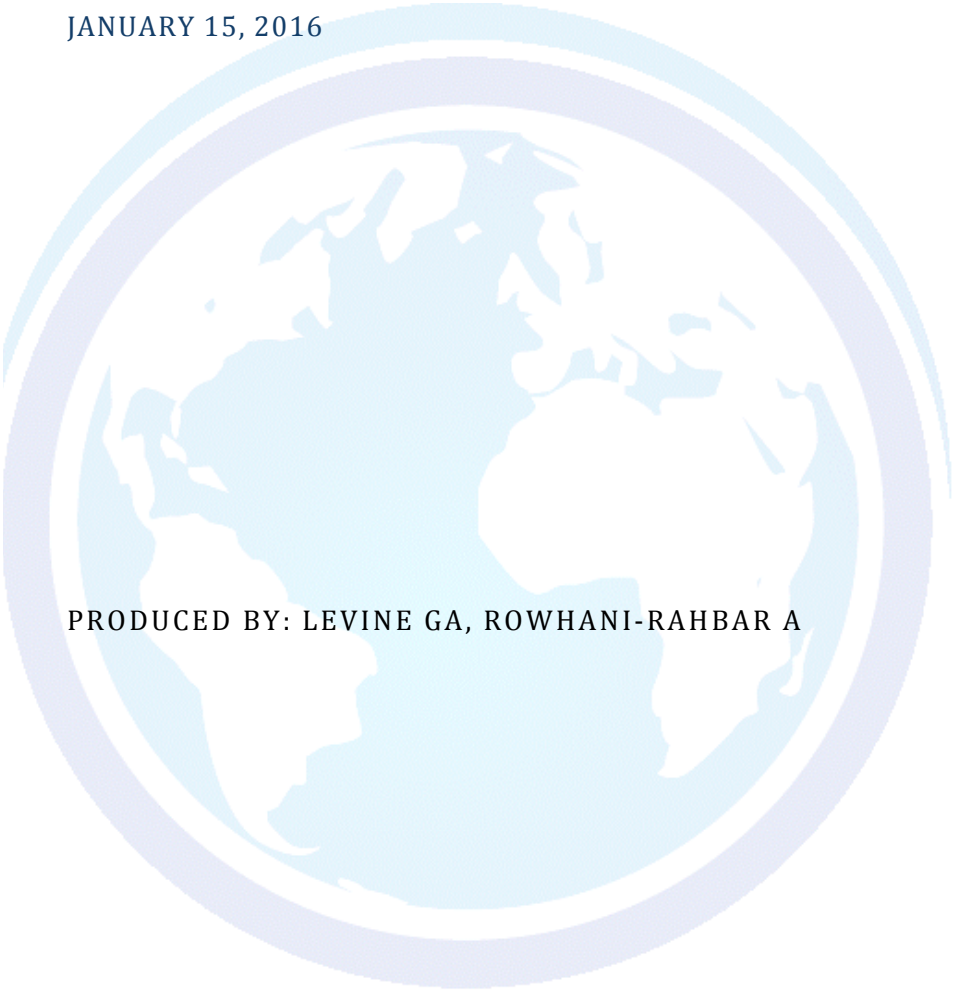
VACCINE DELIVERY RESEARCH DIGEST

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

JANUARY 15, 2016



PRODUCED BY: LEVINE GA, ROWHANI-RAHBAR A

TABLE OF CONTENTS

1. USE OF MOBILE PHONES FOR IMPROVING VACCINATION COVERAGE AMONG CHILDREN LIVING IN RURAL HARD-TO-REACH AREAS AND URBAN STREETS OF BANGLADESH.

Uddin MJ, Shamsuzzaman M, Horng L, Labrique A, Vasudevan L, Zeller K et al.

Vaccine. 2015 Nov 29. [Epub ahead of print]

PMID: 26647290

ABSTRACT

In Bangladesh, full vaccination rates among children living in rural hard-to-reach areas and urban streets are low. We conducted a quasi-experimental pre-post study of a 12-month mobile phone intervention to improve vaccination among 0-11 months old children in rural hard-to-reach and urban street dweller areas. Software named "mTika" was employed within the existing public health system to electronically register each child's birth and remind mothers about upcoming vaccination dates with text messages. Android smart phones with mTika were provided to all health assistants/vaccinators and supervisors in intervention areas, while mothers used plain cell phones already owned by themselves or their families. Pre and post-intervention vaccination coverage was surveyed in intervention and control areas. Among children over 298 days old, full vaccination coverage actually decreased in control areas rural baseline 65.9% to endline 55.2% and urban baseline 44.5% to endline 33.9% - while increasing in intervention areas from rural baseline 58.9% to endline 76.8%, difference +18.8% (95% CI 5.7-31.9) and urban baseline 40.7% to endline 57.1%, difference +16.5% (95% CI 3.9-29.0). Difference-in-difference (DID) estimates were +29.5% for rural intervention versus control areas and +27.1% for urban areas for full vaccination in children over 298 days old, and logistic regression adjusting for maternal education, mobile phone ownership, and sex of child showed intervention effect odds ratio (OR) of 3.8 (95% CI 1.5-9.2) in rural areas and 3.0 (95% CI 1.4-6.4) in urban areas. Among all age groups, intervention effects on age-appropriate vaccination coverage were positive: DIDs +13.1-30.5% and ORs 2.5-4.6 ($p<0.001$ in all comparisons). Qualitative data showed the intervention was well-accepted. Our study demonstrated that a mobile phone intervention can improve vaccination coverage in rural hard-to-reach and urban street dweller communities in Bangladesh. This small-scale successful demonstration should serve as an example to other low-income countries with high mobile phone usage.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.11.024

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

UW EDITORIAL COMMENT: mTika software included the following components: "(i) smart phone-based registration of pregnant women,(ii) short message service (SMS) birth notifications from mothers,(iii) automated SMS vaccination reminders to mothers, (iv) vaccination reminders for health workers, and (v) smart phone and web-based EPI monitoring by supervisors." Authors describe the following implementation challenges: "difficulties with developing new software, multiple other groups working in this space, growing capacity of health workers and field staff to use smart phones, low active mTika usage by mothers, and inability to track SMS notifications by different vaccination coverage categories." Note that while the primary conclusion was that *age-appropriate vaccination* improved more in mTika communities than without mTika, the intervention effect was assessed for vaccinations from 0-11 months of age, but not all children were followed prospectively through 12 months of follow-up at which point "complete vaccination" could be determined, thus the number contributing to the analysis of "full vaccination" was small (n=863). Since tracking is more challenging as children get older and have less contact with the health system, and age is negatively associated with complete coverage, one might expect that coverage would wane overall with age. Also note that the inference on treatment effect was based on outcome status using EPI card records AND maternal recall/vaccination report; use of EPI card alone showed much lower vaccination coverage, and in analysis using only EPI card alone the treatment effect was not statistically significant.

2. DID YOU GET YOUR SHOTS? EXPERIMENTAL EVIDENCE ON THE ROLE OF REMINDERS.

Busso M, Cristia J, Humpage S.

J Health Econ. 2015 Dec;44:226-37. Epub 2015 Sep 25.

PMID:26519909

ABSTRACT

Many families fail to vaccinate their children despite the supply of these services at no cost. This study tests whether personal reminders can increase demand for vaccination. A field experiment was conducted in rural Guatemala in which timely reminders were provided to families whose children were due for a vaccine. The six-month intervention increased the probability of vaccination completion by 2.2 percentage points among all children in treatment communities. Moreover, for children in treatment communities who were due to receive a vaccine, and whose parents were expected to be reminded about that due date, the probability of vaccination completion increased by 4.6 percentage points. The cost of an additional child with complete vaccination due to the intervention is estimated at about $7.50.

WEB: http://dx.doi.org/10.1016/j.jhealeco.2015.08.005

IMPACT FACTOR: 2.58

CITED HALF-LIFE: 9.20

UW EDITORIAL COMMENT: Government electronic administrative health data were used to generate lists of all children in the intervention communities with upcoming vaccinations, based on recommended schedule of vaccinations. Non-governmental organization (NGO)-employed health workers in intervention clinics contacted caregivers to remind them of upcoming scheduled vaccinations. The aim was to test whether *children who received initial vaccinations* would be more likely to receive subsequent vaccinations (endpoint was complete vaccination for age), if community health workers received lists of children with upcoming vaccinations, and were encouraged to contact caregivers to remind them to seek care. Only children for whom administrative records existed were included in the study, which represents a subset of the overall children in the communities, and thus failure to include the "unregistered" children in the analysis may over-represent the treatment effect on a population level. However, authors clarify that the overall intervention aim was to improve follow-through complete vaccination among ever-vaccinated children. Although 167 clinics were randomly assignment to treatment or control (standard of care), only 130 clinics with non-missing data were included in final analysis, and although authors report that baseline characteristics were similar among included and excluded clinics, there may be potential selection bias resulting from exclusion of the other clinics in the analysis. Results from intentional to treat analysis (ITT), and those based on whether the health workers *actually received patient lists* (called local average treatment effect (LATE)), are both reported. The treatment estimates from ITT indicate a smaller magnitude in the treatment effect (2.2% percentage point increase in complete vaccination associated with intervention) than LATE estimates, (4.5% percentage increase in complete vaccination associated with intervention). Authors also report the treatment effect among those for whom a vaccine was indicated during the study period, but this sub-group analysis results in an inflation of the overall estimated effect of the intervention in a target population, since not all children will be of an appropriate age to have vaccinations indicated during any particular administrative time period, and thus the larger analysis is a better representation of the expected effectiveness of the intervention in the population.

3. YOUTH GROUP ENGAGEMENT IN NONCOMPLIANT COMMUNITIES DURING SUPPLEMENTAL IMMUNIZATION ACTIVITIES IN KADUNA, NIGERIA, IN 2014.

Musa A, Mkanda P, Manneh F, Korir C, Warigon C, Gali E, Banda R, Umeh G, Nsubuga P, Chevez A, Vaz RG.

J Infect Dis. 2015 Nov 25. [Epub ahead of print]

PMID: 26609003

ABSTRACT

INTRODUCTION: One of the major challenges being faced in the Global Polio Eradication Initiative program is persistent refusal of oral polio vaccine (OPV) and harassment of vaccination team members by youths. The objective of the study was to describe the strategy of collaborating with recognized youth groups to reduce team harassment during vaccination campaigns and improve vaccination coverage in noncompliant communities.

METHODS: We assessed data from polio vaccination activities in OPV-refusing communities in the Igabi and Zaria local government areas (LGAs) of Kaduna State in Nigeria. We evaluated the following factors to determine trends: enhanced independent monitoring data on the proportion of children missed by vaccination activities (hereafter, "missed children"), lot quality assurance surveys, and vaccination team harassment.

RESULTS: The proportion of missed children decreased in both LGAs after the intervention. In Igabi LGA and Zaria LGA, the lowest proportions of missed children before and after the intervention decreased from 7% to 2% and from 5% to 1%, respectively. Lot quality assurance survey trends showed an improvement in immunization coverage 1 year after youth groups' engagement in both LGAs.

CONCLUSIONS: Systematic engagement of youth groups has a great future in polio interruption as we approach the endgame strategy for polio eradication. It promises to be a veritable innovation in reaching chronically missed children in OPV-refusing communities.

WEB: http://jid.oxfordjournals.org/content/early/2015/11/25/infdis.jiv510.abstract

IMPACT FACTOR: 6.00

CITED HALF-LIFE: 8.70

UW EDITORIAL COMMENT: "Influential" youths for a particular community, including youth specifically thought to be involved in vaccination resistance and harassment, were specifically targeted for involvement. Local community-based organizations and traditional leaders contributed to selecting specific youths for participation. Selected youths underwent 1-day "sensitization" sessions that consisted of interactive training, engagement, discussion and role-playing about the EPI activities in Nigeria, EPI process, challenges, and burden of polio in the community. Youths were then "deployed" to areas in which harassment of vaccination teams was previously documented and where noncompliance was high, and accompanied the vaccination teams for DOPV, house-to-house vaccination and mop-up activities. Youths worked in close collaboration with vaccination team members, security agents, and traditional leaders in their LGAs. Authors report improvements in vaccination coverage following the engagement of youths, but conclusions should be considered in light of some important methodological considerations. The pragmatic evaluation was intended to be informative programmatically, but wasn't designed or conducted as a rigorously controlled trial or prospective study. Other factors, such as changes over time in the communities, other ongoing programmatic polio campaign activities, or differences in insecurity, for instance, may also influence results. Furthermore, the data on program coverage is limited and errors or inconsistencies in measurement may also influence inference. Nevertheless, this pragmatic evaluation indicates this may be one strategy to consider in challenging, high-priority settings.

4. MODELING LONG-TERM VACCINATION STRATEGIES WITH MENAFRIVAC IN THE AFRICAN MENINGITIS BELT.

Karachaliou A, Conlan AJ, Preziosi MP, Trotter CL.

Clin Infect Dis. 2015 Nov 15;61 Suppl 5:S594-600.

PMID: 26553693

ABSTRACT

BACKGROUND: The introduction of MenAfriVac in campaigns targeting people aged 1-29 years across the African meningitis belt has successfully reduced meningitis incidence and carriage due to Neisseria meningitidis group A (MenA). It is important to consider how best to sustain population protection in the long term.

METHODS: We created a mathematical model of MenA transmission and disease to investigate the potential impact of a range of immunization strategies. The model is age structured; includes classes of susceptible, carrier, ill, and immune people (who may be vaccinated or unvaccinated); and incorporates seasonal transmission and a stochastic forcing term that models between year variation in rates of transmission. Model parameters were primarily derived from African sources. The model can describe the typical annual incidence of meningitis in the prevaccine era, with irregular epidemics of varying size. Parameter and structural uncertainty were explored in sensitivity analyses.

RESULTS: Following MenAfriVac introduction at high uptake, the model predicts excellent short-term disease control. With no subsequent immunization, strong resurgences in disease incidence were predicted after approximately 15 years (assuming 10 years' average vaccine protection). Routine immunization at 9 months of age resulted in lower average annual incidence than regular mass campaigns of 1- to 4-year-olds, provided coverage was above approximately 60%. The strategy with the lowest overall average annual incidence and longest time to resurgence was achieved using a combination strategy of introduction into the Expanded Programme on Immunization at 9 months, 5 years after the initial mass campaigns, with a catch-up targeting unvaccinated 1- to 4-year-olds.

CONCLUSIONS: These results can be used to inform policy recommendations for long term vaccination strategies with MenAfriVac.

WEB: http://cid.oxfordjournals.org/content/61/suppl_5/S594.abstract

IMPACT FACTOR: 8.89

CITED HALF-LIFE: 7.00

UW EDITORIAL COMMENT: Vaccine strategies considered introduction and long-term activities, and included initial campaign mass-vaccination only; initial and periodic mass-vaccination campaigns; initial mass vaccination plus routine EPI single-dose vaccination; and a “combination” strategy of initial mass immunization, routine EPI and catch-up. Table 1 describes the different strategies and target populations during introduction and in the long-term. Model parameter (inputs/assumptions) values, and the literature they are based on, are listed in Table 2. Figure 4 is a box plot of the average annual incidence of *Neisseria meningitidis* Group A for different immunization strategies in the 40 years following introduction, from simulations. After an initial decline in incidence, “a strong resurgence” is predicted without a long-term strategy, which is supported by evidence presented in Figure 3: predicted annual incidence following initial mass immunization over a 40-year horizon. Authors determined a combination of routine EPI vaccination after 5 years, together with a catch-up campaign in children 1–4 yrs born after the initial campaigns, was the most effective, although all the long-term strategies were moderately effective in maintaining disease control. This article was part of a supplement in CID focused on MenAfriVac.

5. TRACKING VACCINATION TEAMS DURING POLIO CAMPAIGNS IN NORTHERN NIGERIA BY USE OF GEOGRAPHIC INFORMATION SYSTEM TECHNOLOGY: 2013-2015.

Touray K, Mkanda P, Tegegn SG, Nsubuga P, Erbeto TB, Banda R, et al.

J Infect Dis. 2015 Nov 25. [Epub ahead of print]

PMID: 26609004

ABSTRACT

INTRODUCTION: Nigeria is among the 3 countries in which polio remains endemic. The country made significant efforts to reduce polio transmission but remains challenged by poor-quality campaigns and poor team performance in some areas. This article demonstrates the application of geographic information system technology to track vaccination teams to monitor settlement coverage, reduce the number of missed settlements, and improve team performance.

METHODS: In each local government area where tracking was conducted, global positioning system-enabled Android phones were given to each team on a daily basis and were used to record team tracks. These tracks were uploaded to a dashboard to show the level of coverage and identify areas missed by the teams.

RESULTS: From 2012 to June 2015, tracking covered 119 immunization days. A total of 1149 tracking activities were conducted. Of these, 681 (59%) were implemented in Kano state. There was an improvement in the geographic coverage of settlements and an overall reduction in the number of missed settlements.

CONCLUSIONS: The tracking of vaccination teams provided significant feedback during polio campaigns and enabled supervisors to evaluate performance of vaccination teams. The reports supported other polio program activities, such as review of microplans and the deployment of other interventions, for increasing population immunity in northern Nigeria.

WEB: http://jid.oxfordjournals.org/content/early/2015/11/25/infdis.jiv493.abstract

IMPACT FACTOR: 6.00

CITED HALF-LIFE: 8.70

UW EDITORIAL COMMENT: Regions were selected for tracking based on prioritized need by the polio program. Extensive mapping of the regions was done before the project started, to develop GIS maps of population settlements and also points of interest such as schools and health centers, which could be used to inform program planning. The maps were then used as "background data" for planning purposes and against which to track the activities and geographic coverage of SIA activities. The visual vaccination tracking data was used to identify settlements that were being missed, small settlements that weren't on other administrative maps or lists, and to identify settlements chronically missed by SIA due to insecurity. The frequency and ease of access to data enabled supervisors to make real-time decisions to target missed areas with mop-up activities. This descriptive report is intriguing and indicates that similar programs may be tools to improve coverage. However, the evaluation isn't adequate to determine conclusively the benefit of the program. The information on program activities and descriptive results indicate coverage improvements, but it should be noted that there is no direct comparison of pre-post intervention, nor to comparable program regions that didn't use tracking, and thus trends observed could be due to other factors in addition to the program. Figure 4 is a GIS map with vaccination activities overlaid, and is an example of how the maps with tracking data can be used to identify regions previously missed.

6. TRIVALENT AND QUADRIVALENT INFLUENZA VACCINATION EFFECTIVENESS IN AUSTRALIA AND SOUTH AFRICA: RESULTS FROM A MODELLING STUDY.

Milne GJ, Halder N, Kelso JK, Barr IG, Moyes J, Kahn K, Twine R, Cohen C.

Influenza Other Respir Viruses. 2015 Dec 12. [Epub ahead of print]

PMID: 26663701

ABSTRACT

BACKGROUND: A modelling study was conducted to determine the effectiveness of trivalent (TIV) and quadrivalent (QIV) vaccination in South Africa and Australia.

OBJECTIVES: This study aimed to determine the potential benefits of alternative vaccination strategies which may depend on community-specific demographic and health characteristics.

METHODS: Two influenza A and two influenza B strains were simulated using individual-based simulation models representing specific communities in South Africa and Australia over 11 years. Scenarios using TIV or QIV, with alternative prioritisation strategies and vaccine coverage levels were evaluated using a country-specific health outcomes process.

RESULTS: In South Africa, ~18% fewer deaths and hospitalisations would be expected to result from the use of QIV compared to TIV over the 11 modelled years ($p = 0.031$). In Australia, only 2% ($p = 0.30$) fewer deaths and hospitalisations would result. Vaccinating 2%, 5%, 15% or 20% of the population with TIV using a strategy of prioritising vulnerable age groups, including HIV-positive individuals, resulted in reductions in hospitalisations and mortality of at least 7%, 18%, 57% and 66% respectively, in both communities.

CONCLUSIONS: The degree to which QIV can reduce health burden compared to TIV is strongly dependent on the number of years in which the influenza B lineage in the TIV matches the circulating B lineages. Assuming a moderate level of B cross-strain protection, TIV may be as effective as QIV. The choice of vaccination prioritisation has a greater impact than the QIV/TIV choice, with strategies targeting those most responsible for transmission being most effective.

WEB:http://onlinelibrary.wiley.com/doi/10.1111/irv.12367/abstract;jsessionid=7607BA5EB1E17515D220D2B83793E2E7.f01t01

IMPACT FACTOR: 2.20

CITED HALF-LIFE: 2.70

UW EDITORIAL COMMENT: Authors used a community in a low-income settings in South Africa, where vaccination coverage was very low (approximately <2%) and a community in a high-income country, Australia, where coverage of TIV was approximately 20%, but varied by population (children <5% and elderly > 75%). The range of scenarios considered included TIV or QIV; vaccination coverage levels ranging from 2% to 20% of the population; and different vaccination prioritization strategy (order of prioritization of different sub-groups). QIV results in a significant reduction in deaths and hospitalizations, compared to TIV, in South Africa and Australia, but in Australia the reductions were of smaller magnitude, which the authors attribute to the fact that the B lineage component of the TIV was "less well matched" to B strains circulating in South African than Australia. Authors conclude that the differences in the advantage provided by QIV depends on the ratios of different strains, not differences in the demographic characteristics in the populations. For both communities, TIV and QIV, at vaccination coverage levels of at least 5%, authors report: "the greatest reduction in influenza burden is achieved by the transmitters-first prioritization strategy," due to the indirect effect on herd immunity in the population. Table 2 reports the model-derived estimated outcomes for alternative TIV vaccination coverage and prioritization strategies, and Table 3 reports the model-derived estimated attack rates with varying degree of TIV B-lineage cross protection, by setting and prioritization strategy.

7. MICRONEEDLE PATCHES FOR VACCINATION IN DEVELOPING COUNTRIES.

Arya J, Prausnitz MR.

J Control Release. 2015 Nov 18. [Epub ahead of print]

PMID: 26603347

ABSTRACT

Millions of people die of infectious diseases each year, mostly in developing countries, which could largely be prevented by the use of vaccines. While immunization rates have risen since the introduction of the Expanded Program on Immunization (EPI), there remain major challenges to more effective vaccination in developing countries. As a possible solution, microneedle patches containing an array of micron-sized needles on an adhesive backing have been developed to be used for vaccine delivery to the skin. These microneedle patches can be easily and painlessly applied by pressing against the skin and, in some designs, do not leave behind sharps waste. The patches are single-dose, do not require reconstitution, are easy to administer, have reduced size to simplify storage, transportation and waste disposal, and offer the possibility of improved vaccine immunogenicity, dose sparing and thermostability. This review summarizes vaccination challenges in developing countries and discusses advantages that microneedle patches offer for vaccination to address these challenges. We conclude that microneedle patches offer a powerful new technology that can enable more effective vaccination in developing countries.

WEB: http://dx.doi.org/10.1016/j.jconrel.2015.11.019

IMPACT FACTOR: 7.71

CITED HALF-LIFE: 7.00

UW EDITORIAL COMMENT: The authors list and describe the following advantages of microneedles for vaccination in developing countries: improved vaccine effectiveness; reduced need for trained health care providers; simplified supply chain/eliminating need for cold chair; reduced risk of sharps; reduced vaccine wastage; no requirements for reconstitution; and reduced cost of vaccine and vaccination process. Key considerations and future research needed to advance the field includes more conclusive evidence of: determination in human studies of whether microneedles are associated with improved immunogenicity; determination that vaccine delivery is reliable when delivered by minimally-trained personnel; more extensive research of the thermostability and whether smaller project size does in fact simplify supply chain and effect health care systems; whether there are unintended safety risks associated with MNPs; whether MNPs do in fact result in elimination of need for reconstitution and reduced wastage; manufacturing costs of MNPs, whether terminal sterilization is possible and the cost of manufacturing such a feature; and whether the actual delivery costs to the health system are lower than those association with current vaccination practices.

8. UNDERSTANDING FACTORS INFLUENCING VACCINATION ACCEPTANCE DURING PREGNANCY GLOBALLY: A LITERATURE REVIEW.

Wilson RJ, Paterson P, Jarrett C, Larson HJ.

Vaccine. 2015 Nov 25;33(47):6420-9. Epub 2015 Aug 28.

PMID: 26320417

ABSTRACT

Maternal vaccination has been evaluated and found to be extremely effective at preventing illness in pregnant women and new-borns; however, uptake of such programmes has been low in some areas. To analyse factors contributing to uptake of vaccines globally, a systematic review on vaccine hesitancy was carried out by The Vaccine Confidence Project in 2012. In order to further analyse factors contributing to uptake of maternal immunisation, a further search within the broader systematic review was conducted using the terms 'Pregnan*' or 'Matern*'. Forty-two articles were identified. Pregnancy-related articles were further screened to identify those focused on concerns, trust and access issues regarding maternal vaccination reported by pregnant women and healthcare workers. Thirty-five relevant articles were included which were then searched using the snowballing technique to identify additional relevant references cited in these articles. A search alert was also conducted from February to April 2015 in PubMed to ensure that no new relevant articles were missed. A total of 155 relevant articles were included. Most of the literature which was identified on hesitancy surrounding vaccination during pregnancy reports on determinants of influenza vaccine uptake in North America. Research conducted in low-income countries focused primarily on tetanus vaccine acceptance. The main barriers cited were related to vaccine safety, belief that vaccine not needed or effective, not recommended by healthcare worker, low knowledge about vaacines, access issues, cost, conflicting advice. From the point of view of healthcare workers, barriers included inadequate training, inadequate reimbursement and increased workload. Twenty-seven out of 46 (59%) articles mentioning ethnicity reported lower rates of coverage among ethnic minorities. Barriers to vaccination in pregnancy are complex and vary depending on context and population. There are wide gaps in knowledge regarding the attitudes of healthcare workers and how ethnicity and gender dynamics influence a pregnant woman's decision to vaccinate.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.08.046

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

UW EDITORIAL COMMENT: Almost all included articles focused on influenza vaccination, and the vast majority were from well-resourced settings in North America, but limited articles in low-resource settings and relating to tetanus toxoid were also included. Key factors associated with hesitancy among health care providers/workers (HCP/HCW) included lack of reimbursement, lack of training, workload, cost, conflicting advice/recommendations, and religion. The main consumer concerns were safety and efficacy, but other barriers included lack of knowledge of disease/benefit, lack of a recommendation from a HCP/HCW, and access/availability.

9. NOVEL ADJUVANT FORMULATIONS FOR DELIVERY OF ANTI-TUBERCULOSIS VACCINE CANDIDATES.

Agger EM.

Adv Drug Deliv Rev. 2015 Nov 17. [Epub ahead of print]

PMID: 26596558

ABSTRACT

There is an urgent need for a new and improved vaccine against tuberculosis for controlling this disease that continues to pose a global health threat. The current research strategy is to replace the present BCG vaccine or boost BCG-immunity with subunit vaccines such as viral vectored- or protein-based vaccines. The use of recombinant proteins holds a number of production advantages including ease of scalability, but requires an adjuvant inducing cell-mediated immune responses. A number of promising novel adjuvant formulations have recently been designed and show evidence of induction of cellular immune responses in humans. A common trait of effective TB adjuvants including those already in current clinical testing is a two-component approach combining a delivery system with an appropriate immunomodulator. This review summarizes the status of current TB adjuvant research with a focus on the division of labor between delivery systems and immunomodulators.

WEB: http://dx.doi.org/10.1016/j.addr.2015.11.012

IMPACT FACTOR: 15.04

CITED HALF-LIFE: 7.20

UW EDITORIAL COMMENT: Authors summarize the current state of the science and opportunity resulting from strategies focusing on 1) delivery systems to improve long-term memory or to "tame" PAMP and 2) immunomudulators, which included "novel generation Freund's adjuvant-inspired immunomodulators" and use of TLR ligands to improve protection from BCG. Fig. 1 is a schema that depicts the delivery system characteristics for "optimal" adjuvant effect in TB vaccines. Authors describe the following factors of a delivery system that could be enhanced for optimal adjuvant effect: "A) targeting the antigen to specific organs e.g., lymph nodes or cells e.g., DCs, B) enhance the antigen uptake and antigen presentation in the APC, C) protecting the vaccine antigen from degradation and rapid excretion from the system, D) ensure slow release of antigen from the injection site, E) dampen systemic toxicity of PAMPs by avoiding global activation of all APCs, and F) direct stimulatory effect of the target APC or adjacent cells e.g., NK cells." The authors also list current pre-clinical adjuvant candidates and summarize the "scientific frontier" in TB vaccine research and development, which includes use of new immunomodulators in TB vaccines; combining PAMPs to create "synergy" between different signaling modes; induction of other T cell lineages in addition to CD4 and CD8 T cells; and technologies to "mimick" repeated or booster vaccinations through a single delivery dose, to eliminate required boosting for long-lasting protection.

10. CURRENT ISSUES IN THE ECONOMICS OF VACCINATION AGAINST DENGUE.

Tozan Y.

Expert Rev Vaccines. 2015 Dec 5. [Epub ahead of print]

PMID: 26642099

ABSTRACT

Dengue is a major public health concern in tropical and subtropical areas of the world. The prospects for dengue prevention have recently improved with the results of efficacy trials of a tetravalent dengue vaccine. Although partially effective, once licensed, its introduction can be a public health priority in heavily affected countries because of the perceived public health importance of dengue. This review explores the most immediate economic considerations of introducing a new dengue vaccine and evaluates the published economic analyses of dengue vaccination. Findings indicate that the current economic evidence base is of limited utility to support country-level decisions on dengue vaccine introduction. There are a handful of published cost-effectiveness studies and no country-specific costing studies to project the full resource requirements of dengue vaccine introduction. Country-level analytical expertise in economic analyses, another gap identified, needs to be strengthened to facilitate evidence-based decision-making on dengue vaccine introduction in endemic countries.

WEB: http://dx.doi.org/10.1586/14760584.2016.1129278

IMPACT FACTOR: 4.21

CITED HALF-LIFE: 4.20

UW EDITORIAL COMMENT: Authors stress that while WHO recommends national immunization programs (NIPs) consider *cost-effectiveness*, *affordability*, and *sustainability* in decision-making about vaccination introduction and delivery, for dengue vaccine, there are extremely limited country-level data available to inform such considerations. Authors describe a variety of specific challenges to modeling of public health impact of dengue vaccine to inform *cost-effectiveness*: the complex dynamics of understanding and projecting herd immunity in the dengue context, due to the multiple co-circulating serotypes in many regions, and potential cross-protection; correctly estimating the vaccination threshold needed to eliminate transmission, due to complex interactions between human hosts and mosquito vectors in space and time; consideration of reported serotype-specific efficacy and the potential immunopathogenic effects of vaccine derived immunity and requirement for substantial data to inform questions of immunopathogenic effects of vaccine derived immunity. Regarding *affordability*, authors report that there are no studies that provide country-specific cost estimates of a complete dengue vaccination program (including vaccine and vaccine delivery costs). Based on survey data, authors report policy makers and stake holders consider dengue a high-priority, and thus governments will be under pressure to quickly introduce a vaccine when one is available, even in the face of substantial cost. They report data indicate a potential role of the private sector in dengue vaccine delivery, if the fees set by governments are below willingness-to-pay thresholds. If there is a role for the private sector, methods for regulation and ensuring service quality are not yet well described. Studies to evaluate private-sector demand in low-resource settings have been conducted, but studies have only been conducted in limited settings and aren't yet published. In terms of *sustainability*, authors note that vaccination program financing structures will depend on the country-specific financial commitment to a vaccine strategy and the relative resource commitments of GAVI, other external donors and the national government, and describe the many unknowns currently face regarding financing. Particularly as many countries graduate from GAVI assistance, the vaccine pricing structure and thus direct budget pressure for national governments in unclear.

APPENDIX: PUBMED SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR "supply chain"[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR "Cost effectiveness"[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR "Procurement"[tiab] OR timeliness[tiab] OR systems[tiab])) OR ("vaccine delivery"[tiab])) NOT ("in vitro"[tiab] OR "immune response"[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR "systems biology"[tiab] OR "animal model"[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) AND ("2015/11/15"[PDAT] : "2015/12/14"[PDAT]))

*On December 28, 2015, this search of English language articles published between November 15, 2015 and December 14, 2015 and indexed by the US National Library of Medicine resulted in 241unique manuscripts.