VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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SEPTEMBER 2023

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1. **Advancements in Marburg (MARV) Virus Vaccine Research With Its Recent Reemergence in Equatorial Guinea and Tanzania: A Scoping Review.**

Mane Manohar M, Lee V, Chinedum Odunukwe E, Singh P, Mpofu B, Oxley Md C.
PubMed ID: 37593293

**ABSTRACT**

Given the recent outbreaks of the Marburg (MARV) virus within the first quarter of the year 2023, interest in the MARV virus has been re-ignited given its shared phylogeny with the dreadful Ebola virus. This relation gives some insight into its virulence, associated morbidities, and mortality rates. The first outbreak of MARV recorded was in Germany, in 1967, of which seven died out of 31 reported cases. Ever since, subsequent cases have been reported all over Africa, a continent replete with failing healthcare systems. This reality impresses a need for a contemporary and concise revision of the MARV virus existing publications especially in the areas of vaccine research. A functional MARV vaccine will serve as a panacea to ailing communities within the African healthcare landscape. The objective of this scoping review is to provide pertinent information relating to MARV vaccine research beginning with an outline of MARV’s pathology and pathogenesis in addition to the related morbidities, existing therapies, established outbreak protocols as well as areas of opportunities.

**WEB:** [10.7759/cureus.42014]

**IMPACT FACTOR:** 1.2

**CITED HALF-LIFE:** 2.4
START COMMENTARY

In this review, Mane Manohar et al. provide updates to advancements in Marburg Virus (MARV) vaccine research, in response to recent outbreaks of MARV cases. The two outbreaks in 2023 reported nine confirmed cases, seven deaths, and 20 suspected deaths in Equatorial Guinea, and eight cases, including five deaths in Tanzania. Table 1 summarizes the major MARV virus disease outbreaks since the first in 1967. Prior MARV outbreaks have demonstrated alarmingly high mortality rates, however diagnosis of MARV disease remains highly uncertain, and no vaccine or specific therapy (aside from supportive care) exists. There are several vaccine candidates for MARV, and Phase 2/3 trials will likely be conducted soon. Though outbreaks are rare, quarantine is the best approach to containment, and in the wake of the COVID-19 pandemic, additional research on a vaccine for this contact-spread virus is pressing.

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2. **Towards elimination of cervical cancer - human papillomavirus (HPV) vaccination and cervical cancer screening in Asian National Cancer Centers Alliance (ANCCA) member countries.**


**ABSTRACT**

About 95% of cervical cancers worldwide are caused by human papillomavirus (HPV). Cervical cancer is preventable and curable if it is detected and treated early. We reviewed the latest national cervical cancer indicators, and barriers to HPV vaccination and cervical cancer screening in 21 Asian National Cancer Centers Alliance (ANCCA) member countries. Half (n = 11, 52%) of the countries have introduced HPV vaccination for girls as part of their national vaccination programme, three countries reported coverage of over 90%. Most ANCCA member countries have cervical cancer screening programmes, only five countries reported screening uptake of over 50%. The barriers to HPV vaccination coverage and cervical cancer screening participation have been identified. Ensuring health service accessibility and affordability for women, addressing sociocultural barriers, and strengthening the healthcare system and continuum of care are essential to increase HPV vaccination and cervical cancer screening coverage.

**WEB:** 10.1016/j.lanwpc.2023.100860

**IMPACT FACTOR:** 7.1

**CITED HALF-LIFE:** 1.4

**START COMMENTARY**

In this systematic review, Ong et al. aggregates the latest and most representative country-specific indicators on cervical cancer incidence and mortality and identify barriers to HPV vaccination and cervical cancer screening within ANCCA member states (Bangladesh, Bhutan, Brunei, Cambodia, China, India, Indonesia, Iran, Japan, Laos, Malaysia, Mongolia, Myanmar, Nepal, Pakistan, Philippines, Singapore, South Korea, Sri Lanka, Thailand and Vietnam). Only three countries report coverage about 90% for girls by age 15 (*Figure 2*). Overall, 76% of ANCCA member countries (n = 16) have implemented a national cervical cancer screening program. However, screening coverage is low among women aged 30 to 49, with five countries (Bhutan, Japan, South Korea, Singapore and Thailand) reporting a coverage of over 50%, *Figure 3*. Barriers reported by respondents included: vaccine supply, lack of awareness, stigma, and costs. Switching to a single-dose HPV vaccination schedule, implementation of national programs, and continued education are recommended approaches to addressing these barriers. This is a very comprehensive review of the
state of HPV vaccination and cervical cancer screening in Asia, and highlights the need for a comprehensive approach improving vaccination and screening coverage. Context-specific approaches to addressing cultural barriers, inequalities, and strengthening of healthcare systems are desperately needed to improve coverage.
3. **State-of-the-Science of human papillomavirus vaccination in women with human immunodeficiency Virus: Summary of a scientific workshop.**


PubMed ID: 37576844

**ABSTRACT**

The burden of cervical cancer is disproportionately distributed globally, with the vast majority of cases occurring in low- and middle-income countries. Women with human immunodeficiency virus (HIV) (WWH) are at increased risk of human papillomavirus (HPV) infection and cervical cancer as compared to HIV-negative individuals. HPV vaccination remains a priority in regions with a high burden of cervical cancer and high HIV prevalence. With HPV vaccines becoming more accessible, optimal use beyond the initial World Health Organization-recommended target population of 9 to 14-year-old girls is an important question. In March 2022, a group of experts in epidemiology, immunology, and vaccinology convened to discuss the state-of-the-science of HPV vaccination in WWH. This report summarizes the proceedings: review of HIV epidemiology and its intersection with cervical cancer burden, immunology, HPV vaccination including reduced-dose schedules and experience with other vaccines in people with HIV (PWH), HPV vaccination strategies and knowledge gaps, and outstanding research questions. Studies of HPV vaccine effectiveness among WWH, including duration of protection, are limited. Until data from ongoing research is available, the current recommendation for WWH remains for a multi-dose HPV vaccination regimen. A focus of the discussion included the potential impact of HIV acquisition following HPV vaccination. With no data currently existing for HPV vaccines and limited information from non-HPV vaccines, this question requires further research. Implementation research on optimal HPV vaccine delivery approaches for WWH and other priority populations is also urgently needed.

**WEB:** 10.1016/j.pmedr.2023.102331

**IMPACT FACTOR:** 2.8

**CITED HALF-LIFE:** 3.7

**START COMMENTARY**

In this report, Schuind *et al.* provide a comprehensive overview of HPV-related science in epidemiology, immunology, and vaccinology among women with HIV (WWH). Though regions with high burden of cervical cancer are already prioritized for HPV vaccination, data specific to level and duration of vaccine protection among WWH, as well as immunologic response to post-vaccine acquisition of HIV (*Figure 1*) are major gaps in the science. *Table 1* provides the current list of ongoing HPV vaccination trials among girls and women (for trials registered with ClinicalTrials.gov or
the WHO Trials Registry databases). This report underscores the need for additional research to answer remaining questions about vaccine effectiveness, duration of protection, and proper dosing schedules among immunocompromised recipients of HPV vaccines, both for the benefit of HPV vaccine delivery, and to inform non-HPV-related vaccinology and immunology.

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PubMed ID: 37563051

**ABSTRACT**

**INTRODUCTION:** Timeliness of routine vaccination shapes childhood infection risk and thus is an important public health metric. Estimates of indicators of the timeliness of vaccination are usually produced at the national or regional level, which may conceal epidemiologically relevant local heterogeneities and make it difficult to identify pockets of vulnerabilities that could benefit from targeted interventions. Here, we demonstrate the utility of geospatial modelling techniques in generating high-resolution maps of the prevalence of delayed childhood vaccination in The Gambia. To guide local immunisation policy and prioritize key interventions, we also identified the districts with a combination of high estimated prevalence and a significant population of affected infants.

**METHODS:** We used the birth dose of the hepatitis-B vaccine (HepB0), third-dose of the pentavalent vaccine (PENTA3), and the first dose of measles-containing vaccine (MCV1) as examples to map delayed vaccination nationally at a resolution of 1 × 1-km² pixel. We utilized cluster-level childhood vaccination data from The Gambia 2019-20 Demographic and Health Survey. We adopted a fully Bayesian geostatistical model incorporating publicly available geospatial covariates to aid predictive accuracy. The model was implemented using the integrated nested Laplace approximation-stochastic partial differential equation (INLA-SPDE) approach.

**RESULTS:** We found significant subnational heterogeneity in delayed HepB0, PENTA3 and MCV1 vaccinations. Specific districts in the central and eastern regions of The Gambia consistently exhibited the highest prevalence of delayed vaccination, while the coastal districts showed a lower prevalence for all three vaccines. We also found that districts in the eastern, central, as well as in coastal parts of The Gambia had a combination of high estimated prevalence of delayed HepB0, PENTA3 and MCV1 and a significant population of affected infants.

**CONCLUSIONS:** Our approach provides decision-makers with a valuable tool to better understand local patterns of untimely childhood vaccination and identify districts where strengthening vaccine delivery systems could have the greatest impact.

**WEB:** [10.1016/j.vaccine.2023.08.004](https://doi.org/10.1016/j.vaccine.2023.08.004)
**IMPACT FACTOR:** 5.5
**CITED HALF-LIFE:** 7.2
START COMMENTARY

Wariri et al. utilize geospatial modelling to evaluate The Gambia’s routine childhood vaccination program. Though the immunization program in The Gambia has been very successful, reporting vaccine coverage at or above 90% for most childhood vaccinations, this analysis identifies geographic areas with delayed childhood vaccinations. Authors used data on HepB0, PENTA3, and MCV1 to identify these areas with delayed vaccination at a district-level; maps of the spatial distribution of delayed HepB0, PENTA3, and MCV1 are shown in Figure 6. This novel approach to evaluating immunization programs would be well-suited for application across other contexts to identify weak spots and guide program planning.

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5. **Infant mortality rates and pneumococcal vaccines: a time-series trend analysis in 194 countries, 1950-2020.**
Sanchez C, Rivera-Lozada O, Lozada-Urbano M, Best P.
*BMJ Glob Health.* 2023 Aug 09;8(8).
PubMed ID: 37550006

**ABSTRACT**

Pneumonia due to Streptococcus pneumoniae (pneumococcus) is a major cause of mortality in infants (children under 1 year of age), and pneumococcal conjugate vaccines (PCVs), delivered during the first year of life, are available since the year 2000. Given those two premises, the conclusion follows logically that favourable impact reported for PCVs in preventing pneumococcal disease should be reflected in the infant mortality rates (IMRs) from all causes. Using publicly available datasets, country-level IMR estimates from UNICEF and PCV introduction status from WHO, country-specific time series analysed the temporal relationship between annual IMRs and the introduction of PCVs, providing a unique context into the long-term secular trends of IMRs in countries that included and countries that did not include PCVs in their national immunisation programmes. PCV status was available for 194 countries during the period 1950-2020: 150 (77.3%) of these countries achieved nationwide PCV coverage at some point after the year 2000, 13 (6.7%) achieved only partial or temporary PCV coverage, and 31 (15.9%) never introduced PCVs to their population. One hundred and thirty-nine (92.7%) of countries that reported a decreasing (negative) trend in IMR, also reported a strong correlation with decreasing maternal mortality rates (MMRs), suggesting an improvement in overall child/mother healthcare. Conversely, all but one of the countries that never introduced PCVs in their national immunisation programme also reported a decreasing trend in IMR that strongly correlates with MMRs. IMRs have been decreasing for decades all over the world, but this latest decrease may not be related to PCVs.

**WEB:** [10.1136/bmjgh-2023-012752]

**IMPACT FACTOR:** 8.1

**CITED HALF-LIFE:** 2.7

**START COMMENTARY**

Authors analyze trends in infant mortality rates (IMRs) before and after the introduction of pneumococcal conjugate vaccines (PCVs) and conclude that trends of decreased IMRs may not be related to the introduction of PCVs. Figure 2 shows trends in IMRs for countries where PCVs are administered routinely, and figure 3 shows trends in IMRs for countries where PCVs were never introduced. The explanations suggested are that pneumococcus is no longer an important a factor in infant mortality, non-vaccine serotypes are more likely to be associated with infant mortality, or PCVs
are effective in areas with better population health but not in others where the population is at higher risk of negative health outcomes regardless of PCV status. Authors suggest that expanded testing and surveillance is needed to accurately identify mortality due to specific pneumococcal serotypes and determine if current PCVs match locally circulating serotypes.

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6. **Association of vaccine stockout with immunisation coverage in low-income and middle-income countries: a retrospective cohort study.**

Lee D, Lavayen M, Kim T, Legins K, Seidel M.


PubMed ID: 37524556

**ABSTRACT**

**OBJECTIVES:** This study investigated the association between vaccine stockout and immunisation coverage, and infant/under 5 mortality rates.

**DESIGN:** A retrospective cohort study.

**SETTING:** Low-income and middle-income countries.

**PARTICIPANTS:** A cohort of 131 low-income and middle-income countries from 2004 to 2019.

**PRIMARY OUTCOME MEASURES:** Main outcomes included immunisation coverages of (1) diphtheria-tetanus-pertussis containing vaccine (DTP), (2) measles containing vaccine (MCV), (3) BCG and (4) oral polio vaccine (OPV). We also included infant and under 5 mortality rates as secondary outcomes.

**RESULTS:** The countries that experienced national-level stockouts of DTP and MCV had 3.7 and 4 percentage points lower coverage rates of DTP3 and MCV1, respectively, compared with the countries without the stockout events (p<0.01). Moreover, the statistically significant differences in the immunisation coverage rates across the countries with and without the stockout events are 2.4 percentage points and 2.6 percentage points for BCG and OPV, respectively (p<0.01).

**CONCLUSION:** Our findings show that the incidence of vaccine stockout events is associated with the decreased immunisation coverages for children in low-income and middle-income countries. However, we did not observe a statistically significant association between the increasing frequency of vaccine stockout and infant and under 5 mortality rates.

**WEB:** [10.1136/bmjopen-2023-072364](https://doi.org/10.1136/bmjopen-2023-072364)

**IMPACT FACTOR:** 2.9

**CITED HALF-LIFE:** 4.0

**START COMMENTARY**

A key finding in this study is that low-income countries experienced fewer vaccine stockouts compared to upper- and lower-middle-income countries, which the authors attributed to the
effectiveness of GAVI supply chain strengthening programs. Authors found that 70% of stockouts occurred in the AFR and AMR regions and noted that causes of stockouts were primarily domestic factors such as inadequate forecasting, stock management practices, and government funding delays. The authors suggested that the occurrence of stockouts in these regions could be mitigated by offering technical and skills-based support to strengthen supply chain management skills.

PubMed ID: 37515061

ABSTRACT

Barriers to successful implementation of the human papillomavirus vaccination exist. However, there is limited evidence on implementation strategies in sub-Saharan Africa (SSA). Therefore, this scoping review aimed to identify implementation strategies used in SSA to increase HPV vaccination uptake for adolescent girls. This scoping review was guided by Joanna Briggs Institute guidelines for scoping reviews and an a priori protocol and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis for Scoping Reviews (PRISMA-ScR). We searched PubMed, EMBASE, CINAHL, Scopus, Google Scholar, and gray literature. Two independent reviewers screened article titles and abstracts for possible inclusion, reviewed the full text, and extracted data from eligible articles using a structured data charting table. We identified strategies as specified in the Expert Recommendation for Implementing Change (ERIC) and reported their importance and feasibility. We retrieved 246 articles, included 28 of these, and identified 63 of the 73 ERIC implementation strategies with 667 individual uses, most of which were highly important and feasible. The most frequently used discrete strategies included the following: Build a coalition and change service sites 86% (24/28), distribute educational materials and conduct educational meetings 82% (23/28), develop educational materials, use mass media, involve patients/relatives and families, promote network weaving and stage implementation scale up 79% (22/28), as well as access new funding, promote adaptability, and tailor strategies 75% (21/28). This scoping review shows that implementation strategies of high feasibility and importance were frequently used, suggesting that some strategies may be cross-cutting, but should be contextualized when planned for use in any region.

WEB: 10.3390/vaccines11071246
IMPACT FACTOR: 7.8
CITED HALF-LIFE: 1.6

START COMMENTARY

In this systematic review, Lubeya et al. assess implementation strategies used in SSA from 2011 to 2021 to increase HPV vaccination and reported research gaps using the Expert Recommendation for Implementing Change (ERIC). Overall, 50% of reported vaccine funding across all 28 studies was from GAVI, and 26/28 included studies had international financial support to deliver vaccines.
free of charge to eligible girls. Overall, 63 of the 73 ERIC implementation strategies were used across the studies (n=28), with 10 never mentioned. Table 2 summarizes strategies used. All strategies within cluster 1 (use evaluative iterative and strategies), cluster 2 (provide interactive assistance), cluster 5 (Train and educate stakeholders), and cluster 7 (Engage consumers) were used at least once across the 28 studies. Strategies were also evaluated for importance and feasibility. The reported strategies of high importance and feasibility categories were most commonly found within cluster 1 (use evaluative and iterative strategies), cluster 4 (develop stakeholder interrelationships) and cluster 5 (train and educate stakeholders) and are likely to be applicable across additional contexts in SSA. Improved reporting of implementation strategies and lessons learned across national vaccination program rollout is necessary to increase HPV vaccine uptake in SSA.

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PubMed ID: 37515057

ABSTRACT
The COVID-19 pandemic has focused attention on the use of immunization information systems (IIS) to record and consolidate immunization records from a variety of sources to generate comprehensive patient immunization histories. Operationalization of IIS in the United States is decentralized, and as such, there are over 60 different IIS with wide variations in enabling policies and functionalities. As such, the policies that inform the development and operation of those sub-national IIS exist at the state and sometimes city levels. A targeted literature review was conducted to identify IIS policies and functionalities and assess their impact. The authors identified articles published from 2012 to 2022 that discussed or evaluated IIS policies and functionalities and screened titles, abstracts, and full text for inclusion. When selected for inclusion, authors extracted IIS policy/functional components identified in the targeted literature review, the most commonly evaluated were provider-based patient reminder/recall, IIS-based centralized reminder/recall, and clinical decision support. Patient reminder/recall had the most published research and was associated with increased vaccination rates and vaccine knowledge. Despite the lack of quantitative evidence, there is a consensus that immunization data interoperability is critical to supporting IIS data quality, access, and exchange. Significant evidence gaps remain about the effectiveness of IIS functionalities and policies. Future research should evaluate the impact of policies and functionalities to guide improved utilization of IIS, increase national interoperability and standardization, and ultimately improve vaccination coverage and population health.

WEB: 10.3390/vaccines11071242
IMPACT FACTOR: 7.8
CITED HALF-LIFE: 1.6
START COMMENTARY

This review by Donckels, et al. provides insight into the heterogeneity and effectiveness of policies within immunization information systems (IIS). Of the 39 articles included in this analysis, all but ten were from US, and more than half focused solely on pediatric populations, leaving gaps in understanding of the impact of the policy and functional components on different populations. Only 38% of the findings included a statistical evaluation of the impact of a given policy/functional component. Further research on all identified themes is warranted. Table 3 is a summary of the policy and functional components findings in the literature and includes author definitions of the components evaluated.

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Ensuring vaccine safety: Case studies of falsified influenza vaccines detected in Brazil.
Vaccine X. 2023 Jul 18;14:100343.
PubMed ID: 37457323

ABSTRACT

Falsifications related to health technologies-including vaccines—are a growing threat to patient safety and health systems on a global scale and can cause serious harm to the population (especially vulnerable groups). In Brazil, the manufacturing and spread of counterfeit medicines are prevented through joint actions between different government agencies. In this study, we analyzed three cases of influenza vaccines suspected of counterfeiting. The samples were seized by officials and received by the National Institute for Quality Control in Health (INCQS), the national quality control reference laboratory of the Ministry of Health of Brazil, in 2010, 2017, and 2020. We report the results of our analytical investigations and emphasize the importance of strengthening the partnerships between various national agencies. The seized samples were visually inspected, and their information was compared with that of genuine vaccines (as recorded in the INCQS database). The specific analytical tests were based on quality control tests for biological products. Our results confirmed that all seized samples were falsified. We emphasize the importance of fostering international and intranational collaborations between various national agencies (such as drug regulatory authorities, official laboratories, customs departments, police forces, and civil society). As demonstrated here, such collaborative actions are essential for combating the release of falsified medical products, safeguarding public health, and strengthening health systems.

WEB: 10.1016/j.jvacx.2023.100343
IMPACT FACTOR: 3.8
CITED HALF-LIFE: 1.9

START COMMENTARY

In this article, authors share the process used to identify counterfeit vaccines in Brazil, which is done through visual inspection, database crosschecking, and laboratory analysis. The authors included pictures of packaging irregularities and medication appearance, and detailed their process to crosscheck information with vaccine databases. They include information about the laboratory tests performed on samples, and how they prioritize those based on the amount of available material, beginning with the use of the single radial immunodiffusion assay to measure the concentration of hemagglutinin antigen and compare to a reference standard provided by the National Institute for Biological Standards and Control, as identifying the active ingredient in the suspect samples was
highest priority. The importance of having a clear process to identify suspect vaccines and the ability and capacity to quickly identify and destroy fake vaccinations is emphasized, as is encouraging cooperation between vaccine manufacturers, local, national, and global public health organizations to facilitate the process.

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10. Malawi vaccination drive: An integrated immunization campaign against typhoid, measles, rubella, and polio; health benefits and potential challenges.
Hum Vaccin Immunother. 2023 Jul 12;19(2):2233397.
PubMed ID: 37431661

ABSTRACT
Vaccination stands as one of the most important scientific discoveries and public health achievements in the fight against diseases. For over a century, millions of early childhood deaths have been averted through routine immunizations. However, to prevent the morbidity and mortality associated with vaccine-preventable diseases and their complications and optimize the control of vaccine-preventable diseases in communities, high uptake rates must be achieved. Mass immunization campaigns (MICs) have globally been used to introduce new vaccines for major infectious diseases and improve coverage of routine vaccines through catch-up campaigns. Malawi recently undertook such a campaign to introduce a highly efficacious typhoid conjugate vaccine and provides a catch-up to measles, rubella, and polio. Such campaigns are associated with multiple benefits. However, the MICs are associated with multiple challenges to be successfully administered. In this review, we highlight recent MIC, vaccine coverage, and potential challenges and benefits and offer recommendation for future preventive campaigns.

WEB: 10.1080/21645515.2023.2233397
IMPACT FACTOR: 4.8
CITED HALF-LIFE: 3.9

START COMMENTARY
This article highlights the use of mass immunization campaigns (MICs) within Malawi, a country which has experienced a drop in the number of fully immunized children from 81% in 2010 to 76% in 2016 and where emerging drug-resistant typhoid has made the introduction of a typhoid conjugate vaccine (TCV) a priority. With more than 650,000 people displaced due to natural disaster and disruptions to routine medical care due to the COVID pandemic, the MIC will offer the opportunity for catch-up of routine vaccines and implementation of TCV, and targets more than 9 million children. The only challenge noted was vaccine hesitancy due to COVID-19 conspiracy theories. Future priorities include research on the impact of vaccine hesitancy on the effectiveness of MICs.
Appendix

The literature search for the September 2023 Vaccine Delivery Research Digest was conducted on September 3, 2023. We searched English language articles indexed by the US National Library of Medicine and published between July 15, 2023 and August 14, 2023. The search resulted in 532 items.

SEARCH TERMS