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PRODUCED BY: MESIC, A., LEDUC, S., & SHARMA, M.

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List of Articles

1 Preponderance of vaccine-preventable diseases hotspots in northern Ghana: a spatial and space-time clustering analysis from 2010 to 2014.

{Abstract & START Commentary} {Full Article}

- A geospatial study assessing hot spots of six vaccine-preventable disease in Ghana.

2 Predicting the long-term impact of rotavirus vaccination in 112 countries from 2006 to 2034: A transmission modeling analysis.

{Abstract & START Commentary} {Full Article}

- A modelling study evaluating the long term impact of rotavirus vaccination.

3 The duration of protection against clinical malaria provided by the combination of seasonal RTS,S/AS01E vaccination and seasonal malaria chemoprevention versus either intervention given alone.

{Abstract & START Commentary} {Full Article}

- A secondary analysis from a randomized controlled trial studying the duration of protection with RTS,S,/AS01E vaccination with or without seasonal chemoprevention for malaria.

4 Model-based evaluation of the impact of prophylactic vaccination applied to Ebola epidemics in Sierra Leone and Democratic Republic of Congo.

{Abstract & START Commentary} {Full Article}

- A modeling study exploring various scenarios of prophylactic vaccination on two prior outbreaks (epidemic in Sierra Leone; Kivu outbreak in DRC).

5 Geospatial and Time Trend of Prevalence and Characteristics of Zero-Dose Children in Nigeria from 2003 to 2018.

{Abstract & START Commentary} {Full Article}

- A study assessing prevalence and factors associated with zero-dose child status using Demographic Health Survey data.

6 Changes in on-time vaccination following the introduction of an electronic immunization registry, Tanzania 2016-2018: interrupted time-series analysis.

{Abstract & START Commentary} {Full Article}

- An interrupted time series exploring the impact of the implementation of an electronic immunization registry.

7 Comparing one dose of HPV vaccine in girls aged 9-14 years in Tanzania (DoRIS) with one dose of HPV vaccine in historical cohorts: an immunobridging analysis of a randomised controlled trial.
{Abstract & START Commentary} {Full Article}

- In this immunobridging analysis of an open-label randomised controlled trial evaluating the effect of one dose of HPV vaccination.

8 Feasibility of measles and rubella vaccination programmes for disease elimination: a modelling study.
{Abstract & START Commentary} {Full Article}

- A study modelling the probability of measles and rubella elimination between 2020 and 2100 in 93 countries.

9 Maternal and Child Health Care Service Disruptions and Recovery in Mozambique After Cyclone Idai: An Uncontrolled Interrupted Time Series Analysis.
{Abstract & START Commentary} {Full Article}

- An uncontrolled interrupted time series assessing the impact of Cyclone Idai on 10 maternal child indicators.

10 A Systematic Framework for Prioritizing Burden of Disease Data Required for Vaccine Development and Implementation: The Case for Group A Streptococcal Diseases.
{Abstract & START Commentary} {Full Article}

- A study describing a framework for understanding and prioritizing data required for vaccine development, using Group A Streptococcal Disease as a case study.

Appendix

Details of Articles

1. Preponderance of vaccine-preventable diseases hotspots in northern Ghana: a spatial and space-time clustering analysis from 2010 to 2014.

Amoako-Sakyi D, Obiri-Yeboah D, Ofosu A, Kusi K, Osei K, Adade R, et al.
BMC Public Health. 2022 Oct 14;22(1):1899.
PubMed ID: 36224589

ABSTRACT

BACKGROUND: Vaccine-preventable diseases (VPDs) persist globally with a disproportionately high burden in Low and Middle-Income Countries (LMICs). Although this might be partly due to the failure to sustain vaccination coverage above 90% in some WHO regions, a more nuanced understanding of VPD transmission beyond vaccination coverage may unveil other important factors in VPD transmission and control. This study identified VPDs hotspots and explored their relationships with ecology, urbanicity and land-use variations (Artisanal and Small-scale Gold Mining (ASGM) activities) in Ghana.

METHODS: District-level disease count data from 2010 to 2014 from the Ghana Health Service (GHS) and population data from the Ghana Population and Housing Census (PHC) were used to determine clustering patterns of six VPDs (Measles, Meningitis, Mumps, Otitis media, Pneumonia and Tetanus). Spatial and space-time cluster analyses were implemented in SaTScan using the discrete Poisson model. P-values were estimated using a combination of sequential Monte Carlo, standard Monte Carlo, and Gumbel approximations.

RESULTS: The study found a preponderance for VPD hotspots in the northern parts of Ghana and northernmost ecological zones (Sudan Savannah and Guinea Savannah). Incidence of meningitis was higher in the Sudan Savannah ecological zone relative to: Tropical Rain Forest ($p=0.001$); Semi Deciduous Forest ($p<0.0001$); Transitional Zone ($p<0.0001$); Coastal Savannah ($p<0.0001$) and Guinea Savannah ($p=0.033$). Except for mumps, which recorded a higher incidence in urban districts ($p=0.045$), incidence of the other five VPDs did not differ across the urban-rural divide. Whereas spatial analysis suggested that some VPD hotspots (tetanus and otitis media) occur more frequently in mining districts in the southern part of the country, a Mann-Whitney U test revealed a higher incidence of meningitis in non-mining districts ($p=0.019$). Pneumonia and meningitis recorded the highest (722.8 per 100,000) and least (0.8 per 100,000) incidence rates respectively during the study period.

CONCLUSION: This study shows a preponderance of VPD hotspots in the northern parts of Ghana and in semi-arid ecoclimates. The relationship between ASGM activities and VPD transmission in Ghana remains blurred and requires further studies with better spatial resolution to clarify.

WEB: 10.1186/s12889-022-14307-1
IMPACT FACTOR: 2.521
CITED HALF-LIFE: 6.0

START COMMENTARY

In this study, Amoako-Sakyi *et al.* assess the spatial and space-time clustering of vaccine-preventable disease (VPD) in Northern Ghana from 2010 to 2014. This study identifies VPD hot spots and assess their associations with urbanicity, land-use variations, and ecological factors. This study makes an important contribution as it provides a nuanced understanding of VPD spatial clustering and how this relates to ecology and land use. Such a detailed analysis is not possible when using aggregate measures such as national or regional vaccination coverage. Amoako-Sayki *et al.* used routine data, including district-level VPD counts from the Ghana Health Service and population from the Ghana Population and Housing Census. The analysis was conducted using SaTScan, a geospatial tool that can access spatial trends and spatio-temporal trends.

Amoako-Sakyi *et al.* reported spatial and space-time cube results for six VPDs: measles, meningitis, mumps, otitis media, pneumonia, tetanus. *Figures 1-6* show the incidence and clustering for each disease in Ghana. For each disease, Amoako-Sakyi *et al.* report the top five most likely clusters and three of the most likely space-time clusters. For example, for meningitis, nearly all clusters were in the northern part of the country, whereas for measles, cluster location varied with some found in the northwest, west, and southeast regions. Overall, incidence varied across ecological zones for three diseases: meningitis, otitis media, and pneumonia (Table 1). Meningitis was higher in the Sudan Savannah ecological zone compared to the Topical Rain Forest, Semi-Deciduous Forest, Transitional Zone, Coastal Savannah, and Guinea Savannah. Meningitis, otitis media, and pneumonia were all higher in the Sudan Savannah ecological zone compared to the Semi-Deciduous Forest (*Table 2).* Only mumps incidence had a statistically significant urban-rural difference (higher in rural areas, $p<0.045$). Similarly, only meningitis was shown to have differing trends in mining districts. Meningitis was shown to significantly higher in non-mining areas ($p<0.019$). Lastly, Amoako-Sakyi *et al.* mapped the most likely clusters for all six VPDs, which are shown in *Figure 7.* Overall, this article shows the substantial spatial, and spatio-temporal differences in VPD incidence, which is useful for targeted immunization effort planning.

Return to List of Articles

2. Predicting the long-term impact of rotavirus vaccination in 112 countries from 2006 to 2034: A transmission modeling analysis.

Kraay A, Steele M, Baker J, Hall E, Deshpande A, Saidzosa B, et al.
Vaccine. 2022 Oct 27;40(46):6631-6639.
PubMed ID: 36210251

ABSTRACT

Rotavirus vaccination has been shown to reduce rotavirus burden in many countries, but the long-term magnitude of vaccine impacts is unclear, particularly in low-income countries. We use a transmission model to estimate the long-term impact of rotavirus vaccination on deaths and disability adjusted life years (DALYs) from 2006 to 2034 for 112 low- and middle-income countries. We also explore the predicted effectiveness of a one- vs two- dose series and the relative contribution of direct vs indirect effects to overall impacts. To validate the model, we compare predicted percent reductions in severe rotavirus cases with the percent reduction in rotavirus positivity among gastroenteritis hospital admissions for 10 countries with pre- and post-vaccine introduction data. We estimate that vaccination would reduce deaths from rotavirus by 49.1.% (95.% UI: 46.6-54.3.%) by 2034 under realistic coverage scenarios, compared to a scenario without vaccination. Most of this benefit is due to direct benefit to vaccinated individuals (explaining 69-97.% of the overall impact), but indirect protection also appears to enhance impacts. We find that a one-dose schedule would only be about 57.% as effective as a two-dose schedule 12.years after vaccine introduction. Our model closely reproduced observed reductions in rotavirus positivity in the first few years after vaccine introduction in select countries. Rotavirus vaccination is likely to have a substantial impact on rotavirus gastroenteritis and its mortality burden. To sustain this benefit, the complete series of doses is needed.

WEB: 10.1016/j.vaccine.2022.09.072
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

In this modelling study, Kraay *et al.* estimate the direct effect of rotavirus vaccination for 112 countries, and the indirect effects for four large countries (Pakistan, India, Nigeria, and Ethiopia) which have been prioritized for increased vaccination uptake by Gavi and the Bill and Melinda Gates Foundation. It also examines the impact of a one-dose schedule. Kraay *et al.* developed a Susceptible–Infected–Recovered (SIR) structure model. Children in the following age groups are

modelled: 0-1 month; 2-3 months; 4-11 months; 1 year-old; 2 year-old; 2 year-old; 3 year-old; 4-year-old; 5 year-old and older. Detailed information on the model and the model parameters are provided in the *Supplementary Data*. Three scenarios were included: 1) no vaccination; 2) default scenario (routine vaccination without additional campaigns) and 3) best case (routine and additional campaigns).

Overall, across 112 countries, a total of 103,000 deaths of children under 5 (95% Uncertainty Interval [UI]: 96,000-112,000) would be averted under the default scenario. The best-case scenario is estimated to avert 110,000 deaths (95% UI: 103,000-121,000). The best-case would result in 1.59 million averted deaths from 2006 to 2034. *Figure 2* presents the averted annual deaths by region under the default scenario. In Pakistan, India, Nigeria, and Ethiopia, where direct and indirect impacts were modelled, an estimated 51.4% (95% UI: 46.4 – 59.1%) of deaths per year are protected to be averted by 2034. Direct effects account for 69-97% of the total effect, which varies by country. *Figure 4* present the overall vaccine effect and the direct vaccine effects up to 12 years post vaccination for each country. The effect of a one-dose rotavirus in these four countries would be similar in the short term (i.e., in the first few years) but two doses had substantially more impact (in terms of deaths averted) in the long term (5+ years post-vaccination). *Figure 5* demonstrates these findings. In conclusion, this paper provides evidence of sustained impact of rotavirus vaccine across 112 countries.

Return to List of Articles

3. The duration of protection against clinical malaria provided by the combination of seasonal RTS,S/AS01E vaccination and seasonal malaria chemoprevention versus either intervention given alone.

Cairns M, Barry A, Zongo I, Sagara I, Yerbanga S, Diarra M, et al.
BMC Med. 2022 Oct 10;20(1):352.
PubMed ID: 36203149

ABSTRACT

BACKGROUND: A recent trial of 5920 children in Burkina Faso and Mali showed that the combination of seasonal vaccination with the RTS,S/AS01E malaria vaccine (primary series and two seasonal boosters) and seasonal malaria chemoprevention (four monthly cycles per year) was markedly more effective than either intervention given alone in preventing clinical malaria, severe malaria, and deaths from malaria.

METHODS: In order to help optimise the timing of these two interventions, trial data were reanalysed to estimate the duration of protection against clinical malaria provided by RTS,S/AS01E when deployed seasonally, by comparing the group who received the combination of SMC and RTS,S/AS01E with the group who received SMC alone. The duration of protection from SMC was also estimated comparing the combined intervention group with the group who received RTS,S/AS01E alone. Three methods were used: Piecewise Cox regression, Flexible parametric survival models and Smoothed Schoenfeld residuals from Cox models, stratifying on the study area and using robust standard errors to control for within-child clustering of multiple episodes.

RESULTS: The overall protective efficacy from RTS,S/AS01E over 6 months was at least 60% following the primary series and the two seasonal booster doses and remained at a high level over the full malaria transmission season. Beyond 6 months, protective efficacy appeared to wane more rapidly, but the uncertainty around the estimates increases due to the lower number of cases during this period (coinciding with the onset of the dry season). Protection from SMC exceeded 90% in the first 2-3 weeks post-administration after several cycles, but was not 100%, even immediately post-administration. Efficacy begins to decline from approximately day 21 and then declines more sharply after day 28, indicating the importance of preserving the delivery interval for SMC cycles at a maximum of four weeks.

CONCLUSIONS: The efficacy of both interventions was highest immediately post-administration. Understanding differences between these interventions in their peak efficacy and how rapidly efficacy declines over time will help to optimise the scheduling of SMC, malaria vaccination and the

combination in areas of seasonal transmission with differing epidemiology, and using different vaccine delivery systems.

TRIAL REGISTRATION: The RTS,S-SMC trial in which these data were collected was registered at clinicaltrials.gov: NCT03143218.

WEB: 10.1186/s12916-022-02536-5
IMPACT FACTOR: 6.782
CITED HALF-LIFE: 5.2

START COMMENTARY

Cairns *et al.,* performed a secondary analysis of the RTS,S/AS01$_E$ seasonal malaria vaccination trial data to estimate the changes in RTS,S/AS01$_E$ vaccine efficacy over time and the duration of protection after seasonal malaria chemoprevention (SMC) treatments. While SMC has been deployed successfully at scale in West Africa, several countries with high SMC coverage are still experiencing a high burden of malaria in young children. This study makes an important contribution as RTS,S is newly recommended by WHO for large-scale implementation, and it is not known how best to use the seasonal vaccine in combination with SMC. One strength of this analysis was the assessment of protective efficacy for 12 months of follow up post-vaccine (or booster) for multiple years.

The data is from an individually-randomized controlled trial in Bougouni and Ouélessébougou districts, Mali and in Houndé district, Burkina Faso. Authors included three intervention groups in the analyses: SMC alone, RTS,S alone, and Combined Intervention (*Figure 1).* Protective efficacy was assessed for a year following completion of the primary series, the first booster, and the second booster; doses were given approximately one year apart. The analysis period began 14 days after receipt of doses. Three regression approaches (Piecewise Cox Regression, Flexible Parametric Models, and Smoothed Schoenfeld Residuals) were used to assess the profile of protective efficacy of the Combined treatment group, as compared to the SMC-alone group. All approaches used robust standard errors to account for correlation with repeated measures of participants, and all approaches are stratified by country. *Figure 3* shows the protective efficacy of RTS,S/AS01$_E$ by time since vaccination, demonstrating the most protection in 0-90 days following vaccination, and the largest drop off of protection going from 90-180 days to 180-270 days since vaccine. Overall, the protection provided by RTS,S/AS01$_E$ appears to be relatively high over 6 months post-vaccination. It is important to keep in mind the seasonal timing of malaria cases, introducing uncertainty around the protective efficacy in the 6-12 months following vaccination. *Figure 6* shows the protective efficacy in the first 60 days following SMC, showing considerable drop off in efficacy after the first 30 days. Both interventions were most effective in the time immediately

following completion of treatment (first 30 days) or receipt of vaccine dose (first 6 months). Results can be used to inform programmatic decisions on how to best to utilize SMC and the recently recommended seasonal malaria vaccine in combination.

Return to List of Articles

4. Model-based evaluation of the impact of prophylactic vaccination applied to Ebola epidemics in Sierra Leone and Democratic Republic of Congo.

Potluri R, Kumar A, Oriol-Mathieu V, Van Effelterre T, Metz L, Bhandari H.
BMC Infect Dis. 2022 Oct 05;22(1):769.
PubMed ID: 36192683

ABSTRACT

BACKGROUND: Protection by preventive Ebola vaccines has been demonstrated in clinical trials, but a complete picture of real-world effectiveness is lacking. Our previous study modeling the impact of preventively vaccinating healthcare workers (HCW) alone or with a proportion of the general population (GP) estimated significant reductions in incidence and mortality. The model assumed 100% vaccine efficacy, which is unlikely in the real world. We enhanced this model to account for lower vaccine efficacy and to factor in reduced infectiousness and lower case fatality rate in vaccinated individuals with breakthrough infections.

METHODS: The previous model was enhanced to still permit a risk, although lower, for vaccinated individuals to become infected. The enhanced model, calibrated with data from epidemics in Sierra Leone (SL) and North Kivu, Democratic Republic of the Congo, helped evaluate the impact of preventive Ebola vaccination in different scenarios based on different vaccine efficacy rates (90% and 30% reductions in infection risk in the base and conservative scenarios, respectively; additionally, both scenarios with 50% reductions in infectiousness and mortality) and vaccination coverage among HCWs (30%, 90%) and GP (0%, 5%, and 10%).

RESULTS: The base scenario estimated that, depending upon the proportions of vaccinated HCWs and GP, 33-85% of cases and 34-87% of deaths during the 2014 SL epidemic and 42-89% of cases and 41-89% of deaths during the 2018 North Kivu epidemic would be averted versus no vaccination. Corresponding estimates for the conservative scenario were: 23-74% of cases and 23-77% of deaths averted during the SL epidemic and 31-80% of both cases and deaths averted during the North Kivu epidemic.

CONCLUSIONS: Preventive vaccination targeting HCW alone or with GP may significantly reduce the size and mortality of an EVD outbreak, even with modest efficacy and coverage. Vaccines may also confer additional benefits through reduced infectiousness and mortality in breakthrough cases.

WEB: 10.1186/s12879-022-07723-6
IMPACT FACTOR: 2.668
CITED HALF-LIFE: 5.0

START COMMENTARY

In this modelling study, Potluri *et al.* evaluate the impact of preventative Ebola vaccine under several scenarios of lower vaccine efficacy, infectiousness, and case fatality rates. This study makes an important contribution as it models the impact of vaccination when vaccine efficacy is less than 100%, as it is likely to be in the real world. Portluri *et al.* developed a standard generalized 'susceptible, exposed, infected, and removed (SEIR)' model in this study, which was calibrated to two historical outbreaks: 1) Sierra Leone epidemic in 2014; 2) the Democratic Republic of Congo (DRC) North Kivu outbreak of 2018. *Figure 1* presents the SEIR framework. A strength of this study is the inclusion of differential rates of infection among healthcare workers and non-health care workers. Parameters in the model from the historic outbreaks are presented in *Table 1.*

Potluri *et al.* the model output fit well to empiric data on observed cases in the DRC North Kivu outbreak (*Figure 4*). The model simulated 2,782 cases and 1,876 deaths and the WHO reported 2,791 cases and 1,875 deaths. The base scenario consisted of a vaccine with 90% efficacy and 50% reduction both infectiousness and case fatality rate administered to 346 healthcare workers in Sierra Leone. The base case scenario would avert cases by 33% (n=2,892) and deaths by 34% (n=1,204). In DRC, vaccinating 30% of healthcare workers with the same assumptions would result in a reduction of 42% in cases (n=1,158) and a 41% reduction in deaths (n=778). *Figure 5* presents the impact of prophylactic vaccination in healthcare workers and the general population on the cumulative incidence and mortality associated with Ebola. If part of the general population is also vaccinated, impacts would be substantially greater. For example, if 10% of the general population was vaccinated in addition to healthcare workers, the number of cases and deaths could be reduced by 85% and deaths by 97% in Sierra Leone. Similar results are shown for the DRC outbreak. Potluri *et al.* demonstrated that even in a conservative scenario (a vaccine resulting in a 30% reduced risk of infection and 50% reduced infectiousness and case fatality), the impacts would still be substantial (23-35% reductions in cases/deaths). This article demonstrates the impact of prophylactic vaccination, particularly among healthcare workers, in the context of an outbreak. Although small numbers of healthcare workers were vaccinated in the scenarios, it was very impactful in reducing cases and deaths, particularly when combined with vaccination of the general population.

Return to List of Articles

5. Geospatial and Time Trend of Prevalence and Characteristics of Zero-Dose Children in Nigeria from 2003 to 2018.

Sato R.

Vaccines (Basel). 2022 Sep 28;10(9).
PubMed ID: 36146634

ABSTRACT

INTRODUCTION: While recent years have observed a substantial improvement in vaccination coverage among children in developing countries, many children are still left out and remain unvaccinated. This study analyzes the trend of the prevalence and characteristics of zero-dose children in Nigeria over time.

METHODS: Using data from the Demographic and Health Survey in Nigeria from 2003 to 2018, I analyzed the prevalence and determinants of zero-dose children who had not received any DTP vaccine by geographical zone and over time. In addition, I conducted Blinder-Oaxaca decomposition analysis to evaluate the reasons for the change in the prevalence of zero-dose children over time.

RESULTS: The overall prevalence of zero-dose children reduced from over 60% in 2003 to 40% in 2018 in Nigeria. Rural areas had a higher prevalence of zero-dose children than urban areas and the gap was consistent over time. Southern zones consistently had a lower prevalence of zero-dose children, but northern zones observed more reductions in the prevalence of zero-dose children. The mother's education and wealth level in a household are strongly associated with a lower likelihood of having zero-dose children. In both urban and rural areas, an improvement in the mother's education level strongly explained the reduction in zero-dose children over time, while an increase in the wealth level also explained the reduction in zero-dose children in rural areas.

CONCLUSIONS: While Nigeria has observed a substantial reduction in the prevalence of zero-dose children in the 15 years since 2003, the pattern of and explanatory factors for the reduction differ by geographical region. This analysis can be useful for identifying a targeting strategy to further reduce the prevalence of zero-dose children in Nigeria in the future.

WEB: 10.3390/vaccines10091556
IMPACT FACTOR: 4.086
CITED HALF-LIFE: 3.4

START COMMENTARY

In this descriptive study, Sato describes spatial and time trends in the prevalence of zero-dose children in Nigeria from 2003 to 2018 using Nigeria's Demographic and Health Survey (DHS). The author also assesses factors which may have contributed to reductions in zero-dose children over time. The outcome is zero-dose status defined as not receiving the first dose of Diphtheria-Tetanus-Pertussis (DTP) or Pentavalent vaccine. Authors used ordinary-least squares regression to understand associations between sociodemographic characteristics and likelihood of a child being zero dose and a Blinder-Oaxaca decomposition analysis to examine factors which explain changes in the prevalence of zero dose children.

Figure 1 shows the prevalence of zero dose children over time (2003; 2008; 2018) in urban and rural areas of Nigeria with marked improvements over time. There are substantially more zero-dose children in rural than urban areas across all years. *Table 1,* presents determinants of zero-dose children. Lower likelihood of children being zero-dose was associated with mothers being older, having higher education, and higher household wealth. In *Figure 2,* factors associated with changes in the prevalence of zero-dose children are presented overall and for urban and rural areas. Most of the changes were due to 'unexplained factors'. However, among 'explained factors', increasing levels of maternal education was associated with lower likelihood of children being zero dose. Sato found that improvements in education and wealth levels were associated with change in the prevalence of zero-dose children by region (*Figure 3*). However, the relative importance of each factor differed within regions.

Return to List of Articles

6. Changes in on-time vaccination following the introduction of an electronic immunization registry, Tanzania 2016-2018: interrupted time-series analysis.

Dolan S, Burstein R, Shearer J, Bulula N, Lyons H, Carnahan E, et al.
BMC Health Serv Res. 2022 Sep 23;22(1):1175.
PubMed ID: 36127683

ABSTRACT

BACKGROUND: Digital health interventions (DHI) have the potential to improve the management and utilization of health information to optimize health care worker performance and provision of care. Despite the proliferation of DHI projects in low-and middle-income countries, few have been evaluated in an effort to understand their impact on health systems and health-related outcomes. Although more evidence is needed on their impact and effectiveness, the use of DHIs among immunization programs has become more widespread and shows promise for improving vaccination uptake and adherence to immunization schedules.

METHODS: Our aim was to assess the impact of an electronic immunization registry (EIR) using an interrupted time-series analysis to analyze the effect on proportion of on-time vaccinations following introduction of an EIR in Tanzania. We hypothesized that the introduction of the EIR would lead to statistically significant changes in vaccination timeliness at 3, 6, and>6months post-introduction.

RESULTS: For our primary analysis, we observed a decrease in the proportion of on-time vaccinations following EIR introduction. In contrast, our sensitivity analysis estimated improvements in timeliness among those children with complete vaccination records. However, we must emphasize caution interpreting these findings as they are likely affected by implementation challenges.

CONCLUSIONS: This study highlights the complexities of using digitized individual-level routine health information system data for evaluation and research purposes. EIRs have the potential to improve vaccination timeliness, but analyses using EIR data can be complicated by data quality issues and inconsistent data entry leading to difficulties interpreting findings.

WEB: 10.1186/s12913-022-08504-2
IMPACT FACTOR: 1.987
CITED HALF-LIFE: 5.6

START COMMENTARY

This study by Dolan *et al.* investigated the impact of introducing an electronic immunization registry (EIR) in Tanzania on on-time vaccination over a two-year period. The portion of timely vaccinations per facility per month was assessed for the 1st, 2nd, and 3rd doses of pentavalent vaccine, and the 1st dose of measles-containing vaccine (MVC1). Vaccinations were considered on-time if they were administered within 7 days of the date due, as consistent with the Ministry of Health's (MOH) definition of timeliness. Interestingly, doses administered early were not considered on-time, but were included in the analysis. With a cohort of 246,940 children eligible for DPT1, 243,871 for DTP2, 236,691 for DTP3, and 170,279 for MCV1 vaccines, authors found the DTP1 vaccine was most frequently on-time (57.9%), and the MCV1 to be least likely to be on-time (15.8%). However, the DTP1 vaccine was found to have a mean date of administration of 13 days after the scheduled date, and the MCV1 vaccine had a mean of 25 days off-schedule.

The likelihood of an on-time DTP1 vaccination decreased by 5% (OR:0.95, 95% CI: 0.90-0.99) in the first 3 months following EIR-introduction, but increased 25% (OR:1.26, 95% CI: 1.15-1.35) > 6 months post-EIR, compared to the pre-EIR time period (*Figure 5*). For DTP2, the likelihood of on-time vaccinations was lower post-EIR, compared to pre-EIR, although the reduction decreased over time with 32% (OR:0.68, 95% CI: 0.62-0.75) reduced likelihood 0-3 months post-EIR and 20% (OR:0.80, 95% CI: 0.68-0.93) post-EIR > 6 months after. Authors observed a decrease in the proportion of on-time vaccinations after the introduction of the EIR which plateaued over time (*Figure 3).* There are documented inconsistencies in data entry for vaccine records prior to the EIR introduction and challenges with the complex implementation of the EIR, limiting the accuracy and generalizability of the results.

Return to List of Articles

7. Comparing one dose of HPV vaccine in girls aged 9-14 years in Tanzania (DoRIS) with one dose of HPV vaccine in historical cohorts: an immunobridging analysis of a randomised controlled trial.

Baisley K, Kemp T, Kreimer A, Basu P, Changalucha J, Hildesheim A, et al.
Lancet Glob Health. 2022 Sep 20;10(10):e1485-e1493.
PubMed ID: 3611353236113514

ABSTRACT

BACKGROUND: Human papillomavirus (HPV) vaccines are given as a two-dose schedule in children aged 9-14 years, or as three doses in older individuals. We compared antibody responses after one dose of HPV vaccine in the Dose Reduction Immunobridging and Safety Study (DoRIS), a randomised trial of different HPV vaccine schedules in Tanzania, to those from two observational HPV vaccine trials that found high efficacy of one dose up to 11 years against HPV16 and HPV18 (Costa Rica Vaccine Trial [CVT] and Institutional Agency for Research on Cancer [IARC] India trial).

METHODS: In this immunobridging analysis of an open-label randomised controlled trial, girls were recruited from 54 government schools in Mwanza, Tanzania, into the DoRIS trial. Girls were eligible if they were aged 9-14 years, healthy, and HIV negative. Participants were randomly assigned (1:1:1:1:1:1), using permutated block sizes of 12, 18, and 24, to one, two, or three doses of the 2-valent vaccine (Cervarix, GSK Biologicals, Rixensart, Belgium) or the 9-valent vaccine (Gardasil 9, Sanofi Pasteur MSD, Lyon, France). For this immunobridging analysis, the primary objective was to compare geometric mean concentrations (GMCs) at 24 months after one dose in the per-protocol population compared with in historical cohorts: the one-dose 2-valent vaccine group in DoRIS was compared with recipients of the 2-valent vaccine Cervarix from CVT and the one-dose 9-valent vaccine group in DoRIS was compared with recipients of the 4-valent vaccine Gardasil (Merck Sharp & Dohme, Whitehouse Station, NJ, USA) from the IARC India trial. Samples were tested together with virus-like particle ELISA for HPV16 and HPV18 IgG antibodies. Non-inferiority of GMC ratios (DoRIS trial vs historical cohort) was predefined as when the lower bound of the 95% CI was greater than 0.50. This study is registered with ClinicalTrials.gov, NCT02834637.

FINDINGS: Between Feb 23, 2017, and Jan 6, 2018, we screened 1002 girls for eligibility, of whom 930 were enrolled into DoRIS and 155 each were assigned to one dose, two doses, or three doses of 2-valent vaccine, or one dose, two doses, or three doses of 9-valent vaccine. 154 (99%) participants in the one-dose 2-valent vaccine group (median age 10 years [IQR 9-12]) and 152 (98%) in the one-dose 9-valent vaccine group (median age 10 years [IQR 9-12]) were vaccinated and attended the 24 month visit, and so were included in the analysis. 115 one-dose recipients from the CVT (median age 21 years [19-23]) and 139 one-dose recipients from the IARC India trial

(median age 14 years [13-16]) were included in the analysis. At 24 months after vaccination, GMCs for HPV16 IgG antibodies were 22.9 international units (IU) per mL (95% CI 19.9-26.4; n=148) for the DoRIS 2-valent vaccine group versus 17.7 IU/mL (13.9-22.5; n=97) for the CVT (GMC ratio 1.30 [95% CI 1.00-1.68]) and 13.7 IU/mL (11.9-15.8; n=145) for the DoRIS 9-valent vaccine group versus 6.7 IU/mL (5.5-8.2; n=131) for the IARC India trial (GMC ratio 2.05 [1.61-2.61]). GMCs for HPV18 IgG antibodies were 9.9 IU/mL (95% CI 8.5-11.5: n=141) for the DoRIS 2-valent vaccine group versus 8.0 IU/mL (6.4-10.0; n=97) for the CVT trial (GMC ratio 1.23 [95% CI 0.95-1.60]) and 5.7 IU/mL (4.9-6.8; n=136) for the DoRIS 9-valent vaccine group versus 2.2 IU/mL (1.9-2.7; n=129) for the IARC India trial (GMC ratio 2.12 [1.59-2.83]). Non-inferiority of antibody GMCs was met for each vaccine for both HPV16 and HPV18.

INTERPRETATION: One dose of HPV vaccine in young girls might provide sufficient protection against persistent HPV infection. A one-dose schedule would reduce costs, simplify vaccine delivery, and expand access to the vaccine.

FUNDING: UK Department for International Development/UK Medical Research Council/Wellcome Trust Joint Global Health Trials Scheme, The Bill & Melinda Gates Foundation, and the US National Cancer Institute.

TRANSLATION: For the KiSwahili translation of the abstract see Supplementary Materials section.

WEB: 10.1016/S2214-109X(22)00306-0
IMPACT FACTOR: 21.597
CITED HALF-LIFE: 3.1

START COMMENTARY

In this open-label randomized controlled trial, Baisley *et al.* assessed the antibody response of participants after one, two, or three doses of the 2-valent or 9-valent HPV vaccine at 24 months post- vaccine as part of the Dose Reduction Immunobridging and Safety Study (DoRIS). Although one randomized controlled trial in Kenya assessed efficacy of a single dose HPV vaccine in women aged 18 – 25 years old, prior to this study, evidence on the efficacy of a single dose of HPV vaccine is primarily observational and in the context of incomplete vaccine schedules. This study provides information to fill an important gap: single dose HPV vaccine antibody response in girls aged 9 – 14 years.

Immunogenicity of the 2-valent Cervarix and 9-valent Gardasil-9 vaccines in Tanzania were compared to two observational HPV vaccine trials (the International Agency for Research on Cancer (IARC) HPV vaccine trial in India and the Costa Rica Vaccine Trial (CVT)) chosen for their long-term efficacy data. The DoRIS trial primarily aimed to compare the HPV genotype-specific immune

response in participants with those in historical cohorts who received only one dose of the HPV vaccine, as measured by geometric mean concentrations (GMCs). *Figure 1* shows the distribution of HPV16 and HPV18 antibody concentrations at 24 months following a single dose of HPV vaccine among participants of DoRIS, CT, and IARC India, demonstrating comparable GMCs and individual patient antibody concentrations across trials. *Table 2* shows GMCs and seroconversion rates at 24 months among participants of Doris, CT, and IARC India trials. For both HPV16 and HPV18 IgG antibodies, seroconversion, as defined by concentrations greater than or equal to the laboratory determined cutoff (HPV16=1·309 IU/mL; HPV18=1·109 IU/mL), was shown to be above 99%. Evidence supports non-inferiority of antibody GMC for both 2-valent and 9-valent HPV vaccines. Based on results presented from this trial and others, the WHO's Strategic Advisory Group of Experts on Immunization recommended that the HPV vaccine dose schedule be updated to allow a one-dose or two-dose schedule in April 2022. Evidence supporting a single dose HPV vaccine could have major implications for the costs of vaccine purchase, delivery, supply chain, and access globally.

Return to List of Articles

8. Feasibility of measles and rubella vaccination programmes for disease elimination: a modelling study.

Winter A, Lambert B, Klein D, Klepac P, Papadopoulos T, Truelove S, et al.
Lancet Glob Health. 2022 Sep 20;10(10):e1412-e1422.
PubMed ID: 3611352736113510

ABSTRACT

BACKGROUND: Marked reductions in the incidence of measles and rubella have been observed since the widespread use of the measles and rubella vaccines. Although no global goal for measles eradication has been established, all six WHO regions have set measles elimination targets. However, a gap remains between current control levels and elimination targets, as shown by large measles outbreaks between 2017 and 2019. We aimed to model the potential for measles and rubella elimination globally to inform a WHO report to the 73rd World Health Assembly on the feasibility of measles and rubella eradication.

METHODS: In this study, we modelled the probability of measles and rubella elimination between 2020 and 2100 under different vaccination scenarios in 93 countries of interest. We evaluated measles and rubella burden and elimination across two national transmission models each (Dynamic Measles Immunisation Calculation Engine [DynaMICE], Pennsylvania State University [PSU], Johns Hopkins University, and Public Health England models), and one subnational measles transmission model (Institute for Disease Modeling model). The vaccination scenarios included a so-called business as usual approach, which continues present vaccination coverage, and an intensified investment approach, which increases coverage into the future. The annual numbers of infections projected by each model, country, and vaccination scenario were used to explore if, when, and for how long the infections would be below a threshold for elimination.

FINDINGS: The intensified investment scenario led to large reductions in measles and rubella incidence and burden. Rubella elimination is likely to be achievable in all countries and measles elimination is likely in some countries, but not all. The PSU and DynaMICE national measles models estimated that by 2050, the probability of elimination would exceed 75% in 14 (16%) and 36 (39%) of 93 modelled countries, respectively. The subnational model of measles transmission highlighted inequity in routine coverage as a likely driver of the continuance of endemic measles transmission in a subset of countries.

INTERPRETATION: To reach regional elimination goals, it will be necessary to innovate vaccination strategies and technologies that increase spatial equity of routine vaccination, in addition to investing in existing surveillance and outbreak response programmes.

FUNDING: WHO, Gavi, the Vaccine Alliance, US Centers for Disease Control and Prevention, and the Bill & Melinda Gates Foundation.

WEB: 10.1016/S2214-109X(22)00335-7

IMPACT FACTOR: 21.597
CITED HALF-LIFE: 3.1

START COMMENTARY

In this study, Winter *et al.* model the probability of measles and rubella elimination between 2020 to 2100 in 93 countries. This study is important as it provides evidence on the feasibility of eradicating measles and rubella globally. Two disease transmission models (Dynamic Measles Immunisation Calculation Engine [DynaMICE], Pennsylvania State University [PSU], Johns Hopkins University, and Public Health England models) were used in this study. Two vaccination scenarios are included: 1) routine vaccination ('business as usual' scenario); 2) vaccination campaigns ('intensified investment' scenario). Details on each scenario by vaccine are presented in *Table 1.* Key assumptions for the rubella and measles transmission models are presented in *Table 2.* Authors also assessed a subnational model of Nigeria.

In the 'business as usual' scenario, the burden of rubella is projected to remain high (*Figure 1*). This scenario includes 23 countries not introducing rubella-containing vaccines, which would be the main contributors to the high numbers of infections and deaths; only 17% of 93 countries would achieve elimination by 2020. In the intensified scenarios, where rubella-containing vaccines are introduced in all countries and coverage increases, rubella infections and congenital rubella syndrome cases would reduce drastically (*Figure 2*). However, this impact was not shown as dramatically in elimination; the probability of achieving elimination was higher than 75% in only 39% (36) of the 93 countries by 2050. Results in Nigeria were similar to other national modelling results. However, increasing spatial equity in routine vaccination (i.e., efforts which target lowest coverage districts first), resulted in higher projected reductions in burden and increased probability of elimination. Several countries could eliminate rubella with increased efforts. However, authors conclude that several countries may struggle to reach elimination and highlight the importance of within-country and across-country equity.

Return to List of Articles

9. Maternal and Child Health Care Service Disruptions and Recovery in Mozambique After Cyclone Idai: An Uncontrolled Interrupted Time Series Analysis.

Fernandes Q, Augusto O, Chicumbe S, Anselmi L, Wagenaar B, Marlene R, et al.
Glob Health Sci Pract. 2022 Sep 19;10(Suppl 1).
PubMed ID: 36109066

ABSTRACT

INTRODUCTION: Climate change-related extreme weather events have increased in frequency and intensity, threatening people's health, particularly in places with weak health systems. In March 2019, Cyclone Idai devastated Mozambique's central region, causing infrastructure destruction, population displacement, and death. We assessed the impact of Idai on maternal and child health services and recovery in the Sofala and Manica provinces.

METHODS: Using monthly district-level routine data from November 2016 to March 2020, we performed an uncontrolled interrupted time series analysis to assess changes in 10 maternal and child health indicators in all 25 districts before and after Idai. We applied a Bayesian hierarchical negative binomial model with district-level random intercepts and slopes to estimate Idai-related service disruptions and recovery.

RESULTS: Of the 4.44 million people in Sofala and Manica, 1.83 (41.2%) million were affected. Buzi, Nhamatanda, and Dondo (all in Sofala province) had the highest proportion of people affected. After Idai, all 10 indicators showed an abrupt substantial decrease. First antenatal care visits per 100,000 women of reproductive age decreased by 23% (95% confidence interval [CI]=0.62, 0.96) in March and 11% (95% CI=0.75, 1.07) in April. BCG vaccinations per 1,000 children under age 5 years declined by 21% (95% CI=0.69, 0.90) and measles vaccinations decreased by 25% (95% CI=0.64, 0.87) in March and remained similar in April. Within 3 months post-cyclone, almost all districts recovered to pre-Idai levels, including Buzi, which showed a 22% and 13% relative increase in the number of first antenatal care visits and BCG, respectively.

CONCLUSION: We found substantial health service disruptions immediately after Idai, with greater impact in the most affected districts. The findings suggest impressive recovery post-Idai, emphasizing the need to build resilient health systems to ensure quality health care during and after natural disasters.

WEB: 10.9745/GHSP-D-21-00796
IMPACT FACTOR: 2.352
CITED HALF-LIFE: 3.6

START COMMENTARY

In this uncontrolled interrupted time series, Fernandes *et al.* evaluate the disruptions in maternal and child health care after cyclone Idai in Mozambique. This study is important as climate change-related weather events have become more frequent and intense over time. Quantifying the impact of such events can help with future health system resilience efforts. Fernandes *et al.* used monthly district-level data from November 2016 to March 2020. Outcomes include 10 maternal and child health indicators: 1) first antenatal care visit; 2) completion of 4 doses of intermittent preventive treatment for malaria during pregnancy among women; 3) facility delivery; 4) postpartum care visits; 5) new users of modern contraceptives; 6) BCG vaccine; 7) DPT-Hib3 vaccines; 8) measles vaccines; 9) fully immunized children under 1 year of age; 10) first consultants for at-risk services for children.

Overall, 41.2% of the population in Sofala and Manica provinces was affected by the cyclone. *Table 1* shows the proportion of affected people, including the district-specific populations affected. *Table 2* presents the monthly averages for each of the ten indicators before the cyclone. The cyclone, which occurred in March 2019, resulted in a significant decline in all indicators until April 2019. Before the cyclone, all except two indicators (postpartum visits, first ANC visits), showed positive and consistent trends. For example, in April 2019, there was a 21.0% decrease (95% CI: 0.69 to 0.90) in BCG and measles vaccination per 1,000 children under 5. *Figure 2* shows the average counts for service delivery indicators before and after the cyclone. Relative losses (defined as the ratio between the observed counts during Idai and the expected counts) were estimated. All materenal health delivery indicators had immediate losses but recovered by May 2019. The exception was doses of intermittent preventive treatment for malaria during pregnancy among women. In conclusion, this study shows the negative impact of weather events on women/children's access and uptake of routine services.

Return to List of Articles

10. A Systematic Framework for Prioritizing Burden of Disease Data Required for Vaccine Development and Implementation: The Case for Group A Streptococcal Diseases.

Moore H, Cannon J, Kaslow D, Lamagni T, Bowen A, Miller K, et al.
Clin Infect Dis. 2022 Oct 04;75(7):1245-1254.
PubMed ID: 35438130

ABSTRACT

Vaccine development and implementation decisions need to be guided by accurate and robust burden of disease data. We developed an innovative systematic framework outlining the properties of such data that are needed to advance vaccine development and evaluation, and prioritize research and surveillance activities. We focus on 4 objectives-advocacy, regulatory oversight and licensure, policy and post-licensure evaluation, and post-licensure financing-and identify key stakeholders and specific requirements for burden of disease data aligned with each objective. We apply this framework to group A Streptococcus, a pathogen with an underrecognized global burden, and give specific examples pertinent to 8 clinical endpoints. This dynamic framework can be adapted for any disease with a vaccine in development and can be updated as vaccine candidates progress through clinical trials. This framework will also help with research and innovation priority setting of the Immunization Agenda 2030 (IA2030) and accelerate development of future vaccines.

WEB: 10.1093/cid/ciac291
IMPACT FACTOR: 8.313
CITED HALF-LIFE: 8.3

START COMMENTARY

Moore *et al.* develop a data framework to advance vaccine development and evaluation and apply it to Strep A to identify future research priorities. This framework was developed by the Wellcome Trust–funded Strep A Vaccine Consortium (SAVAC) who established an expert Burden of Disease Working Group. This working group reached consensus on four vaccine objectives: 1) advocacy, 2) regulatory oversight; 3) policy and post-licensure evaluation, 4) and post-licensure financing. *Table 1* summarizes the framework. *Figure 1* summarizes the broad and complex disease syndromes associated with Strep A. *Table 2* summarizes the priorities for data requirements for Acute Group A Strep disease. For pharyngitis among children, some examples within each objective include: advocacy (data on population transmission); regulatory/licensure (monitor adverse events and safety from candidates); policy/post-licensure (economic value of vaccines); and financing (retrospective economic cost of illness data). Similar data requirements are listed for other conditions

including Scarlet fever, Invasive Strep A, Cellulitis, and Impetigo among children. *Table 3* presents similar data priorities for immune-mediated sequalae of Group A Strep. Overall, authors identify four key research priorities for Strep A: 1) establishing sentinel surveillance sites for pharyngitis (and impetigo) measuring age-specific disease burden; 2) collating data to describe the incidence in low- and middle-income countries; 3) assessing the attributable fraction of Strep A to cellulitis; and 4) developing burden of disease estimates.

Return to List of Articles

Appendix

The literature search for the November 2021 Vaccine Delivery Research Digest was conducted on October 31, 2022. We searched English language articles indexed by the US National Library of Medicine and published between September 15, 2022 and October 14, 2022. The search resulted in 577 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]) ("2022/9/15"[PDAT] : "2022/10/14"[PDAT]))