VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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

JULY 2022

Want the Vaccine Delivery Research Digest delivered directly to your inbox?

Subscribe on the Digest website: http://uwstartcenter.org/publication-digests/vaccine-digest

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

List of Articles

1 Vaccine equity in low and middle income countries: a systematic review and meta-analysis.

{Abstract & START Commentary} {Full Article}

- A systematic review and meta-analysis assessing factors on immunization inequality and heterogeneity in vaccine coverage in low- and middle-income countries (LMICs)

2 Cost-effectiveness of COVID-19 vaccination in low- and middle-income countries.

{Abstract & START Commentary} {Full Article}

- A cost-effectiveness study estimating health benefits and donor costs of delivering COVID-19 vaccines for up to 60% of the population in LMICs

3 Efficacy of single-dose HPV vaccination among young African women.

{Abstract & START Commentary} {Full Article}

- A randomized controlled trial assessing single dose nonvalent or bivalent human papillomavirus (HPV0 vaccination compared with meningococcal vaccination

4 Knowledge and willingness of parents towards child girl HPV vaccination in Debre Tabor Town, Ethiopia: a community-based cross-sectional study.

{Abstract & START Commentary} {Full Article}

- A cross-sectional study examining knowledge, willingness, and associated factors for HPV vaccine

5 COVID-19 impact on routine immunisations for vaccine-preventable diseases: Projecting the effect of different routes to recovery.

{Abstract & START Commentary} {Full Article}

- A modelling study estimating the impacts of COVID-19 related disruptions and varying recovery scenarios for ten vaccine-preventable diseases

6 COVID-19 in the 47 countries of the WHO African region: a modelling analysis of past trends and future patterns.

{Abstract & START Commentary} {Full Article}

- A modelling study on the transmission dynamics of COVID-19 in Africa

7 Impact of periodic intensification of routine immunization within an armed conflict setting and COVID-19 outbreak in Cameroon in 2020.

{Abstract & START Commentary} {Full Article}

- A study describing the impact of a periodic intensification of routine immunization amid armed conflict

8 Cost-effectiveness of rotavirus vaccination in children under five years of age in 195 countries: A meta-regression analysis.

{Abstract & START Commentary} {Full Article}

- A meta-regression study estimating cost-effectiveness ratios for rotavirus vaccination

9 How drivers of seasonality in respiratory infections may impact vaccine strategy: a case study in how COVID-19 may help us solve one of influenza's biggest challenges.

{Abstract & START Commentary} {Full Article}

- A case study discussing theories related to seasonal influenza infection outbreaks and COVID-19

10 Measles Vaccination Elicits a Polyfunctional Antibody Response, Which Decays More Rapidly in Early Vaccinated Children.

{Abstract & START Commentary} {Full Article}

- A study examining the antibody response after measles mumps rubella vaccination

Appendix

Details of Articles

1. Vaccine equity in low and middle income countries: a systematic review and meta-analysis.

Ali H, Hartner A, Echeverria-Londono S, Roth J, Li X, Abbas K, et al.

Int J Equity Health. 2022 Jun 16;21(1):82.

PubMed ID: 35701823

ABSTRACT

BACKGROUND: Evidence to date has shown that inequality in health, and vaccination coverage in particular, can have ramifications to wider society. However, whilst individual studies have sought to characterise these heterogeneities in immunisation coverage at national level, few have taken a broad and quantitative view of the contributing factors to heterogeneity in immunisation coverage and impact, i.e. the number of cases, deaths, and disability-adjusted life years averted. This systematic review aims to highlight these geographic, demographic, and sociodemographic characteristics through a qualitative and quantitative approach, vital to prioritise and optimise vaccination policies.

METHODS: A systematic review of two databases (PubMed and Web of Science) was undertaken using search terms and keywords to identify studies examining factors on immunisation inequality and heterogeneity in vaccination coverage. Inclusion criteria were applied independently by two researchers. Studies including data on key characteristics of interest were further analysed through a meta-analysis to produce a pooled estimate of the risk ratio using a random effects model for that characteristic.

RESULTS: One hundred and eight studies were included in this review. We found that inequalities in wealth, education, and geographic access can affect vaccine impact and vaccination dropout. We estimated those living in rural areas were not significantly different in terms of full vaccination status compared to urban areas but noted considerable heterogeneity between countries. We found that females were 3% (95%CI [1%, 5%]) less likely to be fully vaccinated than males. Additionally, we estimated that children whose mothers had no formal education were 28% (95%CI[18%,47%]) less likely to be fully vaccinated than those whose mother had primary level, or above, education. Finally, we found that individuals in the poorest wealth quintile were 27% (95%CI [16%,37%]) less likely to be fully vaccinated than those in the richest.

CONCLUSIONS: We found a nuanced picture of inequality in vaccination coverage and access with wealth disparity dominating, and likely driving, other disparities. This review highlights the complex

landscape of inequity and further need to design vaccination strategies targeting missed subgroups to improve and recover vaccination coverage following the COVID-19 pandemic.

TRIAL REGISTRATION: Prospero, CRD42021261927.

WEB: 10.1186/s12939-022-01678-5
IMPACT FACTOR: 2.595
CITED HALF-LIFE: 4.5

START COMMENTARY

In this systematic review and meta-analysis, Ali *et al.* assess factors associated with vaccine coverage inequality and heterogeneity in coverage with a focus on socioeconomic, geographic, and demographic factors. This study is important as differences in global vaccine coverage inequities are critical for targeted immunization policies. Global coverage of certain vaccines (e.g., diphtheria-tetanus-pertussis vaccination [DTP3] have stagnated in recent years, indicating a need to tailor immunization programs to meet the needs of hard-to-reach populations. Al *et al.* searched for literature in two databases, PubMed and Web of Science. Eligible studies were written in English, focused on vaccines and equality (i.e., equity; fairness; inequality; disparities), took place in in low- or middle-income countries, and mentioned heterogeneity in vaccine access or coverage. Ali *et al.* decided to exclude COVID-19, as they wanted to focus on long-standing inequities. Studies underwent a quality assessment using the Critical Appraisal Skills Program (CASP) guidelines.

In total, 108 studies were included in the systematic review. Many studies (n=24) took place in India and multi-country studies often took place in Africa. Nearly all studies focused on children with only two focusing on adults, and three not specifying the population. Only three studies had poor study quality. One surprising finding was that only 8 of 108 total studies assessed the impact of inequality on the overall impact of vaccination. Geographic variation in vaccination coverage is shown in *Figure 3.* Briefly, most studies found rural and urban differences (although the direction varies depending on study and country), with most showing higher vaccine coverage in urban areas. There was no significant difference in likelihood of being fully vaccinated in rural areas compared to urban. Females were 3% less likely to be vaccinated compared to males (risk ratio RR: 0.97, 95% Confidence Interval [CL]: 0.95-0.99). Children whose mother had no formal education were 27% less likely to be vaccinated compared to any education level was (RR 0.73, 95% CI: 0.64-0.84). Similarly, the poorest quintile was 27% less likely to be vaccinated compared to the wealthiest (RR: 0.73, 95% CI: 0.63-0.84). Factors associated with lower vaccine uptake across studies included travel time/cost, safety concerns, vaccine hesitancy, and others. Overall, Ali *et al.* demonstrate substantial equity issues, particularly for sociodemographic factors.

Return to List of Articles

2. Cost-effectiveness of COVID-19 vaccination in low- and middle-income countries.

Siedner M, Alba C, Fitzmaurice K, Gilbert R, Scott J, Shebl F, et al.

J Infect Dis. 2022 Jun 13.
PubMed ID: 35696544

ABSTRACT

BACKGROUND: Despite the advent of safe and effective COVID-19 vaccines, pervasive inequities in global vaccination persist.

METHODS: We projected health benefits and donor costs of delivering vaccines for up to 60% of the population in 91 low- and middle-income countries (LMICs). We modeled a highly contagious (Re at model start=1.7), low-virulence (IFR=0.32%) “omicron-like” variant and a similarly contagious “severe” variant (IFR=0.59%) over 360 days, accounting for country-specific age structure and healthcare capacity. Costs included vaccination startup (US$630 million) and per-person procurement and delivery (US$12.46/person vaccinated).

RESULTS: In the omicron-like scenario, increasing current vaccination coverage to achieve at least 15% in each of the 91 LMICs would prevent 11 million new infections and 120,000 deaths, at a cost of US$0.95 billion, for an incremental cost-effectiveness ratio (ICER) of US$670/year-of-life saved (YLS). Increases in vaccination coverage to 60% would additionally prevent up to 68 million infections and 160,000 deaths, with ICERs<US$8,000/YLS. ICERs were<US$4,000/YLS under the more severe variant scenario and generally robust to assumptions about vaccine effectiveness, uptake, and costs.

CONCLUSIONS: Funding expanded COVID-19 vaccine delivery in LMICs would save hundreds of thousands of lives, be similarly or more cost-effective than other donor-funded global aid programs, and improve health equity.

WEB: 10.1093/infdis/jiac243
IMPACT FACTOR: 5.022
CITED HALF-LIFE: 9.8

START COMMENTARY

In this modelling study, Siedner *et al.* project health benefits and costs of delivering COVID-19 vaccines in 91 LMICs within COVAX Advance Market Commitment (AMC). This study is important as COVID-19 have disproportionately impacted LMICs, where nearly 60% of the COVID-19 attributable deaths have occurred; of note, this number is likely 2.5-3.1 times higher due to issues with reporting. Despite this disparity, vaccines have not been rolled out equitably, resulting in less

than 40% of people in LMICs receiving the vaccine course compared to 74% in high- and upper-middle countries. This study provides critical insight on the clinical impact and cost-effectiveness of increasing vaccination coverage in 91 LMICs. country-specific Outcomes are estimated over a 360 days time horizon and include infections, deaths, and years of life lost attributable to COVID-19. Input parameters are outlined in *Table 1* and include transmission dynamics, vaccine specifications, costs of vaccine purchase and delivery, and others. One key strength of this analysis is that the authors accounted for the unknown contagiousness and severity of future SAR-CoV-2 variants by including two epidemic scenarios. The first (the base case) is similar to Omicron in terms of epidemic growth rate and infection fatality ratio (IFR), whereas the second scenario has similar transmissibility but with a higher IFR.

COVID-19 vaccination at current coverage was projected to decrease infections by 11% (from 1.2 billion to 1.1 billion) and decrease deaths by 43% (from 3.9 million to 2.3 million). Vaccination would save an estimated 25 million years of life (YLS) across the 91 countries. Detailed findings are presented in *Table 2.* Increasing coverage by 15%, would prevent 11 million infections, 120,000 deaths, at a cost of US$953 (Incremental cost-effectiveness ratio [ICER]: US$670/YLS). With 30% vaccine coverage 101,000 deaths would be prevented (ICER: US$1040/YLS). With 60% vaccine coverage, had an ICER of US$7,820. Siedner *et al.* also conducted one-way sensitivity analyses in the 12 largest LMICs (Bangladesh, Democratic Republic of the Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania, and Vietnam) as they account for 61% of the population in the 91 countries and display a wide range of age structure, hospital capacity, intensive care unit capacity, and current vaccine coverage. Detailed findings are presented in *Table 3.* Overall, ICERs ranged from US$670/YLS for increasing coverage to 15% to US$7820/YLS for increasing coverage to 60% in an Omicron-like scenario. Both estimates are lower than some existing public health interventions (e.g., antiretroviral therapy). Overall, the results indicate substantial benefits for increasing coverage at all levels, and particularly in the scenario of a more severe variant, which support expanding vaccination programs in LMICs.

Return to List of Articles

3. Efficacy of single-dose HPV vaccination among young African women.

Barnabas R, Brown E, Onono M, Bukusi E, Njoroge B, Winer R, et al.
NEJM Evid. 2022 Jun 13;1(5):EVIDoa2100056.
PubMed ID: 35693874

ABSTRACT

BACKGROUND: Single-dose HPV vaccination, if efficacious, would be tremendously advantageous; simplifying implementation and decreasing costs.

METHODS: We performed a randomized, multi-center, double-blind, controlled trial of single-dose nonavalent (HPV 16/18/31/33/45/52/58/6/11) or bivalent (HPV 16/18) HPV vaccination compared to meningococcal vaccination among Kenyan women aged 15-20 years. Enrollment and six monthly cervical swabs and a month three vaginal swab were tested for HPV DNA. Enrollment sera were tested for HPV antibodies. The modified intent-to-treat (mITT) cohort comprised participants who tested HPV antibody negative at enrollment and HPV DNA negative at enrollment and month three. The primary outcome was incident persistent vaccine-type HPV infection by month 18.

RESULTS: Between December 2018 and June 2021, 2,275 women were randomly assigned and followed; 758 received the nonavalent HPV vaccine, 760 the bivalent HPV vaccine, and 757 the meningococcal vaccine; retention was 98%. Thirty-eight incident persistent infections were detected in the HPV 16/18 mITT cohort: one each among participants assigned to the bivalent and nonavalent groups and 36 among those assigned to the meningococcal group; nonavalent Vaccine Efficacy (VE) was 97.5% (95%CI 81.7-99.7%, p=<0.0001), and bivalent VE was 97.5% (95%CI 81.6-99.7%, p=<0.0001). Thirty-three incident persistent infections were detected in the HPV 16/18/31/33/45/52/58 mITT cohort: four in the nonavalent group and 29 in the meningococcal group; nonavalent VE for HPV 16/18/31/33/45/52/58 was 88.9% (95%CI 68.5-96.1%, p<0.0001). The rate of SAEs was 4.5-5.2% by group.

CONCLUSIONS: Over the 18 month time-frame we studied, single-dose bivalent and nonavalent HPV vaccines were each highly effective in preventing incident persistent oncogenic HPV infection, similar to multidose regimens.

WEB: 10.1056/EVIDoa2100056
IMPACT FACTOR: N/A
CITED HALF-LIFE: N/A

START COMMENTARY

In this randomized multi-center, double blind controlled study, Barnabas *et al.* test single-dose nonavalent (Human papillomavirus [HPV] 16/18/31/33/45/52/58/6/11 infection) or bivalent (HPV 16/18 infection) HPV vaccination compared with meningococcal vaccination among Kenyan women 15 to 20 years of age. This study is important as single-dose HPV vaccines could reach many more women given the simplified implementation, logistics, and reduced costs. Participants were recruited from the community and were eligible of they were 15-20, sexual active, female, living within the study area, and able to consent. Barnabas *et al.* selected meningococcal vaccine because the vaccine offers clinical benefits without affecting or being related to HPV outcomes. Randomization was stratified by site (three Kenya Medical Research Institute clinical sites in Thika, Nairobi, and Kisumu). The primary outcome was incident persistent cervical HPV infection among participants with a HPV negative test result at enrollment (verified by external genital and cervical swabs at enrollment and month 3) and a HPV antibody negative test at enrollment. This group was called the modified intent-to-treat [mITT] cohort.

In total, 758 participants enrolled to the nonavalent HPV vaccine group, 760 to the bivalent HPV vaccine group, and 757 to the meningococcal vaccine group. There was high adherence to study protocol – 100% of participants received the assigned vaccine, 98% return for two swabs, 94% for three swabs. In total, 94% of swabs were carnival and 6% were self-collected vaginal swabs. Key results indicate that the incidence of persistent HPV 16/18 was 0.17 per 100 woman-years in the bivalent and nonavalent vaccine groups, compared with 6.83 per 100 woman-years in the meningococcal vaccine control group (bivalent vaccine efficacy [VE]: 97.5%, 95% 81.6 to 99.7%; nonavalent VE: 97.5%, 95% CI 81.7 to 99.7%; P<0.0001). Among the mITTT cohort, 33 incident persistent infections were detected – 4 of which were in the nonavalent vaccine group and 29 in the meningococcal vaccine group. This means nonavalent VE for HPV 16/18/31/33/45/52/58 was 88.9% (95% CI, 68.5 to 96.1%; P<0.0001). Some serious adverse events were reported (e.g., pregnancy-related serious adverse events, infections); however, these were similar between groups. Overall, results from the first 18 months of the ongoing trial demonstrate promising results about the single-dose bivalent and nonavalent HPV vaccine efficacy among young Kenyan women. These findings, if durable, have great potential to improve HPV vaccine coverage and reduce the burden of cervical cancer in Kenya and globally.

Return to List of Articles

4. Knowledge and willingness of parents towards child girl HPV vaccination in Debre Tabor Town, Ethiopia: a community-based cross-sectional study.

Mihretie G, Liyeh T, Ayele A, Belay H, Yimer T, Miskr A.

Reprod Health. 2022 Jun 14;19(1):136.

PubMed ID: 35689288

ABSTRACT

BACKGROUND: Cervical cancer is currently the second-leading cause of cancer death among women in Ethiopia. Vaccination against the human papillomavirus (HPV) is an effective primary prevention strategy for HPV-related illnesses. The knowledge and willingness of parents toward the HPV vaccine are crucial to increasing the uptake of the vaccine. The vaccine's acceptance by children and young adolescents is dependent on parental consent. Therefore, this study aimed to assess knowledge, willingness, and associated factors of the human papillomavirus vaccine among parents of girls aged 9-14 years at Debre Tabor Town.

METHOD: A community-based cross-sectional study was conducted among participants from December 10, 2020, to January 15, 2021. A simple random sample technique was used to include 638 participants. A structured face-to-face interviewer-administered questionnaire was used to collect data. The data were entered and analyzed using Epi-Data and SPSS software, respectively. Bivariate and multivariable analyses were used to examine the association. The Odds Ratio (OR), 95% CI, and p-values less than 0.05 were used to determine the statistical association.

RESULTS: Thirty-five percent (35.4%, 95% CI=31.4%, 38.8%) and 44.8% (95% CI=40.40%, 48.67%) of participants were knowledgeable about HPV vaccination and willing to get it, respectively. Being government employees (AOR=5.46, 95% CI=2.42, 9.34), and having a family history of sexually transmitted diseases (STD) (AOR=1.76, 95% CI=1.14, 2.72) were significantly associated with knowledge of the human papilloma virus (HPV) vaccine. Participants' age (AOR=1.43, 95% CI=1.16, 2.87), secondary education and above (AOR=1.70, 95% CI=1.05, 2.74), fear of HPV infection (AOR=2.29, 95% CI=1.21, 4.32), and having good knowledge of the HPV vaccine (AOR=3.30, 95% CI=2.21, 4.93) were significantly associated with willingness to receive the HPV vaccine.

CONCLUSION AND RECOMMENDATION: The knowledge and willingness of parents toward the HPV vaccine were low. Then, health officials should boost HPV vaccination promotion through public media. In schools, churches, mosques, and health facilities, health extension workers and health professionals provide information about the HPV vaccine for the parents. Mixed quantitative and qualitative studies are preferable for future research to address "why" issues.

WEB: 10.1186/s12978-022-01444-4
IMPACT FACTOR: 1.340
CITED HALF-LIFE: 4.5

START COMMENTARY

In this community-based cross-sectional study, Mihretie *et al.* assess knowledge, willingness to uptake, and associated factors of the HPV vaccine among parents of girls aged 9-13 in Debre Tabor Town, Ethiopia. This study is importance as despite the availability of highly effective HPV vaccines against high-risk types of cancer, coverage remains low. Prior studies have shown that willingness to allow a child to get HPV vaccine may be related to limited knowledge and sociodemographic factors. As such, this study aimed to understand factors associated with willingness among a population of parents in Ethiopia. Participants were randomly sampled using a census of all select kebeles (the smallest administrative unit in Ethiopia) in Debre Tabor Town. For each household, either both a mother and father were interviewed, or one of the parents. Outcomes included parent's knowledge and willingness to receive the HPV vaccine. Knowledge was defined as a serious of correct responses to HPV vaccine questions (50% or greater was considering having knowledge while <50% was considered having no knowledge).

In total, 638 parents were interviewed. Detailed socio-economic factors are shown in *Table 1.* The vast majority did not have family history of cervical cancer (n=636, 99.7%). About half (48.7%) had heard about the HPV vaccine. About 35.1% of participants (95% CI: 31.4-38.8) had good knowledge about HPV and cervical cancer, with about 32.1% knowing that cervical cancer is caused by HPV. Less than half (44.8%, 95% CI: 40.4-48.67%) were willing to receive the HPV vaccine. Reasons for not getting vaccinated among 551 parents including shortage of vaccines at the health facility (57.40%), no information about the vaccine (15.20%), that it affects fertility (14.20%), fear of side effects (7.60%), and fear of needle injections (5.60%). Younger individuals (31-40 year olds) were 1.43 times more likely (adjusted odds ratio [aOR]: 1.43, 95% CI: 1.16-2.87) to have willingness towards the HPV vaccine. Other factors associated with willingness included having a secondary education or above (aOR: 1.7, 95% CI: 1.05-2,74) compared to no education, fear of the HPV infection (aOR: 2.29, 95% CI: 1.21-4.32) compared to no fear, and knowing about the HPV vaccine and cervical cancer (aOR: 3.30, 95% CI: 2.21-4.93). Overall, this study demonstrates the importance of involving parents and educating them to ensure high levels of acceptability and uptake of the HPV vaccine.

Return to List of Articles

5. COVID-19 impact on routine immunisations for vaccine-preventable diseases: Projecting the effect of different routes to recovery.

Toor J, Li X, Jit M, Trotter C, Echeverria-Londono S, Hartner A, et al.

Vaccine. 2022 Jun 21;40(31):4142-4149.

PubMed ID: 35672179

ABSTRACT

Over the past two decades, vaccination programmes for vaccine-preventable diseases (VPDs) have expanded across low- and middle-income countries (LMICs). However, the rise of COVID-19 resulted in global disruption to routine immunisation activities. Such disruptions could have a detrimental effect on public health, leading to more deaths from VPDs, particularly without mitigation efforts. Hence, as routine immunisation activities resume, it is important to estimate the effectiveness of different approaches for recovery. We apply an impact extrapolation method developed by the Vaccine Impact Modelling Consortium to estimate the impact of COVID-19-related disruptions with different recovery scenarios for ten VPDs across 112 LMICs. We focus on deaths averted due to routine immunisations occurring in the years 2020-2030 and investigate two recovery scenarios relative to a no-COVID-19 scenario. In the recovery scenarios, we assume a 10% COVID-19-related drop in routine immunisation coverage in the year 2020. We then linearly interpolate coverage to the year 2030 to investigate two routes to recovery, whereby the immunization agenda (IA2030) targets are reached by 2030 or fall short by 10%. We estimate that falling short of the IA2030 targets by 10% leads to 11.26% fewer fully vaccinated persons (FVPs) and 11.34% more deaths over the years 2020-2030 relative to the no-COVID-19 scenario, whereas, reaching the IA2030 targets reduces these proportions to 5% fewer FVPs and 5.22% more deaths. The impact of the disruption varies across the VPDs with diseases where coverage expands drastically in future years facing a smaller detrimental effect. Overall, our results show that drops in routine immunisation coverage could result in more deaths due to VPDs. As the impact of COVID-19-related disruptions is dependent on the vaccination coverage that is achieved over the coming years, the continued efforts of building up coverage and addressing gaps in immunity are vital in the road to recovery.

WEB: 10.1016/j.vaccine.2022.05.074

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

In this modelling study, Toor *et al.* estimate the impacts of COVID-19-related disruptions associated with different recovery scenarios for ten vaccine-preventable diseases (VPDs) across 112 LMICs (73 currently and formally Gavi-supported countries and 39 other countries). This study is

important as it estimates the long-term impact of recovery scenarios, which are important to understand to scale up efforts and reduce morbidity and mortality from VPDs. Toor *et al.* utilize the impact extrapolation method developed by the Vaccine Impact Modelling Consortium (VIMC) to use prior impact ratios and apply them to new coverage scenarios and estimates. *Table 1* summarizes the included diseases type of vaccination activities, outbreak risk, and expected transmission changes due to other non-pharmaceutical interventions. Three scenarios were modeled: 1) no COVID-19-related disruptions; 2) a 10% absolute drop in routine immunization coverage but coverage in 2030 reaches Immunization Agenda (IA) 2030 targets (coined 'the return scenario'); 3) a 10% absolute drop in routine immunization coverage but coverage in 2030 reaches the IA2030 targets with a 10% absolute reduction ('the default return scenario). Outcomes reported include the change in fully vaccinated persons (FVPs), increase in deaths due to COVID-19, deaths averted and FVPs attributable to routine immunization from 2020-2030.

Table 2 shows detailed results. A COVID-19 drop in vaccine coverage results in 11.26% fewer FVPs and 11.34% more deaths when compared to the non-COVID-19 scenario. In the return scenario, there are 5% fewer FVPs and 5.22% more deaths. However, some vaccines (such as HPV) face a lower effect due to disruption whereas Japanese encephalitis and Neisseria meningitidis serogroup A vaccines are affect more substantially. Overall, the authors show the impact of several recovery scenarios, and how they may vary over time and by vaccine. This extrapolation method can continue being improved with additional inputs (i.e., the inclusion of non-pharmaceutical interventions for COVID-19), to provide better insights into the estimated COVID-19 disruption impact on routine immunization.

Return to List of Articles

6. COVID-19 in the 47 countries of the WHO African region: a modelling analysis of past trends and future patterns.

Cabore J, Karamagi H, Kipruto H, Mungatu J, Asamani J, Droti B, et al.

Lancet Glob Health. 2022 Jun 06.

PubMed ID: 35659911

ABSTRACT

BACKGROUND: COVID-19 has affected the African region in many ways. We aimed to generate robust information on the transmission dynamics of COVID-19 in this region since the beginning of the pandemic and throughout 2022.

METHODS: For each of the 47 countries of the WHO African region, we consolidated COVID-19 data from reported infections and deaths (from WHO statistics); published literature on socioecological, biophysical, and public health interventions; and immunity status and variants of concern, to build a dynamic and comprehensive picture of COVID-19 burden. The model is consolidated through a partially observed Markov decision process, with a Fourier series to produce observed patterns over time based on the SEIRD (denoting susceptible, exposed, infected, recovered, and dead) modelling framework. The model was set up to run weekly, by country, from the date the first infection was reported in each country until Dec 31, 2021. New variants were introduced into the model based on sequenced data reported by countries. The models were then extrapolated until the end of 2022 and included three scenarios based on possible new variants with varying transmissibility, severity, or immunogenicity.

FINDINGS: Between Jan 1, 2020, and Dec 31, 2021, our model estimates the number of SARS-CoV-2 infections in the African region to be 505 6 million (95% CI 476 0-536 2), inferring that only 1 4% (one in 71) of SARS-CoV-2 infections in the region were reported. Deaths are estimated at 439 500 (95% CI 344 374-574 785), with 35 3% (one in three) of these reported as COVID-19-related deaths. Although the number of infections were similar between 2020 and 2021, 81% of the deaths were in 2021. 52 3% (95% CI 43 5-95 2) of the region's population is estimated to have some SARS-CoV-2 immunity, given vaccination coverage of 14 7% as of Dec 31, 2021. By the end of 2022, we estimate that infections will remain high, at around 166 2 million (95% CI 157 5-174 9) infections, but deaths will substantially reduce to 22563 (14970-38831).

INTERPRETATION: The African region is estimated to have had a similar number of COVID-19 infections to that of the rest of the world, but with fewer deaths. Our model suggests that the current approach to SARS-CoV-2 testing is missing most infections. These results are consistent with findings from representative seroprevalence studies. There is, therefore, a need for surveillance of

hospitalisations, comorbidities, and the emergence of new variants of concern, and scale-up of representative seroprevalence studies, as core response strategies.

FUNDING: None.

WEB: 10.1016/S2214-109X(22)00233-9
IMPACT FACTOR: 21.597
CITED HALF-LIFE: 3.1

START COMMENTARY

In this modelling analysis, Cabore *et al.* conduct a study to generate information on the country-specific transmission dynamics of COVID-19 from the beginning of the pandemic to 2022 in the WHO African Region. This study makes an important contribution as the COVID-19 burden has been under-reported in Africa, resulting in a poor understanding of the disease in the African context. Cabore *et al.* used a susceptible, exposed, infected, recovered, and dead (SEIRD) model (presented in *Figure 1*). Input parameters included country population estimates, mortality rates, birth rates, COVID-19 infections, deaths, seroprevalence, and COVID-19 vaccination rates. The authors included a sensitivity analysis to assess the impact of assumptions on the results. The model was built in two different platforms (Excel and R) to check internal consistency.

Overall, from Jan 1, 2020 to December 31, 2021, an estimated 505.6 million (95% CI: 476.0-536.2) people were infected with SARS-CoV-2, suggested that only 1.4% of infections were reported officially. *Table 1* presents estimated infections and deaths by country. Results were also stratified by the country's economic status (*Figure 1A*) and economic regional block (*Figure 1B*). The model estimated that 166.2 million (95% CI: 157.5-174.9) infections and 22,563 deaths are expected in 2022. These estimates would be particularly high in the case of a severe variant. Overall, Cabore *et al.* show the immense COVID-19 burden in the WHO Africa region, which has been poorly understood to date.

Return to List of Articles

7. Impact of periodic intensification of routine immunization within an armed conflict setting and COVID-19 outbreak in Cameroon in 2020.

Njoh A, Saidu Y, Bachir H, Ndoula S, Mboke E, Nembot R, et al.

Confl Health. 2022 Jun 02;16(1):29.

PubMed ID: 35655226

ABSTRACT

INTRODUCTION: Cameroon's Southwest Region (SW) has been hit by an armed conflict for over half a decade now, negatively affecting the region's routine immunization and disease surveillance activities. This negative effect was further acerbated by the COVID-19 pandemic, which alongside the conflict, caused thousands of children to miss out on life-saving vaccinations. Herein, we present the contribution of periodic intensification of routine immunization in improving immunization and surveillance activities amid crises.

METHOD: Periodic intensification of routine immunization (PIRI) and disease surveillance were carried out in three rounds per health district. Before the intervention, the security profile of each district involved was reviewed. Data for this study was extracted on vaccination and surveillance activities from the District Health Information Software and monthly regional reports for 2019 and 2020 from the SW delegation of health.

RESULTS: 54,242 persons were vaccinated in the SW following these interventions. An increase in performance was observed in all 18 health districts in 2020 compared to 2019. Both DPT-HebB-Heb-3 vaccine and OPV-3 coverage rose by 28% points. Similarly, the proportion of health districts that investigated at least a case of acute flaccid paralysis increased by 83%, rising from just three districts in 2019 to all 18 in 2020.

CONCLUSION: PIRI was a practical approach to improving vaccination coverage and surveillance indicators in this region amidst the ongoing armed conflict and COVID-19 pandemic.

WEB: 10.1186/s13031-022-00461-1

IMPACT FACTOR: 4.562

CITED HALF-LIFE: 3.9

START COMMENTARY

In this study, Njoh *et al.* describe the impact of a periodic intensification of routine immunization (PIRI) amid armed conflict in the Southwest Region of Cameroon This study is important as it describes an intervention for issues of worsening vaccination coverage, reduced surveillance, and subsequent increases in vaccine preventable disease (VPD) during crises. The

intervention involved community outreach, health facility vaccinations including of missed doses, administration of Vitamin A and Mebendazole for children under 5, searches of missed cases of acute flaccid paralysis (AFP), suspected cases of neonatal tetanus, yellow fever, and measles. After this, a daily evaluation of activities and corrective performance measures were implemented at health areas. Data was obtained from Dhis2 on a monthly level.

During the intervention, 54,242 people received at least one dose of a missed vaccine. The cost per person vaccinated was estimated to be 4.50 USD. *Figure 2* demonstrates trends in each vaccination type throughout the study period whereas *Figure 3* shows the trends in AFP per health district of the Southwest Region. Overall, authors conclude that there was an improvement in vaccination coverage for all antigens in all districts (shown in *Table 1*). This study indicates that PIRI improved vaccination coverage and disease surveillance. These results are promising for other settings which may be experiencing armed conflict and related crises.

Return to List of Articles

8. Cost-effectiveness of rotavirus vaccination in children under five years of age in 195 countries: A meta-regression analysis.

Janko M, Joffe J, Michael D, Earl L, Rosettie K, Sparks G, et al.

Vaccine. 2022 Jun 15;40(28):3903-3917.
PubMed ID: 35643565

ABSTRACT

BACKGROUND: Rotavirus caused an estimated 151,714 deaths from diarrhea among children under 5 in 2019. To reduce mortality, countries are considering adding rotavirus vaccination to their routine immunization program. Cost-effectiveness analyses (CEAs) to inform these decisions are not available in every setting, and where they are, results are sensitive to modeling assumptions, especially about vaccine efficacy. We used advances in meta-regression methods and estimates of vaccine efficacy by location to estimate incremental cost-effectiveness ratios (ICERs) for rotavirus vaccination in 195 countries.

METHODS: Beginning with Tufts University CEA and Global Health CEA registries we used 515 ICERs from 68 articles published through 2017, extracted 938 additional one-way sensitivity analyses, and excluded 33 ICERs for a sample of 1,418. We used a five-stage, mixed-effects, Bayesian metaregression framework to predict ICERs, and logistic regression model to predict the probability that the vaccine was cost-saving. For both models, covariates were vaccine characteristics including efficacy, study methods, and country-specific rotavirus disability-adjusted life-years (DALYs) and gross domestic product (GDP) per capita. All results are reported in 2017 United States dollars.

RESULTS: Vaccine efficacy, vaccine cost, GDP per capita and rotavirus DALYs were important drivers of variability in ICERs. Globally, the median ICER was $2,289 (95% uncertainty interval (UI): $147-$38,993) and ranged from $85 per DALY averted (95% UI: $13-$302) in Central African Republic to $70,599 per DALY averted (95% UI: $11,030-$263,858) in the United States. Among countries eligible for support from Gavi, The Vaccine Alliance, the mean ICER was $255 per DALY averted (95% UI: $39-$918), and among countries eligible for the PAHO revolving fund, the mean ICER was $2,464 per DALY averted (95% UI: $382-$3,118).

CONCLUSION: Our findings incorporate recent evidence that vaccine efficacy differs across locations, and support expansion of rotavirus vaccination programs, particularly in countries eligible for support from Gavi, The Vaccine Alliance.

WEB: 10.1016/j.vaccine.2022.05.042
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

Janko *et al.* estimate the cost-effectiveness of rotavirus vaccination in children under 5 years of age in 195 countries to provide information for decision-making on rotavirus vaccine scale up globally. Data came from two registries from the Tufts University's Center for Evaluation of Risk and Value in Health: (1) CEA registry with cost per quality-adjusted life year (QALY) estimates and (2) Global Health CEA registry with cost per disability-adjusted life year (DALY) estimates. Variables extracted included the cost discount rate, QALY/DALY, health outcome measure, time horizon, and perspective (e.g., healthcare payer, health sector, others). A logistic regression analysis and a meta-regression were conducted.

For the logistic regression, 1,418 incremental cost-effectiveness ratios (ICERs) were included whereas the meta-regression was comprised of 1,345 ICERs. Janko *et al.* found that most ICERs were reported from the sub-Saharan Africa region (n=440), from a healthcare payer perspective (n=521), measured DALYs (n=1,029) and used a 3% discount rate (n=1,058). Descriptive statistics are presented in *Table 1.* Overall, sub-Saharan Africa and South Asia had the lowest population-weighted mean ICERs. In Africa, the median ICER was 251 USD (90% uncertainty interval [UI]: 38-903). Predicted ICERs are presented by super region in *Table 2* and by country in *Table 3.* When comparing countries, Central African Republic and Chad had the lowest ICERs (85 USD and 120 USD per DALY averted, respectively) as they have the highest burden of rotavirus in the world. In conclusion, the ICERs for each country and region provide estimates of cost-effectiveness which can inform rotavirus immunization implementation globally.

Return to List of Articles

9. How drivers of seasonality in respiratory infections may impact vaccine strategy: a case study in how COVID-19 may help us solve one of influenza's biggest challenges.

Lofgren E, Naumova E, Gorski J, Naumov Y, Fefferman N.

Clin Infect Dis. 2022 May 24.

PubMed ID: 35607766

ABSTRACT

Vaccines against seasonal infections like influenza offer a recurring testbed, encompassing challenges in design, implementation, and uptake to combat a both familiar and ever-shifting threat. One of the pervading mysteries of influenza epidemiology is what causes the distinctive seasonal outbreak pattern. Proposed theories each suggesting different paths forwards in being able to tailor precision vaccines and/or deploy them most effectively. One of the greatest challenges in contrasting and supporting these theories is, of course, that there is no means by which to actually test them. In this communication we revisit theories and explore how the ongoing COVID-19 pandemic might provide a unique opportunity to better understand the global circulation of respiratory infections. We discuss how vaccine strategies may be targeted and improved by both isolating drivers and understanding the immunological consequences of seasonality, and how these insights about influenza vaccines may generalize to vaccines for other seasonal respiratory infections.

WEB: 10.1093/cid/ciac400

IMPACT FACTOR: 8.313

CITED HALF-LIFE: 8.3

START COMMENTARY

In this case study, Lofgren *et al.* discuss theories related to seasonal influenza infection outbreaks and assesses how the COVID-19 pandemic may provide information on circulation of respiratory illnesses. First, Lonfgren *et al.* describe the unknowns regarding influenza seasonality; although there are several theories, there are limited means of testing them. They describe methods of generating evidence and their associated limitations including laboratory experiments (i.e., unknown if this translates to findings 'in the wild') and natural experiments (i.e., COVID-19 and flu outbreaks at the same time).

Lofgren *et al.* describe how a 'twindemic' of seasaonal influenza and COVID-19 cocirculating did not occur, and the theories that might explain the nearly non-existent flu season in 2020 and 2021. Theories including 'reinforcing' (defined as mechanisms that were reinforced during the progression/response to COVID-19 such as seasonal physiological changes like lowered Vitamin D

levels); ‘disruptive’ (defined as mechanisms such as non-pharmaceutical interventions and disruptive travel which reduced COVID-19 and influenza); neutral (defined as drivers of influenza seasonality likely to be neutral in the COVID-19 context such as El Nino Southern Oscillation weather patterns); and conditional (defined as mechanisms that might yield seasonal influenza patterns but depend on manner and scale of the effect such as seasonal crowding). Within each theory, the authors present predictions for testing each hypotheses. Overall, COVID-19 has provided a unique setting to understand and test hypotheses related to seasonal influenza mechanisms.

Return to List of Articles

10. Measles Vaccination Elicits a Polyfunctional Antibody Response, Which Decays More Rapidly in Early Vaccinated Children.

Brinkman I, Butler A, de Wit J, van Binnendijk R, Alter G, van Baarle D.

J Infect Dis. 2022 May 30;225(10):1755-1764.

PubMed ID: 34134138

ABSTRACT

BACKGROUND: Measles outbreaks are reported worldwide and pose a serious threat, especially to young unvaccinated infants. Early measles vaccination given to infants under 12 months of age can induce protective antibody levels, but the long-term antibody functionalities are unknown.

METHODS: Measles-specific antibody functionality was tested using a systems serology approach for children who received an early measles vaccination at 6-8 or 9-12 months, followed by a regular dose at 14 months of age, and children who only received the vaccination at 14 months. Antibody functionalities comprised complement deposition, cellular cytotoxicity, and neutrophil and cellular phagocytosis. We used Pearson's r correlations between all effector functions to investigate the coordination of the response.

RESULTS: Children receiving early measles vaccination at 6-8 or 9-12 months of age show polyfunctional antibody responses. Despite significant lower levels of antibodies in these early-vaccinated children, Fc effector functions were comparable with regular-timed vaccinees at 14 months. However, 3-year follow-up revealed significant decreased polyfunctionality in children who received a first vaccination at 6-8 months of age, but not in children who received the early vaccination at 9-12 months.

CONCLUSIONS: Antibodies elicited in early-vaccinated children are equally polyfunctional to those elicited from children who received vaccination at 14 months. However, these antibody functionalities decay more rapidly than those induced later in life, which may lead to suboptimal, long-term protection.

WEB: 10.1093/infdis/jiab318
IMPACT FACTOR: 5.022
CITED HALF-LIFE: 9.8

START COMMENTARY

Brinkman *et al.* assess antibody response among children after measles mumps rubella (MMR) vaccination. This study fills a critical gap in the literature in understanding long-term antibody functionality after MMR vaccination. Brinkman *et al.* evaluate if the polyfunctional antibody response

is affected by the timing of the first MMR dose. Children who received an early vaccination (between 6 to 8 months or 9 to 12 months) followed by a regular dose (14 months)were compared to those receiving the regular dose at 14 months only. Participants were recruited during a measles outbreak in the Netherlands from 2013 to 2014.

The study included 34 children (13 who received the dose between 6-8 months; 11 who received it from 9 to 12 months). Baseline characteristics are presented in *Table 1.* Brinkman *et al.* used a systems serology platform to measure ADNP, ADCP, ADCD, and antibody-induced NK activation via markers of activation and degranulation: CD107a, IFN-γ, and MIP-1β. There was a decline in ADNP and ADCD 1-3 years after vaccination, and an increase of ADCP over time (*Figure 1A* and *1B,* respectively). Results indicate lower levels of antibodies among children who received early measles vaccines, but no influence on the Fc-effector capacity on the level of a single antibody. There were also some changes in the induction of multiple effector functions simultaneously depending on vaccine timing; the functional response for regular MMR vaccine was more coordinated after 3 years, whereas the early dose (6-8 months) became less coordinated over time. Overall, the study shows that early-vaccinated children induce similar Fc-effector functions as antibodies, showing that this is an appropriate strategy if needed during outbreaks. However, there were some indications of declines in polyfunctionality in the long term (1-3 years after first dose) which should be further explored.

Return to List of Articles

Appendix

The literature search for the July 2022 Vaccine Delivery Research Digest was conducted on June 29, 2022. We searched English language articles indexed by the US National Library of Medicine and published between May 15, 2022 and June 14, 2022. The search resulted in 678 items.

SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR “supply chain”[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR “Cost effectiveness”[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR “Procurement”[tiab] OR timeliness[tiab] OR systems[tiab])) OR (“vaccine delivery”[tiab])) NOT (“in vitro”[tiab] OR “immune response”[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR “systems biology”[tiab] OR “animal model”[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) (“2022/15/05”[PDAT] : “2022/14/06”[PDAT]))