# VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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## 1. [Eliminating Cervical Cancer in Mali and Senegal, Two Sub-Saharan Countries: Insights and Optimizing Solutions.](#)

Haque A, Kouriba B, Aïssatou N, Pant A.

## ABSTRACT

**BACKGROUND:** The number of cases with cervical cancer is rapidly increasing in Sub-Saharan Africa driven by inadequate rates of human papilloma virus (HPV) vaccination and screening programs and accompanied by poor health delivery systems. There are other factors to contend with such as lack of awareness, social myths, reluctance to vaccine acceptance and stigma with sexually transmitted diseases. Here, we formulate strategies to implement intervention programs against HPV infections and other risk factors for cervical cancer in these countries.

**METHODS:** We searched PubMed, Web of Science, and African Journals Online for this review. The current status of anti-HPV vaccination and precancerous screening programs in Mali and Senegal has been assessed by onsite visits. Collaborators from Mali and Senegal collected data and information concerning HPV vaccination and screening programs in these countries.

**FINDINGS:** We found that anti-HPV vaccination and cervical cancer screening have been conducted sporadically mainly in urban areas of Mali and Senegal. No known population-based programs are in progress in either of the two countries. We highlighted the advantages and drawbacks of currently available screening tests and proposed that screening by visual inspection with acetic acid (VIA) accompanied by self-sampling is the most cost-effective, culturally acceptable and most feasible strategy to implement in primary care settings. In addition, HPV DNA testing would be affordable, if local laboratory facilities could be established. We found that many of the factors that increase HPV acquisition and promote the oncogenic effect of the virus are largely widespread in both Senegal and Mali. These include infections with HIV and other sexually transmitted infections (STIs), immunosuppression, polygamous marriages, high parity, early sexual activities, early pregnancies, and multiple sexual partners.

**INTERPRETATION:** Neither vaccines nor screening tests are within the reach of the population in Mali and Senegal because of the high cost. The effective intervention measure would be to integrate

anti-HPV vaccines into the Extended Program for Immunization (EPI), which has saved 3 million young lives per year in Africa with the support of GAVI, to implement cost control mechanisms for HPV vaccinations via price negotiations with manufacturing companies, as has recently been done by Rwanda. The collective efforts by local governments, researchers, private sector, and donors may lead to the introduction of affordable screening tests. A robust awareness campaign coupled with sustained and regular engagement of local communities about the prevention and risk factors is extremely important. The projected solutions may be well applicable to other Sub-Saharan countries that face similar challenges containing cervical cancer.

**WEB:** 10.3390/vaccines8020181
**IMPACT FACTOR:** 4.760
**CITED HALF-LIFE:** 6.9

## START COMMENTARY

Hague et al. review the use of human papillomavirus (HPV) vaccination and cervical cancer screening in the context of Mali and Senegal, two countries with high rates of cervical cancer and high prevalence of high-risk HPV. Table 2 summarizes areas of intervention to eliminate cervical cancer in sub-Saharan Africa. Authors remarked the lack of recognition of cervical cancer as of public health importance, despite the high burden. They also noted the prohibitive cost of the vaccine and screening highlights it as a disease of poverty.

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## 2. Childhood vaccination coverage and equity impact in Ethiopia by socioeconomic, geographic, maternal, and child characteristics.

Geweniger A, Abbas K.

## ABSTRACT

**BACKGROUND:** Ethiopia is a priority country of Gavi, the Vaccine Alliance to improve vaccination coverage and equitable uptake. The Ethiopian National Expanded Programme on Immunisation (EPI) and the Global Vaccine Action Plan set coverage goals of 90% at national level and 80% at district level by 2020. This study analyses full vaccination coverage among children in Ethiopia and estimates the equity impact by socioeconomic, geographic, maternal and child characteristics based on the 2016 Ethiopia Demographic and Health Survey dataset.

**METHODS:** Full vaccination coverage (1-dose BCG, 3-dose DTP3-HepB-Hib, 3-dose polio, 1-dose measles (MCV1), 3-dose pneumococcal (PCV3), and 2-dose rotavirus vaccines) of 2,004 children aged 12-23 months was analysed. Mean coverage was disaggregated by socioeconomic (household wealth, religion, ethnicity), geographic (area of residence, region), maternal (maternal age at birth, maternal education, maternal marital status, sex of household head), and child (sex of child, birth order) characteristics. Concentration indices estimated wealth and education-related inequities, and multiple logistic regression assessed associations between full vaccination coverage and socioeconomic, geographic, maternal, and child characteristics.

**RESULTS:** Full vaccination coverage was 33.3% [29.4-37.2] in 2016. Single vaccination coverage ranged from 49.1% [45.1-53.1] for PCV3 to 69.2% [65.5-72.8] for BCG. Wealth and maternal education related inequities were pronounced with concentration indices of 0.30 and 0.23 respectively. Children in Addis Ababa and Dire Dawa were seven times more likely to have full vaccination compared to children living in the Afar region. Children in female-headed households were 49% less likely to have full vaccination.

**CONCLUSION:** Vaccination coverage in Ethiopia has a pro-advantaged regressive distribution with respect to both household wealth and maternal education. Children from poorer households, rural regions of Afar and Somali, no maternal education, and female-headed households had lower full

vaccination coverage. Targeted programmes to reach under-immunised children in these subpopulations will improve vaccination coverage and equity outcomes in Ethiopia.

**WEB:** 10.1016/j.vaccine.2020.03.040
**IMPACT FACTOR:** 3.269
**CITED HALF-LIFE:** 3.1

## START COMMENTARY

In this analysis of the equity of childhood vaccination coverage in Ethiopia, Geweniger et al. used multiple logistic regression to assess the association between vaccination and measures of socioeconomic, geographic, maternal and child characteristics. Authors found low vaccine coverage and evidence of inequity by several variables. Interestingly, authors also found that households with female heads had lower coverage compared to households with male heads, which counters frameworks of female empowerment; however, authors hypothesize that the head of the household may be a marker for socioeconomic differences. Limitations of this study include reliance on maternal recall of vaccination status of their child(ren). Furthermore, vaccination coverage may not represent current coverage as data were based on the 2016 DHS, and variation in vaccine coverage estimates by data source (e.g., DHS, WUENIC, and official estimates of national authorities) should be accounted for in policy and practice considerations.

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## 3. Immunogenicity and safety of an adjuvanted inactivated polio vaccine, IPV-Al, following vaccination in children at 2, 4, 6 and at 15-18 months.

Sáez-Llorens X, Thierry-Carstensen B, Stoey L, Sørensen C, Wachmann H, Bandyopadhyay A, et al.

## ABSTRACT

**BACKGROUND:** Availability of affordable inactivated polio vaccines (IPV) is of major importance to meet the increasing global supply needs. The results presented here demonstrate non-inferiority of a reduced-dose, aluminium hydroxide-adjuvanted IPV (IPV-Al) to standard IPV.

**METHODS:** A phase 3, observer-blinded, randomised, clinical trial was conducted in Panama in infants who received either IPV-Al (n = 400) or standard IPV (n = 400) at age 2, 4 and 6 months. In the booster trial, subjects received a single dose of IPV-Al at age 15-18 months. The primary endpoint was type-specific seroconversion, defined as an antibody titre ≥4-fold higher than the estimated maternal antibody titre and a titre ≥8, one month after the primary vaccination series. In the booster trial, the primary endpoint was the type-specific booster effects (geometric mean titre (GMT) post-booster (Day 28)/GMT pre-booster (Day 0).

**RESULTS:** Seroconversion rates following primary vaccination with IPV-Al vs IPV were: 96.1% vs 100% (type 1); 100% vs 100% (type 2); and 99.2% vs 100% (type 3) respectively. IPV-Al was non-inferior to IPV, as the lower 95% confidence limits of the treatment differences were above the pre-defined -10%-point limit: 3.94% (-6.51; -2.01) for type 1; 0.0% (-1.30; -1.37) for type 2; -0.85 (-2.46; 0.40) for type 3. The booster effects for the group primed with IPV-Al versus the group primed with IPV were 25.3 vs 9.2 (type 1), 19.1 vs 6.5 (type 2) and 50.4 vs 12.5 (type 3). IPV-Al had a comparable safety profile to that of IPV.

**CONCLUSIONS:** Non-inferiority of IPV-Al to standard IPV with respect to seroconversion after vaccination at 2, 4 and 6 months was confirmed for all three poliovirus serotypes. A robust booster response was demonstrated following vaccination with IPV-Al, regardless of the primary vaccine received. Both vaccines were well tolerated. ClinicalTrials.gov identifiers: NCT03025750 and NCT03671616.

**FUNDING:** Bill & Melinda Gates Foundation.

## START COMMENTARY

Two phase 3 clinical trials conducted in Panama demonstrated non-inferiority of a dose-saving aluminum hydroxide-adjuvanted inactivated polio vaccine (IPV-AI) administered at 2, 4, 6, and 15–18 months compared to the standard inactivated polio vaccine (IPV). Containing only one-tenth the amount of antigen used in the standard IPV, the IPV-AI can have considerable impact on lowering manufacturing costs. The results were in alignment with other clinical trials of IPV-AI conducted in Philippines, the Dominican Republic and Demark, suggesting that there may not be marked differences by geography.

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## 4. [Health and economic burden of respiratory syncytial virus (RSV) disease and the cost-effectiveness of potential interventions against RSV among children under 5 years in 72 Gavi-eligible countries.](#)

Li X, Willem L, Antillon M, Bilcke J, Jit M, Beutels P.

## ABSTRACT

**BACKGROUND:** Respiratory syncytial virus (RSV) frequently causes acute lower respiratory infection in children under 5, representing a high burden in Gavi-eligible countries (mostly low-income and lower-middle-income). Since multiple RSV interventions, including vaccines and monoclonal antibody (mAb) candidates, are under development, we aim to evaluate the key drivers of the cost-effectiveness of maternal vaccination and infant mAb for 72 Gavi countries.

**METHODS:** A static Multi-Country Model Application for RSV Cost-Effectiveness poLicy (MCMARCEL) was developed to follow RSV-related events monthly from birth until 5 years of age. MCMARCEL was parameterised using country- and age-specific demographic, epidemiological, and cost data. The interventions' level and duration of effectiveness were guided by the World Health Organization's preferred product characteristics and other literature. Maternal vaccination and mAb were assumed to require single-dose administration at prices assumed to align with other Gavi-subsidised technologies. The effectiveness and the prices of the interventions were simultaneously varied in extensive scenario analyses. Disability-adjusted life years (DALYs) were the primary health outcomes for cost-effectiveness, integrated with probabilistic sensitivity analyses and Expected Value of Partially Perfect Information analysis.

**RESULTS:** The RSV-associated disease burden among children in these 72 countries is estimated at an average of 20.8 million cases, 1.8 million hospital admissions, 40 thousand deaths, 1.2 million discounted DALYs, and US$611 million discounted direct costs. Strategy 'mAb' is more effective due to its assumed longer duration of protection versus maternal vaccination, but it was also assumed to be more expensive. Given all parameterised uncertainty, the optimal strategy of choice tends to change for increasing willingness to pay (WTP) values per DALY averted from the current situation to maternal vaccination (at WTP > US$1000) to mAB (at WTP > US$3500). The age-specific proportions of cases that are hospitalised and/or die cause most of the uncertainty in the choice of optimal strategy. Results are broadly similar across countries.

**CONCLUSIONS:** Both the maternal and mAb strategies need to be competitively priced to be judged as relatively cost-effective. Information on the level and duration of protection is crucial, but also more and better disease burden evidence-especially on RSV-attributable hospitalisation and death rates-is needed to support policy choices when novel RSV products become available.

**WEB:** 10.1186/s12916-020-01537-6
**IMPACT FACTOR:** 8.285
**CITED HALF-LIFE:** 4.7

## START COMMENTARY

Using a static cohort model, Li et al. compared the health impact and costs of universal maternal respiratory syncytial virus (RSV) vaccination, universal RSV monoclonal antibodies (mAb) administered at birth, and no intervention for 72 Gavi countries. They found that a high willingness to pay was needed for maternal RSV vaccination and mAb to be cost-effective in low-income and lower-middle-income countries (LIC and LMIC). RSV is estimated to cause significant burden globally, especially in LIC and LMIC. There is currently no licensed RSV vaccine. As vaccine development advances, studies such as this one are needed to guide countries and investors in their decision-making around vaccine investments. Li et al. identified factors most influential in determining cost-effectiveness of these iinterventions and highlighted the need to gather more data around areas of uncertainty, including the duration of protection, proportion of RSV cases that are hospitalized, RSV incidence, and case fatality of RSV in hospitals and the community.

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## 5. Vaccination coverage survey and seroprevalence among forcibly displaced Rohingya children, Cox's Bazar, Bangladesh, 2018: A cross-sectional study.

## ABSTRACT

**BACKGROUND:** During August 2017-January 2018, more than 700,000 forcibly displaced Rohingyas crossed into Cox's Bazar, Bangladesh. In response to measles and diphtheria cases, first documented in September and November 2017, respectively, vaccination campaigns targeting children <15 years old were mobilized during September 2017-March 2018. However, in a rapidly evolving emergency situation, poor sanitation, malnutrition, overcrowding, and lack of access to safe water and healthcare can increase susceptibility to infectious diseases, particularly among children. We aimed to estimate population immunity to vaccine-preventable diseases (VPDs) after vaccination activities in the camps to identify any remaining immunity gaps among Rohingya children.

**METHODS AND FINDINGS:** We conducted a cross-sectional serologic and vaccination coverage survey in Nayapara Registered Refugee Camp ("Nayapara") and makeshift settlements (MSs) April 28, 2018 to May 31, 2018, among 930 children aged 6 months to 14 years. MSs are informal, self-settled areas with a population of more than 850,000, the majority of whom arrived after August 2017, whereas Nayapara is a registered camp and has better infrastructure than MSs, including provision of routine immunization services. Households were identified using simple random sampling (SRS) in Nayapara and multistage cluster sampling in MSs (because household lists were unavailable). Dried blood spots (DBSs) were collected to estimate seroprotection against measles, rubella, diphtheria, and tetanus, using Luminex multiplex bead assay (MBA). Caregiver interviews assessed vaccination campaign participation using vaccination card or recall. In Nayapara, 273 children aged 1 to 6 years participated; 46% were female and 88% were registered refugees. In MSs, 358 children aged 1 to 6 years and 299 children aged 7 to 14 years participated; 48% of all children in MSs were female, and none were registered refugees. In Nayapara, estimated seroprotection among 1- to 6-year-olds was high for measles, rubella, diphtheria, and tetanus (91%-98%; 95% confidence interval [CI] 87%-99%); children >6 years were not assessed. In MSs, measles seroprotection was similarly high among 1- to 6-year-olds and 7- to 14-year-olds (91% [95% CI 86%-94%] and 99% [95% CI 96%-100%], respectively, p < 0.001). Rubella and diphtheria seroprotection in MSs were significantly lower among 1- to 6-year-olds (84% [95% CI 79%-88%] and

63% [95% CI 56%-70%]) compared to 7- to 14-year-olds (96% [95% CI 90%-98%] and 77% [95% CI 69%-84%]) (p < 0.001). Tetanus seroprevalence was similar among 1- to 6-year-olds and 7- to 14-year-olds (76% [95% CI 69%-81%] and 84% [95% CI 77%-89%], respectively; p = 0.07). Vaccination campaign coverage was consistent with seroprotection in both camps. However, nonresponse, the main limitation of the study, may have biased the seroprotection and campaign coverage results.

**CONCLUSIONS:** In this study, we observed that despite multiple vaccination campaigns, immunity gaps exist among children in MSs, particularly for diphtheria, which requires serial vaccinations to achieve maximum protection. Therefore, an additional tetanus-diphtheria campaign may be warranted in MSs to address these remaining immunity gaps. Rapid scale-up and strengthening of routine immunization services to reach children and to deliver missed doses to older children is also critically needed to close immunity gaps and prevent future outbreaks.

**WEB:** 10.1371/journal.pmed.1003071
**IMPACT FACTOR:** 11.048
**CITED HALF-LIFE:** 8.2

## START COMMENTARY

Feldstein et al. conducted a vaccine coverage and seroprevalence survey of Rohingya children in Bangladesh in two settings: an established refugee Rohingya camp, Nayapara, and makeshift settlements. They found significant differences in coverage, especially for complete vaccination of measles-rubella and diphtheria-tetanus, between the makeshift settlements and Nayapara (Table 3). Furthermore, they identified gaps in protection from the serosurvey with lower protection levels among children ages 1–6 years in the makeshift settlements compared to children 7–14 years in the makeshift settlements. Interesting, authors noted a small proportion (<5%) of children received vaccination upon entry to Bangladesh, a potential area for intervention. Limitations of the study include included potential bias in maternal recall of vaccination, lack of response from 7–14-year-olds in Nayapara due to Ramadan, and potential discrepancies between serologic results and actual immunity within the population.

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# 6. Qualitative insights into reasons for missed opportunities for vaccination in Kenyan health facilities.

Li A, Tabu C, Shendale S, Okoth P, Sergon K, Maree E, et al.

## ABSTRACT

**BACKGROUND:** In 2016, Kenya conducted a study of missed opportunities for vaccination (MOV)-when eligible children have contact with the health system but are not fully vaccinated-to explore some of the reasons for persistent low vaccination coverage. This paper details the qualitative findings from that assessment.

**METHODS:** Using the World Health Organization MOV methodology, teams conducted focus group discussions among caregivers and health workers and in-depth interviews of key informants in 10 counties in Kenya. Caregivers of children <24 months of age visiting the selected health facilities on the day of the assessment were requested to participate in focus group discussions. Health workers were purposively sampled to capture a broad range of perspectives. Key informants were selected based on their perceived insight on immunization services at the county, sub-county, or health facility level.

**RESULTS:** Six focus group discussions with caregivers, eight focus group discussions with health workers, and 35 in-depth interviews with key informants were completed. In general, caregivers had positive attitudes toward healthcare and vaccination services, but expressed a desire for increased education surrounding vaccination. In order to standardize vaccination checks at all health facility visits, health workers and key informants emphasized the need for additional trainings for all staff members on immunization. Health workers and key informants also highlighted the negative impact of significant understaffing in health facilities, and the persistent challenge of stock-outs of vaccines and vaccination-related supplies.

**CONCLUSIONS:** Identified factors that could contribute to MOV include a lack of knowledge surrounding vaccination among caregivers and health workers, inadequate number of health workers, and stock-outs of vaccines or vaccination-related materials. In addition, vaccination checks outside of vaccination visits lacked consistency, leading to MOV in non-vaccinating departments. Qualitative assessments could provide a starting point for understanding and developing interventions to address MOV in other countries.

## START COMMENTARY

Li et al. conducted a qualitative analysis to better understand reasons for missed opportunities for vaccination (MOV) in Kenya. Purposively selected individuals were invited to participate in focus group discussions or in-depth interviews (summarized in Table 1). From these discussions and interviews, Li et al. captured the following themes: "perceptions of healthcare services and vaccination; vaccination checks and integration with other services; health worker staffing shortages; stock-outs of vaccines and vaccination-related materials; and health education." Several reasons for MOV were identified and, subsequently, informed discussions around interventions to improve vaccination coverage. Limitations of this study included not recording sessions (to encourage more honest discussion), large groups and gender mismatch potentially influencing group dynamics and the ability to have an open conversation, and potential selection bias among caregivers as they all were seeking health services.

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## 7. [Effect of age at vaccination on the measles vaccine effectiveness and immunogenicity: systematic review and meta-analysis.](#)

Carazo S, Billard M, Boutin A, De Serres G.

## ABSTRACT

**BACKGROUND:** The objectives of this review were to evaluate the effect of age at administration of the first dose of a measles-containing vaccine (MCV1) on protection against measles and on antibody response after one- and two-dose measles vaccinations.

**METHODS:** We conducted a systematic review of the PubMed/MEDLINE, Embase, Web of Science and Cochrane databases (1964-2017) to identify observational studies estimating vaccine effectiveness and/or measles attack rates by age at first vaccination as well as experimental studies comparing seroconversion by age at first vaccination. Random effect models were used to pool measles risk ratios (RR), measles odds ratios (OR) and seroconversion RR of MCV1 administered at < 9, 9-11 or ≥ 15 months compared with 12 or 12-14 months of age.

**RESULTS:** We included 41 and 67 studies in the measles protection and immunogenicity analyses. Older age at MCV1, from 6 to ≥15 months, improved antibody response and measles protection among one-dose recipients. Pooled measles RR ranged from 3.56 (95%CI: 1.28, 9.88) for MCV1 at < 9 months to 0.48 (95%CI: 0.36, 0.63) for MCV1 at ≥15 months, both compared to 12-14 months. Pooled seroconversion RR ranged from 0.93 (95%CI: 0.90, 0.96) for MCV1 at 9-11 months to 1.03 (95%CI: 1.00, 1.06) for MCV1 at ≥15 months, both compared to 12 months. After a second dose, serological studies reported high seropositivity regardless of age at administration of MCV1 while epidemiological data based on few studies suggested lower protection with earlier age at MCV1.

**CONCLUSIONS:** Earlier age at MCV1 decreases measles protection and immunogenicity after one dose and might still have an impact on vaccine failures after two doses of measles vaccine. While two-dose vaccination coverage is most critical to interrupt measles transmission, older age at first vaccination may be necessary to keep the high level of population immunity needed to maintain it.

## START COMMENTARY

Carazo et al. conducted a systematic review and meta-analysis of studies to examine differences in vaccine effectiveness and immunogenicity by age at first measles vaccination, finding older ages with higher protection and antibody response. For some pooled analyses, authors commented on heterogeneity unexplained by region, year, vaccine strain, or antibody assay. Interestingly, authors found that infants vaccinated at 11–12 months had higher seroconversion rates compared to those vaccinated at 15 months, but lower antibody titers. Limitations of the study included the low proportion of studies with low risk of bias, low proportion of studies that measured neutralizing antibodies, and lack of data among two-dose recipients. Authors stated that while most participants were born to mothers who acquired natural immunity to measles, studies did not report on maternal status, preventing any sensitivity analyses based on vaccinated mothers (which represents the majority of mothers today). Authors also noted that in high risk settings, immunization at lower ages may be preferred to avoid severe disease among infants.

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## 8. Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization.

Konopka-Anstadt J, Campagnoli R, Vincent A, Shaw J, Wei L, Wynn N, et al.

## ABSTRACT

Enormous progress has been made in global efforts to eradicate poliovirus, using live-attenuated Sabin oral poliovirus vaccine (OPV). However, as the incidence of disease due to wild poliovirus has declined, vaccine-derived poliovirus (VDPV) has emerged in areas of low-vaccine coverage. Coordinated global cessation of routine, type 2 Sabin OPV (OPV2) use has not resulted in fewer VDPV outbreaks, and continued OPV use in outbreak-response campaigns has seeded new emergences in low-coverage areas. The limitations of existing vaccines and current eradication challenges warranted development of more genetically stable OPV strains, most urgently for OPV2. Here, we report using codon deoptimization to further attenuate Sabin OPV2 by changing preferred codons across the capsid to non-preferred, synonymous codons. Additional modifications to the 5' untranslated region stabilized known virulence determinants. Testing of this codon-deoptimized new OPV2 candidate (nOPV2-CD) in cell and animal models demonstrated that nOPV2-CD is highly attenuated, grows sufficiently for vaccine manufacture, is antigenically indistinguishable from Sabin OPV2, induces neutralizing antibodies as effectively as Sabin OPV2, and unlike Sabin OPV2 is genetically stable and maintains an attenuation phenotype. In-human clinical trials of nOPV2-CD are ongoing, with potential for nOPV strains to serve as critical vaccine tools for achieving and maintaining polio eradication.

## START COMMENTARY

Konopka-Anstadt et al. described their work evaluating a codon-deoptimized new oral poliovirus type 2 vaccine (nOPV2-CD) in a preclinical evaluation. Current vaccination strategies present a challenge to polio eradication as unstable strains of poliovirus in vaccines can lead to vaccine-derived poliovirus infections. Mimicking conditions of the human gut, the authors passed both Sabin OPV2 and nOPV2-CD and found nOPV2-CD remained stable while Sabin OPV2 mutated at a key virulent

determinant. The preclinical evaluation serves as the basis for human clinical trials and presents as a more stable option for polio vaccine stockpiles and response to outbreaks.

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# 9. Determinants of geographical inequalities for DTP3 vaccine coverage in sub-Saharan Africa.

Ikilezi G, Augusto O, Sbarra A, Sherr K, Dieleman J, Lim S.

## ABSTRACT

Childhood immunization is one of the most effective health interventions, making it a key indicator of progress towards universal health coverage. In the last decade, improvements in coverage have been made globally, however, slow progress has been documented in sub-Saharan Africa with considerable subnational variations. We explore potential drivers of equitable immunization services based on subnational DTP3 coverage estimates. Using vaccine coverage at the 5 by 5 km area from 2000 to 2016, we quantify inequality using three measures. We assess the shortfall inequality which is the average deviation across subnational units from that with the highest coverage for each country. Secondly we estimate the threshold index, the proportion of children below a globally set subnational coverage target, and lastly, a Gini coefficient representing the within-country distribution of coverage. We use time series analyses to quantify associations with immunization expenditures controlling for country socio-economic and population characteristics. Development assistance, maternal education and governance were associated with reductions in inequality. Furthermore, high quality governance was associated with a stronger relationship between development assistance and reductions in inequality. Results from this analysis also indicate that countries with the lowest coverage suffer the highest inequalities. We highlight growing inequalities among countries which have met national coverage targets such as South Africa and Kenya. In 2016, values for the shortfall inequality ranged from 1% to 43%, the threshold index from 0% to 100% and Gini coefficient from 0.01 to 0.37. Burundi, Comoros, Eswatini, Lesotho, Namibia, Rwanda, and Sao Tome and Principe had the least shortfall inequality (<5%) while Angola, Ethiopia and Nigeria had values greater than 40%. A similar picture was noted for the other dimensions of inequality among these particular countries. Immunization program investments offer promise in addressing inequality, however, domestic mechanisms for resource implementation and accountability should be strengthened to maximize gains in coverage.

# START COMMENTARY

Using high spatial resolution estimates at the 5 by 5 km area level, Ikilezi et al. mapped areas of DTP3 vaccine coverage inequality in 45 sub-Saharan African countries. Figure 2 shows a graphical comparison of national DTP3 coverage and measures of inequality in 2016. Table 1 shows results from the regression analysis at the 5 by 5 km area level. Limitations of this study include information bias and sampling error derived from survey data, excluding domestic spending on immunization programs, and inability to make causal inference due to the cross-sectional nature of the study.

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## 10. [Cervical cancer prevention in Indonesia: An updated clinical impact, cost-effectiveness and budget impact analysis.](#)

Setiawan D, Andrijono D, Hadinegoro S, Meyta H, Sitohang R, Tandy G, et al.

## ABSTRACT

**INTRODUCTION:** The clinical and economic impact of cervical cancer consistently become a serious burden for all countries, including Indonesia. The implementation of HPV vaccination policy for a big country such as Indonesia requires a strong commitment from several decision-makers. The aim of this study was to provide a comprehensive description on cost-effectiveness and the budget-impact of HPV vaccination policy in Indonesia.

**METHOD:** A cohort Markov model was used to evaluate the cost and the clinical impact of HPV vaccination for 10 years old girls in Indonesia. The researchers consider two doses of all three available HPV vaccines adjusted with the HPV infection profilewith 95% vaccination coverage to estimate the national cervical cancer incidence and mortality. The Budget impact analysis explores three different scenarios covering (1) Two districts per year expansion, (2) oneprovince per year expansion and (3) achieving the National Immunization Program in 2024.

**RESULTS:** Upon fully vaccinating almost 2.3 million 10-year-old girls, 34,723; 43,414; and 51,522 cervical cancer cases were prevented by Quadrivalent, Bivalent and Nonavalent vaccines, consecutively. Furthermore, the highest (591 cases) and lowest (399 cases) mortality were prevented by Nonavalent and Quadrivalent vaccines, respectively. Most of the vaccines were considerably cost-effective and only the Bivalent vaccine with the GAVI/UNICEF price which will be considered a cost-saving strategy.To provide national coverage of HPV vaccination in Indonesia, the government has to provide an annual budget of about US$49 million and US$22 million using the government contract price and GAVI/UNICEF price, respectively.

**CONCLUSION:** HPV vaccination shows a cost-effective strategy and the budget required to provide this policy is considerably affordable for Indonesia.

**WEB:** [10.1371/journal.pone.0230359](#)
**IMPACT FACTOR:** 2.776
**CITED HALF-LIFE:** 2.7

## START COMMENTARY

In this cohort Markov modeling study, Setiawan et al. found that human papillomavirus (MPV) vaccination is a cost-effective strategy for Indonesia. Table 3 shows the results of discounted cost, QALYs, and ICER for quadrivalent, bivalent and nonavalent vaccines under two different prices. Tables 4–6 show estimated reductions in cost, incidence, and mortality based on vaccination strategy. Limitations of this study incldue the use of static model, which underestimates HPV impact, and use of 1–3 times GDP as a marker of cost-effectiveness, a controversial measure.

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# Appendix

The literature search for the May 2020 Vaccine Delivery Research Digest was conducted on April 28, 2020. We searched English language articles indexed by the US National Library of Medicine and published between March 15, 2020 and April 14, 2020. The search resulted in 246 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]) ("2020/03/15"[PDAT] : "2020/04/14"[PDAT]))