VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

PRODUCED BY: ARAKAKI L, BABIGUMIRA JB

APRIL 2020

Want the Vaccine Delivery Research Digest delivered directly to your inbox? Subscribe on the Digest website: http://uwstartcenter.org/publication-digests/vaccine-digest/



START
CENTERSTRATEGIC ANALYSIS,
RESEARCH & TRAINING CENTER
Department of Global Health | University of Washington

List of Articles

1. Novel technology for storage and distribution of live vaccines and other biological medicines at ambient temperature.

{Abstract & START Commentary} {Full Article}

- A report describing a series of studies in the preliminary development and testing of a novel, thin-film platform for thermostable vaccines.
- 2. The Response to Re-Emergence of Yellow Fever in Nigeria, 2017. {Abstract & START Commentary} {Full Article}
 - A cross-sectional descriptive study of an outbreak investigation of yellow fever and rapid vaccination coverage assessment in a nomadic population in Nigeria in 2017.
- Geospatial variation in measles vaccine coverage through routine and campaign strategies in Nigeria: Analysis of recent household surveys. {<u>Abstract & START Commentary</u>} {<u>Full Article</u>}
 - A study using geospatial techniques to estimate measles vaccination coverage on a subnational level and identify low coverage areas in Nigeria.
- 4. Field challenges to measles elimination in the Democratic Republic of the Congo. {Abstract & START Commentary} {Full Article}
 - A series of studies describing the measles epidemic in Kunda Province in 2016 and assessing effectiveness of measles vaccination efforts.
- Effects of updated demography, disability weights, and cervical cancer burden on estimates of human papillomavirus vaccination impact at the global, regional, and national levels: a PRIME modelling study.

{Abstract & START Commentary} {Full Article}

 A study detailing data input updates to the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model and their effect on the estimation of cases, deaths, and DALYs averted due to the HPV vaccine.

- Impact of mother's education on full immunization of children aged 12-23 months in Eritrea: population and health survey 2010 data analysis.
 {Abstract & START Commentary} {Full Article}
 - A secondary data analysis of the association between maternal education and full immunization in Eritrea.
- Japanese encephalitis vaccination in the Philippines: A cost-effectiveness analysis comparing alternative delivery strategies.
 {Abstract & START Commentary} {Full Article}
 - A cost-effectiveness analysis comparing three Japanese encephalitis vaccination strategies to children under 5 years of age in the Philippines.
- Health workers' perceptions and challenges in implementing meningococcal serogroup a conjugate vaccine in the routine childhood immunization schedule in Burkina Faso.
 {Abstract & START Commentary} {Full Article}
 - A qualitative study to identify potential opportunities for improving meningococcal serogroup A conjugate vaccine implementation in Burkina Faso.
- Measles antibody levels among vaccinated and unvaccinated children 6-59 months of age in the Democratic Republic of the Congo, 2013-2014.
 {Abstract & START Commentary} {Full Article}
 - A study assessing population seroprotection among children participating in the 2013-2014 Demographic and Health Survey in the Democratic Republic of the Congo.
- Mapping cholera outbreaks and antibiotic resistant *Vibrio cholerae* in India: An assessment of existing data and a scoping review of the literature.
 {Abstract & START Commentary} {Full Article}
 - An analysis of Integrated Disease Surveillance Program data and scoping review of antibiotic resistant *Vibrio cholerae* outbreaks in India to potentially guide policy.

Appendix

Details of Articles

1. Novel technology for storage and distribution of live vaccines and other biological medicines at ambient temperature.

Bajrovic I, Schafer S, Romanovicz D, Croyle M. *Sci Adv.* 2020 Mar 20;6(10):eaau4819. PubMed ID: 32181330

ABSTRACT

A novel, thin-film platform that preserves live viruses, bacteria, antibodies, and enzymes without refrigeration for extended periods of time is described. Studies with recombinant adenovirus in an optimized formulation that supports recovery of live virus through 16 freeze-thaw cycles revealed that production of an amorphous solid with a glass transition above room temperature and nitrogen-hydrogen bonding between virus and film components are critical determinants of stability. Administration of live influenza virus in the optimized film by the sublingual and buccal routes induced antibody-mediated immune responses as good as or better than those achieved by intramuscular injection. This work introduces the possibility of improving global access to a variety of medicines by offering a technology capable of reducing costs of production, distribution, and supply chain maintenance.

WEB: <u>10.1126/sciadv.aau4819</u> IMPACT FACTOR: 12.804 CITED HALF-LIFE: n/a

START COMMENTARY

Bajrovic et al. presented a novel technology (see Figure below) with the potential to make vaccines more accessible to low- and middle-income countries. They conducted several studies to identify the optimal formulation of the thin-film platform, assess its stability and effectiveness to recover virus upon rehydration, test its performance under different environmental conditions (e.g., long-term storage in ambient temperatures, freeze-thaw cycles, and various humidity conditions), and compare the immune response to buccal and sublingual administration of H1N1 influenza virus versus intranasal and intramuscular administration in a mouse model. The results were promising; Bajrovic et al. found the optimized formulation of the thin-film platform was stable in ambient temperatures over a long period of time, effectively recovered live virus, and performed well under stressed

conditions. The authors stated the results of their studies can help further research in the production of thermostable biologicals. They highlighted the potentially significant impact this technology could have as an efficient, cost-saving strategy to provide vaccines to those in low- and middle-income countries.



Figure. Image of the prototype unit dose film. Figure 1A in manuscript.

2. The Response to Re-Emergence of Yellow Fever in Nigeria, 2017

Nwachukwu WE, Yusuff H, Nwangwu U, Okon A, Ogunniyi A, Imuetinyan-Clement J, et al. *Int J Infect Dis.* 2020 Mar;92:189-196. PubMed ID: 31935537

ABSTRACT

Yellow fever (YF) is an acute viral hemorrhagic disease caused by the YF virus (arbovirus) which continues to cause severe morbidity and mortality in Africa. A case of YF was confirmed in Nigeria on the 12th of September 2017, 21 years after the last confirmed case. The patient belongs to a nomadic population with a history of low YF vaccination uptake, in the Ifelodun Local Government Area (LGA) of Kwara State, Nigeria. An active case search in Ifelodun and its five contiguous LGAs led to the listing of 55 additional suspect cases of YF within the period of the outbreak investigation between September 18 to October 6, 2017. The median age of cases was 15 years, and 54.4% were males. Of these, blood samples were collected from 30 cases; nine tested positive in laboratories in Nigeria and six were confirmed positive for YF by the WHO reference laboratory in the region; Institut Pasteur, Dakar. A rapid YF vaccination coverage assessment was carried out, resulting in a coverage of 46% in the LGAs, with 25% of cases able to produce their vaccination cards. All stages of the yellow fever vector, Aedes mosquito were identified in the area, with high larval indices (House and Breteau) observed. In response to the outbreak, YF surveillance was intensified across all States in Nigeria, as well as reactive vaccination and social mobilisation campaigns carried out in the affected LGAs in Kwara State. A state-wide YF preventive campaign was also initiated.

WEB: 10.1016/j.ijid.2019.12.034

IMPACT FACTOR: 3.538 CITED HALF-LIFE: 4.7

START COMMENTARY

Nwachukwu et al. detailed the rapid multi-agency response to an outbreak of yellow fever among a nomadic population in Ifelodun Local Government Area (LGA) in Kwara State, Nigeria. Despite reports of high yellow fever vaccination coverage in Kwara State, the results of the vaccination coverage assessment highlighted limitations of using administrative data to determine vaccination coverage, especially for a nomadic population with "low routine immunization uptake, living in hard-to-reach areas, displaying poor health-seeking [behavior], with associated poor geographic access to health care." The response team quickly obtained approval for the provision of yellow fever

vaccines from the International Coordination Group and deployed three mass vaccination campaigns. Authors recommended activities to remain vigilant, such as training healthcare workers, strengthening yellow fever surveillance and improving vaccination coverage.

3. Geospatial variation in measles vaccine coverage through routine and campaign strategies in Nigeria: Analysis of recent household surveys.

Utazi C, Wagai J, Pannell O, Cutts F, Rhoda D, Ferrari M, et al. *Vaccine*. 2020 Mar 25;38(14):3062-3071. PubMed ID: 32122718

ABSTRACT

Measles vaccination campaigns are conducted regularly in many low- and middle-income countries to boost measles control efforts and accelerate progress towards elimination. National and sometimes first-level administrative division campaign coverage may be estimated through postcampaign coverage surveys (PCCS). However, these large-area estimates mask significant geographic inequities in coverage at more granular levels. Here, we undertake a geospatial analysis of the Nigeria 2017-18 PCCS data to produce coverage estimates at 1 x 1 km resolution and the district level using binomial spatial regression models built on a suite of geospatial covariates and implemented in a Bayesian framework via the INLA-SPDE approach. We investigate the individual and combined performance of the campaign and routine immunization (RI) by mapping various indicators of coverage for children aged 9-59 months. Additionally, we compare estimated coverage before the campaign at 1 x 1 km and the district level with predicted coverage maps produced using other surveys conducted in 2013 and 2016-17. Coverage during the campaign was generally higher and more homogeneous than RI coverage but geospatial differences in the campaign's reach of previously unvaccinated children are shown. Persistent areas of low coverage highlight the need for improved RI performance. The results can help to guide the conduct of future campaigns, improve vaccination monitoring and measles elimination efforts. Moreover, the approaches used here can be readily extended to other countries.

WEB: 10.1016/j.vaccine.2020.02.070

IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

In this geospatial analysis of measles vaccination coverage in Nigeria, Utazi et al. examined six vaccination coverage indicators: 1) coverage before the SIA, 2) SIA coverage among MCV zerodose children, 3) SIA coverage among children vaccinated previously, 4) overall SIA coverage, 5) coverage before and during SIA, and 6) coverage before/or during the SIA (Table 1). Indicator estimates were displayed in maps such as those depicted in the Figure below. Authors found low coverage in the norther regions of Nigeria. Limitations to this analysis included the reliance on caregiver recall when vaccination cards were not available, exclusion of areas affected by conflict, and higher uncertainty in areas with small cluster-level sample sizes—90% of clusters in the post-campaign coverage surveys had sample sizes less than 15). Despite these limitations, Utazi et al. presented methodology that can be expanded to other applications and settings to aid in improving population health.



Figure. Maps of estimated coverage before SIA (top left), overall SIA coverage (top middle), SIA coverage among MCV zero-dose children (top right) and their corresponding standard deviations (bottom row). Figure 2 in manuscript.

4. Field challenges to measles elimination in the Democratic Republic of the Congo.

Coulborn R, Nackers F, Bachy C, Porten K, Vochten H, Ndele E, et al. *Vaccine*. 2020 Mar 09;38(13):2800-2807. PubMed ID: 32111528

ABSTRACT

BACKGROUND: During a measles epidemic, the Ministry of Public Health (MOH) of the Democratic Republic of the Congo conducted supplementary immunization activities (2016-SIA) from August 28-September 3, 2016 throughout Maniema Province. From October 29-November 4, 2016, Médecins Sans Frontières and the MOH conducted a reactive measles vaccination campaign (2016-RVC) targeting children six months to 14 years old in seven health areas with heavy ongoing transmission despite inclusion in the 2016-SIA, and a post-vaccination survey. We report the measles vaccine coverage (VC) and effectiveness (VE) of the 2016-SIA and VC of the 2016-RVC.

METHODS: A cross-sectional VC cluster survey stratified by semi-urban/rural health area and age was conducted. A retrospective cohort analysis of measles reported by the parent/guardian allowed calculation of the cumulative measles incidence according to vaccination status after the 2016-SIA for an estimation of crude and adjusted VE.

RESULTS: In November 2016, 1145 children (6-59 months old) in the semi-urban and 1158 in the rural areas were surveyed. Post-2016-SIA VC (documentation/declaration) was 81.6% (95%CI: 76.5-85.7) in the semi-urban and 91.0% (95%CI: 84.9-94.7) in the rural areas. The reported measles incidence in October among children less than 5 years old was 5.0% for 2016-SIA-vaccinated and 11.2% for 2016-SIA-non-vaccinated in the semi-urban area, and 0.7% for 2016-SIA-vaccinated and 4.0% for 2016-SIA-non-vaccinated in the rural area. Post-2016-SIA VE (adjusted for age, sex) was 53.9% (95%CI: 2.9-78.8) in the semi-urban and 78.7% (95%CI: 0-97.1) in the rural areas. Post 2016-RVC VC (documentation/declaration) was 99.1% (95%CI: 98.2-99.6) in the semi-urban and 98.8% (95%CI: 96.5-99.6) in the rural areas.

CONCLUSIONS: Although our VE estimates could be underestimated due to misclassification of measles status, the VC and VE point estimates of the 2016-SIA in the semi-urban area appear suboptimal, and in combination, could not limit the epidemic. Further research is needed on vaccination strategies adapted to urban contexts.

WEB: <u>10.1016/j.vaccine.2020.02.029</u> IMPACT FACTOR: <u>3.269</u> CITED HALF-LIFE: <u>3.1</u>

START COMMENTARY

Coulborn et al. described a series of activities and studies conducted in response to a measles epidemic in Kunda Province of the Democratic Republic of the Congo (DRC) in 2016. Through their cross-sectional survey of children in semi-urban and rural areas in Kunda, they found higher proportions of vaccination coverage from the reactive vaccination campaign (2016-RVC) than in the supplementary immunization activity (2016-SIA). However, the proportion of children with vaccination cards was drastically lower for the 2016-SIA compared to the 2016-RVC, subjecting coverage estimates for the 2016-SIA to recall bias. Authors found relatively low vaccine effectiveness among the semi-urban participants, though 95% confidence intervals were wide as the study was not powered to assess vaccine effectiveness. Since the measles case definition was based on clinical symptoms, the study was also subject to non-differential misclassification of cases, which could impact vaccine effectiveness estimates. Unfortunately, measles elimination remains a challenge for DRC as indicated by the 2018 epidemic. Authors called for further efforts to better understand the low vaccine effectiveness estimates and to improve vaccination strategies to achieve higher coverage.

5. Effects of updated demography, disability weights, and cervical cancer burden on estimates of human papillomavirus vaccination impact at the global, regional, and national levels: a PRIME modelling study.

Abbas K, van Zandvoort K, Brisson M, Jit M. *Lancet Glob Health*. 2020 Mar 31;8(4):e536-e544. PubMed ID: 32105613

ABSTRACT

BACKGROUND: The Papillomavirus Rapid Interface for Modelling and Economics (PRIME) has been used around the world to assess the health impact and cost-effectiveness of human papillomavirus (HPV) vaccination in girls. We updated PRIME with new data and methods for demography, disability weights, and cervical cancer burden, and generated revised estimates of the health impact of HPV vaccination at the global, regional, and national levels for 177 countries.

METHODS: PRIME was updated with population demography of the UN World Population Prospects (UNWPP) 2019 revision, disability weights of the Global Burden of Disease (GBD) 2017 study, and cervical cancer burden from the Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) 2018 database. We estimated the lifetime health benefits for bivalent or quadrivalent and nonavalent vaccination of 9-year-old and 12-year-old girls at 90% coverage during 2020-29 in 177 countries. Health impact was presented in terms of cervical cancer cases, deaths, or disabilityadjusted life-years (DALYs) averted per 1000 vaccinated girls in comparison with the counterfactual scenario of no vaccination, and the number of girls needed to be vaccinated to prevent a single case, death, or DALY.

FINDINGS: In estimating the health impact of HPV vaccination of 9-year-old girls, the combined updates to demography, disability weights, cervical cancer burden estimates resulted in a 26% increase in the estimated number of cases averted, a 51% increase in deaths averted, and a 72% increase in DALYs averted per 1000 vaccinated girls for both the bivalent or quadrivalent and nonavalent vaccines, compared with previous estimates. With the updated model, the bivalent or quadrivalent HPV vaccine was estimated to avert 15 cases, 12 deaths, and 243 DALYs per 1000 vaccinated girls, and the nonavalent HPV vaccine was estimated to avert 19 cases, 14 deaths, and 306 DALYs per 1000 vaccinated girls. The health benefits of vaccination of 12-year-old girls were estimated to be similar but slightly decreased in comparison with vaccination of 9-year-old girls.

INTERPRETATION: HPV vaccination provides greater health benefits and is more cost-effective than was previously estimated. The demography update, which incorporates population aging, has the largest effect on the health impact estimates. The WHO African region is expected to gain the greatest health benefits and should be prioritised for HPV vaccination.

FUNDING: Gavi, the Vaccine Alliance; Bill & Melinda Gates Foundation.

WEB: <u>10.1016/S2214-109X(20)30022-X</u> IMPACT FACTOR: 15.873 CITED HALF-LIFE: 2.5

START COMMENTARY

Abbas et al. presented data input updates to the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model and explored the effect of these updates to estimated health impacts of the human papillomavirus (HPV) vaccine. With new data, the authors found increased impact of the HPV vaccine globally. The vaccine was found to have the most impact in the African region and South-East Asia region. Authors noted that HPV vaccination could have a greater impact than that estimated from the study because model assumptions were conservative, including exclusion of herd effects and assuming vaccination has no effect after sexual debut. Other limitations included the exclusion of changes in the impact of other non-vaccine interventions and treatment of cervical cancer cases.

6. Impact of mother's education on full immunization of children aged 12-23 months in Eritrea: population and health survey 2010 data analysis.

Kibreab F, Lewycka S, Tewelde A. *BMC Public Health*. 2020 Mar 03;20(1):267. PubMed ID: 32087706

ABSTRACT

BACKGROUND: Although vaccination coverage in Eritrea has improved in recent years, some children are still missing out, and it's important to identify risk factors for lower coverage in order to target campaigns and interventions. The objective of this study was to assess: (1) the impact of maternal education on full immunization of children aged 12-23 months, and (2) whether the association was confounded or modified by other factors.

METHODS: This study was a secondary data analysis of the Eritrean Population and Health Survey 2010 (EPHS 2010). In this analysis 1323 mothers of children aged 12-23 months were included. The outcome of the study was full immunization, defined as receiving all the WHO recommended basic vaccines: one dose of Bacillus Calmette-Gué rin (BCG), three doses of diphtheria-pertussis-tetanus(DPT), three doses of polio, and one dose of measles vaccine. The primary exposure was maternal education. Data on immunization coverage came from vaccination cards and from mothers' or caretakers' verbal reports. Bivariate and multivariable logistic regression analyses were performed.

RESULT: Full vaccination coverage among children aged 12-23 months was 83%. Most children received BCG (95%), DPT1 (97%), DPT2 (96%), DPT3 (93%), polio1 (97%), polio2 (97%), polio3 (91%) and measles (92%). In unadjusted analyses, children of mothers with primary (OR = 2.75, 95% CI 1.74-4.37), and middle or above (OR = 3.16, 95% CI 2.09-4.78) education were more likely to be fully immunised. However, after adjusting for wealth, region, ANC visit, and vaccination card ownership, only the effect for primary education remained significant (OR = 2.34, 95% CI 1.30-4.21).

CONCLUSION: The result of this study suggested that children of mothers who attained primary level were more likely to be fully vaccinated than children of mothers with no education. The association was influenced by wealth index of household, mothers ANC visit, region, and possession of vaccination card. The Expanded Program on Immunization of the Ministry of Health should target strategies to enhance full immunization among children of mothers with no education.

WEB: <u>10.1186/s12889-020-8281-0</u> IMPACT FACTOR: 2.567 CITED HALF-LIFE: 5.5

START COMMENTARY

Kibreab et al. conducted a secondary data analysis of the Eritrea Demographic and Health Survey 2010 to assess the relationship between maternal education and full immunization of children aged 12–23 months. They found higher odds of full immunization among children whose mothers who had primary education compared to no education, adjusting for potential confounders. Interestingly, the association was not statistically significant when comparing mothers with middle or higher education levels and mothers with no education, adjusting for potential confounders. Limitations of this study included the reliance on maternal recall for those who did not have vaccination cards, the cross-sectional nature of the study design (though authors posit that maternal education was likely to occur prior to child immunization), and unmeasured confounding. Authors called for qualitative study to investigate reasons for unimmunized children among mothers with no education.

7. Japanese encephalitis vaccination in the Philippines: A cost-effectiveness analysis comparing alternative delivery strategies.

Vodicka E, Zimmermann M, Lopez A, Silva M, Gorgolon L, Kohei T, et al. Vaccine. 2020 Mar 20;38(13):2833-2840. PubMed ID: 32085954

ABSTRACT

INTRODUCTION: Japanese encephalitis (JE) is a mosquito-borne viral infection of the brain that can cause permanent brain damage and death. In the Philippines, efforts are underway to deliver a live attenuated JE vaccine (CD-JEV) to children under five years of age (YOA), who are disproportionately infected. Multiple vaccination strategies are being considered.

METHODS: We conducted a cost-effectiveness analysis comparing three vaccination strategies to the current state of no vaccination from the societal and government perspectives: (1) national routine vaccination only, (2) sub-national campaign followed by national routine, and (3) national campaign followed by national routine. We developed a Markov model to estimate impact of vaccination or no vaccination over the child's lifetime horizon, assuming an annual incidence of 10.6 cases per 100,000. Costs of illness (\$859/case), vaccine (\$0.50/dose), routine vaccination (\$0.95/dose), and campaign vaccination (\$0.98/dose) were based on hospital financial records, expert opinion and literature. The societal perspective included transportation and opportunity costs of caregiver time, in addition to costs incurred by the health system.

RESULTS: JE vaccination via national campaign followed by national routine delivery was the most cost-effective strategy modeled with a cost per disability adjusted life year (DALY) averted of \$233 and \$29 from the government and societal perspectives, respectively. Results were similar for other delivery strategies with cost/DALY ranging from \$233 to \$265 from the government perspective and \$29-\$57 from the societal perspective. JE vaccination was projected to prevent 27,856-37,277 cases, 5571-7455 deaths, and 173,233-230,704 DALYs among children under five over 20 consecutive birth cohorts. Total incremental costs of vaccination versus no vaccination over 20 birth cohorts were \$6.6-\$9.8 million from the societal perspective (\$230 K-\$440 K annually) and \$45.9-\$53.9 million (\$2.2 M-\$2.7 M annually) from the governmental perspective.

CONCLUSION: Vaccination with CD-JEV in the Philippines is projected to be cost-effective, reducing long-term costs associated with JE illness and improving health outcomes compared to no vaccination.

WEB: <u>10.1016/j.vaccine.2020.02.018</u> IMPACT FACTOR: <u>3.269</u> CITED HALF-LIFE: <u>3.1</u>

START COMMENTARY

Vodicka et al. conducted a cost-effectiveness analysis of three Japanese encephalitis (JE) vaccination strategies in the Philippines, where JE incidence is high. Using a Markov model (see Figuure 1 and Table 1), authors found a national campaign followed by national routine immunization to the most cost-effective strategy. Limitations of this study included lack of age-specific JE incidence data in the Philippines, lack of cost data for JE treatment of confirmed cases, and inability to account for full societal costs.

8. Health workers' perceptions and challenges in implementing meningococcal serogroup a conjugate vaccine in the routine childhood immunization schedule in Burkina Faso.

Nkwenkeu S, Jalloh M, Walldorf J, Zoma R, Tarbangdo F, Fall S, et al. *BMC Public Health*. 2020 Feb 26;20(1):254. PubMed ID: 32075630

ABSTRACT

BACKGROUND: Meningococcal serogroup A conjugate vaccine (MACV) was introduced in 2017 into the routine childhood immunization schedule (at 15-18 months of age) in Burkina Faso to help reduce meningococcal meningitis burden. MACV was scheduled to be co-administered with the second dose of measles-containing vaccine (MCV2), a vaccine already in the national schedule. One year following the introduction of MACV, an assessment was conducted to qualitatively examine health workers' perceptions of MACV introduction, identify barriers to uptake, and explore opportunities to improve coverage.

METHODS: Twelve in-depth interviews were conducted with different cadres of health workers in four purposively selected districts in Burkina Faso. Districts were selected to include urban and rural areas as well as high and low MCV2 coverage areas. Respondents included health workers at the following levels: regional health managers (n = 4), district health managers (n = 4), and frontline healthcare providers (n = 4). All interviews were recorded, transcribed, and thematically analyzed using qualitative content analysis.

RESULTS: Four themes emerged around supply and health systems barriers, demand-related barriers, specific challenges related to MACV and MCV2 co-administration, and motivations and efforts to improve vaccination coverage. Supply and health systems barriers included aging cold chain equipment, staff shortages, overworked and poorly trained staff, insufficient supplies and financial resources, and challenges with implementing community outreach activities. Health workers largely viewed MACV introduction as a source of motivation for caregivers to bring their children for the 15- to 18-month visit. However, they also pointed to demand barriers, including cultural practices that sometimes discourage vaccination, misconceptions about vaccines, and religious beliefs. Challenges in co-administering MACV and MCV2 were mainly related to reluctance among health workers to open multi-dose vials unless enough children were present to avoid wastage.

CONCLUSIONS: To improve effective administration of vaccines in the second-year of life, adequate operational and programmatic planning, training, communication, and monitoring are necessary. Moreover, clear policy communication is needed to help ensure that health workers do not refrain from opening multi-dose vials for small numbers of children.

WEB: <u>10.1186/s12889-020-8347-z</u> IMPACT FACTOR: 2.567 CITED HALF-LIFE: 5.5

START COMMENTARY

Nkwenkeu et al. conducted 12 in-depth interviews of health workers across four purposively selected geographic regions in Burkina Faso—rural and urban areas with low and high coverage of the second dose of the measles-contianing vaccine (MCV2) coverage based on 2016 administrative data. Overall, healthcare workers cited operational challenges to administering the meningococcal serogroup A conjugate vaccine (MACV), areas that can be targeted for improvement. Limitations of the study included potential inconsistencies in the translation of survey questions and responses into local languages other than French, lack of generalizability outside this setting, potential interviewer bias, and not sharing results with interview participants to elicit feedback.

9. Measles antibody levels among vaccinated and unvaccinated children 6-59 months of age in the Democratic Republic of the Congo, 2013-2014.

Ashbaugh H, Cherry J, Hoff N, Doshi R, Alfonso V, Gadoth A, et al. *Vaccine.* 2020 Feb 25;38(9):2258-2265. PubMed ID: 32057333

ABSTRACT

BACKGROUND: Measles is endemic in the Democratic Republic of the Congo (DRC), and 89-94% herd immunity is required to halt its transmission. Much of the World Health Organization African Region, including the DRC, has vaccination coverage below the 95% level required to eliminate measles, heightening concern of inadequate measles immunity.

METHODS: We assessed 6706 children aged 6-59 months whose mothers were selected for interview in the 2013-2014 DRC Demographic and Health Survey. History of measles was obtained by maternal report, and classification of children who had measles was completed using maternal recall and measles immunoglobulin G serostatus obtained from a multiplex chemiluminescent automated immunoassay dried blood spot analysis. A logistic regression model was used to identify associations of covariates with measles and seroprotection, and vaccine effectiveness (VE) was calculated.

RESULTS: Out of our sample, 64% of children were seroprotected. Measles vaccination was associated with protection against measles (OR: 0.15, 95% CI: 0.03, 0.81) when administered to children 12 months of age or older. Vaccination was predictive of seroprotection at all ages. VE was highest (88%) among children 12-24 months of age.

CONCLUSION: Our results demonstrated lower than expected seroprotection against measles among vaccinated children. Understanding the factors that affect host immunity to measles will aid in developing more efficient and effective immunization programs in DRC.

WEB: 10.1016/j.vaccine.2019.09.047 IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

Ashbaugh et al. conducted a serosurvey of children aged 6–59 months who were included in the 2013–2014 Democratic Republic of the Congo (DRC) Demographic and Health Survey to assess population protection against measles among vaccinated and unvaccinated children. They found that seroprotection against measles was lower than expected among vaccinated children. Interestingly, the authors reported 40% of children unvaccinated and with no history of measles were seroprotected against measles, positing either unrecognized measles illness or misclassification of vaccination status. Limitations of the study included potential misclassification of vaccination status (i.e., reliance on maternal recall) and history of measles (i.e., did not have laboratory-confirmed diagnosis of measles). Despite these potential limitations, authors noted that the assessment of seroprotection can inform future policy and research in the efforts to eliminate measles.

10. Mapping cholera outbreaks and antibiotic resistant Vibrio cholerae in India: An assessment of existing data and a scoping review of the literature.

Chatterjee P, Kanungo S, Bhattacharya S, Dutta S. *Vaccine.* 2020 Mar 05;38 Suppl 1:A93-A104. PubMed ID: 31883807

ABSTRACT

Although fluid and electrolyte replenishment remains the mainstay of clinical management of cholera, antibiotics are an important component of the strategy for clinical management of moderate to severe cases of cholera. The emergence of antibiotic resistance (ABR) in Vibrio cholerae has led to difficulties in case management. The past decade has also seen the development of cheap and effective oral cholera vaccines (OCVs). In addition to the two-dose strategy for widespread immunization, OCVs have also been shown to be effective in containing outbreaks using a singledose schedule. In this scoping review we map the states and union territories (SUTs) of India which are prone to cholera outbreaks followed by a scoping review of peer-reviewed publications about ABR outbreaks of cholera employing the Arksey and O'Malley framework. Using the data reported by the Integrated Disease Surveillance Program (IDSP), we identified 559 outbreaks of cholera between 2009 and 2017, affecting 27 SUTs. We defined SUTs which had reported outbreaks in at least three out of the last five years (2012-2016) or had experienced two or more outbreaks in the same year in at least two of the last five years to be outbreak-prone. The scoping review identified 62 ABR outbreaks, with four SUTs accounting for two-thirds of them: West Bengal (14), Maharashtra (10), Odisha (10) and Delhi (7). Overall, this scoping review suggests that there is an increasing trend of ABR in Vibrio cholerae isolated from outbreaks in India. This opens up avenues for exploring the role of antibiotic stewardship in the clinical management of diarrhea, the institution of vaccination as an infection prevention intervention to reduce selection pressure, and the deployment of high quality surveillance systems which report accurate, real-time data allowing appropriate and timely public health responses. It is crucial to counter the issue of ABR in cholera before it assumes a menacing magnitude.

WEB: 10.1016/j.vaccine.2019.12.003 IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

Table 1 and Figure 2 illustrate areas where cholera outbreaks have occurred between 2009 and 2017. Heat maps in Figure 3 indicate the increasing prevalence of antibiotic resistant *Vibrio cholerae*. Chatterjee et al. noted limitations to this study were the under-reporting of cholera cases and wide range of methods used to identify antibiotic resistant burden with overlapping time periods, which made quantification of study findings challenging.

Appendix

The literature search for the April 2020 Vaccine Delivery Research Digest was conducted on March 26, 2020. We searched English language articles indexed by the US National Library of Medicine and published between February 15, 2020 and March 14, 2020. The search resulted in 279 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 pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR