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Department of Global Health | University of Washington

VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

JANUARY 15, 2016

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1. Improving immunisation coverage in rural India: clustered randomised controlled evaluation of immunisation campaigns with and without incentives.

Banerjee A.V., Duflo E; Glennerster R.; Kothari D.

BMJ. 2016 Nov 29;355:i6423.

PMID: 27899349

ABSTRACT

Objective: To assess the efficacy of modest non-financial incentives on immunisation rates in children aged 1-3 and to compare it with the effect of only improving the reliability of the supply of services. Design Clustered randomised controlled study.

Setting: Rural Rajasthan, India. **Participants**: 1640 children aged 1-3 at end point. Interventions 134 villages were randomised to one of three groups: a once monthly reliable immunisation camp (intervention A; 379 children from 30 villages); a once monthly reliable immunisation camp with small incentives (raw lentils and metal plates for completed immunisation; intervention B; 382 children from 30 villages), or control (no intervention, 860 children in 74 villages). Surveys were undertaken in randomly selected households at baseline and about 18 months after the interventions started (end point).**Main outcome measures**: Proportion of children aged 1-3 at the end point who were partially or fully immunised.

Results: Among children aged 1-3 in the end point survey, rates of full immunisation were 39% (148/382, 95% confidence interval 30% to 47%) for intervention B villages (reliable immunisation with incentives), 18% (68/379, 11% to 23%) for intervention A villages (reliable immunisation without incentives), and 6% (50/860, 3% to 9%) for control villages. The relative risk of complete immunisation for intervention B versus control was 6.7 (4.5 to 8.8) and for intervention B versus intervention A was 2.2 (1.5 to 2.8). Children in areas neighbouring intervention B villages were also more likely to be fully immunised than those from areas neighbouring intervention A villages (1.9, 1.1 to 2.8). The average cost per immunisation was $28 (1102 rupees, about £16 or €19) in intervention A and $56 (2202 rupees) in intervention B.

Conclusions: Improving reliability of services improves immunisation rates, but the effect remains modest. Small incentives have large positive impacts on the uptake of immunisation services in resource poor areas and are more cost effective than purely improving supply.

WEB: http://www.dx.doi.org/10.1136/bmj.i6423

IMPACT FACTOR: 3.47

CITED HALF-LIFE: 9.40

START SCIENTIFIC COMMENT: Unreliable access to immunization is a barrier to achieving complete immunization in this region. In Group A villages, investigators introduced visits by monthly, routinely-scheduled, mobile immunization teams ("immunization camps"), conducted by a nurse and assistant. Camps were publicized widely, and a social worker in each village identified children/families that were eligible, educated parents about the benefits of immunization and the availability of the service. Group B villages had a small incentive added to the camp intervention.

Comparing incentive arm (B) to the non-incentive but active intervention arm (A), the largest differences in the proportion vaccinated were for the 3rd and 4th immunization, with a slightly smaller difference observed in the 5th (final) immunization. This is unexpected, since an additional incentive was provided for completing the final immunization, and authors hypothesize the influence of the incentive may be dichotomous, versus incremental. They propose that additional incentives on top of the original incentive may have little or no additional influence. Nevertheless, a substantially larger proportion received the 5th immunization in group B than A. Dose-specific differences aren't quantitatively reported, but Figure 3 indicates immunization 0 (birth dose), 1 and 2 were similar between groups (A) and (B). Notably, adding incentives to the camps reduced the cost per child immunized, because the majority of the costs result from the fixed daily cost of conducting the camps, and camps with incentives tended to serve more children per day, resulting in a lower per-child cost with incentives. As per the erratum (http://www.bmj.com/content/bmj/355/bmj.i6423.full.pdf), the intervention costs in the abstract are reversed; the average cost per child immunized for intervention A was $56 and for B was $28.

2. Map of different vaccine supply chain efficiency measures.
Haidari LA, Brown ST, Wedlock P, Lee BY.
Vaccine. 2017 Jan 3;35(1):199-200.
PMID: 27884477

ABSRACT
Although a number of seemingly disparate measures are being used to evaluate different aspects of vaccine supply chain operations, it may be unclear how they fit together and may overlap. Through our work on vaccine supply chains over the past eight years, our HERMES Team (1) assembled a list of measures that have been used (defined in Appendix A) [1,2]; (2) determined how these measures relate to one another; (3) grouped the measures into those that represent the supply side, demand side, and four domains that incorporate both (agility, costs, resource utilization, and demand fulfillment); and (4) added arrows to represent the relationships between the measures, with each connection labeled as positive (i.e. as one component increases, the other component also increases) or negative (i.e. as one component increases, the other decreases). Fig. 1 shows how some measures are actually calculated or derived from other measures (e.g. total cost per dose administered incorporates logistics costs, vaccine procurement costs, and doses administered). With this map, decision makers such as immunization program managers, ministries of health, and non-governmental organizations can determine whether they are collecting duplicative information, missing measuring certain domains, or could use alternative measures to capture the same or more information.

WEB: http://www.dx.doi.org/10.1016/j.vaccine.2016.11.025

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

START SCIENTIFIC COMMENT: Figure 1 in this article provides a conceptual framework of the measures and how they relate to each other, grouped by domain: supply, demand, agility, costs, resource utilization, and demand fulfillment. The map provides a framework to help decision-makers strategically decide which measures they may want to collect. The definition of each measure considered (Appendix A) is included in the Digest as Appendix 1.

3. Evaluation of a community-based intervention to improve routine childhood vaccination uptake among migrants in urban slums of Ludhiana, India.
Sengupta P, Benjamin AI, Myles PR, Babu BV.
J Public Health (Oxf). 2016 Dec 2. [Epub ahead of print]
PMID**:** 27915261

ABSTRACT

BACHGROUND: Evidence on the effectiveness of community-based interventions in improving vaccination uptake in migrant populations is limited. This study aims to evaluate the effectiveness of a community-based intervention to improve access to and uptake of childhood vaccinations among urban slum-dwelling migrant communities in Ludhiana, India.
METHODS: A mixed-methods evaluation was conducted involving a post-intervention comparison of vaccination uptake in six randomly selected intervention and control slum communities. Multilevel logistic regression to account for clustering of effects was used to investigate the impact of the intervention on vaccination uptake. Thematic analysis was used to analyse qualitative data.
RESULTS: Overall, vaccination uptake was significantly higher in the intervention clusters and the likelihood of full immunization by the age of 1 year was more than twice that in the control clusters [OR: 2.27 (95%CI: 1.12-4.60); P = 0.023]. Qualitative findings showed that stakeholders felt ownership of the intervention and that it was effective in increasing accessibility to and uptake of vaccinations. However, they emphasized the importance of continued government support for the intervention.
CONCLUSIONS: Community-based interventions can significantly increase vaccination coverage in deprived populations with previously low uptake of childhood immunization but such initiatives need to be delivered in partnership with the government.

WEB: http://dx.doi.org/10.1093/pubmed/fdw131

IMPACT FACTOR: 1.27

CITED HALF-LIFE: 5.10

START SCIENTIFIC COMMENT: The intervention aimed to increase access to and utilization of immunization services, by using local stakeholders to conduct outreach activities. Specific activities included government-funded outreach vaccination programs held at local community spaces, and the nomination of a "community guardian" to provide consent for vaccination and supervision after vaccination for children whose parent was deceased or unavailable.

This quasi-experimental study determined intervention and control communities using non-random allocation, and it can't be ruled out that intervention and control communities may have differed at baseline in factors other than the receipt of intervention, that would also influence their vaccination coverage in the post-intervention period. Authors described in the methods that the primary endpoint would be the change since baseline in vaccination coverage, but primary results in Tables 1 and 2 report estimates of post-intervention coverage, rather than a change since baseline, although multi-level logistic regression models do account for baseline levels.

The qualitative component of the study was conducted among community leaders, community members, auxiliary health workers, medical officers, and alternative medical providers. Authors report universal acceptance of the intervention among the different stakeholder groups interviewed, and indicate respondents believed the intervention increased awareness of childhood vaccination and the benefits of childhood vaccination. Authors note community members indicated a feeling of ownership of the intervention, and note the importance of the specific roles played by a range of stakeholders, and the contributions of different stakeholder types to carrying out the intervention.

4. Predicting the relative impacts of maternal and neonatal respiratory syncytial virus (RSV) vaccine target product profiles: A consensus modelling approach.
Pan-Ngum W, Kinyanjui T, Kiti M, Taylor S, Toussaint JF, Saralamba S, et al.
Vaccine. 2017 Jan 5;35(2):403-409.
PMID: 27914740

ABSTRACT

BACKGROUND: Respiratory syncytial virus (RSV) is the major viral cause of infant and childhood lower respiratory tract disease worldwide. Defining the optimal target product profile (TPP) is complicated due to a wide range of possible vaccine properties, modalities and an incomplete understanding of the mechanism of natural immunity. We report consensus population level impact projections based on 2 mathematical models applied to a low income setting.
METHOD: Two structurally distinct age-specific deterministic compartmental models reflecting uncertainty associated with the natural history of infection and the mechanism by which immunity is acquired and lost were constructed. A wide range of vaccine TPPs were explored including dosing regime and uptake, and effects in the vaccinated individual on infectiousness, susceptibility, duration of protection, disease severity and interaction with maternal antibodies and natural induced immunity. These were combined with a range of vaccine implementation strategies, targeting the highest priority age group and calibrated using hospitalization data from Kilifi County Hospital, Kenya.
FINDINGS: Both models were able to reproduce the data. The impact predicted by the two models was qualitatively similar across the range of TPPs, although one model consistently predicted higher impact than the other. For a proposed realistic range of scenarios of TPP combinations, the models predicted up to 70% reduction in hospitalizations in children under five years old. Vaccine designs which reduced the duration and infectiousness of infection were predicted to have higher impacts. Models were sensitive to coverage and rate of loss of vaccine protection but not to the interaction between vaccine and maternal/naturally acquired immunity.
CONCLUSION: The results suggest that vaccine properties leading to reduced virus circulation by lessening the duration and infectiousness of infection upon challenge are of major importance in population RSV disease control. These features should be a focus for vaccine development.

WEB: http://dx.doi.org/10.1016/j.vaccine.2016.10.073

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

START SCIENTIFIC COMMENT: The primary outcome was: *percent reduction in <1 and <5 year old hospital admissions after 10 years of the vaccination program, compared to the pre-vaccination average effects*. The components of the TPP that were varied included:

- *Vaccine effects on individual*: low, medium or high risk of primary infection reduction; duration of infectivity reduction; infectiousness reduction; risk of URTI reduction; risk of LRTI reduction; risk of severe LRTI reduction
- *Dosing regimen*: 2 doses at 0 and 2 months of age; 2 doses at 2 and 4 months of age; 3 doses at 0, 1 and 2 months of age; 3 doses at 2, 4 and 6 months of age
- *Waning effect of vaccine*: 1 or 2 years
- C*overage and compliance level combinations*
- *Interaction with maternal antibodies*: no interaction; “bounce-up”; “drop-back”. I*nteraction with natural immunity*: no effect; multiplicative; “top-up”
- M*aternal vaccination*: range of coverage levels with infant protection lasting 3 or 6 months

Both models demonstrated reasonable fit when calibrated with the Kenya hospitalization data. Results from the models were fairly similar, but the estimated magnitude of the impact was larger in the BWI model than the SAI model, which authors attribute to the higher force of infection used in fitting the SAI model. The impacts estimated by the SAI model were more stable over time.

5. Parental support for human papilloma virus vaccination by adolescents in Ibadan North Local Government Area, Ibadan, Nigeria.
Dairo MD, Adeleke MO, Salawu AT, Adewole AD.
Int J Adolesc Med Health. 2016 Dec 3. [Epub ahead of print]
PMID: 27914213

ABSTRACT

BACKGROUND: Despite changing sexual norms and mores generally perceived to be permissive of sexual expression, parents continue to serve as gateways to uptake of reproductive health services and commodities in our cultural settings. However, their support for adolescent uptake of human papilloma virus (HPV) vaccine are not well explored and documented. This study aims to assess parental knowledge and awareness of HPV infection and cervical cancer and their support for HPV vaccination for their adolescent children.
METHODS: In a descriptive cross sectional study 612 parents from Ibadan North Local Government Area were interviewed using a pre-tested semi structured interviewer administered questionnaire to assess the awareness of HPV infection and cervical cancer as well as parental support for the vaccine.
RESULTS: Only a few of the respondents were aware of HPV infection (10.5%) and the HPV vaccine (6.5%), respectively. About 64.3% of those that were aware of HPV knew it can be transmitted through sexual intercourse. However, 78.4% supported the administration of the vaccine to their adolescent daughters. Reported reasons for not supporting HPV vaccination were high cost of the vaccine (32.2%) and lack of awareness of the vaccine (49.2%). Earning a monthly income above the minimum wage of 18,000 Naira increases the likelihood of parental support for HPV vaccination uptake for adolescents ($p<0.001$).
CONCLUSION: Ignorance and poverty remain as barriers to widespread coverage of the vaccine among adolescents. Health education and promotion on HPV infection and the HPV vaccine to the general public and subsidization of the vaccine to promote its uptake is advocated.

WEB: http://dx.doi.org/10.1515/ijamh-2016-0034

IMPACT FACTOR: 0.75

CITED HALF-LIFE: 0.00

START SCIENTIFIC COMMENT: Although a number of sociodemographic factors were associated with parental support of the vaccine, few are modifiable, and thus may be informative primarily for identifying groups to target for awareness and education campaigns. The following factors were associated with adolescent vaccine acceptance: being a male parent; being in the highest income group (note: there is a typo in the results/discussion section for this result); Christian religion; Yoruba or Ibo ethnic group; occupation as a civil or public servant; and being part of a monogamous family.

The most frequently cited reasons by parents for not supporting adolescent vaccination were fear of infertility from vaccination, vaccination cost, fear of vaccine resulting in fibroids, concerns about adolescent understanding of the vaccine, concerns about discussing sexual behavior with adolescents, cultural beliefs (undefined), and lack of vaccine effectiveness.

6. Oral Cholera Vaccination Delivery Cost in Low- and Middle-Income Countries: An Analysis Based on Systematic Review.

Mogasale V, Ramani E, Wee H, Kim JH.

PLoS Negl Trop Dis. 2016 Dec 8;10(12):e0005124.
PMID: 27930668

ABSTRACT

BACKGROUND: Use of the oral cholera vaccine (OCV) is a vital short-term strategy to control cholera in endemic areas with poor water and sanitation infrastructure. Identifying, estimating, and categorizing the delivery costs of OCV campaigns are useful in analyzing cost-effectiveness, understanding vaccine affordability, and in planning and decision making by program managers and policy makers.
OBJECTIVES: To review and re-estimate oral cholera vaccination program costs and propose a new standardized categorization that can help in collation, analysis, and comparison of delivery costs across countries.
DATA SOURCES: Peer reviewed publications listed in PubMed database, Google Scholar and World Health Organization (WHO) websites and unpublished data from organizations involved in oral cholera vaccination.
STUDY ELIGIBILITY CRITERIA: The publications and reports containing oral cholera vaccination delivery costs, conducted in low- and middle-income countries based on World Bank Classification. Limits are humans and publication date before December 31st, 2014. **PARTICIPANTS**: No participants are involved, only costs are collected. I**NTERVENTION**: Oral cholera vaccination and cost estimation. **STUDY APPRAISAL AND SYNTHESIS METHOD**: A systematic review was conducted using pre-defined inclusion and exclusion criteria. Cost items were categorized into four main cost groups: vaccination program preparation, vaccine administration, adverse events following immunization and vaccine procurement; the first three groups constituting the vaccine delivery costs. The costs were re-estimated in 2014 US dollars (US$) and in international dollar (I$).
RESULTS: Ten studies were identified and included in the analysis. The vaccine delivery costs ranged from US$0.36 to US$ 6.32 (in US$2014) which was equivalent to I$ 0.99 to I$ 16.81 (in I$2014). The vaccine procurement costs ranged from US$ 0.29 to US$ 29.70 (in US$2014), which was equivalent to I$ 0.72 to I$ 78.96 (in I$2014). The delivery costs in routine immunization systems were lowest from US$ 0.36 (in US$2014) equivalent to I$ 0.99 (in I$2014).
LIMITATIONS: The reported cost categories are not standardized at collection point and may lead to misclassification. Costs for some OCV campaigns are not available and analysis does not include direct and indirect costs to vaccine recipients.
CONCLUSIONS AND IMPLICATIONS OF KEY FINDINGS: Vaccine delivery cost estimation is needed for budgeting and economic analysis of vaccination programs. The cost categorization methodology presented in this study is helpful in collecting OCV delivery costs in a standardized manner, comparing delivery costs, planning vaccination campaigns and informing decision-making.

WEB: http://dx.doi.org/10.1371/journal.pntd.0005124

IMPACT FACTOR: 4.45

CITED HALF-LIFE: 3.20

START SCIENTIFIC COMMENT: Vaccine program preparation costs, vaccine administration costs, management of adverse events following immunization and vaccine procurement costs were estimated separately, in addition to total costs. Table 1 describes the costing categories and sub-categories and examples of items contributing to each cost category.

Figure 3 presents cost estimates from the three methods used for prediction, in 10 example countries in sub-Saharan Africa and South Asia, and depicts the sensitively of the estimates to the method used.

Costs estimated in international dollars tended to be higher and to vary more substantially than costs estimated in US dollars. Costs varied substantially across countries as well as by region within country, which authors believe could be attribute to differences in distribution and program activities, differences due to program scale, or explained by lack of standardization in the way costs are documented and reported in different settings.

7. Requirements for global elimination of hepatitis B: a modelling study.
Nayagam S, Thursz M, Sicuri E, Conteh L, Wiktor S, Low-Beer D, Hallett TB.
Lancet Infect Dis. 2016 Dec;16(12):1399-1408.
PMID: 27638356

ABSTRACT

BACKGROUND: Despite the existence of effective prevention and treatment interventions, hepatitis B virus (HBV) infection continues to cause nearly 1 million deaths each year. WHO aspires to global control and elimination of HBV infection. We aimed to evaluate the potential impact of public health interventions against HBV, propose targets for reducing incidence and mortality, and identify the key developments required to achieve them.
METHODS: We developed a simulation model of the global HBV epidemic, incorporating data on the natural history of HBV, prevalence, mortality, vaccine coverage, treatment dynamics, and demographics. We estimate the impact of current interventions and scaling up of existing interventions for prevention of infection and introducing wide-scale population screening and treatment interventions on the worldwide epidemic.
FINDINGS: Vaccination of infants and neonates is already driving a large decrease in new infections; vaccination has already prevented 210 million new chronic infections by 2015 and will have averted 1·1 million deaths by 2030. However, without scale-up of existing interventions, our model showed that there will be a cumulative 63 million new cases of chronic infection and 17 million HBV-related deaths between 2015 and 2030 because of ongoing transmission in some regions and poor access to treatment for people already infected. A target of a 90% reduction in new chronic infections and 65% reduction in mortality could be achieved by scaling up the coverage of infant vaccination (to 90% of infants), birth-dose vaccination (to 80% of neonates), use of peripartum antivirals (to 80% of hepatitis B e antigen-positive mothers), and population-wide testing and treatment (to 80% of eligible people). These interventions would avert 7·3 million deaths between 2015 and 2030, including 1·5 million cases of cancer deaths. An elimination threshold for incidence of new chronic infections would be reached by 2090 worldwide. The annual cost would peak at US$7·5 billion worldwide ($3·4 billion in low-income and lower-middle-income countries), but decrease rapidly and this would be accelerated if a cure is developed.
INTERPRETATION: Scale-up of vaccination coverage, innovations in scalable options for prevention of mother-to-child transmission, and ambitious population-wide testing and treatment are needed to eliminate HBV as a major public health threat. Achievement of these targets could make a major contribution to one of the Sustainable Development Goals of combating hepatitis.

WEB: http://dx.doi.org/10.1016/S1473-3099(16)30204-3

IMPACT FACTOR: 5.82

CITED HALF-LIFE: 4.70

START SCIENTIFIC COMMENT: Authors estimated the relative impact of a package of interventions that included vaccination, PMTCT, screening, and treatment, based on 5 different possible scenarios: a) infant vaccination; b) infant vaccination and birth dose vaccination; c) infant and birth dose vaccination plus prevention by peripartum antiretroviral therapy (PPT); d) infant and birth dose vaccination plus PPT, plus treatment for infection; e) infant and birth dose vaccination plus PPT, plus treatment for infection, plus cure for infection. These scenarios were compared with "status quo" and with a historical comparison of no intervention.

Figure 3 parts A and B summarize the global impact of each intervention approach against HBV on incidence of new chronic infections and on HBV-related deaths, respectively.

8. Current prospects and future challenges for nasal vaccine delivery.
Yusuf H, Kett V.
Hum Vaccin Immunother. 2016 Dec 9:1-12. [Epub ahead of print]
PMID: 27936348

ABSTRACT: Nasal delivery offers many benefits over traditional approaches to vaccine administration. These include ease of administration without needles that reduces issues associated with needlestick injuries and disposal. Additionally, this route offers easy access to a key part of the immune system that can stimulate other mucosal sites throughout the body. Increased acceptance of nasal vaccine products in both adults and children has led to a burgeoning pipeline of nasal delivery technology. Key challenges and opportunities for the future will include translating in vivo data to clinical outcomes. Particular focus should be brought to designing delivery strategies that take into account the broad range of diseases, populations and healthcare delivery settings that stand to benefit from this unique mucosal route.

WEB: http://dx.doi.org/10.1080/21645515.2016.1239668

IMPACT FACTOR: 3.77

CITED HALF-LIFE: 1.80

START SCIENTIFIC COMMENT: The current lack of available safety data from humans is noted as a major bottleneck to the development and utilization of intranasal vaccine delivery, which authors attribute to the substantial investment in time and money which clinical trials require. The article describes the structure and function of the mucosal immune system and the different routes of mucosal vaccination available and their function within the mucosal subcompartments, and explain how mucosal vaccine formulations induce innate and adaptive immune responses within these systems. Authors discuss the benefits of nasal vaccine delivery, summarize therapeutic and preventative nasal vaccines, summarize approaches to formulation, adjuvants, and list current nasal vaccines products which are available or under development.

Table 2 lists a selection of current technologies for intranasal delivery, along with a summary of the presentation, type of drug, current regulatory status and reference for additional information on the technology.

9. Reasons for defaulting from childhood immunization program: a qualitative study from Hadiya zone, Southern Ethiopia.
Zewdie A, Letebo M, Mekonnen T.
BMC Public Health. 2016 Dec 9;16(1):1240.
PMID: 27938363

ABSTRACT

BACKGROUND: Reduction of mortality and morbidity from vaccine-preventable diseases in developing countries involves successfully implementing strategies that ensure high coverage and minimize drop-outs and missed opportunities. Achieving maximum coverage, however, has been a challenge due to many reasons, including high rates of defaulters from the program. The objective of this study was to explore the reasons behind defaulting from the immunization program.
METHODS: A qualitative study was conducted in two districts of Hadiya zone, Southern Ethiopia between November 2014 and April 2015. A total of twenty-six in-depth interviews were held with mothers of defaulted children aged 6-11months old and key informants from the communities, health centers, and health offices. Observations and review of relevant documents were also conducted. Thematic analysis was used to analyze the data.
RESULTS: In this study, the main reason for defaulting from the immunization was inadequate counseling of mothers that led to a lack of information about vaccination schedules and service arrangements, including in unusual circumstances such as after missed appointment, loss of vaccination card and when the health workers failed to make home visits. Provider-client relationships are poor with mothers reporting fear of mistreatment and lack of cooperation from service providers. Contrary to what health workers and managers believe, mothers were knowledgeable about the benefits of vaccination. The high workload on mothers compounded by the lack of support from male partners was also found to contribute to the problem. Health system factors that contributed to the problem were poorly arranged and coordinated immunization services, vaccine and supplies stock outs, and lack of viable defaulter tracking systems in the health facilities.
CONCLUSIONS: The main reasons for defaulting from the immunization program are poor counseling of mothers, unsupportive provider-client relationships, poor immunization service arrangements, and lack of systems for tracking defaulters. Efforts to reduce defaulter rates from the immunization program need to focus on improving counseling of mothers and strengthening the health systems, especially with regards to service arrangements and tracking of defaulters.

WEB: http://dx.doi.org/10.1186/s12889-016-3904-1

IMPACT FACTOR: 2.26

CITED HALF-LIFE: 3.90

START SCIENTIFIC COMMENT: The study regions was served by both “static” health services conducted at facilities and health centers, and outreach services such as home visits and referral linkages. However, authors note that outreach services were inconsistently available or conducted and indicate that the structure and system of outreach services may be confusing to caregivers; they are confused by when/if services may be available and are unsure how to seek out care proactively if a home visit isn’t conducted when anticipated. Furthermore, mothers reported that community health workers were hostile and unsupportive, which authors believe may partially explain why caregivers struggled to complete vaccination when they encounter challenges. Caregivers were reticent to reach out to health workers with questions or for support when facing challenges, as they feared being treated poorly or chastised.

10. Healthcare providers' perspectives on the acceptability and uptake of HPV vaccines in Zimbabwe.
Crann SE, Barata PC, Mitchell R, Mawhinney L, Thistle P, Chirenje ZM, Stewart DE.
J Psychosom Obstet Gynaecol. 2016 Dec;37(4):147-155.
PMID: 27400371

ABSTRACT

BACKGROUND: Human papillomavirus (HPV) vaccines are a critical strategy in the prevention of cervical cancer, especially in countries like Zimbabwe where cervical cancer screening rates are low. In Zimbabwe, cervical cancer is the leading cause of cancer-related deaths in women but the HPV vaccine is not yet widely available. This study examined healthcare providers': (1) perceptions of current hospital practices and issues in cervical cancer prevention and treatment in Zimbabwe; (2) knowledge of HPV and HPV vaccines; and (3) perspectives on introducing HPV vaccination programs in Zimbabwe, including potential facilitators and barriers to successful implementation.
METHOD: In-depth semi-structured interviews were conducted at a rural hospital with 15 healthcare providers in Zimbabwe. Interviews included eight main questions and a number of additional probes that reflected the study's purpose. Data were analyzed using thematic analysis.
RESULTS: Participants reported that women are not consistently being screened for cervical cancer. There were generally low levels of knowledge about HPV and HPV vaccines, but participants asked many questions indicating a desire to learn more. Although they were highly supportive of implementing HPV vaccination programs in Zimbabwe, they also identified a number of likely psychosocial, cultural, and logistical barriers to successful implementation, including cost, vaccine schedule, and hospital infrastructure. However, participants also provided a number of culturally relevant solutions, including education and community engagement.
CONCLUSION: This study provides insight from healthcare providers about barriers to implementation and possible solutions that can be used by policy makers, practitioners, and other stakeholders to facilitate the successful implementation of forthcoming HPV immunization programs in Zimbabwe.

WEB: http://dx.doi.org/10.1080/0167482X.2016.1199544

IMPACT FACTOR: 1.17

CITED HALF-LIFE: 9.30

START SCIENTIFIC COMMENT: Study participants included 15 hospital healthcare providers (primarily nurses but also doctors, educators, counselors, a midwife and a clerk), from one regional hospital in Zimbabwe, selected via convenience sampling methods. The primary logistical barriers to vaccination programs were cost for the vaccine itself, transportation costs, lack of refrigeration and unreliable electricity (although most providers believed generators could provide sufficient back-up), and lack of transportation and transportation costs.

The vaccination schedule was not considered by providers to be a substantial barrier to uptake. Providers were concerned cultural norms that encourage abstinence until marriage could introduce challenges into vaccine acceptance, because individuals may believe encouraging the vaccine could implicitly encourage/condone early sexual initiation. Providers were also concerned that requiring parental permission for vaccination of young girls could introduce a barrier, but indicated that education to mothers and caregivers about the benefits of vaccination could potentially address this challenge.

APPENDIX: *Haidari et al., 2017*

Vaccine supply chain metric definitions

Metric*	Definition
SUPPLY	
Storage capacity	Net storage space available for holding vaccines in their required storage conditions at a location or set of locations
Transport capacity	Net vehicle space available for holding vaccines in their required storage conditions on a route or set of routes
% personnel time dedicated to logistics	Proportion of staff members' normal working hours spent on vaccine supply chain logistics
Number of personnel	Staff members working in vaccine supply chain logistics at a location or set of locations in the supply chain
Doses procured	Vaccine doses purchased and brought into a system in a given time period
DEMAND	
Birth rate	Live births per thousand persons in a population in a given year
Temporal variations in demand	Periodic changes in the rate at which people arrive at immunizing locations seeking vaccines
Immunization schedule	Number and timing of the full set of vaccine doses in a routine immunization program
Target coverage rate	Proportion of needed immunizations a system attempts to provide
Doses needed	Vaccine doses that need to be administered to a population in order to achieve a target coverage rate
Forecasted demand ratio	Ratio of actual consumption of one or more products in a given time period compared to the forecasted consumption
AGILITY	
Lead time	Average number of days from the time a shipment is ordered to the time it is received
Time to meet emergency orders	Average number of days from the time an emergency shipment is ordered to the time it is received
Time through system (or supply chain level)	Average number of days products spend in storage or transport
Annual number of inventory turns	Annual vials consumed or wasted ÷ Average number of vials in inventory
COSTS	
Vaccine procurement costs	Costs of purchasing all vaccines that entered a system, or part of a system, in a given time period
Transport costs	Costs of per diems as well as vehicle fuel, amortization, and maintenance in a given time period

Storage costs	Costs of storage equipment energy, amortization, and maintenance in a given time period
Building costs	Costs of building overhead and amortization in a given time period
Labor costs	Costs of personnel salaries in a given time period
Logistics costs	Operating costs of supply chain logistics in a given time period: storage (energy, amortization, maintenance), transport (fuel, amortization, maintenance, per diems), labor (personnel salaries), and building (overhead, amortization)
Total costs (logistics and vaccines)	Logistics costs + Vaccine procurement costs, in a given time period
RESOURCE UTILIZATION	
% cold chain equipment functional	Proportion of cold chain equipment (CCE) storage devices operable for storing vaccines over a given time period
Peak storage capacity utilization	Maximum percentage of available storage capacity occupied by products at any time
Peak transport capacity utilization	Maximum percentage of available transport capacity needed to complete any shipment
Trips/shipments completed	Number of trips taken for a route or set of routes in a given time period, as a percentage of trips prescribed by policy in a given time period
Extra trips over stated policy	Number of annual trips taken for a route or set of routes on an as-needed basis, above the stated policy, as a percentage of trips prescribed by policy in a given time period in a given time period
Personnel downtime	Percentage of normal working hours dedicated to supply chain logistics spent inactive
Personnel overtime	Hours spent by personnel working on vaccine supply chain logistics in addition to normal working hours
Closed vial wastage	Unused vials discarded due to expiry, heat exposure, or breakage during a given time period
Open vial wastage	Partially used vials expired as a percentage of all vials opened
DEMAND FULFILLMENT	
% shipments completed on time and in full	On-time shipments containing the full amount ordered as a percentage of all shipments
% locations stocked according to plan	Locations maintaining stock levels according to policy as a percentage of all locations
% locations experiencing stockout(s)	Locations experiencing at least one stockout of at least one product in a given time period as a percentage of all locations
% time out of stock	Number of days in a year when a location or set of locations had no inventory on hand for one or more products as a percentage of of total days measured

Liters delivered	Liters of vaccines in packaging delivered to a location or set of locations in a given time period
Doses administered	Vaccine doses administered to patients in a given time period
Vaccine availability	Successful immunizations administered to patients as a percentage of immunizations needed
MULTIPLE CATEGORIES	
Temperature alarm rate	Number of times the temperature inside cold storage or transport equipment exceeds or drops below a reference range in a given time period
Logistics cost per liter delivered	**Logistics costs ÷ Liters delivered**, in a given time period
Logistics cost per dose administered	**Logistics costs ÷ Doses administered**, in a given time period
Total cost per liter delivered	**Total costs (logistics & vaccine procurement) ÷ Liters delivered**, in a given time period
Total cost (logistics and vaccines) per dose administered	**Total costs (logistics & vaccine procurement) ÷ Doses administered**, in a given time period

* While many additional factors (e.g. policy, advocacy, and social norms) may influence the measures included in this analysis, the measures listed here are limited to currently used vaccine supply efficiency measures that can be explicitly defined. Changes in such upstream factors would be captured by many of the measures shown here.

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 ("2016/11/15"[PDAT] : "2016/12/14"[PDAT]))

* On December 29, 2016, this search of English language articles published between November 15, 2016 and December 14, 2016 and indexed by the US National Library of Medicine resulted in 238 unique manuscripts.