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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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List of Articles

1 Ethnic disparities in immunisation: analyses of zero-dose prevalence in 64 countries.

{Abstract & START Commentary} {Full Article}

- A study assessing the in-country ethnic disparities across 64 low- and middle-income countries.

2 Setting-up an Ebola vaccine trial in a remote area of the Democratic Republic of the Congo: Challenges, mitigations, and lessons learned.

{Abstract & START Commentary} {Full Article}

- A study describing the set up and implementation of a vaccine trial in a low resource setting.

3 Challenges and lessons learned during the planning and early implementation of the RTS,S/AS01E malaria vaccine in three regions of Ghana: a qualitative study.

{Abstract & START Commentary} {Full Article}

- A qualitative case study examining the first implementation of the RTS,S/AS01$_E$ malaria vaccine in Ghana.

4 Conducting public health surveillance in areas of armed conflict and restricted population access: a qualitative case study of polio surveillance in conflict-affected areas of Borno State, Nigeria.

{Abstract & START Commentary} {Full Article}

- A qualitative case study assessing the challenges of conducting polio surveillance during armed conflict.

5 It Takes Two to Tango: Combining Conventional Culture With Molecular Diagnostics Enhances Accuracy of *Streptococcus pneumoniae* Detection and Pneumococcal Serogroup/Serotype Determination in Carriage.

{Abstract & START Commentary} {Full Article}

- A study proposing a procedure to increase the accuracy of molecular detection of pneumococci.

6 Public Health Actions to Control Measles Among Afghan Evacuees During Operation Allies Welcome - United States, September-November 2021.

{Abstract & START Commentary} {Full Article}

- A study describing describe the public health actions taken to control measles among Afghan evacuees in August to September 2021.

7 Factors Affecting Human Papillomavirus Vaccination in Men: Systematic Review.
{Abstract & START Commentary} {Full Article}

- A systematic review identifying factors affecting HPV vaccination among men.

8 Health effects of utilising hospital contacts to provide measles vaccination to children 9-59 months-a randomised controlled trial in Guinea-Bissau.
{Abstract & START Commentary} {Full Article}

- A randomized controlled trial protocol describing the methods for a study randomizing children to receive measles vaccine at the time of discharge from a hospital.

9 Estimating the effect of vaccination on antimicrobial-resistant typhoid fever in 73 countries supported by Gavi: a mathematical modelling study.
{Abstract & START Commentary} {Full Article}

- A modelling study assessing the impact of vaccination on typhoid fever cases and antimicrobial resistant cases.

10 Herd Immunity Effects in Cost-Effectiveness Analyses among Low- and Middle-Income Countries.
{Abstract & START Commentary} {Full Article}

- A study investigating the impact of including herd immunity in cost-effectiveness evaluations.

Appendix

Details of Articles

1. Ethnic disparities in immunisation: analyses of zero-dose prevalence in 64 countries.

Cata-Preta B, Santos T, Wendt A, Hogan D, Mengistu T, Barros A, et al.

BMJ Glob Health. 2022 May 19;7(5).
PubMed ID: 35577393

ABSTRACT

BACKGROUND: The Sustainable Development Goals (SDGs) recommend stratification of health indicators by ethnic group, yet there are few studies that have assessed if there are ethnic disparities in childhood immunisation in low-income and middle-income countries (LMICs).

METHODS: We identified 64 LMICs with standardised national surveys carried out since 2010, which provided information on ethnicity or a proxy variable and on vaccine coverage; 339 ethnic groups were identified after excluding those with fewer than 50 children in the sample and countries with a single ethnic group. Lack of vaccination with diphtheria-pertussis-tetanus vaccine-a proxy for no access to routine vaccination or 'zero-dose' status-was the outcome of interest. Differences among ethnic groups were assessed using a 2 test for heterogeneity. Additional analyses controlled for household wealth, maternal education and urban-rural residence.

FINDINGS: The median gap between the highest and lowest zero-dose prevalence ethnic groups in all countries was equal to 10 percentage points (pp) (IQR 4-22), and the median ratio was 3.3 (IQR 1.8-6.7). In 35 of the 64 countries, there was significant heterogeneity in zero-dose prevalence among the ethnic groups. In most countries, adjustment for wealth, education and residence made little difference to the ethnic gaps, but in four countries (Angola, Benin, Nigeria and Philippines), the high-low ethnic gap decreased by over 15 pp after adjustment. Children belonging to a majority group had 29% lower prevalence of zero-dose compared with the rest of the sample.

INTERPRETATION: Statistically significant ethnic disparities in child immunisation were present in over half of the countries studied. Such inequalities have been seldom described in the published literature. Regular analyses of ethnic disparities are essential for monitoring trends, targeting resources and assessing the impact of health interventions to ensure zero-dose children are not left behind in the SDG era.

WEB: 10.1136/bmjgh-2022-008833
IMPACT FACTOR: 4.280
CITED HALF-LIFE: 1.9

START COMMENTARY

In this study, Cata-Preta *et al.* studied the median gap between the highest and lowest zero-dose prevalence ethnic groups in 64 low- and middle-income countries (LMICs). This study is important, as ethnic disparities are common within countries and such inequity is essential to understand to target immunization efforts. Data for this study was obtained from the survey database of the International Center for Equity in health, which included all publicly available datasets from nationally representative Demographic and Health Surveys (DHS). Overall, 64 countries had information on ethnicity and immunization and were included in the analysis. The immunization indicator was no diphtheria-pertussis-tetanus (DPT) vaccination prevalence. Ethnicity was defined as the self-reported ethnicity in 45 surveys, language spoken at home in 17 surveys, skin color in one survey (Cuba), and caste in one survey (India).

A total of 64 countries with 339 ethnic groups and 168,846 children were included in the analysis. Within countries, the number of ethnic groups ranged from 2 to 20. In *Table 1* presents the prevalence of no-DTP overall as well as by the largest ethnic group and in the lowest- and highest prevalence ethnic group. Overall, the median difference between the highest and lowest group was 10 percentage points (PP) (interquartile range [IQR]: 4-22); 35 countries had statistically significant ethnic differences. A strength of this analysis is that the authors considered the impact of other variables known to affect immunization coverage (i.e., wealth, education, urbanicity). Adjusting for household wealth, maternal education, or urban-rural differences did not affect the no-DTP prevalence gap in most countries. About 26 studies remained significant in adjusted analyses. Cata-Preta *et al.* also assessed trends in Gavi eligible countries (40 of the included 64) and found that 72.5% had significant ethnic gaps in no-DTP prevalence. This study demonstrates substantial variability in zero-doses of DTP across ethnic groups, underscoring the need for additional studies to understand unequal access to immunization and additional targeted immunization implementation efforts to reach each child, regardless of ethnicity.

Return to List of Articles

2. Setting-up an Ebola vaccine trial in a remote area of the Democratic Republic of the Congo: Challenges, mitigations, and lessons learned.

Zola Matuvanga T, Larivi re Y, Lemey G, De Bie J, Milolo S, Meta R, et al.

Vaccine. 2022 May 26;40(25):3470-3480.
PubMed ID: 35550847

ABSTRACT

Since the largest Ebola outbreak in West Africa (2013-2016) highlighted the potential threat of the Ebola virus to the world, several vaccines have been under development by different pharmaceutical companies. To obtain vaccine licensure, vaccine trials assessing the safety, immunogenicity and efficacy of new vaccines among different populations (e.g. different in age, gender, race, and ethnicity) play a crucial role. However, while this deadly disease mainly affects Central and West Africa, clinical trial regulations are becoming increasingly complex and consequently more expensive, influencing the affected low- and middle-income countries (LMICs) in performing high quality clinical trials. Consequently, the completion of such trials in LMICs takes more time and vaccines and drugs take longer to be licensed. To overcome some of the obstacles faced, the EBOVAC3 consortium, funded by the European Union's Innovative Medicines Initiative and the Coalition for Epidemic Preparedness Innovations, enabled high quality vaccine trials in Central and West Africa through extensive North-South collaborations. In this article, the encountered challenges, mitigations, recommendations and lessons learned from setting-up an Ebola vaccine trial in a remote area of the Democratic Republic of Congo are presented. These challenges are grouped into eight categories: (1) Regulatory, political and ethical, (2) Trial documents, (3) International collaborations, (4) Local trial staff, (5) Community engagement and sensitization, (6) Logistics, (7) Remoteness and climate conditions, (8) Financial. By sharing the encountered challenges, implemented mitigations and lessons learned for each of these categories, we hope to prepare and inform other researchers aspiring a well-functioning clinical trial unit in similar remote settings in LMICs. ClinicalTrials.gov identifier: NCT04186000.

WEB: 10.1016/j.vaccine.2022.04.094
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

In this paper, Matuvanga *et al.* describe the challenges, mitigations, recommendations, and lessons learned from setting up an Ebola vaccine trial in a remote area of the Democratic Republic of Congo (DRC). This article makes an important contribution, as it can shed light on important considerations for other researchers aiming to set up well-functioning clinical trial units in remote settings in sub-

Saharan Africa. This is critically important, as most clinical trials take place in high income settings, despite the high morbidity and mortality associated with many conditions that are being studied in these areas. For example, of clinical trials targeting Ebola, about 48% are in Africa and 10% are in DRC, despite nearly all cases historically being in these areas.

Table 1 presents challenges encountered by the researchers while setting up the trial, how challenges were mitigated, and lessons learned. Challenges were grouped into seven categories: 1) regulatory, political, and ethical; 2) trial documents; 3) international collaborations; 4) local trial staff; 5) community engagement and sensitization; 6) logistics; and 7) remoteness and climate conditions. One example in the first category was the regulatory capacity of the national regulatory authority and ethics committee being impacted by limited resources (e.g., human capacity, communication). This challenge was mitigated by good contacts with a focal person at the central level to ensure timely follow-up and approval. An important lesson learned was that regular contact and good relations are critical to obtaining clear guidance from authorities. An example of logistical challenges included a lack of electricity, water, internet, cold-chain, well-appointed laboratories, and healthcare infrastructure. These were mitigated by investments and upgrades in infrastructure (e.g., solar panels, borehole, study pharmacy). Some important lessons learned regarding logistics included to foresee enough time to make a new site operational, invest in durable and sustainable material, and to assess needs of the site to select the best options for upgrades. Several challenges, mitigations, and lessons learned are presented, which are highly relevant for other LMICs facing similar issues related to a lack of adequate infrastructure, research experience, and regulatory capacity.

Return to List of Articles

3. Challenges and lessons learned during the planning and early implementation of the RTS,S/AS01E malaria vaccine in three regions of Ghana: a qualitative study.

Grant J, Gyan T, Agbokey F, Webster J, Greenwood B, Asante K.

Malar J. 2022 May 19;21(1):147.

PubMed ID: 35550113

ABSTRACT

BACKGROUND: In 2019, the RTS,S/AS01E malaria vaccine was introduced on a pilot basis in six regions of Ghana by the Ministry of Health/Ghana Health Service as part of the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP). This is the first time a malaria vaccination programme has been implemented in any country. This paper describes the challenges faced, and lessons learned, during the planning and early implementation of the RTS,S/AS01E vaccine in three out of the six regions that implemented the programme in Ghana.

METHODS: Twenty-one in-depth interviews were conducted with regional and district health service managers and frontline health workers three months after the start of MVIP in May 2019. Data were coded using NVivo software version 12 and a coding framework was developed to support thematic analysis to identify the challenges and lessons learned during the RTS,S/AS01E implementation pilot, which were also categorized into the Consolidated Framework for Implementation Research (CFIR).

RESULTS: Participants reported challenges related to the characteristics of the intervention, such as issues with the vaccine schedule and eligibility criteria, and challenges related to how it was implemented as a pilot programme. Additionally, major challenges were faced due to the spread of rumours leading to vaccine refusals; thus, the outer setting of the CFIR was adapted to accommodate rumours within the community context. Health service managers and frontline health workers also experienced challenges with the process of implementing RTS,S/AS01E, including inadequate sensitization and training, as well as issues with the timeline. They also experienced challenges associated with the features of the systems within which the vaccine was being implemented, including inadequate resources for cold-chain at the health facility level and transportation at the district and health facility levels. This study identified the need for a longer, more intensive and sustained delivery of contextually-appropriate sensitization prior to implementation of a programme such as MVIP.

CONCLUSIONS: This study identified 12 main challenges and lessons learned by health service managers and health workers during the planning and early implementation phases of the RTS,S/AS01E pilot introduction in Ghana. These findings are highly relevant to the likely scale-up of

RTS,S/AS01E within Ghana and possible implementation in other African countries, as well as to other future introductions of novel vaccines.

WEB: 10.1186/s12936-022-04168-9
IMPACT FACTOR: 2.631
CITED HALF-LIFE: 5.6

START COMMENTARY

In this qualitative case study, Grant *et al.* describe the implementation of RTS,S/AS01$_E$ malaria vaccine. This study is important as it is the first time that a malaria vaccination has been implemented in any country, providing important insights on challenges and lessons learned. This study was conducted in three regions of Ghana (Bono, Bono East and Ahafo) of the six where the pilot program was conducted. The study recruited health workers at the regional, district, and community levels three months after vaccine administration began. To guide data analysis and reporting, authors used the Consolidated Framework for Implementation research (CFIR), a widely used framework for systematically assessing implementation factors.

Grant *et al.* conducted 21 in-depth interviews with regional and district level health service managers and frontline health workers across the study area (additional details in *Table 1*). Challenges and lessons learned fit into four CFIR domains and eight of the constructs, which are presented in detail in *Table 2* and in *Figure 1.* For intervention characteristics, a few domains were listed as major challenges, including the vaccine schedule (particularly the 4th dose). Health workers stated that the 15-month gap between the 3rd and 4th doses was too long, and caregivers would not remember to return for that dose, indicating a need for greater efforts to increase 4th dose coverage. Relatedly, health workers stated that the strict age eligibility criteria (i.e., the exclusion of children over 6 months) was a challenge. Within inner setting, workers described issues with limited resources, communication (i.e., a lack of communication and experience-sharing in implementation areas), the implementation process (e.g., sensitization, timeline, training). For example, participants stated that the period for sensitization was not long or well-funded enough to provide all the information needed for communities. Within characteristics of individuals and outer setting, the constructs of self-efficacy among community health workers and rumours arose. The majority of health workers stated that some caregivers refused the vaccine due to rumours on social media, such as that the vaccine had not been approved by WHO or the Food and Drug Administration (FDA). This was seen as a challenge unique to the RTS,S/AS01$_E$ malaria vaccine as it was not observed for other vaccines. This study provides insight on the implementation challenges and lessons which can be applied to future efforts to roll out RTS,S/AS01$_E$.

Return to List of Articles

4. Conducting public health surveillance in areas of armed conflict and restricted population access: a qualitative case study of polio surveillance in conflict-affected areas of Borno State, Nigeria.

Wiesen E, Dankoli R, Musa M, Higgins J, Forbi J, Idris J, et al.

Confl Health. 2022 May 10;16(1):20.

PubMed ID: 35526017

ABSTRACT

This study examined the impact of armed conflict on public health surveillance systems, the limitations of traditional surveillance in this context, and innovative strategies to overcome these limitations. A qualitative case study was conducted to examine the factors affecting the functioning of poliovirus surveillance in conflict-affected areas of Borno state, Nigeria using semi-structured interviews of a purposeful sample of participants. The main inhibitors of surveillance were inaccessibility, the destroyed health infrastructure, and the destroyed communication network. These three challenges created a situation in which the traditional polio surveillance system could not function. Three strategies to overcome these challenges were viewed by respondents as the most impactful. First, local community informants were recruited to conduct surveillance for acute flaccid paralysis in children in the inaccessible areas. Second, the informants engaged in local-level negotiation with the insurgency groups to bring children with paralysis to accessible areas for investigation and sample collection. Third, GIS technology was used to track the places reached for surveillance and vaccination and to estimate the size and location of the inaccessible population. A modified monitoring system tracked tailored indicators including the number of places reached for surveillance and the number of acute flaccid paralysis cases detected and investigated, and utilized GIS technology to map the reach of the program. The surveillance strategies used in Borno were successful in increasing surveillance sensitivity in an area of protracted conflict and inaccessibility. This approach and some of the specific strategies may be useful in other areas of armed conflict.

WEB: 10.1186/s13031-022-00452-2

IMPACT FACTOR: 2.723

CITED HALF-LIFE: 4.7

START COMMENTARY

In this qualitative paper, Wiesen *et al.* evaluate the impact of armed conflict on surveillance systems in Borno State, Nigeria with polio as a case study. This study is important as it provides insight to the limitations of traditional surveillance systems, and strategies to address these limitations, which can be useful in other areas of armed conflict and other diseases. Wiesen *et al.* conducted this case study in inaccessible areas (defined as areas where civilians were unable to move in and out due to

the risk of attack by insurgents) of Borno State to understand challenges and strategies in severe conflict areas. One strength of this study is the description of the researcher's characteristics (i.e., background, experience with respondents), highlighting limitations (i.e., one researcher conducting the interviews) and strategies to strengthen the validity despite these limitations. Prior to data collection, a conceptual framework (*Figure 1*) was developed to summarize factors affecting acute flaccid paralysis (AFP) surveillance. This framework was revised during data analysis. The study conducted in-depth interviews with 16 staff members at community, state, and international levels (*Table* 2) and utilized 15 documents, including reports, news articles, and guidelines on polio eradication efforts and the conflict in Borno State (shown in *Table 1*) to obtain a range of perspectives. The coding system involved four categories: inhibitors; strategies; monitoring systems; and collaboration and information sharing.

Overall, findings from document reviews and interviews were highly consistent (shown in *Table 4*). Inhibitors included inaccessibility and the destruction of health centers and communication, which affect ability to report cases. strategies to address the challenges included the use of local community informants (i.e., lay adults who resided or were able to enter inaccessible areas) to search and identify children with suspected AFP through observations or ask adults about paralyzed children in communities. Local level negotiation was used to evacuate AFP cases, which required specimen collection, case investigation, and clinical examination. Another strategy included using geographic information systems (GIS) technology to implement and monitoring surveillance. Satellite imagery provided information on the size and location of inaccessible settlements. Wiesen *et al.* provide a set of recommendations to further improve surveillance performance in inaccessible areas of Borno State, and other areas of armed conflict.

Return to List of Articles

5. It Takes Two to Tango: Combining Conventional Culture With Molecular Diagnostics Enhances Accuracy of Streptococcus pneumoniae Detection and Pneumococcal Serogroup/Serotype Determination in Carriage.

Miellet W, van Veldhuizen J, Litt D, Mariman R, Wijmenga-Monsuur A, Badoux P, et al.

Front Microbiol. 2022 May 07;13:859736.

PubMed ID: 35509314

ABSTRACT

BACKGROUND: The specificity of molecular methods for the detection of Streptococcus pneumoniae carriage is under debate. We propose a procedure for carriage surveillance and vaccine impact studies that increases the accuracy of molecular detection of live pneumococci in polymicrobial respiratory samples.

METHODS: Culture and qPCR methods were applied to detect pneumococcus and pneumococcal serotypes in 1,549 nasopharyngeal samples collected in the Netherlands (n = 972) and England (n = 577) from 946 toddlers and 603 adults, and in paired oropharyngeal samples collected exclusively from 319 Dutch adults. Samples with no live pneumococci isolated at primary diagnostic culture yet generating signal specific for pneumococcus in qPCRs were re-examined with a second, qPCR-guided culture. Optimal Cq cut-offs for positivity in qPCRs were determined via receiver operating characteristic (ROC) curve analysis using isolation of live pneumococci from the primary and qPCR-guided cultures as reference.

RESULTS: Detection of pneumococcus and pneumococcal serotypes with qPCRs in cultured (culture-enriched) nasopharyngeal samples exhibited near-perfect agreement with conventional culture (Cohen's kappa: 0.95). Molecular methods displayed increased sensitivity of detection for multiple serotype carriage, and implementation of qPCR-guided culturing significantly increased the proportion of nasopharyngeal and oropharyngeal samples from which live pneumococcus was recovered ($p < 0.0001$). For paired nasopharyngeal and oropharyngeal samples from adults none of the methods applied to a single sample type exhibited good agreement with results for primary and qPCR-guided nasopharyngeal and oropharyngeal cultures combined (Cohens kappa; 0.13-0.55). However, molecular detection of pneumococcus displayed increased sensitivity with culture-enriched oropharyngeal samples when compared with either nasopharyngeal or oropharyngeal primary cultures ($p < 0.05$).

CONCLUSION: The accuracy of pneumococcal carriage surveillance can be greatly improved by complementing conventional culture with qPCR and vice versa, by using results of conventional and qPCR-guided cultures to interpret qPCR data. The specificity of molecular methods for the detection of live pneumococci can be enhanced by incorporating statistical procedures based on ROC curve

analysis. The procedure we propose for future carriage surveillance and vaccine impact studies improves detection of pneumococcal carriage in adults in particular and enhances the specificity of serotype carriage detection.

WEB: 10.3389/fmicb.2022.859736
IMPACT FACTOR: 5.640
CITED HALF-LIFE: 3.5

START COMMENTARY

In this study, Miellet *et al.* propose a procedure to increase the accuracy of molecular detection of life pneumococci in polymicrobial respiratory samples. This study is important as it can improve the detection of pneumococcal carriage and the specificity of serotype carriage detection, which can be potentially useful for surveillance and research efforts. Miellet *et al.* describe a protocol for combining conventional culturing and pneumococcus-specific quantitative PCR (qPCR) called 'two-to-tango'. Statistical procedures are utilized to interpret results and enhance specificity of the methods. Samples were obtained as part of two cross-sectional prospective observational studies in the Netherlands and in England. *Table 1* presents the methodological differences between *Streptococcus pneumoniae* carriage studies conducted in the two countries.

Figure 1 presents the steps of the new protocol applied to detected S. *pneumoniae* and pneumococcal serotypes in 1,549 nasopharyngeal samples from 946 children and 603 adults. Without the additional qPCR component, live *S. pneumoniae* was detected in 29% of primary cultures of nasopharyngeal swabs. When conducting qPCRs on samples, 38% of samples were positive for S. *pneumoniae.* There were statistically significant differences in the fraction of positive samples among the minimally processed compared with the culture-enriched swabs (36% vs. 31%, $p < 0.0001$). Additional results including the optimal qPCR cycle threshold and corresponding parameters is presented in *Table 2.* The accuracy of *S. pneumoniae* detected in children and in adults are presented in *Table 3* and *Table 4,* respectively. A strength of this study is that Miellet *et al.* evaluated the reproducibility of the molecular methods and agreement in laboratory results between the two sites (*Supplementary Table 6 and 7*) and found near-perfect agreement for all results. The authors demonstrate that this combination of methods may be superior to traditional methods.

Return to List of Articles

6. Public Health Actions to Control Measles Among Afghan Evacuees During Operation Allies Welcome - United States, September-November 2021.

Masters N, Mathis A, Leung J, Raines K, Clemmons N, Miele K, et al.

MMWR Morb Mortal Wkly Rep. 2022 May 02;71(17):592-596.

PubMed ID: 35482557

ABSTRACT

On August 29, 2021, the United States government oversaw the emergent establishment of Operation Allies Welcome (OAW), led by the U.S. Department of Homeland Security (DHS) and implemented by the U.S. Department of Defense (DoD) and U.S. Department of State (DoS), to safely resettle U.S. citizens and Afghan nationals from Afghanistan to the United States. Evacuees were temporarily housed at several overseas locations in Europe and Asia* before being transported via military and charter flights through two U.S. international airports, and onward to eight U.S. military bases with hotel A used for isolation and quarantine of persons with or exposed to certain infectious diseases. On August 30, CDC issued an Epi-X notice encouraging public health officials to maintain vigilance for measles among Afghan evacuees because of an ongoing measles outbreak in Afghanistan (25,988 clinical cases reported nationwide during January-November 2021) (1) and low routine measles vaccination coverage (66% and 43% for the first and second doses, respectively, in 2020) (2).

WEB: 10.15585/mmwr.mm7117a2

IMPACT FACTOR: 13.606

CITED HALF-LIFE: 4.4

START COMMENTARY

In this article, Masters *et al.* describe the public health actions taken to control measles among Afghan evacuees as part of Operation Allies Welcome (OAW). This study is important as it provides a real-world example of controlling an outbreak in an emergency situation. The U.S. government began to evacuate and resettled U.S. citizens and Afghan nationals to the U.S. in August 2021. It was not possible to administer routine, predeparture vaccinations given the urgency of the situation. As such, vaccines including Measles, Mumps, and Rubella (MMR) would have to be provided after arrival to the U.S. This was difficult since Afghanistan had an ongoing national measles outbreak (i.e., 25,988 clinical cases from January to November 2021), making it possible that those being evacuated would have been exposed or infected. Further, in recent years, the U.S. has experienced a spike in measles cases. *Box* shows a timeline of events associated with the measles cases detected among Afghan evacuees during OAW. Some key dates are: August 17, when flights with evacuees began arriving, September 2nd when the rash appeared for the earliest measles case in a

hotel in Virginia, and September 14 when the CDC recommended to pause evacuation flights and initiate mass MMR and varicella vaccination campaigns and a 21 day quarantine.

In total, 47 measles cases were reported among 72,399 evacuees with an estimated attack rate of 0.065 in the U.S. military bases and hotel. The median age was 1 year (range: 0-26 years). All reported cases were either not vaccinated or had an unknown vaccination status. In addition to measles, sites also reported 57 varicella cases, 14 mumps cases, and one rubella case. As aforementioned, the CDC recommended pausing flights on September 14 and conducting mass MMR for all eligible evacuees that were ≥6 months and, and varicella vaccination for all eligible evacuees that were ≥12 months. They also recommended a quarantine for 21 days post vaccine. By September 24, 91% of eligible evacuees at the domestic bases and hotels had been vaccinated with the MMR vaccine. Flights resumed on October 5th, and there was no need for isolation of cases or quarantine of exposed contacts given the high rate of vaccine coverage. Overall, this case highlights the effectiveness of mass vaccination campaigns in minimizing transmission in such cases, which should be considered if/when similar situations arrive.

Return to List of Articles

7. Factors Affecting Human Papillomavirus Vaccination in Men: Systematic Review.

Shin H, Jeon S, Cho I, Park H.

JMIR Public Health Surveill. 2022 Apr 28;8(4):e34070.
PubMed ID: 35471242

ABSTRACT

BACKGROUND: Despite the high risks associated with human papillomavirus (HPV), the HPV vaccination rate of men is far lower than women. Most previous review studies have focused on female vaccination and related affecting factors. However, previous studies have reported that the factors affecting HPV vaccination differ by gender.

OBJECTIVE: The aim of this review was to identify the factors affecting HPV vaccine initiation in men through a systematic review approach.

METHODS: A literature review was conducted across 3 central electronic databases for relevant articles. A total of 30 articles published between 2013 and 2019 met the inclusion criteria and were reviewed in this study.

RESULTS: In total, 50 factors affecting HPV vaccination in men were identified, including 13 sociodemographic factors and social structure factors, 12 belief-related variables, 4 family factors, 4 community factors, 14 variables related to needs, and 3 environmental factors.

CONCLUSIONS: To increase HPV vaccination rates in men, strategies targeting young males and their families should consider frequent visits to or contact with health care providers so that health care professionals can provide recommendations for HPV vaccination.

WEB: 10.2196/34070
IMPACT FACTOR: 4.112
CITED HALF-LIFE: 1.5

START COMMENTARY

In this systematic review, Shin *et al.* identify factors affecting Human Papillomavirus Vaccination (HPV) vaccine initiation in men. This study is important as it summarizes the literature on factors relating to HPV vaccine uptake, an area which is less well-understood among men than women. Understanding the factors affecting HPV vaccine hesitation can aide in establishing public health policies. This study utilized the Behavioral Model of Health Service Use (BMHSU) framework to organize factors influencing men's use of HPV vaccination services. Studies were eligible for

inclusion if they involved heterosexual male participants; included HPV vaccine initiation outcomes; reported factors/predictors associated with HPV vaccination; and were peer-reviewed.

A total of 30 studies were included in the review (*Figure 1*). Details about each study are included in *Table 1.* Nearly all studies (29) were conducted in the US and participants included boys and men aged 9 to 34 years. The limited geographic scope is a limitation of this work along with the exclusion of men who have sex with men. A strength of this study is the reporting of quality scores, which ranged from 2 to 5 (*Table 1* and *Multimedia Appendix 2*). Shin *et al.* identified 50 factors into two components of the framework (47 population characteristics and 3 environmental factors) which are presented in *Textbox 1* and *Table 2.* Some examples include predisposing factors such as sociodemographic and social structure factors (e.g., race/ethnicity, age, education) and beliefs (e.g., parental awareness, awareness of HPV/HPV vaccine); enabling factors such as family (i.e., income, insurance type), community (i.e., region, medical accessibility), and perceived need (i.e., time from last check up, sexual behavior) and evaluated need (i.e., mother's abnormal pap smear result). Environmental factors were all related to the healthcare system and included healthcare provider's recommendations for the vaccine, year that vaccinations were performed, and facility type. Overall, Shin *et al.* concluded that there are many factors identified as being associated with HPV vaccination (e.g., age 10-20), these are often only assessed by single studies, limiting generalizability. However, across studies, healthcare providers recommendations, frequent contact with healthcare providers, and parental awareness of HPV seem to be associated with HPV vaccination in men.

Return to List of Articles

8. Health effects of utilising hospital contacts to provide measles vaccination to children 9-59 months-a randomised controlled trial in Guinea-Bissau.

Fisker A, Martins J, Jensen A, Martins C, Aaby P, Thysen S.

Trials. 2022 Apr 26;23(1):349.

PubMed ID: 35461287

ABSTRACT

BACKGROUND: Measles vaccination coverage in Guinea-Bissau is low; fewer than 80% of children are currently measles vaccinated before 12 months of age. The low coverage hampers control of measles. Furthermore, accumulating evidence indicates that measles vaccine has beneficial non-specific effects, strengthening the resistance towards other infections. Thus, even if children are not exposed to measles virus, measles-unvaccinated children may be worse off. To increase vaccination coverage, WHO recommends that contacts with the health system for mild illness are utilised to vaccinate. Currently, in Guinea-Bissau, curative health system contacts are not utilised.

METHODS: Bandim Health Project registers out-patient consultations and admissions at the paediatric ward of the National Hospital in Guinea-Bissau. Measles-unvaccinated children aged 9-59 months consulting for milder illness or being discharged from the paediatric ward will be invited to participate in a randomised trial. Among 5400 children, randomised 1:1 to receive standard measles vaccine or a saline placebo, we will test the hypothesis that providing a measles vaccine at discharge lowers the risk of admission/mortality (composite outcome) during the subsequent 6 months by 25%. All enrolled children are followed through the Bandim Health Project registration system and through telephone follow-up. The first 1000 enrolled children are furthermore followed through interviews on days 2, 4, 7 and 14 after enrolment.

DISCUSSION: Utilising missed vaccination opportunities can increase vaccination coverage and may improve child health. However, without further evidence for the safety and potential benefits of measles vaccination, these curative contacts are unlikely to be used for vaccination in Guinea-Bissau.

CLINICALTRIALS: gov NCT04220671 . Registered on 5 January 2020.

WEB: 10.1186/s13063-022-06291-z

IMPACT FACTOR: 2.462

CITED HALF-LIFE: 6.6

START COMMENTARY

In this protocol of a randomized controlled trial, Fisker *et al.* plan to test the impact of providing measles vaccines (MV) at hospital contact (discharge or outpatient consultation) on hospital admission and/or death (composite outcome) by 25% during the subsequent 6 months. This article is important as low MV coverage is a threat to disease control efforts in Guinea-Bissau and elsewhere and providing missed doses at healthcare contacts could be a way to address this low coverage. The results of this study will be critical for informing the standard-of-care in Guinea-Bissau and other similar contexts. Participants will include measles-unvaccinated children aged 9-59 months that were in contact with the health system in Bissau, Guinea-Bissau. Participants will be randomized to receive either MV or placebo (saline) at this time of discharge and followed through telephone interviews at 3, 6, and 12 months and through passive case detection at the Hospital National Simao Mendes. The primary composite outcome is death/hospital admission; secondary outcomes include non-accidental mortality within 6 and 2 months, non-accidental hospital admission with an overnight stay within 6 months of enrolment, cause-specific mortality and/or hospital admissions, adverse events, and cost-effectiveness of providing MV at a hospital contact.

Return to List of Articles

9. Estimating the effect of vaccination on antimicrobial-resistant typhoid fever in 73 countries supported by Gavi: a mathematical modelling study.

Birger R, Antill n M, Bilcke J, Dolecek C, Dougan G, Pollard A, et al.

Lancet Infect Dis. 2022 May 06;22(5):679-691.
PubMed ID: 3512367335123674

ABSTRACT

BACKGROUND: Multidrug resistance and fluoroquinolone non-susceptibility (FQNS) are major concerns for the epidemiology and treatment of typhoid fever. The 2018 prequalification of the first typhoid conjugate vaccine (TCV) by WHO provides an opportunity to limit the transmission and burden of antimicrobial-resistant typhoid fever.

METHODS: We combined output from mathematical models of typhoid transmission with estimates of antimicrobial resistance from meta-analyses to predict the burden of antimicrobial-resistant typhoid fever across 73 lower-income countries eligible for support from Gavi, the Vaccine Alliance. We considered FQNS and multidrug resistance separately. The effect of vaccination was predicted on the basis of forecasts of vaccine coverage. We explored how the potential effect of vaccination on the prevalence of antimicrobial resistance varied depending on key model parameters.

FINDINGS: The introduction of routine immunisation with TCV at age 9 months with a catch-up campaign up to age 15 years was predicted to avert 46-74% of all typhoid fever cases in 73 countries eligible for Gavi support. Vaccination was predicted to reduce the relative prevalence of antimicrobial-resistant typhoid fever by 16% (95% prediction interval [PI] 0-49). TCV introduction with a catch-up campaign was predicted to avert 42 5 million (95% PI 24 8-62 8 million) cases and 506,000 (95% PI 187,000-1 9 million) deaths caused by FQNS typhoid fever, and 21 2 million (95% PI 16 4-26 5 million) cases and 342,000 (95% PI 135,000-1 5 million) deaths from multidrug-resistant typhoid fever over 10 years following introduction.

INTERPRETATION: Our results indicate the benefits of prioritising TCV introduction for countries with a high avertable burden of antimicrobial-resistant typhoid fever.

FUNDING: The Bill & Melinda Gates Foundation.

WEB: 10.1016/S1473-3099(21)00627-7
IMPACT FACTOR: 24.446
CITED HALF-LIFE: 4.7

START COMMENTARY

In this modelling study, Birger *et al.* project the burden of antimicrobial resistance typhoid fever across 73 lower income countries eligible for support from Gavi. This study is important as typhoid fever and antimicrobial-resistant typhoid fever pose a substantial risk to people living in LMICs, and it is important to quantify the impact of typhoid conjugate vaccine (TCV) introduction. Birger *et al.* assess the effect of vaccination on total (including resistance) typhoid fever, proportion of cases with fluoroquinolone nonsusceptibility and multidrug resistance, and proportion of cases that are drug resistant. These input parameters, values, and sources are presented in *Table 1.*

Across 73 countries, routine TCV with a catch-up campaign for >15-year-olds was predicted to avert nearly 66.7 million cases of typhoid fever over 10 years (95% PI 48.1-88.3 million), i.e., reductions of 46-74%). *Table 2* presents the number of typhoid cases, deaths, and DALYs averted over 10 years following the introduction of TCV plus a catch-up campaign by country. The authors also considered age structure and drug-resistance for simulations and found a mean reduction in the relative proportion of resistance (16.1%; 95% PI 0-49). The same scenario (routine TCV with a catch-up campaign) was predicted to avert 42.5 million cases of typhoid fever with FQNS (95% PI 24-62.9 million) and 21.2 million with multi-drug resistance over 10 years. Overall 2/3 of cases, deaths, and DALYs associated with FQNS, and multi-drug resistance typhoid could be averted with TCV introduction. This study provides evidence on how TCV may reduce the burden of typhoid fever, FQNS, and multi-drug resistance in settings where it is needed most, indicating the importance of timely and urgent TCV campaigns in Gavi-eligible countries.

Return to List of Articles

10. Herd Immunity Effects in Cost-Effectiveness Analyses among Low- and Middle-Income Countries.

Ma S, Lavelle T, Ollendorf D, Lin P.

Appl Health Econ Health Policy. 2022 Apr 22;20(3):395-404.
PubMed ID: 35001292

ABSTRACT

BACKGROUND: Herd immunity (HI) is a key benefit of vaccination programs, but the effects are not routinely included in cost-effectiveness analyses (CEAs).

OBJECTIVE: This study investigated how the inclusion of HI in CEAs may influence the reported value of immunizations in low- and middle-income countries (LMICs) and illustrated the implications for COVID-19 immunization.

METHODS: We reviewed immunization CEAs published from 2000 to 2018 focusing on LMICs using data from the Tufts Medical Center CEA Registries. We investigated the proportion of studies that included HI, the methods used, and the incremental cost-effectiveness ratios (ICERs) reported. When possible, we evaluated how ICERs would change with and without HI.

RESULTS: Among the 243 immunization CEAs meeting inclusion criteria, 44 studies (18%) included HI. Of those studies, 11 (25%) used dynamic transmission models, whereas the remainder used static models. Sixteen studies allowed for ICER calculations with and without HI (n = 48 ratios). The inclusion of HI always resulted in more favorable ratios. In 20 cases (42%), adding HI decreased the ICERs enough to cross at least one or more common cost-effectiveness benchmarks for LMICs. Among pneumococcal vaccination studies, including HI in the analyses decreased seven of 24 ICERs enough to cross at least one cost-effectiveness benchmark.

CONCLUSION: The full value of immunization may be underestimated without considering a scenario in which HI is achieved. Given the evidence in pneumococcal CEAs, COVID-19 vaccine value assessments should aim to show ICERs with and without HI to inform decision-making in LMICs.

WEB: 10.1007/s40258-021-00711-y
IMPACT FACTOR:
CITED HALF-LIFE:

START COMMENTARY

Ma *et al.* investigate how the inclusion of herd immunity (HI) in cost-effectiveness analyses (CEA) influences the reported value of immunization in low- and middle-income countries (LMICs) and illustrate the implications for COVID-19 immunization. Studies were eligible for inclusion if they were published between 1996 to 2020, included in either the Tufts Medical Center CEA Registry or Tufts Medical Center Global Health CEA Registry, written in English, and included outcomes of cost per quality adjusted year (QALY) or cost per disability-adjusted life year (DALYs). In total, 170 studies from the Global Health CEA registry were included and 73 studies from the CEA registry were included.

In total, 44 vaccine CEAs (18% of the 243 studies) included herd immunity effects (details provided in *Table 1*). Of these, 11 (25%) used dynamic models while the remainder used static models. In the static models (33), herd immunity was estimated in a variety of ways – by adding a fixed percentage improvement, altering model inputs, or applying a multiplier to vaccine efficacy (details provided in *Table 2*). In these papers, the effect of herd immunity could be disentangled, allowing Ma *et al.* to recalculate and compare each incremental cost-effectiveness ratio (ICER). Ma *et al.* found that including herd immunity made all ICERs more favorable, and in more than half (20 of 48 ratio pairs), the ICER decreased enough to cross at least one common cost-effectiveness benchmark. Overall, the authors conclude that although the minority of studies (less than one-fifth) include herd immunity, those that did demonstrated more favorable cost-effectiveness ratios with ICER reductions from 28-61% (shown in *Table 3*). This underscores the importance of including herd immunity, which WHO recommends for CEAs conducted in LMICs.

Return to List of Articles

Appendix

The literature search for the June 2021 Vaccine Delivery Research Digest was conducted on May 30. We searched English language articles indexed by the US National Library of Medicine and published between April 15, 2022 and May 14, 2022. The search resulted in 584 items.

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]) (“2022/15/04”[PDAT] : “2022/14/05”[PDAT]))