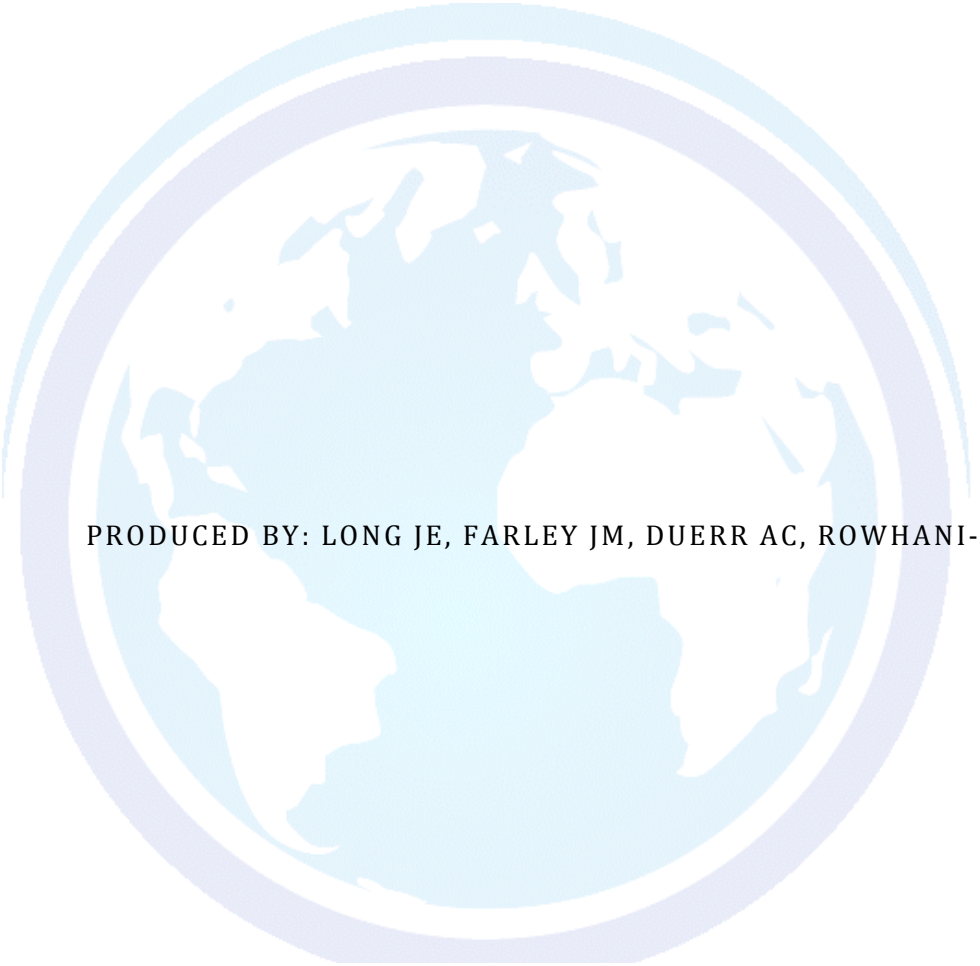
VACCINE DELIVERY RESEARCH DIGEST

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

APRIL 15, 2015



PRODUCED BY: LONG JE, FARLEY JM, DUERR AC, ROWHANI-RAHBAR A

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1. IMMUNOGENICITY AND SAFETY OF MEASLES-MUMPS-RUBELLA VACCINE DELIVERED BY DISPOSABLE-SYRINGE JET INJECTOR IN HEALTHY BRAZILIAN INFANTS: A RANDOMIZED NON-INFERIORITY STUDY.

Martins RM, Curran B, Maia MLS, Ribeiro MGT, Camacho LAB, Freire MS, et al.

Contemp Clin Trials, 2015 Mar; 41:1-8. Epub 2014 Dec 1.

PMID: 25476584

ABSTRACT

This study aimed to determine if immunogenicity to measles-mumps-rubella vaccine delivered to infants via a disposable-syringe jet injector (DSJI) was non-inferior to that administered by needle and syringe (NS). Vaccination safety was evaluated, as were the use, performance, and acceptability of each delivery method. The DSJI was the PharmaJet® 2009 generation-1 device (G1) and the vaccine was measles-mumps-rubella vaccine from Bio-Manguinhos. Five hundred eighty-two healthy Brazilian infants were randomized to receive vaccine via G1 or NS. Seroconversion rates against measles and mumps viruses in the G1 treatment group did not meet non-inferiority criteria when compared with the NS group; however, responses in the G1 group to rubella virus were non-inferior to those of NS vaccinees. Most adverse events were mild or moderate. Crying after injection was more frequent in the NS group, and local skin reactions were more common in the G1 group. Five serious adverse events were judged causally unrelated to treatment and all resolved. Parents/guardians expressed a strong preference for G1 over NS for their children. Vaccinators found the G1 easy to use but noted incomplete vaccine delivery in some cases. Although the G1 has been superseded by an updated device, our results are important for the continued improvement and evaluation of DSJIs, which have the potential to overcome many of the challenges and risks associated with needle-based injections worldwide. Recommendations for future DSJI clinical studies include rigorous training of vaccinators, quantitative measurement of wetness on the skin following injection, and regular monitoring of device and vaccinator performance.

WEB: http://dx.doi.org/10.1016/j.cct.2014.11.014

IMPACT FACTOR: 1.99

CITED HALF-LIFE: 4.00

UW EDITORIAL COMMENT: Table 1 shows the seroconversion rates and geometric mean concentrations for antibodies against measles, mumps, and rubella by treatment group among baseline-negative subjects following an injection of measles–mumps–rubella vaccine (per-protocol [PP] population). Only rubella met the criteria for non-inferiority. Table 2 summarizes adverse effects (observed in at least 4% of vaccinees) among those who received disposable-syringe jet injector and needle and syringe vaccinations.

2. FEASIBILITY OF DELIVERING HPV VACCINE TO GIRLS AGED 10 TO 15 YEARS IN UGANDA.

Mugisha E, LaMontagne DS, Katahoire AR, Murokora D, Kumakech E, Seruyange R, et al.

Afr Health Sci. 2015 Mar;15(1):33-41.

PMID: 25834528

ABSTRACT

BACKGROUND: Cervical cancer is a leading cause of mortality among women in Uganda. The availability of the human papillomavirus (HPV) vaccine presents an opportunity to prevent cervical cancer. The Government of Uganda conducted a demonstration project exploring the feasibility of two delivery strategies.

OBJECTIVE: To explore the feasibility of two HPV vaccine delivery strategies: 1) a stand-alone school-based strategy that selected girls based on their enrolment in grade 5 (known as the "grade-based" strategy); and 2) an age-based strategy that delivered the HPV vaccine based on the girls' age (10-year-olds). This strategy combined the delivery of the vaccine with the distribution of deworming medication and vitamin A through an existing Child Days Plus program.

METHODS: A qualitative study that explored the feasibility of the two delivery strategies from the perspective of health workers, district leaders, and staff of the Uganda National Expanded Programme on Immunization, utilizing in-depth interviews and focus group discussions.

RESULTS: Coverage data showed that more girls (88%) were vaccinated using the grade-based strategy and completed all three doses compared to those (73%) vaccinated using the age-based strategy. Health workers and teachers indicated that deter- mining vaccination eligibility was easier by grade than by age and there were minor disruptions to health services and school programs during vaccinations, as reported by health workers and teachers using the grade-based strategy.

CONCLUSION: HPV vaccine delivery at schools using grade eligibility was more feasible than selecting girls by age. Lessons learned in Uganda could be relevant for countries considering implementing HPV vaccinations.

WEB: http://dx.doi.org/10.4314/ahs.v15i1.5

IMPACT FACTOR: .66

CITED HALF-LIFE: 5.10

UW EDITORIAL COMMENT: This demonstration project explored two delivery platforms for HPV vaccination in Uganda: grade-based and age-based. Providers and teachers reported that a grade-based strategy is more effective, as it is often difficult to determine age, and girls of the same age are frequently scattered across multiple grades and classrooms. This article also highlights the importance of teacher involvement in vaccination logistics and follow-up. Table 2 shows vaccine uptake percentages for both delivery platforms.

3. OVERCOMING CHALLENGES TO SUSTAINABLE IMMUNIZATION FINANCING: EARLY EXPERIENCES FROM GAVI GRADUATING COUNTRIES.

Saxenian H, Hecht R, Kaddar M, Schmitt S, Ryckman T, Cornejo S.

Health Policy Plan. 2015 Feb;30:197-205. Epub 2014 Feb 4.

PMID: 24510369

ABSTRACT

Over the 5-year period ending in 2018, 16 countries with a combined birth cohort of over 6 million infants requiring life-saving immunizations are scheduled to transition (graduate) from outside financial and technical support for a number of their essential vaccines. This support has been provided over the past decade by the GAVI Alliance. Will these 16 countries be able to continue to sustain these vaccination efforts? To address this issue, GAVI and its partners are supporting transition planning, entailing country assessments of readiness to graduate and intensive dialogue with national officials to ensure a smooth transition process. This approach was piloted in Bhutan, Republic of Congo, Georgia, Moldova and Mongolia in 2012. The pilot showed that graduating countries are highly heterogeneous in their capacity to assume responsibility for their immunization programmes. Although all possess certain strengths, each country displayed weaknesses in some of the following areas: budgeting for vaccine purchase, national procurement practices, performance of national regulatory agencies, and technical capacity for vaccine planning and advocacy. The 2012 pilot experience further demonstrated the value of transition planning processes and tools. As a result, GAVI has decided to continue with transition planning in 2013 and beyond. As the graduation process advances, GAVI and graduating countries should continue to contribute to global collective thinking about how developing countries can successfully end their dependence on donor aid and achieve self-sufficiency.

WEB: http://dx.doi.org/10.1093/heapol/czu003

IMPACT FACTOR: 3.00

CITED HALF-LIFE: 7.20

UW EDITORIAL COMMENT: Table 1 provides an overview of the graduating countries. Table 2 shows the expected financial transition from GAVI/country co-financing to exclusive country financing between 2012 and 2018. While the transitioning countries are diverse, financing, procurement, and strengthening regulations and capacity at the country level were identified as the key priorities for a successful transition.

4. AN ECONOMIC MODEL ASSESSING THE VALUE OF MICRONEEDLE PATCH DELIVERY OF THE SEASONAL INFLUENZA VACCINE.

Lee BY, Bartsch SM, Mvundura M, Jarrahian C, Zapf KM, Marinan K, et al.

Vaccine. 2015 Mar 3. pii: S0264-410X(15)00288-1. [Epub ahead of print].

PMID: 25772675

ABSTRACT

BACKGROUND: New vaccine technologies may improve the acceptability, delivery (potentially enabling self- administration), and product efficacy of influenza vaccines. One such technology is the microneedle patch (MNP), a skin delivery technology currently in development. Although MNPs hold promise in preclinical studies, their potential economic and epidemiologic impacts have not yet been evaluated.

METHODS: We utilized a susceptible-exposed-infectious-recovered (SEIR) transmission model linked to an economic influenza outcomes model to assess the economic value of introducing the MNP into the current influenza vaccine market in the United States from the third-party payer and societal perspectives. We also explored the impact of different vaccination settings, self-administration, the MNP price, vaccine efficacy, compliance, and MNP market share. Outcomes included costs, quality-adjusted life years (QALYs), cases, and incremental cost-effectiveness ratios (ICERs; cost/QALY).

RESULTS: With healthcare provider administration, MNP introduction would be cost-effective (ICERs ≤$23,347/QALY) at all MNP price points ($9.50–$30) and market shares (10–60%) assessed, except when compliance and efficacy were assumed to be the same as existing vaccines and the MNP occupied a 10% market share. If MNP self-administration were available (assuming the same efficacy as current technologies), MNP compliance or its efficacy would need to increase by ≥3% in order to be cost- effective (ICERs ≤$1401/QALY), assuming a 2% reduction in administration success with unsupervised self-administration. Under these conditions, MNP introduction would be cost-effective for all price points and market shares assessed.

CONCLUSIONS: When healthcare providers administered the MNP, its introduction would be cost-effective or dominant (i.e., less costly and more effective) in the majority of scenarios assessed. If self-administration were available, MNP introduction would be cost-effective if it increased compliance enough to overcome any decrease in self-administration success or if the MNP presentation afforded an increase in efficacy over current delivery methods for influenza vaccines.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.02.076

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 3 shows the effect of MNP efficacy on mean number of cases averted and mean incremental cost for multiple scenarios. Table 4 shows the impact of MNP compliance on the additional number of vaccinations and vaccination costs, as well as the effect on the number of cases averted and influenza-related costs from the third-party payer and societal perspectives.

5. ENGAGING COMMUNITIES WITH A SIMPLE TOOL TO HELP INCREASE IMMUNIZATION COVERAGE.

Jain M, Taneja G, Amin R, Steinglass R, Favin M.

Glob Health Sci Pract. 2015 Mar 5;3(1):117-125.

PMID: 25745125

ABSTRACT

The level of vaccination coverage in a given community depends on both service factors and the degree to which the public understands and trusts the immunization process. This article describes an approach that aims to raise awareness and boost demand. Developed in India, the "My Village Is My Home" (MVMH) tool, known as Uma Imunizasaun (UI) in Timor-Leste, is a poster-sized material used by volunteers and health workers to record the births and vaccination dates of every infant in a community. Introduction of the tool in 5 districts of India (April 2012 to March 2013) and in 7 initial villages in Timor-Leste (beginning in January 2012) allowed community leaders, volunteers, and health workers to monitor the vaccination status of every young child and guided reminder and motivational visits. In 3 districts of India, we analyzed data on vaccination coverage and timeliness before and during use of the tool; in 2 other districts, analysis was based only on data for new births during use of the tool. In Timor-Leste, we compared UI data from the 3 villages with the most complete data with data for the same villages from the vaccination registers from the previous year. In both countries, we also obtained qualitative data about perceptions of the tool through interviews with health workers and community members. Assessments in both countries found evidence suggesting improved vaccination timeliness and coverage. In India, pilot communities had 80% or higher coverage of identified and eligible children for all vaccines. In comparison, overall coverage in the respective districts during the same time period was much lower, at 49% to 69%. In Timor-Leste, both the number of infants identified and immunized rose substantially with use of the tool compared with the previous year (236 vs. 155, respectively, identified as targets; 185 vs. 147, respectively, received Penta 3). Although data challenges limit firm conclusions, the experiences in both countries suggest that "My Village Is My Home" is a promising tool that has the potential to broaden program coverage by marshalling both community residents and health workers to track individual children's vaccinations. Three states in India have adopted the tool, and Timor-Leste had also planned to scale-up the initiative.

WEB: http://dx.doi.org/10.9745/GHSP-D-14-00180

IMPACT FACTOR: 0.00

CITED HALF-LIFE: 0.00

UW Editorial Comment: This study explores the topic of community participation within vaccination efforts. While poor data precluded drawing firm conclusions from this study, the qualitative feedback from health workers suggested that this tool was easy to use and did not disrupt normal workflow. While privacy issues were not raised in India or Timor-Leste, this may be a concern in other contexts. Figure 1 provides an example of two posters, and the photo on page 120 shows an actual poster with data filled in.

6. ACCELERATING MEASLES ELIMINATION AND STRENGTHENING ROUTINE IMMUNIZATION SERVICES IN GUIZHOU PROVINCE, CHINA, 2003-2009.

Zuo S, Cairns L, Hutin Y, Liang X, Tong Y, Zhu Q, et al.

Vaccine. 2015 Apr 21;33(17):2050-5. Epub 2015 March 11.

PMID: 25769207

ABSTRACT

BACKGROUND: To develop a successful model for accelerating measles elimination in poor areas of China, we initiated a seven-year project in Guizhou, one of the poorest provinces, with reported highest measles incidence of 360 per million population in 2002.

METHODS: Project strategies consisted of strengthening routine immunization services, enforcement of school entry immunization requirements at kindergarten and school, conducting supplemental measles immunization activities (SIAs), and enhancing measles surveillance. We measured coverage of measles containing vaccines (MCV) by administrative reporting and population-based sample surveys, systematic random sampling surveys, and convenience sampling surveys for routine immunization services, school entry immunization, and SIAs respectively. We measured impact using surveillance based measles incidence.

RESULTS: Routine immunization coverage of the 1st dose of MCV (MCV1) increased from 82% to 93%, while 2nd dose of MCV (MCV2) coverage increased from 78% to 91%. Enforcement of school entry immunization requirements led to an increase in MCV2 coverage from 36% on primary school entry in 2004 to 93% in 2009. Province-wide SIAs achieved coverage greater than 90%. The reported annual incidence of measles dropped from 200 to 300 per million in 2003 to 6 per million in 2009, and sustained at 0.9–2.2 per million in 2010–2013.

CONCLUSION: This project found that a package of strategies including periodic SIAs, strengthened routine immunization, and enforcing school entry immunization requirements, was an effective approach toward achieving and sustaining measles elimination in less-developed area of China.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.02.078

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This study addresses the importance of a dynamic package of interventions. The success of this project ultimately led China to scale-up supplementary measles immunization activities to the national level in 2010. Figure 3 shows the number of confirmed measles cases, by month, over the study period. Figure 4 shows measles incidence by age groups over the same period.

7. PROVIDER'S AND USER'S PERSPECTIVE ABOUT IMMUNIZATION COVERAGE AMONG MIGRATORY AND NON-MIGRATORY POPULATION IN SLUMS AND CONSTRUCTION SITES OF CHANDIGARH.

Sharma V, Singh A, Sharma V.

J Urban Health. 2015 Feb 18. [Epub ahead of print].

PMID: 25690459

ABSTRACT

Strengthening routine immunization is a corner stone for countries to achieve the United Nations Millennium Development Goal 4 (MDG 4) which aims to reduce under-five mortality by two-thirds and MDG 5 improving maternal health compared to 1990 estimates by 2015. The poor urban newborns are more vulnerable to many health and nutrition problems compared to the non-poor urban counterparts. Therefore there is a need to strengthen health system to cater the needs of urban poor. Standardized WHO30*7 cluster sampling for slums and convenience sampling for construction sites. In depth interviews were conducted for user's as well as provider's perspective about immunization coverage. Two hundred ten children and 210 mothers were enrolled in slums and 100 were sampled from construction sites. The slum workers are considered as non-migratory groups whereas construction site workers are considered as migratory population. Among children, 23 % were fully immunized, 73 % were partially immunized and 3 % were unimmunized in non-migratory population whereas 3 % were fully immunized, 91 % were partially immunized and 6 % were unimmunized in migratory population. Among mothers, 43 and 39 % were fully immunized, 13 and 15 % partially immunized and 43 and 46 % were unimmunized in non-migratory and migratory population, respectively. The various reasons attributed for low coverage are (a) dissatisfaction of the users with the service delivery and procedural delays (bureaucracy), (b) lack of faith in health workers, (c) insistence upon ID/vaccination card/aadhar card by the health worker before vaccinating child and (d) ignorance of the need of immunization by the people and migration of the population.

WEB: http://dx.doi.org/10.1007/s11524-015-9939-2

IMPACT FACTOR: 1.94

CITED HALF-LIFE: 6.40

UW EDITORIAL COMMENT: This study addresses immunization coverage and attitudes among migrant populations; relatively little research has been done in this area. Table 1 shows immunization coverage among migratory and non-migratory populations, while Table 3 gives reasons that parents and caregivers cited for partial and non-immunization for their children. The suggestions in this article, such as offering condition-free vaccinations and training healthcare workers to address the needs of migrant populations, are applicable to many low-income settings. This study was limited, however, by the different sampling strategies used for the two study populations—WHO cluster sampling for the non-migratory population and convenience sampling for the migratory population.

8. VACCINES, OUR SHARED RESPONSIBILITY.

Pagliusi S, Jain R, Suri RK, DCVMN Executive Committee Group

Vaccine. 2015 Mar 4. pii: S0264-410X(15)00265-0. [Epub ahead of print].

PMID: 25749248

ABSTRACT

The Developing Countries Vaccine Manufacturers' Network (DCVMN) held its fifteenth annual meeting from October 27-29, 2014, New Delhi, India. The DCVMN, together with the co-organizing institution Panacea Biotec, welcomed over 240 delegates representing high-profile governmental and nongovernmental global health organizations from 36 countries. Over the three-day meeting, attendees exchanged information about their efforts to achieve their shared goal of preventing death and disability from known and emerging infectious diseases. Special praise was extended to all stakeholders involved in the success of polio eradication in South East Asia and highlighted challenges in vaccine supply for measles-rubella immunization over the coming decades. Innovative vaccines and vaccine delivery technologies indicated creative solutions for achieving global immunization goals. Discussions were focused on three major themes including regulatory challenges for developing countries that may be overcome with better communication; global collaborations and partnerships for leveraging investments and enable uninterrupted supply of affordable and suitable vaccines; and leading innovation in vaccines difficult to develop, such as dengue, Chikungunya, typhoid-conjugated and EV71, and needle-free technologies that may speed up vaccine delivery. Moving further into the Decade of Vaccines, participants renewed their commitment to shared responsibility toward a world free of vaccine-preventable diseases.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.02.065

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Regulation, collaboration and partnerships, and vaccine innovation were the three themes that emerged in this meeting. WHO representatives discussed barriers to regulatory requirements in low-resource settings, including limited expertise among regulators and manufacturers, limited compliance, and long registration and review processes. Solutions include trainings and workshops, pre-submission meetings with manufacturers, strengthening review and processes, and using existing global networks. Representatives from a number of organizations discussed collaboration and partnerships within the context of reliable vaccine supply chains and financing. Finally, there was a dialogue around how to prioritize vaccine development for neglected tropical disease, and support innovative vaccine delivery technologies, such as needle-free devices and nasal and aerosol vaccines.

9. AN EXTENDED COST-EFFECTIVENESS ANALYSIS OF PUBLICLY FINANCED HPV VACCINATION TO PREVENT CERVICAL CANCER IN CHINA.

Levin CE, Sharma M, Olson Z, Verguet S, Shi JF, Wang SM, et al.

Vaccine. 2015 Mar 12. pii: S0264-410X(15)00241-8. [Epub ahead of print]

PMID: 25770785

ABSTRACT

INTRODUCTION: Cervical cancer screening and existing health insurance schemes in China fall short of reaching women with prevention and treatment services, especially in rural areas where the disease burden is greatest. We conducted an extended cost-effectiveness analysis (ECEA) to evaluate public financing of HPV vaccination to prevent cervical cancer, adding new dimensions to conventional cost-effectiveness analysis through an explicit inclusion of equity and impact on financial risk protection.

METHODS: We synthesized available epidemiological, clinical, and economic data from China using an individual-based Monte Carlo simulation model of cervical cancer to estimate the distribution of deaths averted by income quintile, comparing vaccination plus screening against current practice. We also estimated reductions in cervical cancer incidence, net costs to the government (HPV vaccination costs minus cervical cancer treatment costs averted), and patient cost savings, as well as the incremental government health care costs per death averted.

RESULTS: HPV vaccination is cost-effective across all income groups when the cost is less than US $50 per vaccinated girl. Compared to screening alone, adding preadolescent HPV vaccination followed by cervical cancer screening in adulthood could reduce cancer by 44 percent across all income groups, while providing relatively higher financial protection to the poorest women. The absolute numbers of cervical cancer deaths averted and the financial risk protection from HPV vaccination are highest among women in the lowest quintile; women in the bottom income quintiles received higher benefits than those in the upper wealth quintiles. Patient cost savings represent a large proportion of poor women's average per capita income, reaching 60 percent among women in the bottom income quintile and declining to 15 percent among women in the wealthiest quintile.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.02.052

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 1 summarizes the parameters used in the study model addressing impacts and costs of a publicly financed HPV vaccination policy in China. Table 2 shows the benefits and costs of this policy. These cost-effectiveness results have large implications for policy, as the HPV vaccine is not yet available in China.

10. ROUTINE EPI COVERAGE: SUBDISTRICT INEQUALITIES AND REASONS FOR IMMUNIZATION FAILURE IN A RURAL SETTING IN PAKISTAN.

Khowaja AR, Zaman U, Feroze A, Rizvi A, Zaidi AKM.

Asia Pac J Public Health. 2015 Mar;27(2):1050-9. Epub 2011 Dec 20.

PMID: 22186395

ABSTRACT

High vaccine coverage at the district level may not translate with the same vigor to subdistrict levels; therefore, it is important to understand coverage inequalities. This study underscored vaccine coverage inequalities at subdistrict levels and explored reasons for immunization failure in a high-performing rural district of Pakistan. Parents of children aged 12 to 23 months were randomly selected and interviewed for child's vaccination history through a cross-sectional survey in 2008. Using secondary data (GIS maps and population census), coverage was plotted in respect to sociodemographic and presence of lady health workers. The proportion of children fully immunized was found notably low (75%) than officially reported (85%). Coverage inequalities were observed at subdistrict levels, ranging from 58% to 85% in rural to urban areas and from 60% to 80% in lower to higher income quintiles. Distance to immunization facility, parental unawareness, and wrong ideas about vaccination were statistically significant for immunization failure. Focus of immunization microplans at the subdistrict level are needed to achieve universal immunization goals.

WEB: http://dx.doi.org/10.1177/1010539511430850

IMPACT FACTOR: 1.11

CITED HALF-LIFE: 4.20

UW EDITORIAL COMMENT: This study addresses a gap in the literature surrounding vaccine coverage disparities in subdistrict levels among areas that have generally high coverage. Table 2 provides reasons for immunization failure or partial immunization among the study population.

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 ("2015/2/15"[PDAT] : "2015/03/14"[PDAT]))

*On April 4, 2015, this search of English language articles published between February 15, 2015 and March 14, 2015 and indexed by the US National Library of Medicine resulted in 186 unique manuscripts.