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REPORT TO THE BILL & MELINDA GATES FOUNDATION

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Appendix

Details of Articles

1. Malaria vaccines: facing unknowns.

Palacpac N, Horii T.

F1000Res. 2020 May 16;9.

PubMed ID: 32399189

ABSTRACT

Much of the gain in malaria control, in terms of regional achievements in restricting geographical spread and reducing malaria cases and deaths, can be attributed to large-scale deployment of antimalarial drugs, insecticide-treated bed nets, and early diagnostics. However, despite impressive progress, control efforts have stalled because of logistics, unsustainable delivery, or short-term effectiveness of existing interventions or a combination of these reasons. A highly efficacious malaria vaccine as an additional tool would go a long way, but success in the development of this important intervention remains elusive. Moreover, most of the vaccine candidate antigens that were investigated in early-stage clinical trials, selected partly because of their immunogenicity and abundance during natural malaria infection, were polymorphic or structurally complex or both. Likewise, we have a limited understanding of immune mechanisms that confer protection. We reflect on some considerable technological and scientific progress that has been achieved and the lessons learned.

WEB: 10.12688/f1000research.22143.1

IMPACT FACTOR: N/A CITED HALF-LIFE: N/A

START COMMENTARY

This commentary provides an update on the progress of the development of a malaria vaccine, highlighting challenges such as the immunogenicity and polymorphic concerns with vaccine candidates in early stage clinical trials, a limited understanding of immune responses and natural immunity to malaria, and opportunities such as newly developed tools like controlled human malaria infection and novel adjunctive. This article is impactful as it provides a detailed review of malaria vaccination developments and lessons learned which can inform future efforts. Malaria vaccines that can either prevent infections, or control parasite growth and the duration of infection, would be highly effective in malaria control, an area that is in dire need of new interventions given the high burden of disease, limited and short-term effectiveness of existing control strategies (i.e. insecticides, artemisinin combination treatment), and coverage gaps. The study highlights areas that need

additional research efforts including the use of structural epitopes for antigen selection, the development of novel vectors and adjuvants, and new developments in delivery methods and vaccine schedules. Further, this study highlights the need for cooperative global efforts to develop effective vaccines that can complement each other.

2. A single dose of quadrivalent human papillomavirus (HPV) vaccine is immunogenic and reduces HPV detection rates in young women in Mongolia, six years after vaccination.

Batmunkh T, Dalmau M, Munkhsaikhan M, Khorolsuren T, Namjil N, Surenjav U, et al.

Vaccine. 2020 Jun 02;38(27):4316-4324.

PubMed ID: 32387009

ABSTRACT

BACKGROUND: Emerging observational evidence suggests a single-dose of human papillomavirus (HPV) vaccine may be protective against vaccine-targeted HPV infection and associated cervical dysplasia. We aimed to demonstrate whether a single dose of quadrivalent HPV (4vHPV) vaccine was immunogenic and reduced HPV detection rates in young women in Mongolia. We also assessed knowledge and attitudes regarding HPV and the HPV vaccine.

METHODS: A retrospective paired cohort study was undertaken to evaluate the effect of a single dose of 4vHPV, given at age 11-17 years in 2012, on HPV detection rates, when compared with unvaccinated women. Real time PCR was performed on self-administered vaginal swabs for HPV detection. An immunological analysis detecting neutralising antibodies (NAb) to high-risk HPV (HRHPV) genotypes 16 and 18 was performed on sera from a subset of 58 participants. Questionnaires evaluated knowledge, attitudes and self-swab acceptability.

FINDINGS: A total of 475 women (mean age 20.4 years \pm 1.6) were recruited; 118 vaccinated and 357 unvaccinated women. The prevalence of vaccine-targeted HRHPV16 and 18 was reduced by 92% (95%Cl 44-99%) in the vaccinated (1·1%) compared with the unvaccinated (15.4%) group. The percentage of non-vaccine HPV genotypes was similar between vaccinated (26.5%) and unvaccinated (26.7%) groups. Approximately 90% and 58% of vaccinated women remained seropositive after six years for HRHPV16 and 18, respectively, with neutralising antibody levels 5-and 2-fold higher than unvaccinated women (p < 0.001).

INTERPRETATION: One dose of 4vHPV vaccine reduces vaccine-targeted HPV genotypes, six years following vaccination, with high levels of HR genotype seropositivity among young Mongolian women.

WEB: 10.1016/j.vaccine.2020.04.041

IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

A retrospective paired cohort study of 475 women in Mongolia found that a single dose of quadrivalent HPV vaccine reduced high-risk HPV (HRHPV) genotypes 16 and 18 by 92% (95%CI 44-99%) in the vaccinated compared to unvaccinated group. Six years after vaccination, about 90% and 58% of vaccinated women were seropositive for HRHPV16 and 18, respectively, indicating an effective reduction in vaccine-targeted HPV genotypes. In this retrospective cohort, participants were requested to collect self-administered vaginal swabs and to complete a questionnaire with questions on demographic characteristics, sexual and reproductive history, knowledge and attitudes towards HPV, HPV vaccine and cervical cancer, and acceptability of the self-administered swabs. Additional results indicated that positivity for HRHPV16 and 18 was associated with having two to four lifetime sexual partners (aOR 3.01, 95%Cl 1.32–6.83, p = 0.009). Knowledge levels on HPV, HPV vaccines, or cervical cancer were low (about 86% of participants did not achieve 50% correct), and selfswabbing was highly acceptable (about 98.9% of participants stated the instructions were clear and exhaustive). This study has many strengths, including the long follow up period (six years), reliable testing methods, and the collection of demographic and sexual history data that are potential confounders. Limitations include that this is an observational study—women (or their parents) self-selected to receive only one dose, against WHO guidelines. Similarly, the study sample of one-dose vaccinated women was small (N=118), and women who were vaccinated with one-dose were not compared to women who were vaccinated with two- or three-doses, making comparisons of immunogenicity difficult. This article is impactful as it extends evidence of the persistent immune response after receiving a single dose of HPV vaccine, contributing to efforts to reduce barriers to vaccine uptake in low- and middle-income settings.

3. Eliminating yellow fever epidemics in Africa: Vaccine demand forecast and impact modelling.

Jean K, Hamlet A, Benzler J, Cibrelus L, Gaythorpe K, Sall A, et al.

PLoS Negl Trop Dis. 2020 Jun 04;14(5):e0008304.

PubMed ID: 32379756

ABSTRACT

BACKGROUND: To counter the increasing global risk of Yellow fever (YF), the World Health Organisation initiated the Eliminate Yellow fever Epidemics (EYE) strategy. Estimating YF burden, as well as vaccine impact, while accounting for the features of urban YF transmission such as indirect benefits of vaccination, is key to informing this strategy.

METHODS AND FINDINGS: We developed two model variants to estimate YF burden in sub-Saharan Africa, assuming all infections stem from either the sylvatic or the urban cycle of the disease. Both relied on an ecological niche model fitted to the local presence of any YF reported event in 34 African countries. We calibrated under-reporting using independent estimates of transmission intensity provided by 12 serological surveys performed in 11 countries. We calculated local numbers of YF infections, deaths and disability-adjusted life years (DALYs) lost based on estimated transmission intensity while accounting for time-varying vaccination coverage. We estimated vaccine demand and impact of future preventive mass vaccination campaigns (PMVCs) according to various vaccination scenarios. Vaccination activities conducted in Africa between 2005 and 2017 were estimated to prevent from 3.3 (95% CI 1.2-7.7) to 6.1 (95% CI 2.4-13.2) millions of deaths over the lifetime of vaccinees, representing extreme scenarios of none or maximal herd effects, respectively. By prioritizing provinces based on the risk of urban YF transmission in future PMVCs, an average of 37.7 million annual doses for PMVCs over eight years would avert an estimated 9,900,000 (95% CI 7,000,000-13,400,000) infections and 480,000 (180,000-1,140,000) deaths over the lifetime of vaccinees, corresponding to 1.7 (0.7-4.1) deaths averted per 1,000 vaccine doses.

CONCLUSIONS: By estimating YF burden and vaccine impact over a range of spatial and temporal scales, while accounting for the specificity of urban transmission, our model can be used to inform the current EYE strategy.

WEB: 10.1371/journal.pntd.0008304

IMPACT FACTOR: 4.487 CITED HALF-LIFE: 4.4

START COMMENTARY

This modeling study estimates yellow fever disease burden and vaccine impact, while accounting for urban transmission, across 34 countries in sub-Saharan Africa using serological surveys from 11 countries. Jean et al. found that preventative mass vaccination campaigns since 2005 have prevented 3 to 6 million deaths, and further allocating a 37.7 million doses per year between 2018 and 2026 would prevent 9.89 (6.96–13.3) million yellow fever infections. This modelling study informs global yellow fever elimination strategies by extending prior disease modeling efforts and integrating specific inter-human transmission estimates to determine the burden, vaccine impact, and potential scenarios of preventative mass vaccination campaigns aimed at averting yellow fever infections and mortality.

This modeling study's strengths lie in the integration of serological data on a spectrum of severity, which may provide more reliable disease burden results compared to other methodologies. Further, this paper provides many vaccination scenarios, including targeted approaches of high-risk areas compared to widespread vaccination campaigns, to suggest options for immunization activities and vaccine allocation.

4. Stemming cholera tides in Zimbabwe through mass vaccination.

Mukandavire Z, Manangazira P, Nyabadza F, Cuadros D, Musuka G, Morris J.

Int J Infect Dis. 2020 Jun 08:96:222-227.

PubMed ID: 32371191

ABSTRACT

BACKGROUND: In 2018, Zimbabwe declared another major cholera outbreak a decade after recording one of the worst cholera outbreaks in Africa.

METHODS: A mathematical model for cholera was used to estimate the magnitude of the cholera outbreak and vaccination coverage using cholera cases reported data. A Markov chain Monte Carlo method based on a Bayesian framework was used to fit the model in order to estimate the basic reproductive number and required vaccination coverage for cholera control.

RESULTS: The results showed that the outbreak had a basic reproductive number of 1.82 (95% credible interval [CrI] 1.53-2.11) and required vaccination coverage of at least 58% (95% CrI 45-68%) to be contained using an oral cholera vaccine of 78% efficacy. Sensitivity analysis demonstrated that a vaccine with at least 55% efficacy was sufficient to contain the outbreak but at higher coverage of 75% (95% CrI 58-88%). However, high-efficacy vaccines would greatly reduce the required coverage, with 100% efficacy vaccine reducing coverage to 45% (95% CrI 35-53%).

CONCLUSIONS: These findings reinforce the crucial need for oral cholera vaccines to control cholera in Zimbabwe, considering that the decay of water reticulation and sewerage infrastructure is unlikely to be effectively addressed in the coming years.

WEB: 10.1016/j.ijid.2020.03.077

IMPACT FACTOR: 3.538 CITED HALF-LIFE: 4.9

START COMMENTARY

Mukandavire et al. fit a model using a Markov chain Monte Carlo method based on a Bayesian framework to estimate that a recent cholera outbreak in Zimbabwe had a basic reproductive number of 1.82 (95% credible interval [Crl] 1.53-2.11) and required vaccination coverage of at least 58% (95% Crl 45-68%) to be contained using an oral cholera vaccine of 78% efficacy. This study highlights the critical role of oral cholera vaccines for both short-term relief during outbreaks and for long term control. Models were fit using data from reported cholera cases from Harare, where the

outbreak began. The basic reproductive number was high (>1), indicating that the outbreak had the potential to spread to other areas, which it ultimately did. However, this study shows that it would have been possible to contain this outbreak and prevent it from spreading if targeted oral cholera vaccines were implemented in a timely manner. These results show that oral vaccine is a viable option for controlling cholera outbreaks especially in communities where there are significant structural and operational challenges with sewerage and water systems. However, one key limitation of this study is that it only collected data from an urban area (Harare) and did not assess dynamics of the outbreak in suburban areas (Budirio and Glen View) due to limited data, which would have enhanced the understanding of the outbreak and control measures.

5. Assessment of a novel scanner-supported system for processing of child health and immunization data in Uganda.

Äijö A, Schäffner I, Waiswa P, Kananura R, Tessma M, Hanson C.

BMC Health Serv Res. 2020 May 05;20(1):367.

PubMed ID: 32349755

ABSTRACT

BACKGROUND: Electronic data capturing has the potential to improve data quality and user-friendliness compared to manually processed, paper-based documentation systems. The MyChild system uses an innovative approach to process immunization data by employing detachable vouchers integrated into a vaccination booklet which are then scanned and converted into individual-level health data. The aim was to evaluate the MyChild data capturing system by assessing the proportion of correctly processed vouchers and to compare the user-friendliness in term of time spent on documentation and health worker experiences with the standard health information system at health facilities in Uganda.

METHODS: We used a mixed method approach. Documented data were manually copied and compared to processed health records to calculate the proportion of correctly registered vouchers. To compare time spend on documentation we did a continuous observational time-motion study and analyzed data using a Mann-Whitney U test. Semi-structured interviews were conducted to assess health workers' experiences and analyzed using conventional content analysis. Data was collected in 14 health facilities in two districts in Uganda using different systems.

RESULTS: The MyChild system processed 97% (224 of 231) of the vouchers correctly. Recording using the MyChild system increased time spend on documentation of vaccination follow-up visits by 24 s compared to the standard system (02:25 vs. 02:01 min/child, Mann-Whitney U = 6293, n1 = 115, n2 = 151, p < 0.001 two-tailed, Z = -3.861, r = 0.186). However, high variance between health centers using the same health information system suggests that documentation time differences can be attributed to other factors than the way information was processed. Health workers perceived both health management information systems as predominantly functional and easy to use, while the MyChild system achieved a higher level of satisfaction.

CONCLUSIONS: The MyChild system electronically processes individual-level immunization data correctly without increasing significantly time spent on recording and is appreciated by health providers making it a potential solution to overcome shortcomings of present paper-based health information systems in health centers.

WEB: 10.1186/s12913-020-05242-1

IMPACT FACTOR: 1.932 CITED HALF-LIFE: 5.4

START COMMENTARY

This mixed methods study of health records from 14 health centers and semi-structured interviews showed that MyChild, an electronic data capturing system, accurately processed 97% (224 of 231) of individual-level immunization vouchers, while slightly increasing the time spent on documentation during visits, compared to the standard system (02:25 vs. 02:01 min/child, Mann-Whitney U = 6293, n1 = 115, n2 = 151, p < 0.001 two-tailed, Z = -3.861, r = 0.186). Data was collected from seven randomly selected intervention health centers in Dokolo district and seven randomly selected control health centers in Bukedea district. At each intervention health center, a healthcare worker was purposefully selected for a semi-structured interview. Limitations of this study design that should be noted include that the study was not blinded, which may have introduced reactive bias that affected the accuracy and speed of documentation. Further, interviews were conducted with only English-speaking staff, and in the presence of others, which may have introduced selection bias.

Based on positive study results, including nearly all vouchers being correctly scanned and processed substantially increasing time spent on recording, and high acceptability among healthcare workers, this intervention could be a solution to overcome issues with manual processing, paper-based systems. These results show that this intervention, MyChild, which is paper-based at point of care, and then scanned and processed into digital health records, could improve data quality on immunization services, and better inform planning and development of immunization service delivery. This study is impactful as it demonstrates effectiveness of an electronic data capturing system which relies on scanning handwritten health records and digitizing them to improve data quality and user-friendliness.

6. Human papillomavirus vaccine coverage in Rwanda: A population-level analysis by birth cohort.

Sayinzoga F, Umulisa M, Sibomana H, Tenet V, Baussano I, Clifford G.

Vaccine. 2020 Jun 01;38(24):4001-4005.

PubMed ID: 32336599

ABSTRACT

BACKGROUND: In 2011, Rwanda became the first African nation to implement a national human papillomavirus (HPV) vaccination program, conceived to protect girls aged <15 years (i.e. born ≥1997). After an initial school-grade-targeted catch-up campaign, there was a transition to routine vaccination of 12 year-olds only. We aimed to produce population-level vaccine coverage estimates.

METHODS: The Rwandan Expanded Program on Immunization (EPI) collected data on number of eligible girls and HPV vaccines delivered, stratified by calendar year (2011-2018), girl's age, district and vaccination round. HPV vaccine coverage was estimated by birth cohort (reconstituted using calendar year and age), as a proportion of (1) eligible target, and (2) the 2012 Rwandan census population.

RESULTS: 1,156,863 girls received first dose of HPV vaccine between 2011 and 2018, corresponding to 98% of the eligible target. Median vaccination age was 15 years (interquartile range [IQR] 13-16) in 2011-2013 (school grade-targeted catch-up), 13 years (IQR 12-14) in 2014 (transition) and 12 years in 2015-2018 (routine). Population-level coverage versus the census increased from 10 to 40% for girls born in 1993-1995 (median vaccination age = 17 years) to 50-65% for 1996-2000 birth cohorts (14 years), and 80-90% for 2001-2006 birth cohorts (12 years). Coverage trends were similar across provinces and in the capital, Kigali. Second and third round coverage suggested most vaccinated girls completed their recommended dosing regimen (which reduced from 3 to 2 doses in 2015).

CONCLUSIONS: Birth cohorts provide a clear picture of population-level HPV vaccine coverage after a pragmatic catch-up campaign, particularly in Rwanda where eligible school grades included wide age ranges. Whilst the catch-up campaign resulted in some coverage gaps in out-of-school teenagers, coverage remains high in cohorts routinely targeted as 12 year-olds.

WEB: 10.1016/j.vaccine.2020.04.021

IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

Sayinzoga et al. estimated annual population-level human papillomavirus (HPV) vaccine coverage for girls in Rwanda from 2011–2018. While first dose HPV vaccine coverage estimates were high when using number of eligible girls based on school registers (i.e., number of girls in targeted primary and secondary school grades) as denominators, authors found estimates were lower when denominators were defined using census estimates, though steadily increased over time (Table 1). As HPV vaccination strategies shifted away from a school-based approach to a "single-cohort agebased immunization approach," vaccination coverage gaps, namely among girls out of school, became more apparent. Authors identified two main limitations of the study. The first limitation was measuring vaccination by campaign round, rather than individual-level dose number. Campaign round may not necessarily correlate to individual-level dose number as those missed in the first campaign round may have received their first dose in a subsequent round. Additional studies to assess HPV vaccine completeness and timeliness would be beneficial. The second limitation was the use of three-year floating averages to estimate coverage and median age at vaccination since exact date of birth and exact date of vaccination were not available. This analysis is impact because it provides insight into HPV vaccine implementation in Rwanda and valuable birth cohort HPV vaccine coverage data for future studies.

7. Documentation of vaccine wastage in two different geographic contexts under the universal immunization program in India.

Das M, Sood M, Tambe M, Sharma T, Parande M, Surwade J, et al. *BMC Public Health*. 2020 Apr 30;20(1):556.

PubMed ID: 32334554

ABSTRACT

BACKGROUND: Government of India is introducing new and relatively costly vaccines under immunization program. Monitoring of vaccine wastage is needed to guide the program implementation and forecasting. Under pilot introduction of rotavirus vaccine in two districts both 5-and 10-doses vials were used, which was considered as an opportunity for documenting the wastage. The wastage rates for other routine vaccines were also documented.

METHODS: A survey conducted in two districts (Kangra, Himachal Pradesh and Pune, Maharashtra) covered 49 vaccine stores, 34 sub-centres and 34 outreach sessions collected vaccine receipt, distribution and usage data for two complete years 2016 and 2017.

RESULTS: The overall wastage rates for almost all vaccines were higher in Kangra district (BCG 37.1%, DPT 32.1%, Measles 32.2%, OPV 50.8%, TT 34.1% and pentavalent 18.4%) than Pune district (BCG 35.1%, DPT 25.4%, Measles 21.7%, OPV 14.3%, TT 23.1% and pentavalent 13.2%). Wastage for pneumococcal conjugate and measles-rubella vaccines in Kangra district were 27 and 40.5%, respectively. With transition from 5- to 10-doses vials for rotavirus vaccine, wastage at stores levels increased in both Kangra (29 to 33.2%) and Pune (17.8 to 25.7%) districts. With transition from intramuscular to intradermal fractional inactivated polio vaccine, the wastage increased from 36.1 to 54.8% in Kangra and 18.4 to 26.9% in Pune district.

CONCLUSIONS: The observed vaccine wastage rates for several vaccines were relatively higher than program assumption for forecasting. The observed variations in the vaccine wastage indicates need for state or region based documentation and monitoring in India for appropriate programmatic action.

WEB: 10.1186/s12889-020-08637-1

IMPACT FACTOR: 2.567 CITED HALF-LIFE: 5.5

START COMMENTARY

In the interest of reducing vaccine wastage and costs, Das et al. assessed vaccine wastage rates for rotavirus vaccine, poliovirus vaccine, and other routine childhood vaccines from select facilities in two districts of India, Kangra and Pune. Authors reported higher wastage rates for several vaccines than what was recommended by the Ministry of Health and Family Welfare. Higher wastage was also observed for 10-dose vials of rotavirus vaccine compared to 5-dose vials. Importantly, authors also observed variation in wastage by several factors including vaccine antigen, district, vial size, and distribution site. Based on semi-structured interviews, Das et al. found that beneficiary case load seemed to explain differences in wastage for 10-dose vials and 5-dose vials of rotavirus vaccine. Furthermore, health workers attempted to limit wastage with the 10-dose vials by reorganizing vaccination sessions to increase number of beneficiaries at a given session. This study may have limited generalizability since authors only examined select facilities in two districts. There may also be potential bias in estimating wastage depending on the accuracy of doses issued and doses administered data. The study was also limited by the lack of data in a number of areas (e.g., doses returned for vaccines under the open vial policy, small sample for MR and PCV). Despite these limitations, this study is impactful as it exposes deviations from wastage assumptions for Kangra and Pune and highlights the need for continued wastage monitoring at various level of vaccine implementation.

8. Questions for future evidence-informed policy initiatives: insights from the evolution and aspirations of National Immunization Technical Advisory Groups.

Buffardi A, Njambi-Szlapka S.

Health Res Policy Syst. 2020 Apr 27;18(1):40.

PubMed ID: 32321521

ABSTRACT

BACKGROUND: Attention to evidence-informed policy has grown; however, efforts to strengthen the quality and use of evidence are not starting from a blank slate. Changes in health architectures and financing pose different considerations for investments in evidence-informed policy than in the past. We identify major trends that have shifted the environment in which health policies are made, and use the evolution and future aspirations of National Immunization Technical Advisory Groups (NITAGs) in low- and middle-income countries to identify questions the sector must confront when determining how best to structure and strengthen evidence-informed health policy.

DISCUSSION: Trends over the last two decades have resulted in a dense arena with many issue-specific groups, discrete initiatives to strengthen evidence-informed policy and increasing responsibility for subnational institutions. Many countries face a shifting resource base, which for some reduces the amount of resources for health. There is global momentum around universal health coverage, reflecting a broader systems approach, but few examples of how the vast array of stakeholders relate within it are available. NITAG aspirations reflect four interconnected themes related to their scope, their integration in national policy processes, health financing and relationships with ministries of finance, and NITAG positioning relative to other domestic and international entities, raising questions such as, What are the bounds of issue-specific groups and their relationship to allocation decision-making processes across health areas? How do technical advisory groups interface with what are inherently political processes? When are finances considered, by whom and how? What is the future of existing groups whose creation was intended to enhance national ownership but who need continued external support to function? When should new entities be created, in what form and with what mandate?

CONCLUSIONS: Countries must determine who makes decisions about resources, when, using what criteria, and how to do so in a robust yet efficient way given the existing and future landscape. While answers to these questions are necessarily country specific, they are collective matters that

cannot be addressed by specialised groups alone and have implications for new investments in evidence-informed policy.

WEB: 10.1186/s12961-020-00551-7

IMPACT FACTOR: 2.218 CITED HALF-LIFE: 4.6

START COMMENTARY

In this report, Buffardi and Njambi-Szlapka explored questions for consideration to support growing interest in evidence-informed policy in the health and international development sectors. These questions and considerations were illustrated through the future aspirations of National Immunization Technical Advisory Groups (NITAGs). The authors grounded the analysis of four core themes (referenced in the abstract) with the following thought: "The question, therefore, is not simply, 'how can the quality and use of evidence on issue X be improved'. We must also ask 'how do new or renewed efforts to enhance evidence-informed policy relate to existing, and in some cases, shifting structures and resources?'" The questions Buffardi and Njambi-Szlapka presented go beyond common considerations for issue-specific groups and help facilitate holistic system-level, rather than siloed, development of evidence-informed policymaking. As NITAGs evolve, putting forth deliberate and continued attention on these issues in collaboration with other stakeholders may promote more efficient and globally-informed health policies.

9. Hepatitis B virus seroepidemiology data for Africa: Modelling intervention strategies based on a systematic review and metaanalysis.

McNaughton A, Lourenço J, Bester P, Mokaya J, Lumley S, Obolski U, et al. *PLoS Med.* 2020 Apr 28;17(4):e1003068.

PubMed ID: 32315297

ABSTRACT

BACKGROUND: International Sustainable Development Goals (SDGs) for elimination of hepatitis B virus (HBV) infection set ambitious targets for 2030. In African populations, infant immunisation has been fundamental to reducing incident infections in children, but overall population prevalence of chronic hepatitis B (CHB) infection remains high. In high-prevalence populations, adult catch-up vaccination has sometimes been deployed, but an alternative Test and Treat (T&T) approach could be used as an intervention to interrupt transmission. Universal T&T has not been previously evaluated as a population intervention for HBV infection, despite high-profile data supporting its success with human immunodeficiency virus (HIV).

METHODS AND FINDINGS: We set out to investigate the relationship between prevalence of HBV infection and exposure in Africa, undertaking a systematic literature review in November 2019. We identified published seroepidemiology data representing the period 1995-2019 from PubMed and Web of Science, including studies of adults that reported prevalence of both hepatitis B surface antigen (HBsAg; prevalence of HBV infection) and antibody to hepatitis B core antigen (anti-HBc; prevalence of HBV exposure). We identified 96 studies representing 39 African countries, with a median cohort size of 370 participants and a median participant age of 34 years. Using weighted linear regression analysis, we found a strong relationship between the prevalence of infection (HBsAg) and exposure (anti-HBc) (R2 = 0.45, p < 0.001). Region-specific differences were present, with estimated CHB prevalence in Northern Africa typically 30% to 40% lower (p = 0.007) than in Southern Africa for statistically similar exposure rates, demonstrating the need for intervention strategies to be tailored to individual settings. We applied a previously published mathematical model to investigate the effect of interventions in a high-prevalence setting. The most marked and sustained impact was projected with a T&T strategy, with a predicted reduction of 33% prevalence by 20 years (95% CI 30%-37%) and 62% at 50 years (95% CI 57%-68%), followed by routine neonatal vaccination and prevention of mother to child transmission (PMTCT; at 100% coverage). In contrast, the impact of catch-up vaccination in adults had a negligible and transient effect on population prevalence. The study is constrained by gaps in the published data, such that we could

not model the impact of antiviral therapy based on stratification by specific clinical criteria and our model framework does not include explicit age-specific or risk-group assumptions regarding force of transmission.

CONCLUSIONS: The unique data set collected in this study highlights how regional epidemiology data for HBV can provide insights into patterns of transmission, and it provides an evidence base for future quantitative research into the most effective local interventions. In combination with robust neonatal immunisation programmes, ongoing PMTCT efforts, and the vaccination of high-risk groups, diagnosing and treating HBV infection is likely to be of most impact in driving advances towards elimination targets at a population level.

WEB: 10.1371/journal.pmed.1003068

IMPACT FACTOR: 11.048 CITED HALF-LIFE: 8.2

START COMMENTARY

McNaughton et al. conducted a review of literature on hepatitis B virus (HBV) burden in Africa to inform a modeling analysis, which examined the impact of hepatitis B interventions in a high-prevalence setting. The Markov chain Monte Carlo model included complexities around age-specific risk of infection for acute and chronic hepatitis B (Figure 2). They found, in a high-prevalence setting, a test and treat strategy had the largest impact decreasing prevalence of HBV over time and low impact from an all ages catch-up vaccination campaign strategy. Authors noted that successful test and treat approaches have been widely documented in the HIV sphere, but recognized that, unlike hepatitis B, there is no vaccine for HIV. Limitations of the study included not considering the risk of reactivation among individuals who were HBsAg negative and anti-HBc positive, but still have HBV cccDNA in their liver. Another limitation is the potential bias introduced by using data from various studies where the sensitivity and specificity of serological assays may vary.

10. Effect of a school-based educational intervention on HPV and HPV vaccine knowledge and willingness to be vaccinated among Chinese adolescents: a multi-center intervention follow-up study.

Zhang X, Liu C, Wang Z, Ren Z, Feng X, Ma W, et al.

Vaccine. 2020 Apr 13;38(20):3665-3670.

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ABSTRACT

BACKGROUND: Middle school students are recommended as the primary target population for human papillomavirus (HPV) vaccination. This study aimed to assess HPV and HPV vaccine knowledge, and to evaluate the effect of a school-based educational intervention, immediately and one year later, on HPV knowledge and vaccine acceptability among adolescents in mainland China.

METHODS: A school-based interventional follow-up study was conducted in seven representative cities in mainland China from May 2015 to May 2017. "Train-the-trainer" strategy was employed to educate school teachers in this study. Students aged 13 to 14 years old were assigned to intervention classes and control classes. All students were required to complete the baseline questionnaire. Students in the intervention classes were given a 45-minute lecture regarding HPV and HPV vaccine knowledge and were then asked to complete a post-education questionnaire. One year later, all students were asked to complete the post-education questionnaire again.

RESULTS: Baseline HPV knowledge was low among Chinese adolescents, with only 12.6% and 15.7% of students having heard of HPV and HPV vaccines, respectively. After the intervention, the level of HPV-related knowledge increased immediately, and students with higher knowledge levels of HPV and HPV vaccines were more willing to get vaccinated. One year after the intervention, the knowledge of HPV and HPV vaccines was dramatically diminished. However, knowledge was significantly higher in intervention classes compared to control classes.

CONCLUSIONS: Knowledge and awareness of HPV and vaccination are generally deficient among Chinese adolescents. School-based health education was very effective in improving awareness and positive attitudes about HPV and HPV vaccines within a short time. Integrating health education on HPV into the existing school-based sexual health curriculum could be an effective way to increase HPV vaccination coverage and help to eliminate preventable HPV-associated cancers in China.

WEB: 10.1016/j.vaccine.2020.03.032

IMPACT FACTOR: 3.269 CITED HALF-LIFE: 3.1

START COMMENTARY

Zhang et al. conducted an evaluation of a school-based educational HPV intervention in China. Preand post-intervention assessments demonstrated students who received the educational lecture had greater knowledge and more positive attitudes towards HPV vaccination compared to those who did not receive the lecture. However, these differences were less pronounced one year after the intervention. Limitations of this study included lack of generalizability among youths out of school, potential for reporting bias among students, and not including parent and teacher knowledge and attitudes towards HPV and HPV vaccination, which may highly influence vaccination uptake.

Appendix

The literature search for the June 2020 Vaccine Delivery Research Digest was conducted on May 18, 2020. We searched English language articles indexed by the US National Library of Medicine and published between April 15, 2020 and May 14, 2020. The search resulted in 276 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 murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) ("2020/04/15"[PDAT] : "2020/05/14"[PDAT]))