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List of Articles

1 Cost-effectiveness of a reactive oral cholera immunization campaign using Shanchol™ in Malawi.

{Abstract & START Commentary} {Full Article}

- A cost-effectiveness study assessing the direct and indirect protective effects and cost-effectiveness of a reactive cholera immunization campaign.

2 Impact and effect mechanisms of mass campaigns in resource-constrained health systems: quasi-experimental evidence from polio eradication in Nigeria.

{Abstract & START Commentary} {Full Article}

- A longitudinal study utilizing multi-level mixed-effects regression models to assess the impact of polio eradication campaigns on health system performance measured by routine immunization attainment, maternal healthcare utilization, and child survival.

3 Botched Ebola Vaccine Trials in Ghana: An Analysis of Discourses in the Media.

{Abstract & START Commentary} {Full Article}

- A qualitative study of media discourses to understand the cultural, historical, and political influences which influenced the suspension of the 2015 Ebola vaccine trials in Ghana.

4 Allocating epidemic response teams and vaccine deliveries by drone in generic network structures, according to expected prevented exposures.

{Abstract & START Commentary} {Full Article}

- A study utilizing a network-based SIERVD model to simulate the spatial spread of an epidemic, assess the feasibility of drones as a resource allocation strategy, and consider several resource allocation scenarios.

5 Measles outbreak in complex emergency: estimating vaccine effectiveness and evaluation of the vaccination campaign in Borno State, Nigeria, 2019.

{Abstract & START Commentary} {Full Article}

- A study describing the 2019 measles outbreak in Nigeria and assessing measles-containing vaccine coverage and vaccine effectiveness to determine the public-level impact of outbreak respond immunization campaigns.

6 The epidemiologic impact and cost-effectiveness of new tuberculosis vaccines on multidrug-resistant tuberculosis in India and China.

{Abstract & START Commentary} {Full Article}

- A study assessing the epidemiological impact, cost-effectiveness, and budget impact of a hypothetical TB vaccine on rifampicin-resistant and multidrug-resistant tuberculosis.

7 A scorecard of progress towards measles elimination in 15 west African countries, 2001-19: a retrospective, multicountry analysis of national immunisation coverage and surveillance data.

{Abstract & START Commentary} {Full Article}

- A retrospective analysis of national immunization coverage of measles-containing vaccines, immunization activities, and measles incidence rates across 15 countries to track progress on measles elimination.

8 Assessing the impact of preventive mass vaccination campaigns on yellow fever outbreaks in Africa: A population-level self-controlled case series study.

{Abstract & START Commentary} {Full Article}

- A self-controlled case series method on the association between the occurrence of yellow fever outbreaks and the implementation of preventive mass vaccination campaigns at the province level.

9 Cost-effectiveness and budget impact analyses for the prioritisation of the four available rotavirus vaccines in the national immunisation programme in Thailand.

{Abstract & START Commentary} {Full Article}

- A study utilizing a transmission dynamic model to estimate the costs and outcomes of four WHO-prequalified rotavirus vaccines among children <1 year compared to no vaccination.

10 Direct and indirect effect of 10 valent pneumococcal vaccine on nasopharyngeal carriage in children under 2 years of age in Matiari, Pakistan.

{Abstract & START Commentary} {Full Article}

- A study determining carriage-rates over time for vaccine-type and non-vaccine-type pneumococcus and associated factors after the 2012 introduction of ten-valent pneumococcal-conjugate-vaccine.

Appendix

Details of Articles

1. Cost-effectiveness of a reactive oral cholera immunization campaign using Shanchol™ in Malawi.

Ilboudo P, Mengel M, Gessner B, Ngwira B, Cavailler P, Le Gargasson J.

Cost Eff Resour Alloc. 2021 Mar 14;19(1):17.
PubMed ID: 33691725

ABSTRACT

BACKGROUND: Oral cholera vaccines (OCV) have been recommended as additional measures for the prevention of cholera. However, little is known about the cost-effectiveness of OCV use in sub-Saharan Africa, particularly in reactive outbreak contexts. This study aimed to investigate the cost-effectiveness of the use of OCV Shanchol in response to a cholera outbreak in the Lake Chilwa area, Malawi.

METHODS: The Excel-based Vaccine Introduction Cost-Effectiveness model was used to assess the cost-effectiveness ratios with and without indirect protection. Model input parameters were obtained from cost evaluations and epidemiological studies conducted in Malawi and published literature. One-way sensitivity and threshold analyses of cost-effectiveness ratios were performed.

RESULTS: Compared with the reference scenario i.e. treatment of cholera cases, the immunization campaign would have prevented 636 and 1 020 cases of cholera without and with indirect protection, respectively. The cost-effectiveness ratios were US$19 212 per death, US$500 per case, and US$738 per DALY averted without indirect protection. They were US$10 165 per death, US$264 per case, and US$391 per DALY averted with indirect protection. The net cost per DALY averted was sensitive to four input parameters, including case fatality rate, duration of immunity (vaccine's protective duration), discount rate and cholera incidence.

CONCLUSION: Relative to the Malawi gross domestic product per capita, the reactive OCV campaign represented a cost-effective intervention, particularly when considering indirect vaccine effects. Results will need to be assessed in other settings, e.g., during campaigns implemented directly by the Ministry of Health rather than by international partners.

WEB: 10.1186/s12962-021-00270-y
IMPACT FACTOR: 1.413
CITED HALF-LIFE: 7.8

START COMMENTARY

In this cost-effectiveness analysis, Ilboudo *et al.* evaluated the cost-effectiveness of implementing Shanchol oral cholera vaccine in the context of an outbreak. This analysis builds on prior work by the authors on the costs of the vaccine campaign (including cost of vaccine delivery per dose), and on household and health facility costs of treating cholera. Reactive immunization costs were extracted from program documents, budgets, and financial reports from implementers and were presented in US dollars. Costs included the vaccine, personnel, per diems, materials, equipment, transportation, rentals, catering, wasted vaccines, and other miscellaneous costs. Treatment costs borne by households (i.e., direct medical and non-medical costs and indirect costs of lost wages) were collected through interviews with heads of households. Treatment costs for health facilities included the cost of staff, medicines, and consumables were estimated through health facility cholera registries and interviews with health personnel. The cost effectiveness was determined using the Vaccine Introduction Cost-Effectiveness Calculator, a tool for estimating the cost-effectiveness of vaccination programs by determining the net cost per case, cost per death, and cost per DALY averted. Direct effects of vaccination were determined via vaccination coverage surveys whereas indirect effects were estimated using previously published epidemiological models which predict vaccine effectiveness as a function of vaccine coverage. In this study, Ilboudo *et al.* assumed a protective efficacy of 93% (95 confidence interval [CI]: 82%-99%) for the double dose coverage rate.

Key findings included that with a vaccine efficacy of 58% (the base case), 636 cases and 430 DALYs could be averted for a total cost of US$397,358. When considering indirect protection and a vaccine efficacy of 93%, as aforementioned, 1,020 vases and 690 DALYs could be averted under this scenario. The latter scenario would result in US$127,938 and US$268,420 treatment-related costs being averted for households and health facilities, respectively. The authors noted that the net costs per case and death averted were most sensitive to cholera incidence, vaccine efficacy, vaccine delivery cost, cost of illness, case fatality, and duration of protection. Limitations of this study include the lack of primary data on indirect protection effects for this study or from Malawi, and the lack of consideration of complex transmission dynamics of cholera. This study is an important contribution to the literature on cost-effectiveness of oral cholera vaccine use in reactive campaigns, which has been largely understudied but is required for policy-making for future outbreaks.

Return to List of Articles

2. Impact and effect mechanisms of mass campaigns in resource-constrained health systems: quasi-experimental evidence from polio eradication in Nigeria.

Haenssgen M, Closser S, Alonge O.

BMJ Glob Health. 2021 Mar 22;6(3).

PubMed ID: 33685940

ABSTRACT

BACKGROUND: Mass campaigns are a key strategy for delivering life-saving interventions under Global Health Initiatives, especially in weak health system contexts. They are frequently designed parallel to the health system to rapidly achieve programme targets such as vaccination coverage, but we lack quantitative evidence demonstrating their impact and effect mechanisms on health system performance at sub-/national level. This longitudinal study responds to this gap through an analysis of polio eradication campaigns in Nigeria.

METHODS: Using four rounds of Demographic and Health Surveys in Nigeria between October 2000 and December 2017, we created a longitudinal dataset containing 88 881 under-5 children/pregnancies. We estimated the relationships between individuals' campaign exposure and health system performance indices (full RI schedule attainment, maternal healthcare services utilisation and child survival) using multilevel, mixed-effects regression models applied nationally and stratified by the six geopolitical zones in Nigeria.

RESULTS: Nationally, high-frequency mass campaigns had detrimental health systems effects that potentially left 3.6 million children deprived of full immunisation. The frequency of campaigns was most concentrated in regions with weak health systems, where the operations of RI were disrupted, alongside negative effects on child survival and institutional delivery. In contrast, regions with relatively strong health systems and few campaigns experienced beneficial effects on maternal healthcare service utilisation.

CONCLUSIONS: As we provide evidence that well-functioning health systems can benefit from mass campaigns under Global Health Initiatives, our work also challenges the established wisdom to intensify mass campaigns in weaker health systems to bypass service provision bottlenecks. Mass campaigns do not inherently benefit or damage a health system, but frequent campaigns in weak health system contexts can impede service provision. We call for an additional burden of proof and active efforts to integrate mass campaigns into routine health services by harmonising implementation plans and service delivery in weak health system contexts.

WEB: 10.1136/bmjgh-2020-004248
IMPACT FACTOR: 4.280
CITED HALF-LIFE: 1.9

START COMMENTARY

In the following study, Haenssgen *et al.* analyze supplementary immunization activities (SIAs) for polio eradication in Nigeria to understand how they positively or negatively influence national health system performance. SIAs are mass immunization campaigns conducted to immunize every child under five with two doses or oral polio vaccine regardless of prior immunization status via fixed sites for immunization and with door-to-door campaigns. Authors utilized Demographic Health Survey (DHS) data from 2003, 2008, 2013, and 2018 matched data for each local government area (LGA) with dates and information on 312 national and subnational SIA campaigns from 2000-2017. Matched data allowed authors to estimate the number of rounds to which children and pregnancies were exposed in three periods: pregnancy period, routine immunization period (i.e., birth until 10 months), and follow up period (age after 10 months where children catch up on missed vaccines during the routine immunization period). Haenssgen *et al.* utilized multi-level logistic and linear regression models with SIA exposure as the predictor and the following three outcomes: full childhood immunization (defined as completing three doses of DPT vaccine, one dose of BCG and one dose of measles vaccine); maternal healthcare utilization (defined by the number of antenatal healthcare visits and tetanus toxoid injections, and place of delivery), and child survival. Models included covariates frequently used in the childhood immunization literature (e.g., age of child, age of mother, mother's highest education).

Authors found that SIAs were concentrated in regions with relatively poorer health system performance and lower wealth, such as the Northwest and Northeast region. The analysis showed a negative overall relationship between mass campaign exposure of any type (i.e., national immunization days, immunization plus days, mop-up campaigns, etc.,) and routine health services. This was particularly pronounced for catch up immunizations (i.e., during the third period) for older children. In regions with stronger health systems, SIAs were associated with increased maternal health service utilization, indicating substantial subnational variation in the impacts of SIAs on health system performance. Limitations of note include the assumption that all children in a target area were covered by SIAs, and the inability to account for other interventions which may have affected health system performance in Nigeria. Despite these limitations, this article underscores the importance of understanding the impacts of mass immunization campaigns on health system performance; mass campaigns may benefit well-functioning health systems but negatively impact service provision and utilization in weaker health systems.

Return to List of Articles

3. Botched Ebola Vaccine Trials in Ghana: An Analysis of Discourses in the Media.

Thompson E.

Vaccines (Basel). 2021 Mar 10;9(2).
PubMed ID: 33669759

ABSTRACT

In June 2015, proposed Ebola vaccine trials were suspended by the Ministry of Health of Ghana amid protests from members of parliament and the general public. Scholarship has often focused on the design, development, and administration of vaccines. Of equal importance are the social issues surrounding challenges with vaccine trials and their implementation. The purpose of this study was to analyze discourses in the media that led to the suspension of the 2015 Ebola vaccine trials in Ghana. I use a sociological lens drawing on moral panic and risk society theories. The study qualitatively analyzed discourses in 18 semi-structured interviews with media workers, selected online publications, and user comments about the Ebola vaccine trials. The findings show that discourses surrounding the Ebola vaccine trials drew on cultural, biomedical, historical, and even contextual knowledge and circumstances to concretize risk discourses and garner support for their positions. Historical, political, and cultural underpinnings have a strong influence on biomedical practices and how they are (not) accepted. This study highlights the complexity and challenges of undertaking much needed vaccine tests in societies where the notion of drug trials has underlying historical and sociological baggage that determine whether (or not) the trials proceed.

WEB: 10.3390/vaccines9020177
IMPACT FACTOR: 4.086
CITED HALF-LIFE: 3.4

START COMMENTARY

In this qualitative study, Thompson describes the discourses surrounding the suspended 2015 Ebola vaccine trials. The author conducted semi-structured interviews with 18 workers in television, radio, and newspapers in Accra, and conducted content analysis from digital news sites of four radio stations (Myjoyonline.com, citifmonline.com, peacefmonline.com, and starrfmonline.com) and of the leading Ghanaian digital news site (ghanaweb.com). This work was grounded in theories related to moral panic and risk society. Eligible workers included those that worked at a legacy media organization (e.g., radio, newspaper, television) and covered stories about the Ebola vaccine trials. Participants were recruited using purposive snowball sampling and interviewed in August and September 2015.

The study highlighted many interesting social, political, and cultural factors which affected views on the vaccine trials. There were mixed findings regarding the coverage of the vaccine trials; some interviewees felt that the negative portrayal of the trials was warranted whereas others stated that it harmed the image of the media. The author highlights several moral panic discourses that were present in the interviews and online media content. One such example included stigmatizing discourses such as claims that the vaccines were not safe, trial implementers were conducting trials for their own benefit while harming Ghanaian citizens, and that the vaccine may cause Ebola. Risk society context states that people view things skeptically to deal with unknown risk. Interviews, news stories, and user comments all highlighted concerns about the risks of the vaccine, including fears that it would carry the Ebola virus. Further, the author stated this risk society context contributes to an environment where there is limited trust in science. Further, there were several concerns about the selection of Ghana as the location for the clinical trial, given that the country had not recorded any Ebola cases, and many mentions of prior negative examples of trials (e.g., polio vaccine; Tuskegee syphilis trials). One key limitation of note is that this study only relied on legacy media (e.g., news, radio) without considering social media platforms, where many people in Ghana, and globally get information and share opinions about biomedical research. Overall, this study shows the importance of understanding the cultural, contextual, and historical factors which may affect a vaccine trial's acceptance and success in a country.

Return to List of Articles

4. Allocating epidemic response teams and vaccine deliveries by drone in generic network structures, according to expected prevented exposures.

Matter D, Potgieter L.

PLoS One. 2021 Mar 16;16(3):e0248053.
PubMed ID: 33667263

ABSTRACT

The tumultuous inception of an epidemic is usually accompanied by difficulty in determining how to respond best. In developing nations, this can be compounded by logistical challenges, such as vaccine shortages and poor road infrastructure. To provide guidance towards improved epidemic response, various resource allocation models, in conjunction with a network-based SEIRVD epidemic model, are proposed in this article. Further, the feasibility of using drones for vaccine delivery is evaluated, and assorted relevant parameters are discussed. For the sake of generality, these results are presented for multiple network structures, representing interconnected populations-upon which repeated epidemic simulations are performed. The resource allocation models formulated maximise expected prevented exposures on each day of a simulated epidemic, by allocating response teams and vaccine deliveries according to the solutions of two respective integer programming problems-thereby influencing the simulated epidemic through the SEIRVD model. These models, when compared with a range of alternative resource allocation strategies, were found to reduce both the number of cases per epidemic, and the number of vaccines required. Consequently, the recommendation is made that such models be used as decision support tools in epidemic response. In the absence thereof, prioritizing locations for vaccinations according to susceptible population, rather than total population or number of infections, is most effective for the majority of network types. In other results, fixed-wing drones are demonstrated to be a viable delivery method for vaccines in the context of an epidemic, if sufficient drones can be promptly procured; the detrimental effect of intervention delay was discovered to be significant. In addition, the importance of well-documented routine vaccination activities is highlighted, due to the benefits of increased pre-epidemic immunity rates, and targeted vaccination.

WEB: 10.1371/journal.pone.0248053
IMPACT FACTOR: 2.740
CITED HALF-LIFE: 5.6

START COMMENTARY

In this modelling study, Matter *et al.* describe various resource allocation models which could be considered in the context of an epidemic in developing countries that may face challenges including vaccine shortages, poor road conditions, and a lack of resources during outbreaks. To

address these logistical difficulties, authors describe the feasibility of delivering vaccines via drones and the parameters that are most relevant for determining a resource allocation strategy. The authors use a network-based SEIRVD epidemic model to stimulate the spread of an epidemic by considering the progression of the epidemic, the transmission rate of disease, the movement of individuals, and the number of vaccinations performed. This model has been validated previously for a measles outbreak in Niger from 2003-2004. They also present several alternate dynamic resource allocation methods. The first strategy considers team allocation strategies that that either allocate teams evenly across locations, or alternatively, allocate teams based on the location's characteristics such as the size of the total population, the susceptible population, the infected population, or the ratio of infections to the total population. The second allocation method assesses vaccine allocation via drones to communities based on population size (i.e., total population, susceptible population, infected population) and by delivery time. Matter *et al.* concluded that both resource allocation models formulated were highly effective in reducing cases of disease and increasing vaccine usage. Models indicated that allocating teams uniformly or proportionally to the number of infections in a location was ineffective, indicating the need for more sophisticated targeting during outbreaks, such as those that prioritize locations based on the susceptible population, which performed well. Authors also conducted sensitivity analyses to understand the role of intervention delays and drone-related parameters. This article contributes important findings on how to improve resource allocation of personnel and vaccines in current and future epidemics in developing countries.

Return to List of Articles

5. Measles outbreak in complex emergency: estimating vaccine effectiveness and evaluation of the vaccination campaign in Borno State, Nigeria, 2019.

Jean Baptiste A, Wagai J, Luce R, Masresha B, Klinkenberg D, Veldhuijzen I, et al.

BMC Public Health. 2021 Mar 08;21(1):437.
PubMed ID: 33663439

ABSTRACT

BACKGROUND: From January to May 2019, large measles outbreaks affected Nigeria. Borno state was the most affected, recording 15,237 suspected cases with the state capital of Maiduguri having 1125 cases investigated and line-listed by March 2019. In Borno state, 22 of the 27 Local Government Areas (LGAs or Districts), including 37 internally displaced persons (IDPs) camps were affected. In response to the situation, an outbreak response immunization (ORI) campaign was conducted in the 13 most affected LGAs. In addition to conventional vaccination teams, special teams were deployed in security compromised areas, areas with migrants, and for nomadic and IDPs. Here we describe the outbreak and the ORI campaign. We also assess the measles-containing vaccine (MCV) coverage and vaccine effectiveness (VE) in order to quantify the population-level impact.

METHODS: We reviewed the ORI activities, and conducted an analysis of the surveillance and the outbreak investigation reports. We assessed VE of MCV by applying the screening-method. Sensitivity analyses were also conducted to assess the effect of final classification of cases on the VE of MCV. The MCV coverage was assessed by a post-campaign coverage survey after completion of the ORI through a quantitative survey in the 12 LGAs that were accessible.

RESULTS: Of the total 15,237 reported measles cases, 2002 cases were line-listed and investigated, and 737 were confirmed for measles by week 9 of 2019. Of the investigated cases 67.3% (n = 1348) were between 9 and 59 months of age. Among the 737 confirmed cases, only 9% (n = 64) stated being vaccinated with at least 1 dose of MCV. The overall VE for MCV was 98.4% (95%CI: 97.8-98.8). No significant differences were observed in the VE estimates of lab-confirmed and epi-linked cases when compared to the original estimates. The aggregated weighted vaccination coverage was 85.7% (95% CI: 79.6-90.1).

CONCLUSION: The experience in Borno demonstrates that adequate VE can be obtained in conflict-affected areas. In complex emergencies affected by measles outbreaks, health authorities may consider integration with other health strategies and the engagement of security personnel as part of the ORI activities.

WEB: 10.1186/s12889-021-10436-1
IMPACT FACTOR: 2.521
CITED HALF-LIFE: 6.0

START COMMENTARY

In the following article, Jean Baptiste *et al.* describe the outbreak response immunization (ORI) and the associated population-level impacts of a large measles outbreak in Borno, Nigeria in 2019. Data that was used for this study included routine case-based surveillance for measles, which has been shown to be reliable and sensitive to identify and confirm measles through annual performance monitoring indicators, and a post-campaign coverage survey. In this two-stage cluster household survey, participants were randomly selected from a sampling frame of 1044 settlements and deemed eligible if they had children aged from 9 to 71 months. Authors estimate age-specific vaccine effectiveness (VE) for measles containing vaccines (MCV). Further, they conducted a sensitivity analysis comparing VE for lab-confirmed cases compared to the VE for epidemiological-linked cases.

Jean Baptiste *et al.* report that of 737 confirmed cases, 9% (n=64) report being vaccinated with at least one dose of MCV. The overall VE among all age groups was 98.4 (95%CI: 97.8–98.8), with the oldest group (60-71 months) reporting the highest VE. In the sensitivity analysis, authors only found one age group had any significant differences in VE estimates in two scenarios (lab-confirmed vs. epi-linked) when compared to the initial estimates; among 9-11 months for lab-confirmed cases, the VE was 68.3% (95%CI: − 509 – 99.5), compared to 88.5% (95%CI: 72.1–96.1) for epi-linked cases. Both estimates were lower than the original estimate of 96.2% (95%CI: 92.6–98.3) for this group. In the post campaign coverage survey, the aggregate weighted coverage was 85.7% (95%CI: 79.6–90.1) which children 24-35 months reporting the highest coverage. One notable limitation is the exclusion of internally displaced persons (IDP) camps, 37 of which were affected by measles outbreaks, which may have resulted in higher estimates of VE. Relatedly, many participants (53.2%) who were vaccinated did not have a vaccination card and given the lag between ORI phases and the survey, there may have been recall bias. Overall, this study provides critical insights for future measles prevention activities in Nigeria and vaccination efforts in the context of outbreaks and emergency settings in Nigeria and elsewhere.

Return to List of Articles

6. The epidemiologic impact and cost-effectiveness of new tuberculosis vaccines on multidrug-resistant tuberculosis in India and China.

Weerasuriya C, Harris R, McQuaid C, Bozzani F, Ruan Y, Li R, et al.

BMC Med. 2021 Mar 21;19(1):60.

PubMed ID: 33632218

ABSTRACT

BACKGROUND: Despite recent advances through the development pipeline, how novel tuberculosis (TB) vaccines might affect rifampicin-resistant and multidrug-resistant tuberculosis (RR/MDR-TB) is unknown. We investigated the epidemiologic impact, cost-effectiveness, and budget impact of hypothetical novel prophylactic prevention of disease TB vaccines on RR/MDR-TB in China and India.

METHODS: We constructed a deterministic, compartmental, age-, drug-resistance- and treatment history-stratified dynamic transmission model of tuberculosis. We introduced novel vaccines from 2027, with post- (PSI) or both pre- and post-infection (P&PI) efficacy, conferring 10 years of protection, with 50% efficacy. We measured vaccine cost-effectiveness over 2027-2050 as USD/DALY averted-against 1-times GDP/capita, and two healthcare opportunity cost-based (HCOC), thresholds. We carried out scenario analyses.

RESULTS: By 2050, the P&PI vaccine reduced RR/MDR-TB incidence rate by 71% (UI: 69-72) and 72% (UI: 70-74), and the PSI vaccine by 31% (UI: 30-32) and 44% (UI: 42-47) in China and India, respectively. In India, we found both USD 10 P&PI and PSI vaccines cost-effective at the 1-times GDP and upper HCOC thresholds and P&PI vaccines cost-effective at the lower HCOC threshold. In China, both vaccines were cost-effective at the 1-times GDP threshold. P&PI vaccine remained cost-effective at the lower HCOC threshold with 49% probability and PSI vaccines at the upper HCOC threshold with 21% probability. The P&PI vaccine was predicted to avert 0.9 million (UI: 0.8-1.1) and 1.1 million (UI: 0.9-1.4) second-line therapy regimens in China and India between 2027 and 2050, respectively.

CONCLUSIONS: Novel TB vaccination is likely to substantially reduce the future burden of RR/MDR-TB, while averting the need for second-line therapy. Vaccination may be cost-effective depending on vaccine characteristics and setting.

WEB: 10.1186/s12916-021-01932-7

IMPACT FACTOR: 6.782

CITED HALF-LIFE: 5.2

START COMMENTARY

In this modelling study, Weerasuriya *et al.* explore the potential epidemiological impact and cost-effectiveness of a novel vaccine for rifampicin-resistant and multidrug-resistant tuberculosis (RR/MDR-TB). The authors developed an an age-, treatment history-, and drug resistance- stratified compartmental transmission model which included five states of TB (susceptible, latently infected, active disease, on treatment, and recovered from disease, stratified by drug resistance and treatment history). The model was calibrated to India and China by considering historical rates of prevalence, incidence, notification, and mortality for TB, and RR/MDR-TB incidence rates and percentage RR/MDR-TB among all TB notifications. Vaccine introduction with post- (PSI) or both pre- and post- (P&PI) efficacy with 10 years of protection was stimulated to begin in 2027 and impact was assessed from 2027 to 2050. Two vaccination strategies were modeled: routine annual vaccination to 9-year-olds and mass vaccination campaigns delivered every decade to those 10 years or older. Vaccine, delivery, and program costs were estimated from existing literature.

Weerasuriya *et al.* found that P&PI vaccines would reduce RR/MDR-TB incidence by 70% for both strategies. A PSI vaccine would reduce incidence by 50% in India and 30% in China. Vaccination averted more cases and deaths in India compared to China, due to higher TB mortality in India. Authors noted that both vaccines priced at US$10 were highly likely to be cost-effective in both countries, with P&PI vaccines being more cost-effective. Results projected significant cost savings from vaccination; across both countries, vaccination would avert the need for 1 million 1 million RR/MDR-TB regimens by 2050. Limitations of note included scarce literature for several input parameters (e.g., on RR/MDR-TB transmission rates) and the exclusion of targeted vaccination strategies, which could be more impactful and cost-effective for countries to implement. In conclusion, this study shows the substantial potential of a novel TB vaccine to reduce to RR/MDR-TB morbidity and mortality and the associated health treatment costs, further underscoring the need for new TB vaccines globally.

Return to List of Articles

7. A scorecard of progress towards measles elimination in 15 west African countries, 2001-19: a retrospective, multicountry analysis of national immunisation coverage and surveillance data.

Wariri O, Nkereuwem E, Erondu N, Edem B, Nkereuwem O, Idoko O, et al.

Lancet Glob Health. 2021 Mar 09;9(3):e280-e290.
PubMed ID: 33607028

ABSTRACT

BACKGROUND: The WHO Regional Office for the Africa Regional Immunization Technical Advisory Group, in 2011, adopted the measles control and elimination goals for all countries of the African region to achieve in 2015 and 2020 respectively. Our aim was to track the current status of progress towards measles control and elimination milestones across 15 west African countries between 2001 and 2019.

METHODS: We did a retrospective multicountry series analysis of national immunisation coverage and case surveillance data from Jan 1, 2001, to Dec 31, 2019. Our analysis focused on the 15 west African countries that constitute the Economic Community of West African States. We tracked progress in the coverage of measles-containing vaccines (MCVs), measles supplementary immunisation activities, and measles incidence rates. We developed a country-level measles summary scorecard using eight indicators to track progress towards measles elimination as of the end of 2019. The summary indicators were tracked against measles control and elimination milestones.

FINDINGS: The weighted average regional first-dose MCV coverage in 2019 was 66% compared with 45% in 2001. 73% (11 of 15) of the west African countries had introduced second-dose MCV as of December, 2019. An estimated 4 588 040 children (aged 12-23 months) did not receive first-dose MCV in 2019, the majority (71%) of whom lived in Nigeria. Based on the scorecard, 12 (80%) countries are off-track to achieving measles elimination milestones; however, Cape Verde, The Gambia, and Ghana have made substantial progress.

INTERPRETATION: Measles will continue to be endemic in west Africa after 2020. The regional measles incidence rate in 2019 was 33 times the 2020 elimination target of less than 1 case per million population. However, some hope exists as countries can look at the efforts made by Cape Verde, The Gambia, and Ghana and learn from them.

FUNDING: None.

WEB: 10.1016/S2214-109X(20)30481-2
IMPACT FACTOR: 21.597
CITED HALF-LIFE: 3.1

START COMMENTARY

Wariri *et al.* assessed progress towards measles control and elimination milestones between 2001 to 2019 in 15 west African countries (Benin, Burkina Faso, Cape Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, and Togo). Authors obtained data on population, measles-containing virus (MCV) 1 and MCV 2 coverage, measles cases, and joint external evaluation scores (a score which useless measles vaccine coverage to determine a country's public health preparedness). Data was extracted from the UN World Population Prospects 2019, the WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) database, Multiple Indicator Cluster Survey (MICS), and Demographic and Health Surveys (DHS), the WHO measles surveillance database, and Joint External Evaluation reports. Wariri *et al.* estimated the following outcomes across data sources; MC1 coverage, population reached by supplementary immunization activities (SIAs), number of children unvaccinated for MCV1 in 2019, intra-county geographical equity gaps, the number of measles cases, and the annual measles incidence rate. Authors used these estimates and others to develop a scorecard with eight country-level indicators to track progress towards elimination.

Wariri *et al.* reported mixed success for measles control and elimination; MCV1 improved from 45% in 2001 to a maximum of 72% in 2017. However, progress was not consistent nor sustained over the time. Authors noted variation between countries on MCV1 coverage (as shown in Figure 2), and an inverse relationship between the weighted mean MCV1 coverage and the weighted mean of measles incidence rate (Figure 4a). Ghana, The Gambia, and Cape Verde made substantial progress towards elimination, and are on track to achieving elimination milestones by 2020, whereas all other nations have made little progress (measured by having met only one or two of eight measles scorecard benchmarks). This study is impactful as it demonstrates the reality that measles will continue to be endemic in this region without further attempts to coordinate control/elimination strategies and strengthen health systems.

Return to List of Articles

8. Assessing the impact of preventive mass vaccination campaigns on yellow fever outbreaks in Africa: A population-level self-controlled case series study.

Jean K, Raad H, Gaythorpe K, Hamlet A, Mueller J, Hogan D, et al.

PLoS Med. 2021 Mar 16;18(2):e1003523.

PubMed ID: 33600451

ABSTRACT

BACKGROUND: The Eliminate Yellow fever Epidemics (EYE) strategy was launched in 2017 in response to the resurgence of yellow fever in Africa and the Americas. The strategy relies on several vaccination activities, including preventive mass vaccination campaigns (PMVCs). However, to what extent PMVCs are associated with a decreased risk of outbreak has not yet been quantified.

METHODS AND FINDINGS: We used the self-controlled case series (SCCS) method to assess the association between the occurrence of yellow fever outbreaks and the implementation of PMVCs at the province level in the African endemic region. As all time-invariant confounders are implicitly controlled for in the SCCS method, this method is an alternative to classical cohort or case-control study designs when the risk of residual confounding is high, in particular confounding by indication. The locations and dates of outbreaks were identified from international epidemiological records, and information on PMVCs was provided by coordinators of vaccination activities and international funders. The study sample consisted of provinces that were both affected by an outbreak and targeted for a PMVC between 2005 and 2018. We compared the incidence of outbreaks before and after the implementation of a PMVC. The sensitivity of our estimates to a range of assumptions was explored, and the results of the SCCS method were compared to those obtained through a retrospective cohort study design. We further derived the number of yellow fever outbreaks that have been prevented by PMVCs. The study sample consisted of 33 provinces from 11 African countries. Among these, the first outbreak occurred during the pre-PMVC period in 26 (79%) provinces, and during the post-PMVC period in 7 (21%) provinces. At the province level, the post-PMVC period was associated with an 86% reduction (95% CI 66% to 94%, $p < 0.001$) in the risk of outbreak as compared to the pre-PMVC period. This negative association between exposure to PMVCs and outbreak was robustly observed across a range of sensitivity analyses, especially when using quantitative estimates of vaccination coverage as an alternative exposure measure, or when varying the observation period. In contrast, the results of the cohort-style analyses were highly sensitive to the choice of covariates included in the model. Based on the SCCS results, we estimated that PMVCs were associated with a 34% (95% CI 22% to 45%) reduction in the number of outbreaks in Africa from 2005 to 2018. A limitation of our study is the fact that it does not account for potential time-varying confounders, such as changing environmental drivers of yellow fever and possibly improved disease surveillance.

CONCLUSIONS: In this study, we provide new empirical evidence of the high preventive impact of PMVCs on yellow fever outbreaks. This study illustrates that the SCCS method can be advantageously applied at the population level in order to evaluate a public health intervention.

WEB: 10.1371/journal.pmed.1003523
IMPACT FACTOR: 10.5
CITED HALF-LIFE: 8.4

START COMMENTARY

In this self-controlled case series (SCCS), Jean *et al.* assess associations between implementation of preventative mass vaccination campaigns (PMVCs) and yellow fever outbreaks across yellow-fever endemic regions in Africa. Specifically, the study focused on 33 provinces in 11 countries that were affected by outbreaks and targeted for PMVC. This study utilized secondary data sources, including case data from the WHO Regional Officer for Africa yellow fever surveillance database (which covers 21 countries in West and Central Africa) and PMCV information for the Yellow Fever Initiative and Eliminate Yellow Fever Epidemics strategy. Jean *et al.* found a substantial dose-response preventative effect of PMVCs on the risk of yellow fever in provinces across several models. Authors found that the first outbreak in each province occurred during the pre-PMVC period in 78.8% (n=26) of provinces compared to 21.2% (n=7) outbreaks in the post-PMVC period, corresponding to a reduced incidence rate ratio (IRR) of 0.14 (95% CI 0.06–0.34) for exposed (post-PMVC) versus the unexposed (pre-PMVC). Figure 2 highlights the PMVC campaigns for each province in the unexposed and exposed periods. In the comparison cohort-style analysis, results were very similar: exposure to PMVC led to a significant reduction in risk of an outbreak (IRR 0.37, 95% CI 0.15–0.92). Jean *et al.* also estimated the 10% increases in vaccine coverage led to significant decreases of risk of an outbreak (IRR:0.59, 95% CI 0.49-0.76).

A key strength of this study is the extension of the self-controlled case series design at the population level to control from known and unknown time invariant confounders at the population level. Another strength of this study was the sensitivity analyses conducted; authors varied population-level vaccination coverages (0-19%. 20-39%, etc.), included several SCCS models to understand the influence of model assumptions and conducted a classic cohort design analysis to compare results. Some limitations of note include missing data (e.g., missing PMVC dates) and issues with confounding (e.g., environmental factors which may have affected the risk of yellow fever over time). This study underscores the importance of vaccination campaigns to prevent yellow fever outbreaks among endemic areas in Africa.

Return to List of Articles

9. Cost-effectiveness and budget impact analyses for the prioritisation of the four available rotavirus vaccines in the national immunisation programme in Thailand.

Luangasanatip N, Mahikul W, Poovorawan K, Cooper B, Lubell Y, White L, et al.

Vaccine. 2021 Feb 17;39(9):1402-1414.
PubMed ID: 33531197

ABSTRACT

BACKGROUND: Rotavirus is a major cause of diarrhoea in children less than five years old in Thailand. Vaccination has been shown to be an effective intervention to prevent rotavirus infections but has yet to be enlisted in the national immunisation programme. This study aimed to assess the cost-utility of introducing rotavirus vaccines, taking all WHO-prequalified vaccines into consideration.

METHODS: A cost-utility analysis was performed using a transmission dynamic model to estimate, from a societal perspective, the costs and outcomes of four WHO-prequalified rotavirus vaccines: Rotarix®, RotaTeq®, ROTAVAC® and ROTASIIL®. The model was used to simulate the impact of introducing the vaccines among children aged < 1 year and compare this with no rotavirus vaccination. The vaccination programme was considered to be cost-effective if the incremental cost-effectiveness ratio was less than a threshold of USD 5,110 per QALY gained.

RESULTS: Overall, without the vaccine, the model predicted the average annual incidence of rotavirus to be 312,118 cases. With rotavirus vaccination at a coverage of more than 95%, the average number of rotavirus cases averted was estimated to be 144,299 per year. All rotavirus vaccines were cost-saving. ROTASIIL® was the most cost-saving option, followed by ROTAVAC®, Rotarix® and RotaTeq®, providing average cost-savings of USD 32, 31, 23 and 22 million per year, respectively, with 999 QALYs gained. All vaccines remained cost-saving with lower QALYs gained, even when ignoring indirect beneficial effects. The net saving to the healthcare system when implementing any one of these vaccines would be between USD 13 and 33 million per year.

CONCLUSION: Rotavirus vaccines should be included in the national vaccination programme in Thailand. Implementing any one of these four WHO-prequalified vaccines would reduce government healthcare spending while yielding health benefits to the population.

WEB: 10.1016/j.vaccine.2021.01.051
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

In this cost-effectiveness and budget impact analysis, Luangasanatip *et al.* assess the cost implications of including rotavirus vaccination into the national immunization program in Thailand. Four WHO-prequalified rotavirus vaccines Rotarix®, RotaTeq®, ROTAVAC® and ROTASIIL® were considered in this analysis. This article contributes to an existing literature on the cost-effectiveness of introducing rotavirus vaccines in Thailand which have demonstrated mixed findings. Further, this article fills a critical gap in the literature as it considers all four WHO-prequalified rotavirus vaccines and includes estimates of indirect vaccine effects, both of which have not been done previously. The authors employed an age-structure epidemiological transmission model with several input parameters (e.g., surveillance data; duration of latency; vaccine efficacy), described in detail in Table 1. The model estimated the age-specific incidence and outcomes of rotavirus, and combined these estimates with costs information from the National Health Security Office and existing literature to project the cost-effectiveness and budget impact of introducing vaccines.

Luangasanatip *et al.* projected that rotavirus vaccination would avert an average of 144,299 cases per year from 2020 to 2024, 47.2% (n=67,427) which would have required hospitalization. About 58.3% of the cases averted were due to direct vaccination effects, compared to 41.7% of cases being averted by indirect protection. Authors found that all rotavirus vaccines were cost-saving and lead to substantial QALY gain when compared to no immunization. Analyses indicated that ROTASIIL® was the most cost-effective option. Importantly, sensitivity analyses indicated that two of the vaccines, Rotarix® and RotaTeq®, were no longer considered cost-effective when only considering the direct vaccine effects. Budget impact analyses indicate that net savings to the healthcare budget would be between US$20-29 million per year compared to no vaccination. One key limitation of note which may have overstated the cost-effectiveness and cost savings is the healthcare utilization assumptions; data was not available for diarrheal disease health seeking in Thailand, leading authors to base healthcare utilization assumptions on other settings (e.g., 65% of diarrhea cases seeking healthcare in LMICs). Luangasanatip *et al.* assessed the cost-utility of introducing rotavirus vaccines into the national immunization program and determined any of the WHO-prequalified vaccines would be beneficial for health outcomes and cost-saving.

Return to List of Articles

10. Direct and indirect effect of 10 valent pneumococcal vaccine on nasopharyngeal carriage in children under 2 years of age in Matiari, Pakistan.

Nisar M, Ahmed S, Jehan F, Shahid S, Shakoor S, Kabir F, et al.

Vaccine. 2021 Mar 05;39(8):1319-1327.
PubMed ID: 33422379

ABSTRACT

BACKGROUND: Pakistan introduced Ten-valent pneumococcal-conjugate-vaccine PCV10 in 2012 as a 3 + 0 schedule without catch-up.

METHODS: Children <2 years old in Matiari, Sindh provided nasopharyngeal swabs between 2014 and 2018, which were cultured for pneumococcus and serotyped through multiplex PCR at the Aga Khan University Hospital. Carriage rates over time for Vaccine-Type (VT) and Non-VT (NVT) serotypes were used to estimate direct, indirect, total and overall effects of vaccination. Regression analysis was used to determine factors associated with VT carriage.

RESULTS: Pneumococcus was detected in 2370/3140 (75%). VT carriage decreased overall, 16.1-9.6% (p-trend <0.001); vaccinated (all 3 doses of PCV10 received) 11.3-8.1% (p-trend 0.031) and unvaccinated (no PCV10 dose received) 17.4-10.3% (p-trend 0.003) with a decline in serotypes 6B, 9V/9A and 19F. Immunization increased from 41.0% to 68.4% (p-trend 0.001). Direct effect of vaccine was 32.8% (95% CI 14.7-47.0%) and indirect effect 44.6%(95% CI 40.6-48.6%). Factors associated with decreased VT colonization were education 1-5 years (aOR 0.7, 95%CI 0.6-1.0), history of difficulty breathing (aOR 0.7, 95%CI 0.5-1.0), exposure to smoke (aOR 0.8, 95% CI 0.6-1.0), child fully immunized (aOR 0.7, 95%CI 0.5-1.0) and enrolled in 3rd (aOR 0.6, 95%CI 0.4-0.8) and 4th (aOR 0.6, 95%CI 0.5-0.9) year of the study whereas history of runny nose (aOR 1.5, 95% CI 1.2-1.9) was positively associated.

CONCLUSIONS: Decrease in VT pneumococcal carriage in vaccinated and unvaccinated children indicates herd immunity. Sustained increase in vaccine coverage and close long-term surveillance is warranted.

WEB: 10.1016/j.vaccine.2020.12.066
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

Nisar *et al.* describe the impact and factors associated pneumococcal carriage in vaccinated and unvaccinated children after the introduction of Ten-valent pneumococcal-conjugate-vaccine

(PCV10). PCV10 was introduced in early 2013 as per the national immunization schedule without any catchup immunizations. Weekly, 15 age-eligible children were selected, vaccination status was assessed with parental interviews, and nasopharyngeal specimens were collected. Authors estimated direct, indirect, and overall effects using a modified Halloran Model. Carriage rates among vaccine naïve children were estimated from a prior cross-sectional survey that took place in January and February 2013 before vaccine introduction.

All samples (n=2,370) were analyzed, and results showed that pneumococcal carriage and VT carriage decreased significantly from year 2014/15 to 2017/2018 (80.8% vs. 72.8% and 16.1% vs. 9.6%, respectively). Similar trends were observed among those vaccinated with one, two, or three doses of PCV10.The estimated direct effect of the vaccine was 32.7% (95% CI 14.7–47.0) and the estimated indirect effect was 44.5% (95% CI 40.6–48.6). Authors noted that only one factor, runny nose in the prior two weeks, was significantly associated with VT carriage. One limitation of this study was that vaccination status was determined by recall, which could have introduced bias. Overall, authors demonstrated substantial carriage rate declines with the introduction of PCV10. This study supports evidence that a three dose without catch up provides both direct and indirect protection to young children in LMICs.

Return to List of Articles

Appendix

The literature search for the April 2021 Vaccine Delivery Research Digest was conducted on March 18, 2021. We searched English language articles indexed by the US National Library of Medicine and published between February 15, 2021 and March 14, 2021. The search resulted in 369 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]) (“2021/02/15”[PDAT] : “2021/03/14”[PDAT]))