

VACCINE DELIVERY RESEARCH DIGEST

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

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1. SUPPORTING COUNTRIES IN ESTABLISHING AND STRENGTHENING NITAGS: LESSONS LEARNED FROM 5 YEARS OF THE SIVAC INITIATIVE.

Adjagba A, Senouci K, Biellik R, Batmunkh N, Faye PC, Durupt A et al.

Vaccine. 2015 Jan 29;33(5):588-595. Epub 2014 Dec 26.

PMID: 25545597

ABSTRACT

To empower governments to formulate rational policies without pressure from any group, and to increase the use of evidence-based decision-making to adapt global recommendations on immunization to their local context, the WHO has recommended on multiple occasions that countries should establish National Immunization Technical Advisory Groups (NITAGs). The World Health Assembly (WHA) reinforced those recommendations in 2012 when Member States endorsed the Decade of Vaccines Global Vaccine Action Plan (GVAP). NITAGs are multidisciplinary groups of national experts responsible for providing independent, evidence-informed advice to health authorities on all policy-related issues for all vaccines across all populations. In 2012, according to the WHO-UNICEF Joint Reporting Form, among 57 countries eligible for immunization program financial support from the GAVI Alliance, only 9 reported having a functional NITAG. Since 2008, the Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) Initiative (at the Agence de Médecine Préventive or AMP) in close collaboration with the WHO and other partners has been working to accelerate and systematize the establishment of NITAGs in low- and middle-income countries. In addition to providing direct support to countries to establish advisory groups, the initiative also supports existing NITAGs to strengthen their capacity in the use of evidence-based processes for decision-making aligned with international standards. After 5 years of implementation and based on lessons learned, we recommend that future efforts should target both expanding new NITAGs and strengthening existing NITAGs in individual countries, along three strategic lines: (i) reinforce NITAG institutional integration to promote sustainability and credibility, (ii) build technical capacity within NITAG secretariats and evaluate NITAG performance, and (iii) increase networking and regional collaborations. These should be done through the development and dissemination of tools and guidelines, and information through a variety of adapted mechanisms.

WEB: <http://dx.doi.org/10.1016/j.vaccine.2014.12.026>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This paper provides an overview of the challenges that have been associated with establishing new NITAGs and supporting existing ones, which are enumerated in section 3.1 of the paper. In light of these lessons, recommendations for how to move forward in the support of NITAGs are suggested. These recommendations include: institutional integration into the existing health system to support credibility and sustainability, strengthening the technical capacity and resources available to NITAGs so they have the infrastructure necessary to fulfill their responsibilities, provision of technical support and training for new NITAGs to easily integrate into the position, development of a protocol for official evaluation, and networking with other NITAGs in similar regions.



2. CONTROLLING MEASLES USING SUPPLEMENTAL IMMUNIZATION ACTIVITIES: A MATHEMATICAL MODEL TO INFORM OPTIMAL POLICY.

Verguet S, Johri M, Morris SK, Gauvreau CL, Jha P, Jit M.

Vaccine. 2015 Mar 3;33(10):1291-6. Epub 2014 Dec 23.

PMID: 25541214

ABSTRACT

BACKGROUND: The Measles & Rubella Initiative, a broad consortium of global health agencies, has provided support to measles-burdened countries, focusing on sustaining high coverage of routine immunization of children and supplementing it with a second dose opportunity for measles vaccine through supplemental immunization activities (SIAs). We estimate optimal scheduling of SIAs in countries with the highest measles burden.

METHODS: We develop an age-stratified dynamic compartmental model of measles transmission. We explore the frequency of SIAs in order to achieve measles control in selected countries and two Indian states with high measles burden. Specifically, we compute the maximum allowable time period between two consecutive SIAs to achieve measles control.

RESULTS: Our analysis indicates that a single SIA will not control measles transmission in any of the countries with high measles burden. However, regular SIAs at high coverage levels are a viable strategy to prevent measles outbreaks. The periodicity of SIAs differs between countries and even within a single country, and is determined by population demographics and existing routine immunization coverage.

CONCLUSION: Our analysis can guide country policymakers deciding on the optimal scheduling of SIA campaigns and the best combination of routine and SIA vaccination to control measles.

WEB: <http://dx.doi.org/10.1016/j.vaccine.2014.11.050>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 2 shows the results of computer simulations of measles incidence over 50 years at increasing time intervals between SIAs. The model found that when assuming an $R_0=16$ and 90% coverage, up to 3 years between SIA campaigns is sufficient to control measles, while periods of longer than 3 years will result in increasingly large resurgences. Figure 3 shows how the inter-SIA period required for measles control changes depending on the percent of population receiving routine coverage and the effective coverage of the SIA campaign. One limitation of this study is that it did not account for variations in vaccine effectiveness or intensity in measles infection by regions within countries.



3. USING A SCHOOL-BASED APPROACH TO DELIVER IMMUNIZATION-GLOBAL UPDATE.

Vandelaer J, Olaniran M.

Vaccine. 2015 Jan 29;33(5):719-25. Epub 2014 Dec 15.

PMID: 225523525

ABSTRACT

Vaccines, such as HPV vaccine, are increasingly administered to school-age children, and school-based immunization is an approach that can be used to reach these children. Limited information has thus far been published that provides an overview of the school-based approach worldwide. This article, based on self-reported data from countries, summarizes the extent to which a school-based immunization approach is used around the world, and what antigens are most frequently being administered. Of the 174 countries for which data on school-based immunization were available, ninety five countries reported using a school-based approach for immunization. Children in grades 1 and 6 (or at an age corresponding with these grades) are most often targeted, and tetanus and diphtheria toxoids are the most frequently administered antigens. The impact of the school-based approach may be reduced in areas with low school attendance, unless specific measures are taken to target out-of-school children. Methods to monitor coverage need to be standardized and data on coverage and on the reach of the approach need to be more systematically analyzed and reported.

WEB: <http://dx.doi.org/10.1016/j.vaccine.2014.11.037>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 1 shows a global map of where school-based immunization is implemented. Figure 3 provides information on the number of countries administering each antigen through school-based programs, and how many doses are given. The authors note that this approach was used less often in low income countries, and hypothesized that this is due to low attendance at schools (shown in Table 2) and lack of resources to implement programs.



4. QUADRIVALENT HPV VACCINATION AND RISK OF MULTIPLE SCLEROSIS AND OTHER DEMYELINATING DISEASES OF THE CENTRAL NERVOUS SYSTEM.

Scheller NM, Svanström H, Pasternak B, Arnheim-Dahlström L, Sundström K, Fink K, et al.

JAMA. 2015 Jan 6;313(1):54-61.

PMID: 25562266

ABSTRACT

IMPORTANCE: Case reports have suggested a link between human papillomavirus (HPV) vaccination and development of multiple sclerosis and other demyelinating diseases.

OBJECTIVES: To investigate if quadrivalent HPV (qHPV) vaccination is associated with an increased risk of multiple sclerosis and other demyelinating diseases.

DESIGN, SETTING, AND PARTICIPANTS: Using nationwide registers we identified a cohort of all females aged 10 years to 44 years in Denmark and Sweden, followed up from 2006 to 2013, information on qHPV vaccination, and data on incident diagnoses of multiple sclerosis and other demyelinating diseases. The primary analysis used a cohort design including vaccinated and unvaccinated study participants. A secondary analysis used a self-controlled case-series design including only cases. Both analyses used a 2-year risk period following vaccination. ...

RESULTS: The study included 3,983,824 females, among whom 789,082 received a total of 1,927,581 qHPV vaccine doses. During follow-up, 4322 multiple sclerosis cases and 3300 cases of other demyelinating diseases were identified, of which 73 and 90, respectively, occurred within the risk period. In the cohort analysis, there was no increased risk of multiple sclerosis (crude incidence rates, 6.12 events/100,000 person-years [95% CI, 4.86-7.69] and 21.54 events/100,000 person-years [95% CI, 20.90-22.20] for the vaccinated and unvaccinated periods; adjusted rate ratio, 0.90 [95% CI, 0.70-1.15]) or other demyelinating diseases (crude incidence rates, 7.54 events/100,000 person-years [95% CI, 6.13-9.27] and 16.14 events/100,000 person-years [95% CI, 15.58-16.71]; adjusted rate ratio, 1.00 [95% CI, 0.80-1.26]) associated with qHPV vaccination. Similarly, no increased risk was found using the self-controlled case-series design (multiple sclerosis: incidence ratio, 1.05 [95% CI, 0.79-1.38]; other demyelinating diseases: incidence ratio, 1.14 [95% CI, 0.88-1.47]).

CONCLUSION AND RELEVANCE: In this study with nationwide coverage of 2 Scandinavian countries, qHPV vaccination was not associated with the development of multiple sclerosis or other demyelinating diseases. These findings do not support concerns about a causal relationship between qHPV vaccination and demyelinating diseases.

WEB: <http://dx.doi.org/10.1001/jama.2014.16946>

IMPACT FACTOR: 30.39

CITED HALF-LIFE: 9.40

UW EDITORIAL COMMENT: Table 2 summarizes the results of the analysis, showing that there was no evidence of an increased risk of multiple sclerosis or other demyelinating diseases following qHPV vaccination.



5. HUMAN PAPILLOMA VIRUS VACCINATION: IMPACT AND RECOMMENDATIONS ACROSS THE WORLD.

Bonanni P, Bechini A, Donato R, Capei R, Sacco C, Levi M, et al.

Ther Adv Vaccines. 2015 Jan;3(1):3-12.

PMID: 25553242

ABSTRACT

Human papilloma virus (HPV) vaccination has been implemented in several countries for about the past 7 years, mainly in the adolescent female population, with varying coverage results. Although the impact of immunization on cervical and other HPV-related cancers will be evident in the next decades, a marked decrease of prevalent HPV infections, precancerous lesions and genital warts is already dramatic in the vaccinated cohorts, and also in their sexual partners, thus providing clear evidence of the effectiveness of HPV vaccination, including a herd-protection effect. Today, recommendations and implementation of universal HPV vaccination for adolescent girls are a public-health priority in all countries of the world. Countries with limited resources are presently involved in demonstration projects and, in some cases, have launched national programmes with the help of international agencies and alliances. Extension of immunization offer to young women and to adolescent male subjects has become an important additional opportunity for several countries, with a special focus needed on homosexual men with HIV infection who are at particularly increased risk of HPV-related diseases. Public-health authorities are confronted with the need to enlarge HPV-vaccination offer to all target groups, especially pre-adolescent girls, so that they can be saved from dreadful cancers by reaching high immunization coverage.

WEB: <http://dx.doi.org/10.1177/2051013614557476>

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT: This review article highlights the current evidence of the impact of HPV vaccination on cancer and genital warts. While this vaccine is currently available mostly in high income countries (Figure 1), GAVI negotiated a low-price HPV vaccine in 2013 and approved eleven countries, mainly in Sub-Saharan Africa, to begin receiving support. Additional countries were included in 2014, with a goal of over 20 countries total supported in 2015. Figure 2 displays the countries targeted for GAVI support for HPV vaccines.



6. TWENTY-FIVE YEARS OF THE WHO VACCINES PREQUALIFICATION PROGRAMME (1987-2012): LESSONS LEARNED AND FUTURE PERSPECTIVES.

Dellepiane N, Wood D.

Vaccine. 2015 Jan 1;33(1):52-61. Epub 2013 Dec 2.

PMID: 24300593

ABSTRACT

The World Health Organization (WHO) vaccines prequalification programme was established in 1987. It is a service provided to United Nations procurement agencies to ensure that the vaccines supplied through these agencies are consistently safe and effective under conditions of use in national immunization programmes. This review describes the purpose and aims of the programme, its evolution during 25 years of existence, its added value, and its role in the context of the WHO strategy to ensure the global availability of vaccines of assured quality. The rationale for changes introduced during the implementation of the programme is provided. The paper also discusses the resources involved, both human and financial, its performance, strengths and weaknesses and steps taken to maximize its efficiency. This historical perspective is used to inform proposed future changes to the service.

WEB: <http://dx.doi.org/10.1016/j.vaccine.2013.11.066>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This paper provides a history of how the WHO vaccine prequalification program evolved over time. Table 1 shows how different aspects of the procedure for prequalification developed with new iterations of the procedures. Figure 1 provides information regarding national regulatory authority (NRA) regulatory functions prioritized by the source of the vaccine. Moving forward, the program plans to rely more on national capacity for procurement in individual countries, and therefore increase country responsibility in vaccine regulation and procurement.



7. CONCEPTUAL FRAMEWORKS AND KEY DIMENSIONS TO SUPPORT COVERAGE DECISIONS FOR VACCINES.

González-Lorenzo M, Piatti A, Coppola L, Gramegna M, Demicheli V, Melegaro A, et al.

Vaccine. 2015 Feb 25;33(9):1206-17. Epub 2014 Dec 19.

PMID: 25533328

ABSTRACT

BACKGROUND: Health policy makers often have to face decisions on whether and how to incorporate new vaccines into immunisation plans. This study aims to review and catalogue the relevant current frameworks and taxonomies on vaccines and connect these to the DECIDE Evidence to Decision framework (EtD), a general framework based on evidence-based criteria to guide decision-making on intervention adoption.

METHODS: We systematically searched MEDLINE, EMBASE, Cochrane Library and funding agency websites from 1990 to 2013. We included systematic reviews and primary studies presenting decision-making tools for community vaccine adoption. We qualitatively summarised the reports by purpose, targeted country, principal results, and decisional models. We then extracted and compared the dimensions adopted by vaccine frameworks across studies.

RESULTS: Fourteen studies (five systematic reviews and nine primary studies) were included. Several factors frequently influenced decision-makers' views on vaccines: the most frequent political-context factors considered were Importance of illness or problem, Vaccine characteristics, Resource use, and Feasibility. Others such as Values and preferences and Acceptability were less consistently reported. We did not find evidence on the reasons why a framework for vaccine adoption differs from that for decisions on the adoption of an intervention in general, such as the EtD. There are limited data on how dimensions are explained in practical factors and directly linked to coverage decisions.

CONCLUSIONS: This review summarises conceptual models and taxonomy of a heterogeneous and evolving area in health policy decisions. A shared and comprehensive framework on vaccine coverage remains to be achieved with its single dimensions (epidemiologic, effectiveness, economic, and social) valued differently across studies. A generic tool such as the EtD conceptualises all relevant dimensions, and might reduce inconsistencies.

WEB: <http://dx.doi.org/10.1016/j.vaccine.2014.12.020>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: The purpose of this review was to determine criteria to help guide stakeholders in making health policy decisions on vaccine delivery and coverage. Table 3 shows the main sources the authors used to determine which dimensions are most important in decision making related to vaccine adoption. Table 4 summarizes the results of this review as a conceptual framework containing a list of dimensions, such as burden of disease and feasibility, and the criteria that should be used within each dimension to create an Evidence-to-Decision framework for policy surrounding vaccine coverage.



8. GAPS IN USING BRONCHODILATORS, INHALED CORTICOSTEROIDS AND INFLUENZA VACCINE AMONG 23 HIGH- AND LOW-INCOME SITES.

Gnatiuc L, Buist AS, Kato B, Janson C, Ait-Khaled N, Nielsen R, et al.

P Int J Tuberc Lung Dis. 2015 Jan;19(1):21-30.

PMID: 25519786

ABSTRACT

BACKGROUND: Increasing access to essential respiratory medicines and influenza vaccination has been a priority for over three decades. Their use remains low in low- and middle-income countries (LMICs), where little is known about factors influencing use, or about the use of influenza vaccination for preventing respiratory exacerbations.

METHODS: We estimated rates of regular use of bronchodilators, inhaled corticosteroids and influenza vaccine, and predictors for use among 19 000 adults in 23 high-income countries (HICs) and LMIC sites.

RESULTS: Bronchodilators, inhaled corticosteroids and influenza vaccine were used significantly more in HICs than in LMICs, after adjusting for similar clinical needs. Although they are used more commonly by people with symptomatic or severe respiratory disease, the gap between HICs and LMICs is not explained by the prevalence of chronic obstructive pulmonary disease or doctor-diagnosed asthma. Site-specific factors are likely to influence use differently. The gross national income per capita for the country is a strong predictor for use of these treatments, suggesting that economics influence under-treatment.

CONCLUSIONS: We still need a better understanding of determinants for the low use of essential respiratory medicines and influenza vaccine in low-income settings. Identifying and addressing these more systematically could improve the access and use of effective treatments.

WEB: <http://dx.doi.org/10.5588/ijtld.14.0263>

IMPACT FACTOR: 2.76

CITED HALF-LIFE: 6.00

UW EDITORIAL COMMENT: Figure 3 shows adjusted odds ratios for factors that influence influenza vaccine uptake. The graph shows difference in predictors of vaccine use between HICs and LMICs, with older age and severe symptoms showing a greater uptake in HICs but not LMICs. The authors note that the influenza vaccination rates found by this study were very low in LMICs, possibly due to the heavy emphasis in these countries on childhood vaccination as opposed to adult vaccination. Figure 4 shows how influenza vaccination uptake falls off as gross national income per capita declines.



9. CONQUERING ROTAVIRUS: FROM DISCOVERY TO GLOBAL VACCINE IMPLEMENTATION.

Bines JE, Kirkwood CD.

J Paediatr Child Health. 2015 Jan;51(1):34-9.

PMID: 25586843

ABSTRACT

Rotavirus, the commonest cause of severe dehydrating gastroenteritis world-wide, was discovered less than 50 years ago. It causes about 450 000 deaths per year in children <5 years of age and hospitalises millions more. Rotavirus vaccines have been shown to have a major impact on hospital admissions due to rotavirus gastroenteritis and all-cause gastroenteritis and reduce mortality in developing countries. In Australia, there has been a 71% decrease in rotavirus hospitalisations in children 0-5 years of age. From the discovery of rotavirus as the major causative agent for severe gastroenteritis, through vaccine development and vaccine post-marketing surveillance activities, Australian scientists and clinicians have played a significant role in the global effort to reduce the burden of rotavirus infection.

WEB: <http://dx.doi.org/10.1111/jpc.12815>

IMPACT FACTOR: 1.19

CITED HALF-LIFE: 7.60

UW EDITORIAL COMMENT: This review paper discusses the current burden of rotavirus worldwide, as well as the current methods used to prevent and treat children with rotavirus. Figure 1 shows the burden of disease across the globe, highlighting the high mortality rate due to rotavirus in Africa. In 2009 the WHO recommended vaccinating all children against rotavirus. By May 2014, 61 countries had included it into their National Immunization Programs, 26 of which are GAVI eligible (Figure 4). GAVI has offered assistance in financing of the vaccine to 53 countries, based on cost-effectiveness analyses. Some barriers to the implementation of rotavirus vaccination programs include cost, storage temperature requirements (2-8 degrees Celsius), refrigerated transport, and age limitations for vaccination eligibility, all of which make these vaccines hard to implement in areas with poor health care infrastructure. Table 1 provides a review of the current rotavirus vaccines available and in development, some of which could potentially address the barriers above and lead to expanded access to the vaccine.



10. INNOVATIVE APPLICATIONS OF IMMUNISATION REGISTRATION INFORMATION SYSTEMS: EXAMPLE OF IMPROVED MEASLES CONTROL IN TAIWAN.

Liu D, Wang E, Pan Y, Cheng Sh.

Euro Surveill. 2014 Dec 18;19(50).

PMID: 25597542

ABSTRACT

Immunisation registry systems have been shown to be important for finding pockets of under-immunised individuals and for increasing vaccination coverage. The National Immunisation Information System (NIIS) was established in 2003 in Taiwan. In this perspective, we present the construction of the NIIS and two innovative applications, which were implemented in 2009, which link the NIIS with other databases for better control of measles. Firstly, by linking the NIIS with hospital administrative records, we are able to follow up contacts of measles cases in a timely manner to provide the necessary prophylaxis, such as immunoglobulin or vaccines. Since 2009, there have been no measles outbreaks in hospitals in Taiwan. Secondly, by linking the NIIS with an immigration database, we are able to ensure that young citizens under the age of five years entering Taiwan from abroad become fully vaccinated. Since 2009, the measles-mumps-rubella vaccine coverage rate at two years of age has increased from 96% to 98%. We consider these applications of the NIIS to be effective mechanisms for improving the performance of infectious disease control in Taiwan. The experience gained could provide a valuable example for other countries.

WEB: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20994>

IMPACT FACTOR: 4.66

CITED HALF-LIFE: 3.20

UW EDITORIAL COMMENT: Figure 1 shows the structure of the National Immunization Information System (NIIS) utilized in Taiwan. The database contains a registry of immunizations, vaccine management information, and information on unvaccinated children, coverage rates, and vaccination statistics. Registration in the database occurs within 24 hours of birth in a hospital and contains information on the entire population of Taiwan born after 1995. Figure 2 demonstrates how, in accordance with the timeline of NIIS introduction, confirmed measles cases have plummeted and vaccination coverage of major routine vaccines has greatly increased. In addition to general vaccination tracking, the NIIS system has been used to contain nosocomial measles outbreaks by identifying contacts of the cases and verifying vaccination status. Additionally, NIIS has been linked with immigration records to monitor children coming into Taiwan without measles vaccination. While this system would be difficult to implement in many low income settings, it presents a novel way of increasing vaccination coverage by identifying and targeting those at highest risk for measles infection and transmission.



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 ("2014/12/15"[PDAT] : "2015/01/14"[PDAT]))

*On February 6, 2015, this search of English language articles published between December 15, 2014 and January 14, 2015 and indexed by the US National Library of Medicine resulted in 163 unique manuscripts.

