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STRATEGIC ANALYSIS, RESEARCH & TRAINING CENTER

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

MARCH 15, 2017

PRODUCED BY: LEVINE, GA; SLYKER, J.

TABLE OF CONTENTS

1. **Vial usage, device dead space, vaccine wastage, and dose accuracy of intradermal delivery devices for inactivated poliovirus vaccine (IPV).**

Jarrahian C, Rein-Weston A, Saxon G, Creelman B, Kachmarik G, Anand A, Zehrung D.

Vaccine. 2017 Feb 8. [Epub ahead of print]

PMID: 28189403

ABSTRACT

INTRODUCTION: Intradermal delivery of a fractional dose of inactivated poliovirus vaccine (IPV) offers potential benefits compared to intramuscular (IM) delivery, including possible cost reductions and easing of IPV supply shortages. Objectives of this study were to assess intradermal delivery devices for dead space, wastage generated by the filling process, dose accuracy, and total number of doses that can be delivered per vial.

METHODS: Devices tested included syringes with staked (fixed) needles (autodisable syringes and syringes used with intradermal adapters), a luer-slip needle and syringe, a mini-needle syringe, a hollow microneedle device, and disposable-syringe jet injectors with their associated filling adapters. Each device was used to withdraw 0.1-mL fractional doses from single-dose IM glass vials which were then ejected into a beaker. Both vial and device were weighed before and after filling and again after expulsion of liquid to record change in volume at each stage of the process. Data were used to calculate the number of doses that could potentially be obtained from multidose vials.

RESULTS: Results show wide variability in dead space, dose accuracy, overall wastage, and total number of doses that can be obtained per vial among intradermal delivery devices. Syringes with staked needles had relatively low dead space and low overall wastage, and could achieve a greater number of doses per vial compared to syringes with a detachable luer-slip needle. Of the disposable-syringe jet injectors tested, one was comparable to syringes with staked needles.

DISCUSSION: If intradermal delivery of IPV is introduced, selection of an intradermal delivery device can have a substantial impact on vaccine wasted during administration, and thus on the required quantity of vaccine that needs to be purchased. An ideal intradermal delivery device should be not only safe, reliable, accurate, and acceptable to users and vaccine recipients, but should also have low dead space, high dose accuracy, and low overall wastage to maximize the potential number of doses that can be withdrawn and delivered.

WEB: http://dx.doi.10.1016/j.vaccine.2016.11.098

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

START SCIENTIFIC COMMENT: Authors estimate that, accounting for variability in dead space, dose accuracy, and overall wastage, the number of ID doses available in a 5-dose IM vial could range from 15.7 to 27.1, and from anywhere between 29.8 and 50.8 ID doses in a 10-dose IM vial. Authors point out that variability in the amount of vaccine wasted in different delivery devices results in excess production and substantially inflates the cost of purchasing vaccines. Figure 1 shows photographs of a range of specific intradermal delivery devises evaluated by authors, each of which can be filled onsite and used for IPV delivery.

2. Investigating socio-economic inequity in access to and expenditures on routine immunization services in Anambra state.

Sibeudu FT, Uzochukwu BS, Onwujekwe OE.

BMC Res Notes. 2017 Feb 1;10(1):78.

PMID: 28143605

ABSTRACT

Introduction: Addressing existing inequities in the utilization of priority health services such as routine immunization is a current public health priority. Increasing access to routine immunization from the current low levels amongst all socio-economic status groups in Nigeria is challenging. However, little is known on the level of SES inequity in utilization of routine immunization services and such information which will inform the development of strategies for ensuring equitable provision of routine immunization services in the country. The study was a cross sectional household survey, which was undertaken in two randomly selected communities in Anambra State, southeast Nigeria. A pre-tested interviewer administered questionnaire was used to collect data on levels of access to RI by children under-2 years from randomly selected households. In each household, data was collected from the primary care givers or their representative (in their absence). The relationship between access to routine immunization and socio-economic status of households and other key variables was explored in data analysis.

RESULT: Households from high socio-economic status (well-off) groups utilized routine immunization services more than those that belong to low socio-economic status (poor) groups ($X^2 = 9.97$, $p < 0.002$). It was found that higher percentage of low socio-economic status households compared to the high socio-economic status households received routine immunization services at public health facilities. Households that belong to low socio-economic status groups had to travel longer distance to get to health facilities consequently incurring some transportation cost. The mean expenditures on service charge for routine immunization services (mostly informal payments) and transportation were US$1.84 and US$1.27 respectively. Logistic regression showed that access to routine immunization was positively related to socio-economic status and negatively related to distant of a household to a health facility.

CONCLUSION: Ability to pay affects access to services, even when such services are free at point of consumption with lower socio-economic status groups having less access to services and also having other constraints such as transportation. Hence, innovative provision methods that will bring routine immunization services closer to the people and eliminate all formal and informal user fees for routine immunization will help to increase and improve equitable coverage with routine immunization services.

WEB: http://dx.doi.10.1186/s13104-017-2407-1

IMPACT FACTOR: 1.60

CITED HALF-LIFE: 0.00

START SCIENTIFIC COMMENT: Although the proportion accessing private routine immunization services was higher in the highest wealth quintile, and the proportion accessing public services was higher in the lowest wealth quintile, all SES groups accessed services in both sectors. Approximately 27% of the lowest quintile SES group accessed private services and approximately 57% of the highest wealth quintile accessed public services. But again, although the proportion paying direct costs for immunization services was highest among the highest wealth quintile, even among the lowest quintile more than half of respondents paid at least some direct costs. Although the distance traveled to access services was slightly longer among the lower SES group, the expenditure on transportation was similar between the highest and lowest quintiles. This might be partially explained by a difference in the distribution of transportation modes used across SES groups. Table 5 reports logistic regression model coefficients for specific factors associated with access to routine immunization services; although these demonstrate which co-factors are statistically significant in multivariable models, coefficients are difficult to interpret. We therefore provide exponentiated coefficients below, which can be interpreted as odds ratios (ORs). Note that the "geographic location" variable was not defined, and thus what constituted each "geographic location" category compared is unclear. Also note that only "geographic location" and SES coefficients were statistically significant.

Geographic location: OR = 0.94;
Distance (km): OR = 0.99;
SES (one-unit higher quintile compared with one-unit lower quintile): OR = 1.05; **Formal education** (years): OR = 0.99.
**(ORs estimate difference in access (accessing versus not accessing services) associated with each explanatory factor, comparing a one-higher to a one-unit lower value of the factor, adjusting for all other factors listed.)*

3. **The polio endgame: rationale behind the change in immunisation.**

Garon J, Patel M.

Arch Dis Child. 2017 Jan 17. [Epub ahead of print]

PMID:28096107

ABSTRACT

The decades long effort to eradicate polio is nearing the final stages and oral polio vaccine (OPV) is much to thank for this success. As cases of wild poliovirus continue to dwindle, cases of paralysis associated with OPV itself have become a concern. As type-2 poliovirus (one of three) has been certified eradicated and a large proportion of OPV-related paralysis is caused by the type-2 component of OPV, the World Health Assembly endorsed the phased withdrawal of OPV and the introduction of inactivated polio vaccine (IPV) into routine immunisation schedules as a crucial step in the polio endgame plan. The rapid pace of IPV scale-up and uptake required adequate supply, planning, advocacy, training and operational readiness. Similarly, the synchronised switch from trivalent OPV (all three types) to bivalent OPV (types 1 and 3) involved an unprecedented level of global coordination and country commitment. The important shift in vaccination policy seen through global IPV introduction and OPV withdrawal represents an historical milestone reached in the polio eradication effort.

WEB: http://dx.doi.org/10.1136/archdischild-2016-311171

IMPACT FACTOR: 0.19

CITED HALF-LIFE: 10.00

START SCIENTIFIC COMMENT: Authors conclude that important relevant questions currently for IPV strategy are the length of time that will be required for IPV administration following eradication certification, and the ideal dosing strategy in low-resource settings. Authors recommend that following eradication certification, “personnel, infrastructure, resources and processes” be leveraged to address other global health priorities.
Figure 4 is a map depicting endemic countries and case counts in 1988 and 2016.

4. **Modeling the Potential for Vaccination to Diminish the Burden of Invasive Non-typhoidal Salmonella Disease in Young Children in Mali, West Africa.**

Bornstein K, Hungerford L, Hartley D, Sorkin JD, Tapia MD, et al.

PLoS Negl Trop Dis. 2017 Feb 9;11(2):e0005283.

PMID:28182657

ABSTRACT

BACKGROUND: In sub-Saharan Africa, systematic surveillance of young children with suspected invasive bacterial disease (e.g., septicemia, meningitis) has revealed non-typhoidal Salmonella (NTS) to be a major pathogen exhibiting high case fatality (~20%). Where infant vaccination against Haemophilus influenzae type b (Hib) and Streptococcus pneumoniae has been introduced to prevent invasive disease caused by these pathogens, as in Bamako, Mali, their burden has decreased markedly. In parallel, NTS has become the predominant invasive bacterial pathogen in children aged <5 years. While NTS is believed to be acquired orally via contaminated food/water, epidemiologic studies have failed to identify the reservoir of infection or vehicles of transmission. This has precluded targeting food chain interventions to diminish disease transmission but conversely has fostered the development of vaccines to prevent invasive NTS (iNTS) disease. We developed a mathematical model to estimate the potential impact of NTS vaccination programs in Bamako.

METHODOLOGY/PRINCIPAL FINDINGS: A Markov chain transmission model was developed utilizing age-specific Bamako demographic data and hospital surveillance data for iNTS disease in children aged <5 years and assuming vaccine coverage and efficacy similar to the existing, successfully implemented, Hib vaccine. Annual iNTS hospitalizations and deaths in children <5 years, with and without a Salmonella Enteritidis/Salmonella Typhimurium vaccine, were the model's outcomes of interest. Per the model, high coverage/high efficacy iNTS vaccination programs would drastically diminish iNTS disease except among infants age <8 weeks.

CONCLUSIONS/SIGNIFICANCE: The public health impact of NTS vaccination shifts as disease burden, vaccine coverage, and serovar distribution vary. Our model shows that implementing an iNTS vaccine through an analogous strategy to the Hib vaccination program in Bamako would markedly reduce cases and deaths due to iNTS among the pediatric population. The model can be adjusted for use elsewhere in Africa where NTS epidemiologic patterns, serovar prevalence, and immunization schedules differ from Bamako.

WEB: http://dx.doi.org/10.1371/journal.pntd.0005283

IMPACT FACTOR: 4.45

CITED HALF-LIFE: 3.20

START SCIENTIFIC COMMENT: Authors estimated iNTS coverage for parameter inputs from a small sample of 61 caretakers of infants 6-8 months old in Bamako, based on Hib vaccine coverage. Among this sample 98% had received > 1 dose and 90% had received all 3. Ranges were further expanded based on data from a larger population-based sample in Kenya. iNTS vaccine efficacy parameter inputs were based on Hib and pneumococcal conjugate vaccine from African countries. Figure 5 reports the age-specific expected numbers of cases and fatal cases under scenarios of iNTS vaccination: a) no iNTS vaccination; b) 6-week iNTS vaccination at 100% efficacy and 100% coverage; 3) 6, 10 and 14-week vaccination with coverage varying by dose (3 doses 90% and 1 dose 98%) and efficacy depending on number of doses received (3 doses 95%, 1 dose 45%). Table 5 reports the proportional reduction in iNTS cases and deaths in scenarios with different vaccine efficacy, serovar distribution and dosing regimen assumptions. Most scenarios resulted in similar proportional reductions in deaths (approximately 30-45% reduction), but assuming S. *Typhimurium* was the only causal pathogen, authors estimate an 80% reduction is iNTS-related mortality. Proportional reductions in cases ranged from approximately 50% for 3-dose with low efficacy due to immune suppression, and 80%, with high vaccine efficacy estimates.

In absolute terms, authors estimate a minimum of between 4-23 pediatric cases per year would be prevented by vaccination, assuming the lowest ranges of vaccine efficacy, and a maximum of 29 pediatric cases prevented per year, assuming the highest vaccine efficacy. Three-dose vaccination at 6, 10 and 14 weeks was estimated to prevent between 21-23 cases per year and 1-3 deaths, assuming efficacy and effectiveness similar to a trial in the Gambia.

5. **Estimated Effect of Inactivated Poliovirus Vaccine Campaigns, Nigeria and Pakistan, January 2014-April 2016.**

Shirreff G, Wadood MZ, Vaz RG, Sutter RW, Grassly NC.

Emerg Infect Dis. 2017 Feb;23(2):258-263.

PMID:27861118

ABSTRACT

In 2014, inactivated poliovirus vaccine (IPV) campaigns were implemented in Nigeria and Pakistan after clinical trials showed that IPV boosts intestinal immunity in children previously given oral poliovirus vaccine (OPV). We estimated the effect of these campaigns by using surveillance data collected during January 2014-April 2016. In Nigeria, campaigns with IPV and trivalent OPV (tOPV) substantially reduced the incidence of poliomyelitis caused by circulating serotype-2 vaccine-derived poliovirus (incidence rate ratio [IRR] 0.17 for 90 days after vs. 90 days before campaigns, 95% CI 0.04-0.78) and the prevalence of virus in environmental samples (prevalence ratio [PR] 0.16, 95% CI 0.02-1.33). Campaigns with tOPV alone resulted in similar reductions (IRR 0.59, 95% CI 0.18-1.97; PR 0.45, 95% CI 0.21-0.95). In Pakistan, the effect of IPV+tOPV campaigns on wild-type poliovirus was not significant. Results suggest that administration of IPV alongside OPV can decrease poliovirus transmission if high vaccine coverage is achieved.

WEB: http://dx.doi.org/10.3201/eid2302.161210

IMPACT FACTOR: 4.89

CITED HALF-LIFE: 6.30

START SCIENTIFIC COMMENT: Figure 1 depicts the effect of mass vaccination campaigns with inactivated poliovirus vaccine plus trivalent oral poliovirus vaccine (IPV+tOPV) or tOPV alone on poliovirus detection in people and from environmental samples, in Nigeria and Pakistan from 2014–2016. Results demonstrate the substantial differences in effect across these two settings. Authors also note that across states/regions within a country, there was substantial variation in the effect of the strategies; within a country, the incidence of cases and prevalence of pathogens isolated from environmental sample varied substantially. Because of this within-country heterogeneity, authors preferred a mixed-effects regression model (as opposed to fixed-effect), which allows the effect of the strategies to differ across location.

Authors propose that the lack of effect of IPV + tOPV mass campaigns on WPV1 incidence or environmental prevalence could be explained by low statistical power, low coverage during the campaigns and restriction in the target age groups for vaccination.

6. **Knowledge, attitudes, practices and willingness to vaccinate in preparation for the introduction of HPV vaccines in Bamako, Mali.**

De Groot AS, Tounkara K, Rochas M, Beseme S, Yekta S, et al.

PLoS One. 2017 Feb 13;12(2):e0171631.

PMID:28192460

ABSTRACT

Although screening for pre-cancerous cervical lesions and human papilloma virus (HPV) vaccination are accepted and effective means to prevent cervical cancer, women in Mali have limited access to these interventions. In addition, cervical cancer prevention by HPV vaccination has been controversial in some settings. To reduce cervical cancer prevalence and increase HPV vaccine uptake, it is important to understand the level of knowledge about cervical cancer screening and practices related to vaccination in at-risk populations. In this study, the level of knowledge about HPV and cervical cancer and attitudes towards vaccination were assessed among 301 participants (male and female, adults and adolescents) in a house-to-house survey in two urban neighborhoods in Bamako, Mali. The survey was combined with a brief educational session on HPV. Prior to the education session, overall knowledge of HPV infection and cervical cancer was very low: only 8% knew that HPV is a sexually transmitted infection (STI). Less than 20% of women had ever consulted a gynecologist and less than 3% had ever had cervical cancer screening. After hearing a description of HPV vaccine, more than 80% would accept HPV vaccination; fathers and husbands were identified as primary decisions makers and local clinics or the home as preferred sites for vaccination. This study provides information on STI knowledge and vaccine acceptance in Bamako, Mali in 2012, prior to the introduction of HPV vaccination.

WEB: http://dx.doi.org/10.1371/journal.pone.0171631

IMPACT FACTOR: 3.23

CITED HALF-LIFE: 2.70

START SCIENTIFIC COMMENT: After receiving the brief HPV educational intervention, respondents reported community clinics and their homes were their preferred locations for receiving HPV vaccination. When prompted for their preferred method of receiving information about HPV vaccine-related appointments, respondents reported preferring home visits to SMS reminders.

Figure 4 describes the individual decision-making and decision-making autonomy for HPV vaccination among different ages and genders. About a third of adult women reported that the decision to vaccine her child would be made by her spouse, a quarter reported they would make the decision themselves, and 16% said both she and her partner would decide together. In contrast, no adult males reported their spouse would make the decision alone, about 10% said they themselves would make the decision alone and approximately 1% said the decision would be made together with their spouse.

Adolescent females and males also had different perceptions about decision-making autonomy. Whereas approximately 16% of females reported they would make the decision with their parents, 44% of males said they would make the decision with their parents. Among females, 27% said they themselves would make the decision, but only about half of that, approximately 15% of males, felt the decision would be theirs independently.

7. **Leveraging contact network structure in the design of cluster randomized trials.**

Harling G, Wang R, Onnela JP, De Gruttola V.

Clin Trials. 2017 Feb;14(1):37-47.

PMID:27798376

ABSTRACT

BACKGROUND: In settings like the Ebola epidemic, where proof-of-principle trials have provided evidence of efficacy but questions remain about the effectiveness of different possible modes of implementation, it may be useful to conduct trials that not only generate information about intervention effects but also themselves provide public health benefit. Cluster randomized trials are of particular value for infectious disease prevention research by virtue of their ability to capture both direct and indirect effects of intervention, the latter of which depends heavily on the nature of contact networks within and across clusters. By leveraging information about these networks-in particular the degree of connection across randomized units, which can be obtained at study baseline-we propose a novel class of connectivity-informed cluster trial designs that aim both to improve public health impact (speed of epidemic control) and to preserve the ability to detect intervention effects.

METHODS: We several designs for cluster randomized trials with staggered enrollment, in each of which the order of enrollment is based on the total number of ties (contacts) from individuals within a cluster to individuals in other clusters. Our designs can accommodate connectivity based either on the total number of external connections at baseline or on connections only to areas yet to receive the intervention. We further consider a "holdback" version of the designs in which control clusters are held back from re-randomization for some time interval. We investigate the performance of these designs in terms of epidemic control outcomes (time to end of epidemic and cumulative incidence) and power to detect intervention effect, by simulating vaccination trials during an SEIR-type epidemic outbreak using a network-structured agent-based model. We compare results to those of a traditional Stepped Wedge trial.

RESULTS: In our simulation studies, connectivity-informed designs lead to a 20% reduction in cumulative incidence compared to comparable traditional study designs, but have little impact on epidemic length. Power to detect intervention effect is reduced in all connectivity-informed designs, but "holdback" versions provide power that is very close to that of a traditional Stepped Wedge approach.

CONCLUSION: Incorporating information about cluster connectivity in the design of cluster randomized trials can increase their public health impact, especially in acute outbreak settings. Using this information helps control outbreaks-by minimizing the number of cross-cluster infections-with very modest cost in terms of power to detect effectiveness.

WEB: http://dx.doi.org/10.1177/1740774516673355

IMPACT FACTOR: 1.84

CITED HALF-LIFE: 5.60

START SCIENTIFIC COMMENT: Figure 1 is a flow chart to guide appropriate selection and typology of the different connectivity-informed designs described in the paper, based on attributes of the research scenario. Figure 2 is a depiction of between-cluster connectivity (or “ties”), and a schematic for how it is calculated at different times in a cluster randomized trial, based on different numbers of individuals connected within and between clusters, in the different types of connectivity-informed designs.

Authors describe that the basic trade-off between a traditional cluster-RCT and a connectivity-informed design is that the former has more statistical power to detect intervention effects, while the latter types provide faster epidemic control. However, the magnitude of the trade-off depends on a number of factors, including the types and amount of connectedness in the study population, design used, timing of planned analyses, and features of the causative agent. Knowledge of the structure of the connectedness within the study population (how connected are those within and between clusters) is essential in determining the balance of such trade-offs. Authors emphasize the potential utility of this class of designs for effectiveness trials, when efficacy has already been established.

8. **The role of the vaccines industry in Mission Grand Convergence.**

Almond J, Medaglini D.

Vaccine. 2017 Jan 20;35 Suppl 1:A24-A28.

PMID:28017440

ABSTRACT

The vast majority of vaccines used throughout the world are supplied by the private sector. It is essential therefore that the industry is closely engaged in future policy developments at a national and international level and is able to respond to the changing needs and priorities that may be required to ensure the success of Mission Grand Convergence. Uniquely, the major vaccine companies have the expertise and technical capacity to develop, produce and supply vaccines on a global scale. Through partnering with Governments, charities and NGOs, they must play a pivotal role in the Mission and, at the same time as agreeing on objectives that may not be entirely market driven, must be able to sustain their commercial obligations to shareholders. Similarly, small and medium sized companies, with the global investor market and government incentives that underpin and support them, also have a very important role to play; for example in innovation around a given disease and on technology, process and platform development across the whole value chain. The industry at large is therefore an essential player. Indeed Mission Grand Convergence can only succeed with the full and willing participation of the vaccines industry.

WEB: http://dx.doi.org/doi.10.1016/j.vaccine.2016.10.084

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

START SCIENTIFIC COMMENT: Authors discuss the importance for private vaccine manufacturers to analyze well-informed "business cases" to determine prioritization in research and development, production, and distribution of vaccines. A business case would include the following:

- Determining region-specific estimates of the cost of disease treatment
- Assuming a "price-neutral" approach to vaccine development/production/distribution costs relative to treatment costs among health authorities that would procure it
- Determining indirect disease costs/assessing "population benefits" above and beyond treatment benefit
- Assessing quality-adjusted life-years lost associated with the disease (encourages higher possible pricing)
- Assessing global vaccine development costs (including clinical research and licensure; capital costs and production facility costs)
- Forecasting vaccine sales to estimate potential revenue
- Calculation of Net Present Value

Authors explain that if the Net Present Value is positive, there is a business case for development. The next step would be evaluation of "scientific feasibility", based on expert determination of the following:

- Whether antigens/components to use to produce a protective immune response in recipient are known;
- Whether the product is safe;
- How "complex" the vaccine needs to be;
- Whether there is a feasible clinical development pathway and whether the process is likely to be "industrialisable" to produce adequate product at scale, at reasonable price.

Authors emphasize the importance to the field of having people in vaccinology who are trained in both academic disciplines and in industry skills and processes, and recommend joint and collaborative training programs with diverse components across disciplines. They encourage the development of training and engagement opportunities via partnership and collaboration across the sectors.

9. **Timeliness and risk factors associated with delay for pneumococcal conjugate 10-valent routine immunization in Brazilian children.**

Sartori AL, Minamisava R, Afonso ET, Policena GM, Pessoni GC, et al.

Vaccine. 2017 Feb 15;35(7):1030-1036.

PMID:28108230

ABSTRACT

BACKGROUND: Vaccination coverage is the usual metrics to evaluate the immunization programs performance. For the 10-valent pneumococcal conjugate (PCV10) vaccine, measuring the delay of vaccination is also important, particularly as younger children are at increased risk of disease. Routinely collected administrative data was used to assess the timeliness of PCV10 vaccination, and the factors associated with delay to receive the first and second doses, and the completion of the PCV10 3+1 schedule.

METHODS: A population-based retrospective cohort study was conducted with children born in 2012 in Central Brazil. Children who received the PCV10 first dose in public health services were followed-up until 23months of age. Timeliness of receiving each PCV10 dose at any given age was defined as receiving the dose within 28days grace period from the recommended age by the National Immunization Program. Log-binomial regression models were used to examine risk factors for delays of the first dose and the completion PCV10 3+1 schedule.

RESULTS: In total, 14,282 children were included in the cohort of study. Delayed vaccination occurred in 9.4%, 23.8%, 36.8% and 39.9% children for the first, second, third and the booster doses, respectively. A total of 1912 children (12.8% of the cohort) were not adequately vaccinated at the 6months of life; 1,071 (7%) received the second dose after 6months of age, 784 (5.4%) did not receive the second dose, and 57 (0.4%) received the first dose after six months of life.

CONCLUSION: A considerable delay was found in PCV10 third and booster doses. Almost 2 thousand children had not received the recommended PCV10 doses at 6 months of age. Timeliness of vaccination is an issue in Brazil although high vaccination coverages.

WEB: http://dx.doi.org/10.1016/j.vaccine.2017.01.012

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

START SCIENTIFIC COMMENT: Authors found that higher level of maternal educational attainment and receipt of more prenatal visits were both associated with larger likelihood of receipt without delay in first dose of PCV10 in the child, and in completion. In multiple regression analysis, authors found that the influence of receipt of adequate prenatal care on completion of PCV10 3+1 among those who received first dose, depended on maternal education. Among those with low educational attainment, having less than 7 prenatal visits was a particularly strong risk factor for not completing PCV10 3+1.

10. **Perspective on Global Measles Epidemiology and Control and the Role of Novel Vaccination Strategies.**

Coughlin MM, Beck AS, Bankamp B, Rota PA.

Viruses. 2017 Jan 19;9(1).

PMID:28106841

ABSTRACT

Measles is a highly contagious, vaccine preventable disease. Measles results in a systemic illness which causes profound immunosuppression often leading to severe complications. In 2010, the World Health Assembly declared that measles can and should be eradicated. Measles has been eliminated in the Region of the Americas, and the remaining five regions of the World Health Organization (WHO) have adopted measles elimination goals. Significant progress has been made through increased global coverage of first and second doses of measles-containing vaccine, leading to a decrease in global incidence of measles, and through improved case based surveillance supported by the WHO Global Measles and Rubella Laboratory Network. Improved vaccine delivery methods will likely play an important role in achieving measles elimination goals as these delivery methods circumvent many of the logistic issues associated with subcutaneous injection. This review highlights the status of global measles epidemiology, novel measles vaccination strategies, and describes the pathway toward measles elimination.

WEB: http://dx.doi.org/10.3390/v9010011

IMPACT FACTOR: 1.98

CITED HALF-LIFE: 6.30

START SCIENTIFIC COMMENT: Authors describe key challenges in vaccine delivery systems for measles vaccine as relating to 1) cold chain requirements; 2) injection safety and disposal of contaminated waste; and 3) requirements for available trained personnel to administer the vaccine, and discuss novel strategies to address these needs. One strategy under investigation was determining methods to block placentally-transferred maternal antibodies in infants, so that the vaccine could be delivered earlier and still produce a lasting infant response. Alternate delivery systems, which may help alleviate challenges in waste management and requirements for skilled personnel, include intradermal microneedles and respiratory administration via aerosolized vaccine (nebulized liquid and dry powder formulations). Unfortunately, though trials in aerosolized routes appeared to result in sufficient immune response in older children, results in infants indicated less immune response, although increased exposure time to nebulized vaccine did induce sufficient immune response among infants. Unfortunately, a major challenge in developing aerosolized formulations is lower consistency in the dose delivered than compared to subcutaneous delivery methods. Dry power formulations, which improve thermostability, have relatively more limited human data; phase 1 data suggests acceptable immunogenicity and safety, but this formulation has not been evaluated in children to date. Although microneedle patches are a promising new approach which would reduce the need for trained staff, lack of human clinical data or a plan for large-scale commercial production limit utility in the short-term. Table 1 summarizes clinical research on alternative (non-subcutaneous injection) vaccine delivery approaches.

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]) ("2017/1/15"[PDAT] : "2017/2/14"[PDAT]))

* On March 2, 2017, this search of English language articles published between January 15, 2017 and February 14, 2017 and indexed by the US National Library of Medicine resulted in 191 unique manuscripts.