REVIEW: Rotavirus vaccines are playing a pivotal role in improving lives of infants and young children in low and middle-income countries (LMICs). Many of these countries have adopted the vaccine into their routine immunization, whereas others are considering introduction. This article provides an update on the impact of rotavirus vaccines in LMICs on morbidity and mortality in children aged less than 5 years, and their cost-effectiveness.
RECENT FINDINGS: The WHO, in 2013, updated its recommendation to prioritize introduction of rotavirus vaccines in the routine immunization schedule, without age restrictions. Despite the decreased efficacy of the vaccines in LMICs, data from Sub-Saharan Africa have demonstrated a decrease in rotavirus-related morbidity, with some sites reporting an indirect protective effect on children age ineligible to receive the vaccine. Even with improvements in sanitation, nutritional status in children, and other health-related indices in LMICs, the use of rotavirus vaccines will play an important role in preventing rotavirus-related gastroenteritis. Economic models predict a reduction in economic burden because of rotavirus-related health costs, making vaccine introduction cost-effective in resource-constrained settings.
SUMMARY: Increasing evidence from impact studies shows the significant impact of rotavirus vaccination on hospitalizations and economic burden because of rotavirus gastroenteritis in LMICs. Universal rotavirus vaccination is recommended, and introductions should be monitored by robust surveillance systems to measure effectiveness and impact.

WEB: 10.1097/QCO.0000000000000397
IMPACT FACTOR: 3.18
CITED HALF-LIFE: 5.40

START Scientific Comment: There is an opportunity to decrease much of the rotavirus disease burden, which persist among infants, through the recommended WHO vaccination strategy. Table 1 features a compilation of studies from LMICs (by region) reporting rotavirus vaccine reduction/projected reduction of annual deaths or gastroenteritis hospitalizations among children less than 5. Table 2 presents cost-effectiveness analysis of rotavirus vaccines on gastroenteritis in LMICs by region. Economic models are useful to project anticipated cost-savings; however, models are not applicable across regions. There were 99 countries as of April 2017 that did not intend to introduce the rotavirus vaccine due to "competing priorities, lack of local epidemiological data, possible safety issues," and lower vaccine efficacy in LMIC settings. Figure 1 maps the location of rotavirus impact assessment studies and vaccine availability in LMICs and further highlights the need for additional research.

10. Using Cluster Analysis to Group Countries for Cost-Effectiveness Analysis: An Application to Sub-Saharan Africa
    Russell LB, Bhanot G, Kim SY, Sinha A
    Med Decis Making. 2017 Aug 01. [Epub ahead of print]
    Pubmed ID: 28823186

ABSTRACT
OBJECTIVE: To explore the use of cluster analysis to define groups of similar countries for the purpose of evaluating the cost-effectiveness of a public health intervention-maternal immunization-within the constraints of a project budget originally meant for an overall regional analysis.
METHODS: We used the most common cluster analysis algorithm, K-means, and the most common measure of distance, Euclidean distance, to group 37 low-income, sub-Saharan African countries on the basis of 24 measures of economic development, general health resources, and past success in public health programs. The groups were tested for robustness and reviewed by regional disease experts.
RESULTS: We explored 2-, 3- and 4-group clustering. Public health performance was consistently important in determining the groups. For the 2-group clustering, for example, infant mortality in Group 1 was 81 per 1,000 live births compared with 51 per 1,000 in Group 2, and 67% of children in Group 1 received DPT immunization compared with 87% in Group 2. The experts preferred four groups to fewer, on the ground that national decision makers would more readily recognize their country among four groups.
CONCLUSIONS: Clusters defined by K-means clustering made sense to subject experts and allowed a more detailed evaluation of the cost-effectiveness of maternal immunization within the constraint of the project budget. The method may be useful for other evaluations that, without having the resources to conduct separate analyses for each unit, seek to inform decision makers in numerous countries or subdivisions within countries, such as states or counties.

WEB: 10.1177/0272989X17724773
IMPACT FACTOR: 1.53
CITED HALF-LIFE: 8.20

START Scientific Comment: Authors utilized an adapted model previously used for cost-effectiveness analysis in South Africa and removed "risk factor-based intrapartum prophylaxis during delivery" as it would not be feasible in low income countries. Antenatal care and public health measure variables primarily defined the clusters, with GDP per capita, urbanization, and general health resources contributing least to the differences between the two groups (Table 1). For the 3- and 4- group clusters, "general health resources and economic development" played a bigger role in groupings and Nigeria was in its own group (Table 2). The authors conducted robustness checks of the selected variables and identified data imputation as influential to the cluster assignments. This methodological approach improved clustering of countries by utilizing public health records, which may better inform decision makers. A limitation of the analysis was due to the absence of country-level analysis, cost-effectiveness results with variations in groupings cannot be compared. Additionally, the authors suggest weighting of features/variables that may improve the clusters.

APPENDIX

(((((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]) ("2017/7/15"[PDAT] : "2017/8/14"[PDAT]))

* August 23, 2017, this search of English language articles published between July 15, 2017 and August 14, 2017 and indexed by the US National Library of Medicine resulted in 223 unique manuscripts.