VACCINE DELIVERY RESEARCH DIGEST

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

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1. ISSUES AND CONSIDERATIONS IN THE USE OF SEROLOGIC BIOMARKERS FOR CLASSIFYING VACCINATION HISTORY IN HOUSEHOLD SURVEYS.

MacNeil A, Lee CW, Dietz V.

Vaccine. 2014 Sep 3;32(39):4893-900. Epub 2014 Jul 18

PMID: 25045821

ABSTRACT

Accurate estimates of vaccination coverage are crucial for assessing routine immunization program performance. Community based household surveys are frequently used to assess coverage within a country. In household surveys to assess routine immunization coverage, a child's vaccination history is classified on the basis of observation of the immunization card, parental recall of receipt of vaccination, or both; each of these methods has been shown to commonly be inaccurate. The use of serologic data as a biomarker of vaccination history is a potential additional approach to improve accuracy in classifying vaccination history. However, potential challenges, including the accuracy of serologic methods in classifying vaccination history, varying vaccine types and dosing schedules, and logistical and financial implications must be considered. We provide historic and scientific context for the potential use of serologic data to assess vaccination history and discuss in detail key areas of importance for consideration in the context of using serologic data for classifying vaccination history in household surveys. Further studies are needed to directly evaluate the performance of serologic data compared with use of immunization cards or parental recall for classification of vaccination history in household surveys, as well assess the impact of age at the time of sample collection on serologic titers, the predictive value of serology to identify a fully vaccinated child for multi-dose vaccines, and the cost impact and logistical issues on outcomes associated with different types of biological samples for serologic testing.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.07.005

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 1 summarizes the key issues discussed throughout the paper, assessing the feasibility and impact of using serology to determine vaccination history. Table 4 summarizes the areas of research that need to be further explored before serologic biomarkers could be used in coverage surveys. The conclusion notes that the use of serological biomarkers, considering all the issues discussed, would have to depend on the added value the information would provide in assessing vaccine coverage and EPI performance.

2. A GLOBAL PERSPECTIVE OF VACCINATION OF HEALTHCARE PERSONNEL AGAINST MEASLES: SYSTEMATIC REVIEW.

Fiebelkorn AP, Seward JF, Orenstein WA.

Vaccine. 2014 Aug 27;32(38):4823-39. Epub 2013 Nov 24.

PMID: 24280280

ABSTRACT

Measles transmission has been well documented in healthcare facilities. Healthcare personnel who are unvaccinated and who lack other evidence of measles immunity put themselves and their patients at risk for measles. We conducted a systematic literature review of measles vaccination policies and their implementation in healthcare personnel, measles seroprevalence among healthcare personnel, measles transmission and disease burden in healthcare settings, and impact/costs incurred by healthcare facilities for healthcare-associated measles transmission. Five database searches yielded 135 relevant articles; 47 additional articles were found through cross-referencing. The risk of acquiring measles is estimated to be 2 to 19 times higher for susceptible healthcare personnel than for the general population. Fifty-three articles published worldwide during 1989-2013 reported measles transmission from patients to healthcare personnel; many of the healthcare personnel were unvaccinated or had unknown vaccination status. Eighteen articles published worldwide during 1982-2013 described examples of transmission from healthcare personnel to patients or to other healthcare personnel. Half of European countries have no measles vaccine policies for healthcare personnel. There is no global policy recommendation for the vaccination of healthcare personnel against measles. Even in countries such as the United States or Finland that have national policies, the recommendations are not uniformly implemented in healthcare facilities. Measles serosusceptibility in healthcare personnel varied widely across studies (median 6.5%, range 0-46%) but was consistently higher among younger healthcare personnel. Deficiencies in documentation of two doses of measles vaccination or other evidence of immunity among healthcare personnel presents challenges in responding to measles exposures in healthcare settings. Evaluating and containing exposures and outbreaks in healthcare settings can be disruptive and costly. Establishing policies for measles vaccination for healthcare personnel is an important strategy towards achieving measles elimination and should be a high priority for global policy setting groups, governments, and hospitals.

WEB: http://dx.doi.org/10.1016/j.vaccine.2013.11.005

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 2 illustrates how the African countries represented tend to have low seronegativity due to endemic measles in the population, while the Middle Eastern and Asian countries have the highest rates of seronegativity. The authors note that the prevalence of seronegativity in healthcare workers in a region could be useful when developing vaccination policy.

3. FINDINGS FROM A HEPATITIS B BIRTH DOSE ASSESSMENT IN HEALTH FACILITIES IN THE PHILIPPINES: OPPORTUNITIES TO ENGAGE THE PRIVATE SECTOR.

Patel MK, Capeding RZ, Ducusin JU, de Quiroz Castro M, Garcia LC, Hennessey K.

Vaccine. 2014 Sep 3;32(39):5140-4. Epub 2013 Dec 19.

PMID: 24361121

ABSTRACT

BACKGROUND: Hepatitis B vaccination in the Philippines was introduced in 1992 to reduce the high burden of chronic hepatitis B virus (HBV) infection in the population; in 2007, a birth dose (HepB-BD) was introduced to decrease perinatal HBV transmission. Timely HepB-BD coverage, defined as doses given within 24h of birth, was 40% nationally in 2011. A first step in improving timely HepB-BD coverage is to ensure that all newborns born in health facilities are vaccinated.

METHODS: In order to assess ways of improving the Philippines' HepB-BD program, we evaluated knowledge, attitudes, and practices surrounding HepB-BD administration in health facilities. Teams visited selected government clinics, government hospitals, and private hospitals in regions with low reported HepB-BD coverage and interviewed immunization and maternity staff. HepB-BD coverage was calculated in each facility for a 3-month period in 2011.

RESULTS: Of the 142 health facilities visited, 12 (8%) did not provide HepB-BD; seven were private hospitals and five were government hospitals. Median timely HepB-BD coverage was 90% (IQR 80%-100%) among government clinics, 87% (IQR 50%-97%) among government hospitals, and 50% (IQR 0%-90%) among private hospitals (p=0.02). The private hospitals were least likely to receive supervision (53% vs. 6%-31%, p=0.0005) and to report vaccination data to the national Expanded Programme on Immunization (36% vs. 96%-100%, p<0.0001).

CONCLUSIONS: Private sector hospitals in the Philippines, which deliver 18% of newborns, had the lowest timely HepB-BD coverage. Multiple avenues exist to engage the private sector in hepatitis B prevention including through existing laws, newborn health initiatives, hospital accreditation processes, and raising awareness of the government's free vaccine program.

WEB: http://dx.doi.org/10.1016/j.vaccine.2013.11.097

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 1 highlights how government clinics performed better than government hospitals and private hospitals in vaccine knowledge, practices, and management. Table 2 compares the timely vaccination rates and total vaccination rates across clinic type, again showing that government clinics outperformed the other health facilities. Box 1 at the end of the article provides improvements that could be made to private sector care.

4. MATERNAL AND NEONATAL TETANUS

Thwaites CL, Beeching NJ, Newton CR.

Lancet. 2014 Aug 19. pii: S0140-6736(14)60236-1. [Epub ahead of print]

PMID: 25149223

ABSTRACT

Maternal and neonatal tetanus is still a substantial but preventable cause of mortality in many developing countries. Case fatality from these diseases remains high and treatment is limited by scarcity of resources and effective drug treatments. The Maternal and Neonatal Tetanus Elimination Initiative, launched by WHO and its partners, has made substantial progress in eliminating maternal and neonatal tetanus. Sustained emphasis on improvement of vaccination coverage, birth hygiene, and surveillance, with specific approaches in high-risk areas, has meant that the incidence of the disease continues to fall. Despite this progress, an estimated 58 000 neonates and an unknown number of mothers die every year from tetanus. As of June, 2014, 24 countries are still to eliminate the disease. Maintenance of elimination needs ongoing vaccination programmes and improved public health infrastructure.

WEB: http://dx.doi.org/10.1016/S0140-6736(14)60236-1

IMPACT FACTOR: 39.06

CITED HALF-LIFE: 9.10

UW EDITORIAL COMMENT: This review provides an update to a 2007 Lancet Seminar on maternal and neonatal tetanus. Figure 1 shows the global state of maternal and neonatal tetanus elimination, emphasizing the countries, mainly in Africa, where elimination has not yet been achieved. Figure 2 shows the progress that has been made in the last 20 years, with global deaths due to tetanus rapidly decreasing as tetanus vaccine coverage increases. The article highlights the need for more up to date research, citing only 4 clinic trials of tetanus treatment since the 2007 seminar was completed.

5. ADVANCING THE APPLICATION OF SYSTEMS THINKING IN HEALTH: UNDERSTANDING THE GROWING COMPLEXITY GOVERNING IMMUNIZATION SERVICES IN KERALA, INDIA.

Varghese J, Kutty VR, Paina L, Adam T.

Health Res Policy Syst. 2014 Aug 26;12(1):47.

PMID: 25160531

ABSTRACT

BACKGROUND: Governing immunization services in a way that achieves and maintains desired population coverage levels is complex as it involves interactions of multiple actors and contexts. In one of the Indian states, Kerala, after routine immunization had reached high coverage in the late 1990s, it started to decline in some of the districts. This paper describes an application of complex adaptive systems theory and methods to understand and explain the phenomena underlying unexpected changes in vaccination coverage.

METHODS: We used qualitative methods to explore the factors underlying changes in vaccination coverage in two districts in Kerala, one with high and one with low coverage. Content analysis was guided by features inherent to complex adaptive systems such as phase transitions, feedback, path dependence, and self-organization. Causal loop diagrams were developed to depict the interactions among actors and critical events that influenced the changes in vaccination coverage.

RESULTS: We identified various complex adaptive system phenomena that influenced the change in vaccination coverage levels in the two districts. Phase transition describes how initial acceptability to vaccination is replaced by a resistance in northern Kerala, which involved new actors; actors attempting to regain acceptability and others who countered it created several feedback loops. …

CONCLUSION: As illustrated in this study, a complex adaptive system lens helps to uncover the 'real' drivers for change. This approach assists researchers and decision makers to systematically explore the driving forces and factors in each setting and develop appropriate and timely strategies to address them. The study calls for greater consideration of dynamics of vaccine acceptability while formulating immunization policies and program strategies. The analytical approaches adopted in this study are not only applicable to immunization or Kerala but to all complex interventions, health systems problems, and contexts.

WEB: http://dx.doi.org/10.1186/1478-4505-12-47

IMPACT FACTOR: 1.86

CITED HALF-LIFE: 0.00

UW EDITORIAL COMMENT: Figure 2 shows a causal feedback loop in which vaccination is accepted and coverage is high, compared to Figure 3 which introduces factors that lead to low vaccination coverage, using the polio vaccination campaign as an example.

6. MEASLES AND RUBELLA VACCINATION COVERAGE IN HAITI, 2012: PROGRESS TOWARDS VERIFYING AND CHALLENGES TO MAINTAINING MEASLES AND RUBELLA ELIMINATION.

Tohme RA, François J, Wannemuehler K, Magloire R, Danovaro-Holliday MC, Flannery B, et al.

Trop Med Int Health. 2014 Sep;19(9):1105-15. Epub 2014 Jul 16.

PMID: 25041586

ABSTRACT

OBJECTIVES: We conducted a nationwide survey to assess measles containing vaccine (MCV) coverage among children aged 1-9 years in Haiti and identify factors associated with vaccination before and during the 2012 nationwide supplementary immunisation activities (SIA).

METHODS: Haiti was stratified into five geographic regions (Metropolitan Port-au-Prince, North, Centre, South and West), 40 clusters were randomly selected in each region, and 35 households were selected per cluster.

RESULTS: Among the 7000 visited households, 75.8% had at least one child aged 1-9 years; of these, 5279 (99.5%) households consented to participate in the survey. Of 9883 children enrolled, 91% received MCV before and/or during the SIA; 31% received MR for the first time during the SIA, and 50.7% received two doses of MCV (one before and one during the 2012 SIA). Among the 1685 unvaccinated children during the SIA, the primary reason of non-vaccination was caregivers not being aware of the SIA (31.0%). Children aged 1-4 years had significantly lower MR SIA coverage than those aged 5-9 years (79.5% vs. 84.8%) ($P < 0.0001$). A higher proportion of children living in the West (12.3%) and Centre (11.2%) regions had never been vaccinated than in other regions (4.8-9.1%). Awareness, educational level of the mother and region were significantly associated with MR vaccination during and before the SIA ($P < 0.001$).

CONCLUSIONS: The 2012 SIA successfully increased MR coverage; however, to maintain measles and rubella elimination, coverage needs to be further increased among children aged 1-4 years and in regions with lower coverage.

WEB: http://dx.doi.org/10.1111/tmi.12335

IMPACT FACTOR: 2.94

CITED HALF-LIFE: 6.30

UW EDITORIAL COMMENT: Table 1 displays overall measles and rubella vaccination rates by region as a result of the 2012 nationwide supplemental immunization activities (SIA) campaign, showing that a total of 82.2% of children received a vaccination, compared to 65% reported by 2012 DHS findings prior to the SIA campaign. Table 4 summarizes the factors associated with not being vaccinated. One potential limitation of this study is that it relied on caregiver recall when a vaccination card was not available, which accounted for 30.3% of recorded MCV vaccination before the 2012 SIA.

7. KILLED ORAL CHOLERA VACCINES: HISTORY, DEVELOPMENT AND IMPLEMENTATION CHALLENGES.

Lopez AL, Gonzales ML, Aldaba JG, Nair GB.

Ther Adv Vaccines. 2014 Sep;2(5):123-36.

PMID: 25177492

ABSTRACT

Cholera is still a major global health problem, affecting mainly people living in unsanitary conditions and who are at risk for outbreaks of cholera. During the past decade, outbreaks are increasingly reported from more countries. From the early killed oral cholera vaccine, rapid improvements in vaccine development occurred as a result of a better understanding of the epidemiology of the disease, pathogenesis of cholera infection and immunity. The newer-generation oral killed cholera vaccines have been shown to be safe and effective in field trials conducted in cholera endemic areas. Likewise, they have been shown to be protective when used during outbreak settings. Aside from providing direct protection to vaccinated individuals, recent studies have demonstrated that these killed oral vaccines also confer indirect protection through herd immunity. Although new-generation oral cholera vaccines should not be considered in isolation from other preventive approaches in countries where they are most needed, especially improved water quality and sanitation, these vaccines serve as immediately available public health tools for preventing further morbidity and mortality from cholera. However, despite its availability for more than two decades, use of these vaccines has not been optimized. Although there are limitations of the currently available oral cholera vaccines, recent data show that the vaccines are safe, feasible to use even in difficult circumstances and able to provide protection in various settings. Clear identification of the areas and target population groups who will benefit from the use of the cholera vaccines will be required and strategies to facilitate accessibility and usage of these vaccines in these areas and population groups will need to be developed.

WEB: http://dx.doi.org/10.1177/2051013614537819

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT: This review provides a brief history of the killed oral cholera vaccine and the current state of use. Table 2 outlines the research trials that were used to establish efficacy in the OCVs discussed in the article. Table 3 identifies the challenges and barriers to use for OCVs in developing countries.

8. POTENTIAL FUTURE IMPACT OF A PARTIALLY EFFECTIVE HIV VACCINE IN A SOUTHERN AFRICAN SETTING.

Phillips AN, Cambiano V, Nakagawa F, Ford D, Lundgren JD, Roset-Bahmanyar E, Roman F, et al.

PLoS One. 2014 Sep 10;9(9):e107214. eCollection 2014.

PMID: 25207973

ABSTRACT

BACKGROUND: It is important for public health and within the HIV vaccine development field to understand the potential population level impact of an HIV vaccine of partial efficacy-both in preventing infection and in reducing viral load in vaccinated individuals who become infected-in the context of a realistic future implementation scenario in resource limited settings.

METHODS: An individual level model of HIV transmission, progression and the effect of antiretroviral therapy was used to predict the outcome to 2060 of introduction in 2025 of a partially effective vaccine with various combinations of efficacy characteristics, in the context of continued ART roll-out in southern Africa.

RESULTS: In the context of our base case epidemic (in 2015 HIV prevalence 28% and incidence 1.7 per 100 person years), a vaccine with only 30% preventative efficacy could make a substantial difference in the rate with which HIV incidence declines; the impact on incidence in relative terms is projected to increase over time, with a projected 67% lower HIV incidence in 2060 compared with no vaccine introduction. The projected mean decline in the general adult population death rate 2040-2060 is 11%. …

INTERPRETATION: Introduction of a partially effective preventive HIV vaccine would make a substantial long-term impact on HIV epidemics in southern Africa, in addition to the effects of ART. Development of an HIV vaccine, even of relatively low apparent efficacy at the individual level, remains a critical global public health goal.

WEB: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160197/

IMPACT FACTOR: 3.53

CITED HALF-LIFE: 2.40

UW EDITORIAL COMMENT: This paper considers the effect of vaccines that reduce HIV acquisition but have no effect of HIV viral load, vaccines that have no effect on HIV acquisition but reduce post-infection viral load and vaccines that do both; models are constructed for the South African population at current and projected coverage levels of antiretroviral therapy. Figure 1 shows a summary of the variables that influenced the model. Figure 2 shows the outcomes of vaccination under 8 different scenarios chosen by the investigators. This paper builds upon and updates a large number of modeling studies of partially effective HIV vaccines (for example, PMID:17589368).

9. VALUING VACCINATION.

Bärnighausen T, Bloom DE, Cafiero-Fonseca ET, O'Brien JC.

Proc Natl Acad Sci U S A. 2014 Aug 26;111(34):12313-9. Epub 2014 Aug 18

.PMID: 25136129

ABSTRACT

Vaccination has led to remarkable health gains over the last century. However, large coverage gaps remain, which will require significant financial resources and political will to address. In recent years, a compelling line of inquiry has established the economic benefits of health, at both the individual and aggregate levels. Most existing economic evaluations of particular health interventions fail to account for this new research, leading to potentially sizable undervaluation of those interventions. In line with this new research, we set forth a framework for conceptualizing the full benefits of vaccination, including avoided medical care costs, outcome-related productivity gains, behavior-related productivity gains, community health externalities, community economic externalities, and the value of risk reduction and pure health gains. We also review literature highlighting the magnitude of these sources of benefit for different vaccinations. Finally, we outline the steps that need to be taken to implement a broad-approach economic evaluation and discuss the implications of this work for research, policy, and resource allocation for vaccine development and delivery.

WEB: http://dx.doi.org/10.1073/pnas.1400475111

IMPACT FACTOR: 9.81

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Table 1 summarizes both the narrow definition of vaccine benefits that are usually attributed to vaccines in economic analyses, as well as a broader set of benefits the authors argue should also be considered when conducting an economic evaluation. Table 2 expands on this broad view, summarizing detailed and potentially overlooked benefits of specific vaccines and vaccine programs.

10. COSTS AND COST-EFFECTIVENESS OF 9-VALENT HUMAN PAPILLOMAVIRUS (HPV) VACCINATION IN TWO EAST AFRICAN COUNTRIES.

Kiatpongsan S, Kim JJ.

PLoS One. 2014 Sep 8;9(9):e106836. eCollection 2014..

PMID: 25198104

ABSTRACT

BACKGROUND: Current prophylactic vaccines against human papillomavirus (HPV) target two of the most oncogenic types, HPV-16 and -18, which contribute to roughly 70% of cervical cancers worldwide. Second-generation HPV vaccines include a 9-valent vaccine, which targets five additional oncogenic HPV types (i.e., 31, 33, 45, 52, and 58) that contribute to another 15-30% of cervical cancer cases. The objective of this study was to determine a range of vaccine costs for which the 9-valent vaccine would be cost-effective in comparison to the current vaccines in two less developed countries (i.e., Kenya and Uganda).

METHODS AND FINDINGS: The analysis was performed using a natural history disease simulation model of HPV and cervical cancer. The mathematical model simulates individual women from an early age and tracks health events and resource use as they transition through clinically-relevant health states over their lifetime. Epidemiological data on HPV prevalence and cancer incidence were used to adapt the model to Kenya and Uganda. Health benefit, or effectiveness, from HPV vaccination was measured in terms of life expectancy, and costs were measured in international dollars (I$). The incremental cost of the 9-valent vaccine included the added cost of the vaccine counterbalanced by costs averted from additional cancer cases prevented. All future costs and health benefits were discounted at an annual rate of 3% in the base case analysis. We conducted sensitivity analyses to investigate how infection with multiple HPV types, unidentifiable HPV types in cancer cases, and cross-protection against non-vaccine types could affect the potential cost range of the 9-valent vaccine. …

CONCLUSION: This study provides a threshold range of incremental costs associated with the 9-valent HPV vaccine that would make it a cost-effective intervention in comparison to currently available HPV vaccines in Kenya and Uganda. These prices represent a 71% and 61% increase over the price offered to the GAVI Alliance ($5 per dose) for the currently available 2- and 4-valent vaccines in Kenya and Uganda, respectively. Despite evidence of cost-effectiveness, critical challenges around affordability and feasibility of HPV vaccination and other competing needs in low-resource settings such as Kenya and Uganda remain.

WEB: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4157790/

IMPACT FACTOR: 3.53

CITED HALF-LIFE: 2.40

UW EDITORIAL COMMENT: Tables 1 and 2 demonstrate that the 9-valent vaccine is very cost effective. Some limitations of the model used for this analysis is that it was not designed to capture herd immunity, and it did not test varying levels of vaccine uptake and completion.

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 ("2014/08/15"[PDAT] : "2014/09/14"[PDAT]))

*On September 22, 2014, this search of English language articles published between August 15, 2014 and September 14, 2014 and indexed by the US National Library of Medicine resulted in 174 unique manuscripts.