Measuring the impact of development assistance on vaccination coverage: evidence from low- and middle- income recipient countries.

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A dissertation

Submitted in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy

University of Washington

2019

Reading Committee:

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Program Authorized to Offer Degree:

Global Health

University of Washington

Abstract

Measuring the impact of development assistance on vaccination coverage: evidence from low- and middle- income recipient countries.

Chair of the Supervisory Committee:

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Global Health

Over the last decade, substantial amounts of development assistance have been invested among low and middle income countries to strengthen the performance and outcomes of the immunization program. Multiple development partners have collectively instituted different financing obligations targeting both new vaccine introductions and scale up of traditional vaccines. This dissertation explores the development assistance landscape and the impact on vaccination outcomes, with the goal of making a timely contribution to guide subsequent investment decisions as the end of the decade of vaccines draws nearer.

In the first chapter, *Tracking donor funding towards achieving the Global Vaccine Action Plan (GVAP) goals: A landscape analysis (1990-2016),* development assistance for immunization is characterized by purpose, recipient and time. The study utilized data from existing project databases, annual reports, and audited financial statements of multi-sectoral agencies supporting immunization where

funding was categorized by objective, estimating allocations to different vaccine types versus health systems strengthening. Using generalized linear models, funding projections were made to inform the progress of current global targets. While development assistance has remained resilient over time, findings from this analysis suggest that resource targets stipulated in the Global Vaccine Action Plan may not be met by 2020. This as a result calls for renewed financial assessments while strengthening existing resource efficiency at recipient level in order to achieve the desired child health outcomes.

The second chapter, *Effect of donor funding for immunization from Gavi and other development assistance channels on vaccine coverage: evidence from 120 low and middle income recipient countries,* builds on the first chapter further evaluating any impacts of aid on vaccine coverage. Following the launch of Gavi in 2000, recipient countries have not only continued to scale up underused vaccines but have concurrently expanded the scope of their routine immunization products which to date include thirteen new vaccine introductions. In this study we apply a novel approach where disbursements are disaggregated into funding for specific vaccines versus that for health systems strengthening. For these aid categories, we evaluate the impact on coverage for a wide spectrum of routinely administered vaccines namely; DPT3, pneumococcal vaccine (PCV3), Pentavalent3, Measles2 and Rotavirus2 vaccines. Findings from this analysis suggest varying improvements in coverage as a result of aid with stronger effects occurring among the newer vaccines. From a policy perspective, these findings offer promise for continued investments in immunization, but perhaps even more importantly, highlight the need for improved strategies for fiscal sustainability and efficiency in order to achieve universal immunization coverage.

The last chapter, *Determinants of inequality in vaccination coverage for DPT3 among sub-Saharan countries,* investigates predictors of inequality for DPT3 vaccine coverage. Different measures of inequality are computed using 5km by 5km level vaccine coverage estimates to quantify existing geographical disparities in coverage in sub-Sahara. Using vaccine coverage estimates from 2000 to 2016, we quantify inequity using three measures. First, 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 which is the proportion of children below a globally set subnational coverage target, and lastly, a Gini coefficient which represents 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, with governance augmenting the observed relationship between development assistance and inequality. Results from this analysis also indicate that countries with the lowest coverage suffer the highest inequalities. We also demonstrate growing inequalities among countries which have since met national coverage targets such as South Africa and Kenya. Burundi, Comoros, Lesotho, Namibia, Rwanda, Sao Tome and Principe and Swaziland had the least shortfall inequality (<5%) while Angola, Ethiopia and Nigeria had values greater that 40%. A similar picture was noted for the other dimensions of inequality among these particular countries. The value of current immunization program in addressing inequality is evident, however, mechanisms for resource implementation and accountability should be strengthened to maximize gains in vaccine coverage.

Acknowledgements

I am indebted to many who have provided guidance, mentorship and support throughout the process of undertaking this research.

I am very grateful to my advisor Stephen Lim for your thorough mentorship, encouragement and support through the years. Thank you for giving me the opportunity to grow in my career, first by supporting my enrollment into the PhD program, and for continuing to challenge me to become a more independent researcher while providing any necessary support in both the academic and research components of this program. I am extremely grateful that throughout the years, especially with your highly demanding schedule you still remained an active force in my learning and well-being while in Seattle. Thank you.

I would like to thank my committee members. Joseph Dieleman, thank you for teaching me everything I know regarding the different methodologies I encountered during the process of writing my dissertation. Thank you for patiently helping me to understand various complex statistical approaches of which I likely would have never reckoned on my own. Your door has always been open and I am grateful that every discussion we had, ranging from development assistance, research methods, or even parenting was a great eye opening lesson. Thank you for seeing my potential and for continuing to support me during times of doubt and indecisiveness.

To Kenneth Sherr, I am thankful for the great insights and thoughtful perspectives that challenged me to broaden my understanding on global health matters. Thank you for being a source of encouragement and a voice of reason whenever I needed to make critical decisions during the course of my program.

To my GSR, Patrick Heagerty, thank you for teaching me statistics and for remaining a constant source of wisdom after taking your class and throughout the rest of my program.

I am thankful for the IHME leadership, most especially to Emmanuela Gakidou. Thank you for supporting my enrollment in the program, for challenging me to step out into unfamiliar territories of global health and mostly for your support, both as a student and on a personal level. You have been a great source of inspiration and have enabled opportunities I will always be grateful for.

To my colleagues in the program, past and present, thank you for your friendship, for being open to sharing knowledge and for fostering an environment of friendly collaboration. David Phillips, Orvalho Augusto, Roy Burstein, Matt Schneider, Reed Sorensen, Wisal Hassan, William Msemburi, Sarah Wulf, Hong Xiao, Xioachen Dai, Emily Dansereau and others, I am grateful that our paths crossed.

I am grateful for the friendships I have built while at IHME. Kelsey Bannon, Kelsey Pierce, Chris Odell, Angela Micah, Damaris Kinyoki, and the DAH team, thank you for your friendship and support.

I would like to thank my mentors back at home in Uganda. Prof. Moses R. Kamya, Dr. Jane Achan and Dr. Anne Gasasira, thank you for paving the way for me.

To my beloved family; Dad, Mum, my brothers Caesar and Chief, and my sister Carol, I could not have done this without your daily encouragement. Thank you for being an active part of this process no matter how far apart we were. Special gratitude to my husband Roy for your unconditional support, and to my daughter Tamba for being my constant source of joy.

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Chapter 1: Tracking donor funding towards achieving the Global Vaccine Action Plan (GVAP) goals: A landscape analysis (1990-2016)

Reference (https://doi.org/10.1016/j.vaccine.2018.10.062)

Abstract

Efforts driving universal coverage have recently been strengthened through implementation of the Global Vaccine Action Plan (GVAP) where cost estimates for immunization support were developed totaling US$40 billion of donor assistance by 2020. In addition to resource mobilization, there has been an increasing focus on improving both vaccine access and delivery systems. We track donor assistance for immunization by funding objective and channel from 1990 to 2016, and illustrate projections through 2020 to inform progress of the GVAP.

Using available data from development agencies supporting immunization, we categorize funding by vaccine and quantify support for systems strengthening. We split time into four periods including the post universal childhood immunization era (1990-1999) and Gavi's three funding phases between 2000 and 2015, during which annualized funding changes are estimated. Lastly, we perform a linear extrapolation through 2020 to predict the success of stipulated resource mobilization targets. Double counting was eliminated and results presented in real 2017 US dollars.

Over the last 27 years, funding for immunization increased by 10.5% annually, with non-Gavi funding increasing by 7.1% and Gavi funding by 23.6% in the last 17 years. Gavi disbursements targeting vaccines and health system improvements increased uniformly at 15%, compared to 22.5% for vaccines and 11.7% for system strengthening from non-Gavi channels. Funding fluctuated for non-Gavi

channels with disbursements declining before 2000 and during Gavi funding phase II, while Gavi disbursements continued to grow relative the previous phase. New and underused vaccines were prioritized by Gavi whereas non-Gavi channels focused on elimination efforts. Projected funding targets were estimated to be on track for Gavi contrary to non-Gavi support which was estimated to remain 40% below the stipulated target.

Renewed assessments for funding requirements need to be undertaken, while strengthening existing resource efficiencies in order to achieve current global universal coverage targets.

Key words

Vaccine, Gavi, development assistance for health, GVAP, HSS, universal coverage

Introduction

Global efforts towards achieving optimal universal immunization coverage have evolved since the introduction of the Expanded Programme on Immunization in 1974 [1], an initiative of the World Health Organization (WHO). Subsequent initiatives include Gavi, the Vaccine Alliance in 2000, the Global Immunization Vision and Strategy in 2006 and more recently the Global Vaccine Action Plan (GVAP), a multi sectoral initiative launched in 2012 [2].

The GVAP was approved by 194 Member States of the World Health Assembly in 2012 specifying renewed and targeted strategies towards achieving universal vaccination coverage by 2020. Development and implementation of GVAP has involved multiple stakeholders comprising governments, professional institutions, academia, manufacturers, global agencies, development partners, civil society, media and the private sector with designated responsibilities monitored collectively through a coordinated mechanism. The plan describes potential

health returns on investment in immunization using vaccine coverage and child mortality as target outcomes.
Specific goals resulting from this investment included reductions in childhood deaths, meeting set elimination targets, improving coverage for both routine and newly introduced vaccines at both national and subnational levels, and fostering up to five additional vaccine introductions among low and middle income countries by 2020.
Substantial progress has since been made [3] mainly regarding new vaccine introduction particularly among Gavi eligible countries, and in case containment and reduced transmission of polio. However, elimination efforts towards tetanus and measles and current coverage estimates for both new and routine vaccines still fall below the intended targets.

Resource estimates towards implementation were developed based on analyses restricted to low and middle income countries [4] aimed at scaling up and sustaining both current routine immunization and supplemental activities in order to reach elimination and eradication goals. Costs were informed using both planned vaccine introductions and scale up over 10 years totaling $40 billion of donor assistance by 2020. Of this, $12 billion was stipulated to be channeled through Gavi the Vaccine Alliance, and $28 billion through other development agencies and organizations.
In addition to resources specific for commodities such as vaccines and vaccine supplies, additional investments have been made targeting particular processes through which service delivery is optimized. For example, development assistance for health (DAH) specific to immunization has been disaggregated to include support for health system strengthening activities [5] aimed at addressing any existing bottlenecks along the chain of immunization delivery as well as vaccine support.
Where funding support can be distinguished by purpose, resource tracking within the given categories over time for different programs provides an opportunity to accurately describe investment flows, and estimate their potential impacts. Distinguishing between support for new and underused vaccine availability and support for activities aimed at addressing health system constraints will be useful

in understanding resource area gaps within the immunization program in order to further guide planning and targeted spending processes.

Expenditure tracking over time has been performed for overall assistance for health [6, 7] by funding channel [8, 9], and by program area such as maternal and child health [10, 11]. Similar work on immunization has focused on tracking overall aid for immunizations with an emphasis on donors to recipient flows [12]. In order to characterize development assistance for immunization, we track aid for immunization by channel assessing trends of Gavi and non-Gavi support from 2000 to 2016, and 1990 to 2016 respectively. Non-Gavi channels comprised all other aid agencies that provided development assistance for immunization outside Gavi including UNICEF, the World Health Organization (WHO), private philanthropies and development banks, among others. We categorize aid into funding for procurement of vaccine and vaccine supplies, and funding for health system strengthening for the immunization program.

In addition, we examine trends of support at specific time points starting in the period 1990-1999 (post universal childhood immunization), and during the first three 5-year funding periods of Gavi representing fundraising processes including 2000-2005 (phase I), 2005-2010 (phase II) and 2010-2015 (phase III). We incorporate an additional time category representing Gavi phase IV which together with phase III straddles the GVAP timeframe to measure progress towards projected funding targets between 2011 and 2020 from both Gavi and other channeling agencies.

This updated and comprehensive assessment of immunization program support provides evidence against which development assistance partners can track their progress and make informed strategies to achieve universal access to immunization.

Methodology

Project-level disbursement data by expense year from Gavi were obtained from the Gavi website [5] spanning 2000 to 2016. Data were available for different programs supported at country level for each year funds were disbursed, including categories to which funding was allocated. These included cold chain equipment optimization platforms (CCEOP), civil society organizations (CSO), cash support, Ebola EPI recovery plan, graduation grants, health systems strengthening (HSS), Injection safety support (INS), Immunization system strengthening (ISS), investment cases, new vaccine support (NVS), operational support, product switch grants, and vaccine introduction grants.

Based on the specific objectives for each of these programs, we re-classified financial data into 'vaccine support' (cash support, NVS, vaccine introduction grants, product switch grants, and investment cases), and 'health systems strengthening (HSS) support' (CCEOP, CSO, HSS, ISS, operational support, graduation grants, and epidemic recovery grants).

Disbursement data from non-Gavi funding channels were obtained from the development assistance for health (DAH) database compiled by the Institute for Health Metrics and Evaluation (IHME). The database contains updated estimates of DAH by funding source (donor), channel, health focus area, and where possible, recipient location [6]. The data are typically compiled using revenue and expenditure data from online project databases, financial statements, budgets, audited reports and through correspondence where data are not publicly available [7]. The database includes data from bilateral agencies which comprise 23 OECD (Organization for Economic Co-operation and Development) member countries the European Commission whose disbursement records are reported through the Credit Reporting System (CRS) each year, development banks, UN agencies, the Global Fund, non-governmental organizations (NGO's) and private philanthropies including the Bill and Melinda Gates Foundation (Gates Foundation). [1]

[1] The OECD member countries include Austria, Australia, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Luxembourg, the Netherlands, New

For the non-Gavi group, we included channels that reported DAH specific for vaccines or immunization program activities. These comprised WHO, NGO's, PAHO, UNICEF, Gates Foundation, US foundations, World Bank International Development Association (WB-IDA), bilateral agencies, and development banks including the Asian Development Bank (ADB) and the Inter-American Development Bank (IDB). DAH from bilateral agencies excluded funds from other donor agencies transferred to any of these channels in order to avoid double-counting. Methods detailing this process have been detailed and published previously [8, 9]. In addition, we describe original sources, funding channels and recipient regions illustrating DAH flows to channels and across different channels. Total funding envelopes for immunization were estimated from channel specific data ranging from 1990 to 2016, while funding classifications into vaccine versus health systems strengthening support as defined for Gavi DAH were assigned using available project-level disbursement data from the CRS also spanning 1990 to 2016, the most recent year for which these data were available. These data consisted over 16,000 projects with respective objective descriptions detailing the intended purposes for the funds tagged to corresponding annual disbursements within specified country or regional locations. We assessed and report the completeness of these data by year compared to data obtained directly from specific channels.

To allocate disbursements into vaccine-specific funding or funding for health systems strengthening, we applied a previously peer reviewed keyword search process used to assign projects to different health focus areas [7]. The key words that were used to identify disbursements in the vaccine specific category included: 'Pentavalent', 'Pneumococcal', 'Rotavirus', 'Injectable polio', 'Polio' 'Human papilloma virus', 'HPV', 'Hep B', 'Hepatitis', 'JEV', 'Japanese Encephalitis', 'HiB mono', 'H. influenza type B', 'Yellow fever', 'DPT' 'DTP', 'Tdap', 'Tetanus', 'Meningitis', 'Men-A', 'Measles' and 'Measles-Rubella (MR)'.

Zealand, Norway, Portugal, South Korea, Spain, Sweden, Switzerland, the United Kingdom, and the United States.

We disaggregated funding for vaccines by vaccine type by identifying all projects that were described as supporting specific vaccines and allocated these funds to the named vaccine.
Similarly, we used a set of key words capturing health systems support activities informed by objectives outlined in country Gavi HSS proposals including 'training', 'cold chain', 'monitoring and evaluation' 'information systems', infrastructure', 'surveillance', 'maintenance', 'delivery', 'health worker', 'capacity', 'immunization system support', 'advocacy', 'civil society', 'demand', 'distribution', 'cascade', 'mentorship', 'data quality', 'equipment', 'mobilization', and 'management', among others. To account for the robustness of the key word search process, multiple projects were selected at random and assigned categories *a priori*, which were then compared to categories following the key word assignment to ensure the different projects were meaningfully categorized.

We demonstrate funding trends over time for total DAH for immunization starting in 1990, disaggregating Gavi from all other channels, by funding category, and vaccine type.
Time was stratified starting 1990-1999 representing the era post universal childhood immunization, 2000-2005 representing Gavi phase I, 2005-2010 for Gavi phase II, and 2010-2015 for phase III. We further illustrate the total DAH trends by income level of recipient countries classified by their gross national income per capita.

In order to estimate the annualized change in funding for immunization from Gavi and non-Gavi channels, we used a generalized linear model with time segments as specified, in order to capture the slope for each segment and level changes between consecutive segments relative to the previous cycle's final year, while relaxing the assumption of linearity between DAH and time. Our results remained robust to varying model specifications where the link and family combinations were interchanged as presented in the supplementary materials.

Furthermore, we developed projection models to inform the progress and potential realization of the GVAP funding targets based on segmented linear regression analyses between 2011, the commencement of GVAP, and 2016 the last year for which real time data were available. We applied a linear extrapolation model with uncertainty intervals to predict the funding trajectory of the GVAP through 2020. Our unit of analysis was cumulative DAH aggregating disbursements for 2011, 2012, 2013, 2014, 2015 and 2016. Projections were made for total development assistance, disaggregated by channel group.
All DAH were converted to 2017 USD to account for inflation. We used Stata 15.1 for all analyses.

Results

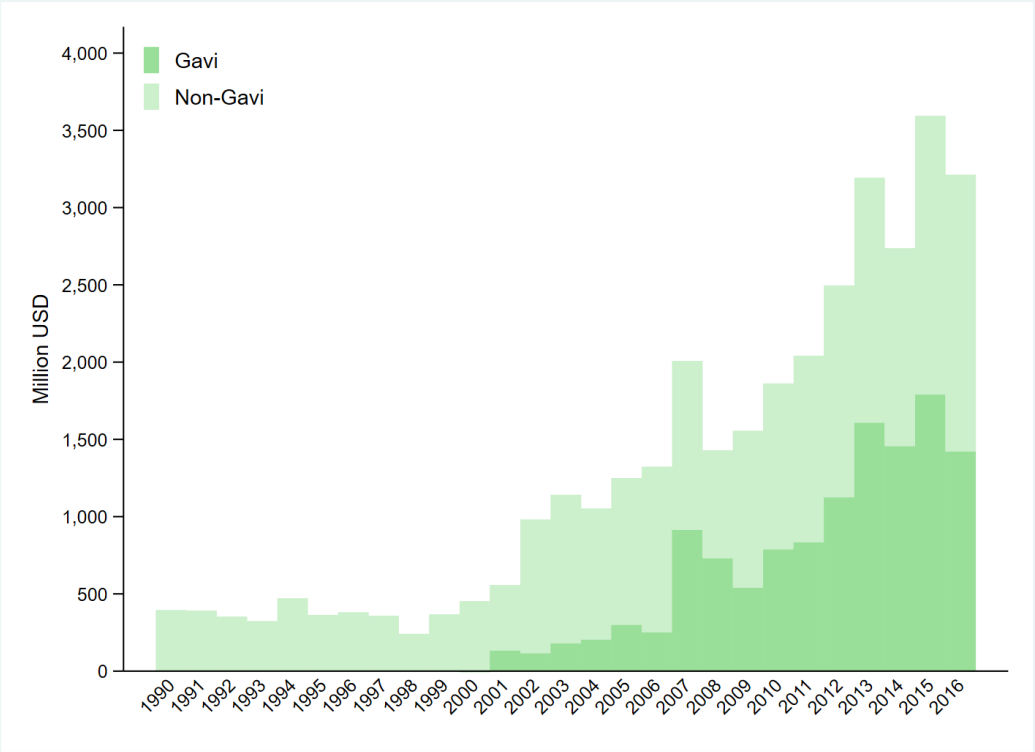
Overall, donor funding for immunization totaled $34.5 billion between 1990 and 2016. Of this, $12.4 billion was channeled through Gavi starting 2000, while $22.1 billion was from other DAH channels between 1990 and 2016. In 2016 alone, immunization DAH was estimated at $3.2 billion, with $1.4 billion from Gavi and $1.8 billion from other channels (Figure 1).

The largest sources of funding for Gavi include the United Kingdom, Gates Foundation and the United States, contributing $3.2 billion, $2.1 billion, and $1.5 billion respectively. Of the $5.1 billion of vaccine funding channeled through UNICEF from 1990 to 2016, $1.5 billion was contributed by private philanthropy, $614 million was contributed by the United States, and $386 million by the United Kingdom. WHO, the third largest channel of immunization funding over this period, was largely funded by the United States and United Kingdom, which provided $687 million and $393 million, respectively. The largest public sources of funding were the United States, United Kingdom, Norway, and Germany, funding $4.6 billion, $4.5 billion, $1.9 billion, and $1.3 billion respectively. Other private sources of funding made up a significant $3.2 billion.
While Gavi is the major implementing agency, it provided funding to other implementing channels such as UNICEF and the WHO. From 2000 to 2016, these

transfers to UNICEF amounted to $33.5 million, and transfers to WHO from 2006 to 2016 totaled $77.0 million.

Between 1990 and 2016 the annual increase in total funding was 10.5% (95%CI: 9.2%-11.9%), with Gavi funding increasing by 23.6% (95% CI: 17.3%-30.3%) after 2000, and other channels increasing by 7.1% (95%CI: 5.9%-8.3%) from 1990 to 2016.

Figure 1: Total development assistance for immunization, by funding channel, 1990–2016



Values are real currency expressed in 2017 USD
Non-Gavi channels include: WHO, NGO's, PAHO, UNICEF, BMGF, US foundations, World Bank International Development Association (WB-IDA), and development banks including the Asian Development Bank (ADB) and the Inter-American Development Bank (IDB)

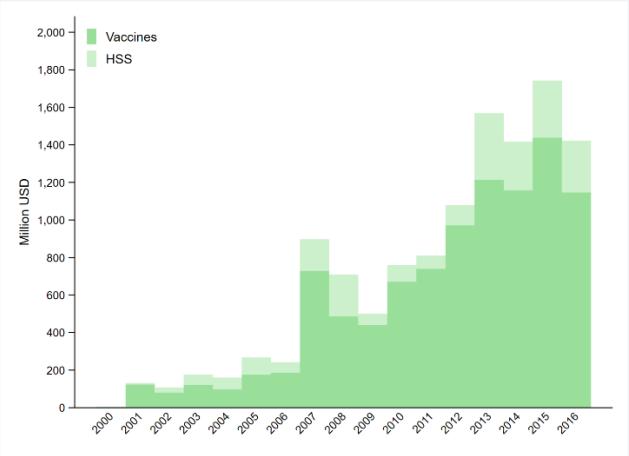
We distinguished immunization DAH by purpose contingent on the availability and extent of granularity of project-level data. For Gavi, about one fifth of total disbursements from 2000 to 2016 were estimated as funds targeting HSS, with allocations increasing over time from 5.1% in 2001, to 18.9% in 2016, peaking in 2008 and 2013 where HSS funds comprised 31.3% and 22.6% of all disbursements

respectively (Figure 2). The annual increase in funding specific for vaccines was comparable to that for HSS estimated at 15.6% (95%CI: 11.7% to 19.6%), and 14.8% (95%CI: 7.9% to 22.2%), respectively.

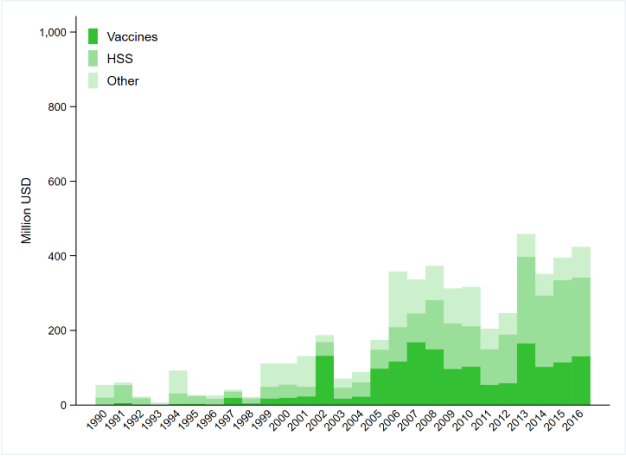
To characterize funding by specific purpose from non-Gavi channels, we used project-level data from CRS detailing 16,113 projects reported predominantly from bilateral agencies, comprising 67.8% of all immunization-related projects. Other channels reporting through the CRS platform included NGOs (which made up 24.9% of available projects), UNICEF, WHO and the EC (which made up 3.5%, 2.6% and 1% of projects, respectively). In terms of DAH reported, these data represent about one quarter of the total DAH from non-GAVI channels, with reporting levels varying from year to year ranging between approximately 5% (1993) to close to 40% (2008).

Vaccine DAH alone made up 32.4% ($1.3billion), funding for HSS comprised 40.9% ($2.0billion), while that for other immunization and vaccine-related activities comprised 26.7% ($1.3billion), which included projects supporting operational research pertaining to immunization programs, vaccine clinical trials, and vaccine manufacturing or development (Figure 2). Between 1990 and 2016, funding for vaccines grew by 22.5% (95%CI: 14.2%-31.5%), funding for HSS by 11.7% (95%CI: 8.1%-13.5%), and funding for other activities by 7.7% (95%CI: 3.2%- 12.4%). Furthermore, the trend for funding for vaccines specifically was noted to vary substantially before and after the formation of Gavi, decreasing from 33.8% (95%CI: 8.6% to 65.1%) to 4.8% (95%CI: -1.6% to 11.8%) after 2000. However, funding trends for HSS and other activities during the two time periods were not found to vary significantly.

Figure 2: Development assistance for immunization by purpose, 1990 to 2016



Gavi



Non- Gavi

Complementary to Gavi, UN agencies have by far been the most dominant channels through which immunization programs are funded, with UNICEF and WHO accounting for 23.1% ($5.1billion) and 20.4% ($4.5billion) of non-Gavi DAH, respectively. Bilateral agencies provided a comparable amount of funding at 19.9% ($4.4billion), while the Gates Foundation has since disbursed 18.0% ($3.9billion) starting in 1999. In addition, NGOs disbursed 11.8% ($2.6 billion), the WB 4.9% ($1.1billion), while PAHO, the EC, development banks and US foundations disbursements each accounted for less than 1% of vaccine DAH channeled outside Gavi.

Following the formation of Gavi, funding trends for other channels have varied over time. Between 2000 and 2016, annual disbursements increased for most, with the highest increases in absolute terms coming from NGO's (25.7%), Gates Foundation (14.9%), US foundations (14.5%), World Bank (12.8%), UNICEF (8.0%), and development banks (5.9%). Whereas, funding from bilateral agencies sustained a positive trend, (Figure 3) the growth in annual disbursements slowed down by 7.8% since the formation of Gavi.

Figure 3: Annualized change in development assistance for vaccination among Non-Gavi channels

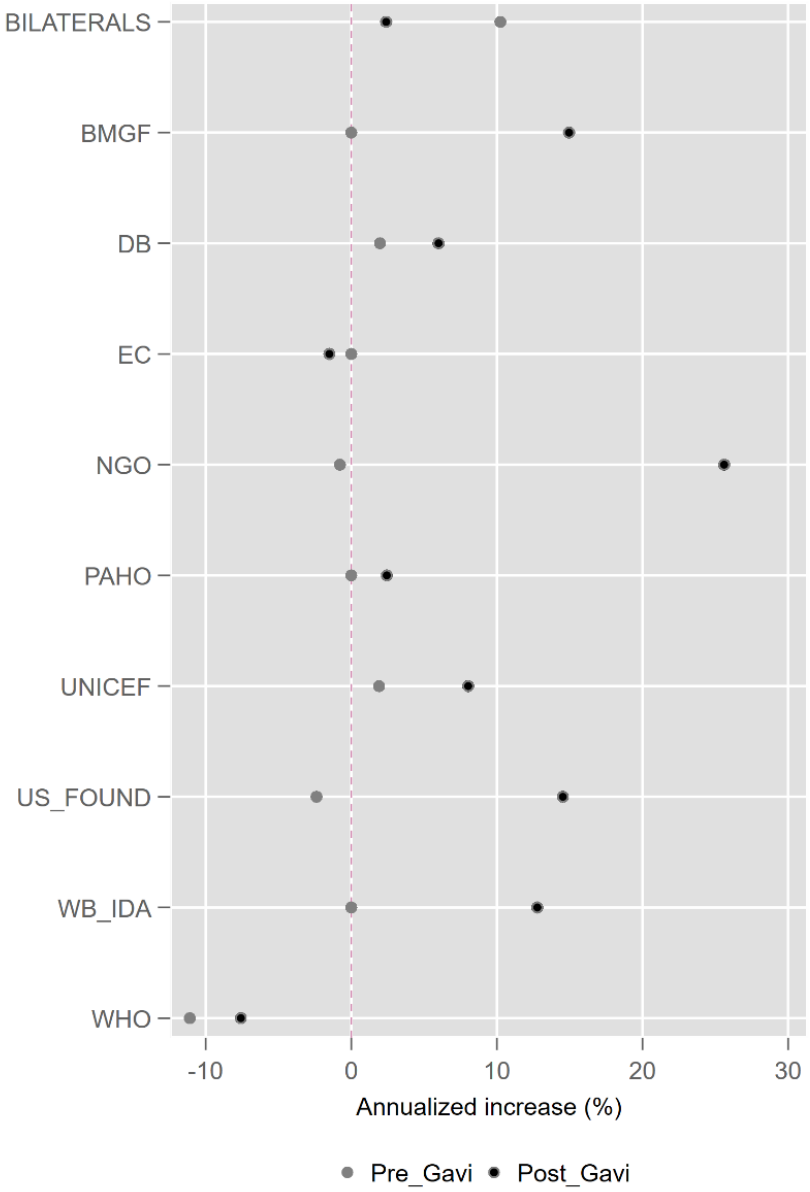


Table 1: Non-Gavi channel trajectories before and after the creation of Gavi

Channel	Pre_Gavi(1990-2000)	Post Gavi(2001-2016)
WHO		
Absolute	-24.2 (-36.3 to – 12.0)	-18.5 (-24.8 to -12.2)
Relative	-11.1 (-20.3 to -2.0)	-7.6 (-10.2 to -4.9)
UNICEF		
Absolute	5.9 (1.1 to 33.5)	16.6 (12.0 to 21.2)
Relative	1.9 (0.1 to 3.8)	8.0 (6.4 to 9.6)
BMGF	-	
Absolute		22.5 (17.5 – 27.4)
Relative		12.1 (6.5 to 18.0)
PAHO	-	
Absolute		0.5 (0.2 to 0.9)
Relative		2.4 (0.9 to 4.0)
Bilateral agencies		
Absolute	7.4 (0.2 to 14.5)	4.6 (-1.2 to 10.5)
Relative	10.2 (0.9 to 20.5)	2.4 (-0.8 to 5.7)
European Commission	-	
Absolute		-0.3 (-9 to 0.3)
Relative		-3.3 (-10.4 to 4.3)
NGO's		
Absolute	-0.2 (-0.4 to 1.1)	17.1 (13.5 to 20.7)
Relative	-0.8 (-2.1 to 0.5)	25.6 (16.1 to 35.8)
Development banks		
Absolute	0.0 (0.0 to 0.0)	0.9 (0.3 to 1.5)
Relative	1.9 (0.1 to 3.9)	6.0 (-10.3 to 25.2)
World Bank-IDA	-	
Absolute		7.4 (5.1 to 9.7)
Relative		11.6 (4.3 to 19.5)
US Foundations		
Absolute	-0.0 (-0.2 to 0.1)	0.1 (-0.0 to 0.2)
Relative	-2.4 (-11.4 to 7.6)	14.5 (3.5 to 26.8)

Absolute amounts in millions of USD
Relative (%)
BMGF, PAHO, European Commission and World Bank-do not have sufficient data points to estimate changes before

Furthermore, funding channeled through WHO continued to decrease, albeit at a slower rate at 7.6% compared to 11.1% before 2000. Table 1 shows the changes in both absolute and relative terms for all non Gavi channels providing immunization DAH.

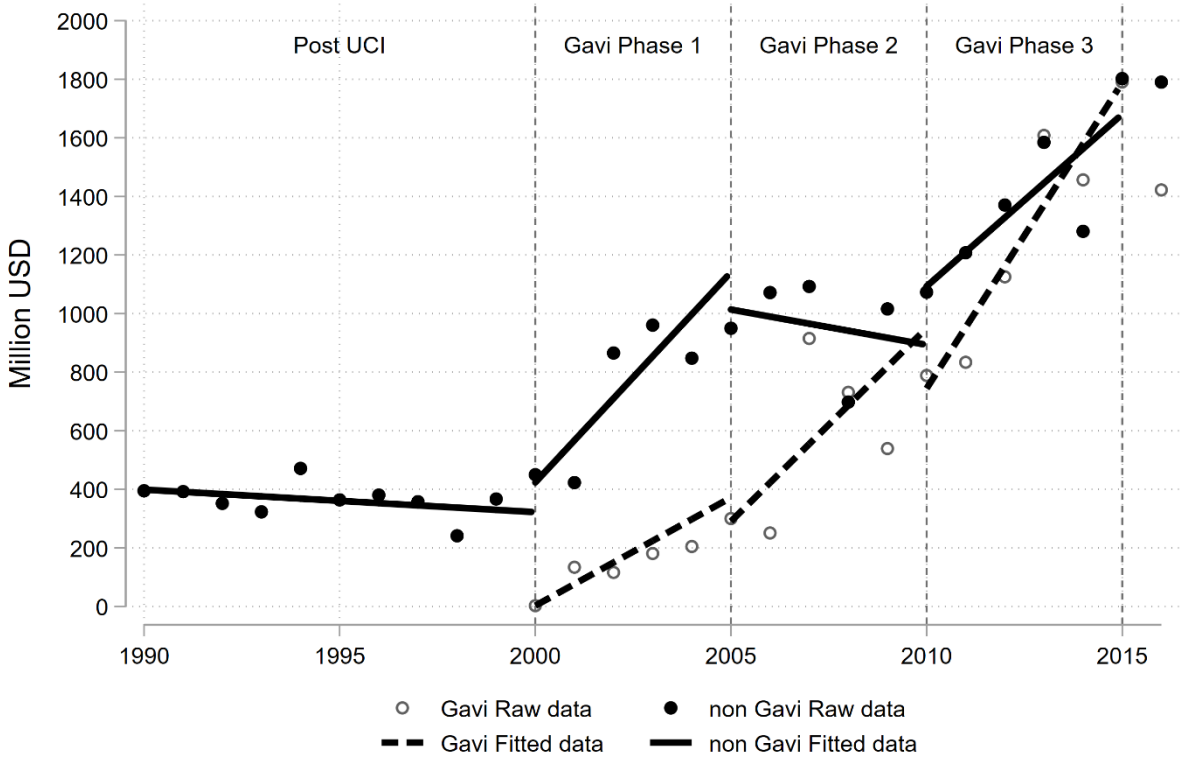
DAH was further disaggregated by vaccine for Gavi, with pentavalent and pneumococcal vaccines being the highest funded vaccines totaling 40.2% ($3.9billion) and 39.0% ($3.8billion), respectively. Rotavirus vaccine accounted for 5.9% ($576million), meningitis A 2.3% ($283million), Hepatitis B mono 1.9% ($187million), Injectable Polio 1.9% ($188million), measles-rubella 2.9% ($283million), Tetravalent DPT-HepB 1.8% ($178million) and yellow fever 2.1% ($203million). Human Papilloma Vaccine, Haemophillus Influenza B mono, Japanese Encephalitis, and Tetravalent DPT-HiB vaccines each accounted for less than 1%.

A similar approach was taken for non-Gavi project-level data. The majority of non-Gavi DAH targeted towards specific vaccines was highest for polio and measles vaccines, amounting to 64.8% ($1.74billion) and 29.1% ($780million), respectively. Pentavalent vaccine support made up about 2% ($53million), while all the other vaccines each comprised of less than 1% funding tagged towards specific vaccines.

Despite the observed general growth in funding, the trends within different time periods as defined varied considerably for both development channel categories (Figure 4). Prior to the introduction of Gavi in 2000, DAH for immunization was noted to decline by an estimated -2.1% (95%CI: -4.2% to 0.1%) annually through 1999. During Gavi phase I, funding grew substantially by 53.9% (95%CI: -2.8 to 110.7%), and remained a priority for other agencies with funding increasing by 21.0% (95%CI: 12.6% to 29.4%) annually. Relative to the previous funding cycle, Gavi disbursements maintained an upward trend increasing at 22.9% (95%CI: 2.1% to 43.6%), while non Gavi disbursements receded changing by an estimated -2.5%(95%CI: -7.7% to 2.7%) during phase II. In the recently completed phase ending 2015, funding for both Gavi and non-Gavi channels sustained an upward

trend growing annually at 17.6% (95%CI: 14.6% to 20.4%) and 8.5% (95%CI: 6.0% to 11.0%) respectively.

Figure 4: Annualized changes in absolute amounts of development assistance for immunization for Gavi and Non-Gavi channels from 1990 to 2016



**Post UCI (post universal childhood immunization)*

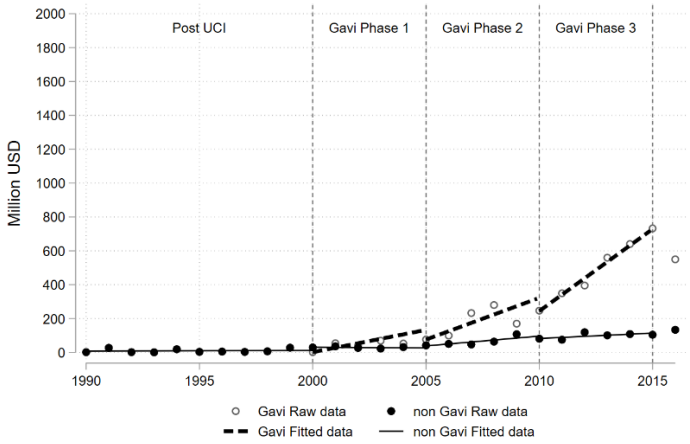
We made similar assessments by economic status of recipient countries for which substantial DAH was disbursed to low income and lower middle income countries (Figure 5). Non Gavi DAH decreased or remained flat across the different categories prior to 2000, increasing marginally among both low income and lower- middle income countries. Gavi DAH grew steadily among low income and lower middle income countries compared to upper middle income countries which received less DAH overall, with reductions starting in phase II and plateauing during phase III as shown.

Changes in total DAH disbursed by the two channel groups in both relative and absolute terms using different model specifications are presented in supplementary sections I and II.

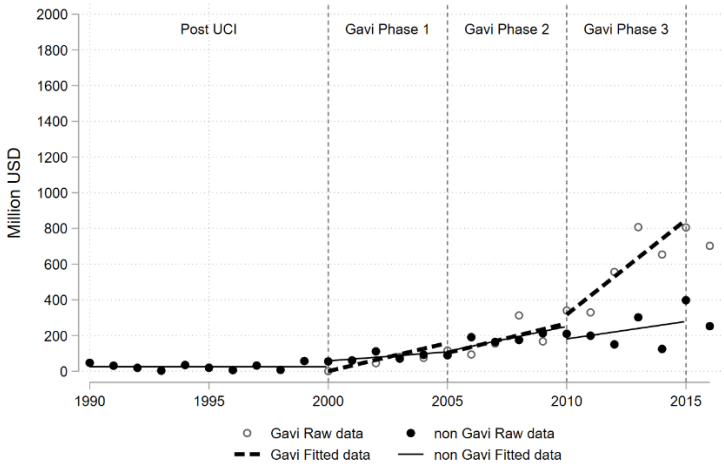
Figure 6 illustrates the total development assistance for immunization by year for the duration of the GVAP period, suggesting that projected target totaling $12billion for Gavi has since been achieved, while non-Gavi support is estimated to remain approximately 40% less than the intended target of $28billion by 2020. Cumulative amounts by year for the subsequent years through 2020 are presented in Table 2 with a corresponding figure in supplementary section III.

Figure 5: Annualized changes in absolute amounts of development assistance for immunization for Gavi and Non-Gavi channels from 1990 to 2016 by income level

Low Income countries



Low and middle income countries



Upper middle countries

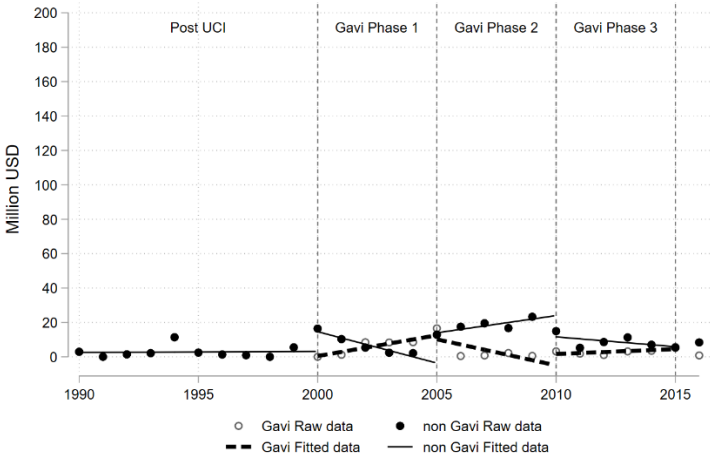
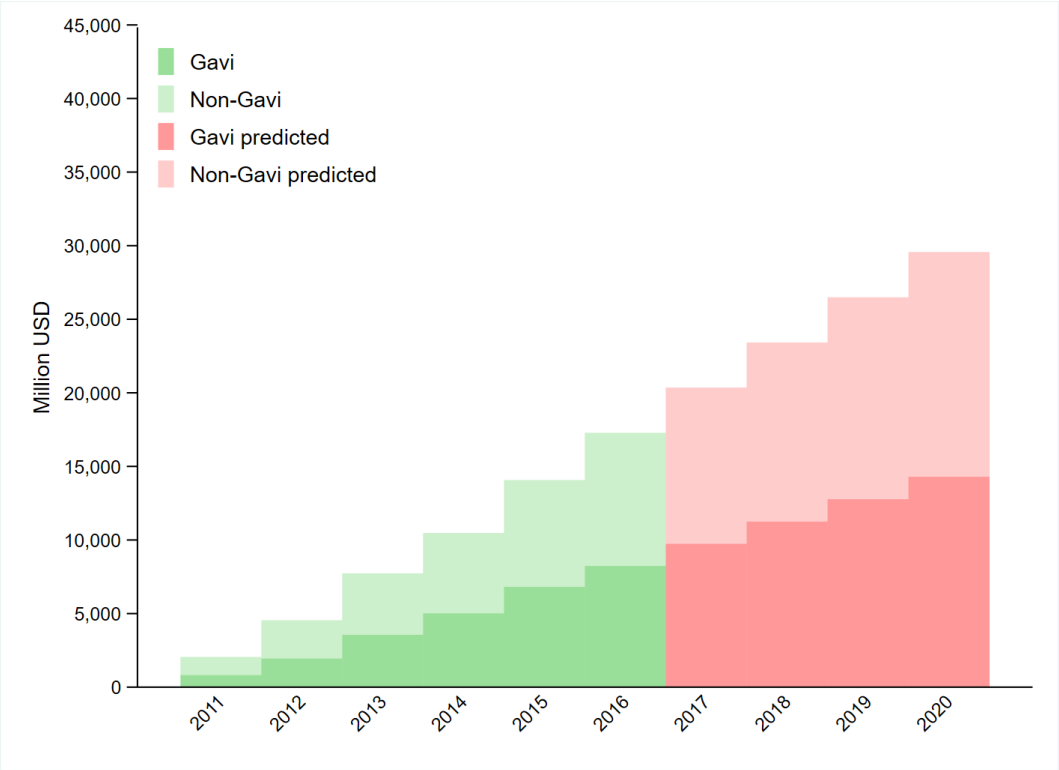


Figure 6: Estimated projections for the Global Vaccine Action Plan funding targets



Values are real currency expressed in 2017 USD
Non- Gavi channels include: WHO, NGO's, PAHO, UNICEF, BMGF, US foundations, World Bank International Development Association (WB-IDA), and development banks including the Asian Development Bank (ADB) and the Inter-American Development Bank (IDB)

Discussion

We demonstrate that while donor support for immunization has been substantial, funding trends have shifted over time, and priorities redefined in the recent past. Our analysis provides a detailed description of development assistance for immunization using project-level data from which funds are disaggregated by purpose. We present the trends in funding differentiating investments for vaccine products from immunization program strengthening, which provides insight into the value of implementing and sustaining an existing infrastructure base through which vaccines are delivered. It also allows for additional evaluations on the impact of specific funding categories on vaccination outcomes, although this is beyond the scope of this analysis. We also illustrate the need for continued assessments given current advances in different program outcomes and changes in previous market conditions as we approach the end of what is considered the decade of vaccines.

The commitment from Gavi to increase access to vaccines in low and middle-income countries is evident through the notable focus on vaccine introductions targeting highly prevalent vaccine preventable diseases (VPDs), as much as that on immunization program system strengthening [10].

There is indeed continued support for vaccine products from both Gavi and non-Gavi channels, although the annualized rate for vaccine specific disbursements from the latter was noted to substantially decline after 2000 likely related to a shift in channeling mechanisms through Gavi. This funding trend followed a different course in the recently completed phase, with a surge in 2013 through 2016 driven by an increase in vaccine specific spending echoing the 2013-2018 Polio Eradication & Endgame Strategic Plan (PEESP) [11] endorsed by the 66th World Health Assembly. The PEESP consists of four principal objectives that address polio eradication including withdrawal of trivalent to a bivalent [12] vaccine by 2020 as part of the Global Polio Eradication Initiative. These findings illustrate the shift in mandate and redefined focus among development partners for immunization.

Our data demonstrate that over 90% of vaccine funding from non-Gavi sources targeted polio and measles vaccines, with polio dominating at about 65%, and measles accounting for over 25% of all vaccine-specific funding. This supports the mission of the global eradication strategy that purposes to transition polio resources [13] to measles and rubella (MR) elimination following the 99% success rate] in eradicating all three types of wild polio viruses. The last 1% of polio cases has posed challenges in the elimination agenda mostly due to conflict, political instability, hard-to-reach populations and poor infrastructure [14, 15]. As such, a substantial amount of polio resources support surveillance, and using a diagonal approach [13], focusing on measles control would boost case detection for polio among other VPDs hence accelerating progress towards elimination, coverage and equity. It is important to note however, that polio control strategies to achieve the PEESP objectives vary across implementing countries [16,17,18] to suit their contextual challenges.

With support from non-Gavi channels largely focusing on disease elimination and eradication efforts, our analyses suggest complementarity given Gavi's focus on scaling up new and under-used vaccinations against highly prevalent VPDs. Pentavalent previously administered as tetravalent, pneumococcal, and rotavirus vaccines have made up over 80% of vaccine introduction grants from Gavi, targeting childhood pneumonia and diarrhea, which together with malaria account for one third of childhood deaths globally and 40% of deaths in sub-Saharan Africa [19,20]. The sustained prioritization of vaccines overall with a scale up approach from Gavi and a complementary mop up approach from non-Gavi channels offers promise towards improving new vaccine coverage while continuing to reach marginalized populations.

In terms of program system strengthening, Gavi supported specific activities addressing system constraints through its ISS programs prior to the introduction of country driven [21] health systems cash support processes formally in 2005, which overall has been estimated to grow at 15% annually, analogous to vaccine funding. The decline in Gavi DAH disbursed to upper and middle income countries starting in phase II aligns with the funding objective to strengthen broader health

services [22] beyond the immunization program for which lower income countries continued to benefit compared to upper income recipient countries.

Nonetheless, funding prospects for non-Gavi channels based on observed trends appear to remain unfeasible at this point relative to initial funding estimates. In order to achieve the GVAP objectives between 2011 and 2020, an estimated $50billion to $60billion was required [2] contingent on a number of market shaping assumptions and conditionalities from both government and donor perspectives. Donor commitments totaled $40billion, of which $12billion would be mobilized from Gavi and $28billion from other development partners. Funding targets as per our analyses were estimated to be on track for Gavi, which is estimated to reach the stipulated targets by the end of 2018, in contrast to non-Gavi channels for which our projections suggest that funding is likely to remain short by an estimated 40% by the end of the 2020.
This may be attributable to continued stagnation or deceleration among different channels supporting immunization following the creation of Gavi. As indicated, UN agencies, bilateral agencies and the Gates Foundation disbursed the highest amounts of aid overall among the non-Gavi channels; however, we also highlight reductions after 2000 from WHO and bilateral agencies in relative terms. And while there were considerable increases in annual funding from the Gates Foundation, support for immunization channeled outside Gavi has predominantly targeted technology and innovation through research and development [23, 24].On the other hand, the downward trend might have resulted from changes in different determinants from which initial funding targets were estimated. For example, vaccine prices [25] have declined over time, and market conditions for some vaccines such as rotavirus and HPV have created shortages which potentially might have led to downward pressure on total expenditures [26].

Based on initial estimates, the observed trajectory poses a threat towards achieving universal immunization coverage and disease elimination targets as described in the current global agenda for immunization. Past trends suggest that fluctuations in funding are influenced by the development agenda [27,28] where partner mandates and funding priorities are redefined to align with changes to

the global agenda. Therefore, timely and detailed resource tracking assessments such as ours provide critical evidence to guide discussions or decisions on how to sustain allocations primarily from governments, with development partners playing a supplementary role where gaps exist. With interim resource tracking assessments, country multi-year plans can be updated to allow for changes in resource mobilization efforts based on real time evidence. Furthermore, available funding at points of implementation can be redirected to underserved regions or populations where the net gain from existing resources would be maximized.

The main limitation for our study is the incomplete nature and potentially unrepresentative project-level data for non-Gavi channels based off the OECD-CRS database. Relatedly, in using the keyword search, DAH is allocated proportionally to purpose category or specific vaccine based on the number of keywords found. Although this process may affect the construct validity of specific funding distributions, the potential impact on allocations is non-disproportionate. Different approaches estimating DAH for maternal and child health have used different time periods and rationales [29,30] against which disaggregation is performed resulting into quantitative disparities in program level DAH. Missing data could have led to underestimation of the funding envelopes for the three categories overall, and masked the true changes in funding priorities for these channels following the formation of Gavi. This echoes the appeal for continued improvements in reporting procedures [24,31] from development partners by instituting complete, timely and standardized project level data allowing for comprehensive, comparable and accurate assessments of financial disbursements. In this analysis, we do not examine the role of domestic funding for immunization or primary health care expenditure, both of which are critical drivers of development assistance. Previous assessments suggest that countries spending on immunization are positively and significantly correlated with their gross national income [32,33], and have covered over 80% of their budgets. However, projections call for significant increases in the investment functions of reporting countries in order to meet 2020 targets. Data on government expenditure on immunization are available through WHO/UNICEF joint reporting

form, although concerns remain regarding reliability arising from variation in data quality, timeliness and accuracy [34]. Continued improvements in the data quality for government expenditure by health program area would improve resource tracking practices overall, allow for a bidirectional resource mobilization process where one source is lacking, and test for potential program specific subadditionality. In addition, future analyses should also include primary health care (PHC) expenditure of which immunization is an essential component [35] to assess how PHC resources compare with immunization expenditure.

Global initiatives are increasingly adopting program or disease specific approaches with time sensitive indicators of success. The current global agenda for immunization takes on a multidimensional pursuit towards enlarging the scope of vaccines while reinforcing elimination and eradication efforts. This analysis measures financial resources to evaluate progress towards these efforts highlighting areas of success as seen for Gavi, and where renewed strategies are imperative as for the other channels of immunization DAH. Iterative assessments such as this provide key information to facilitate more focused evaluation, advocacy, and resource allocation approaches towards achieving universal coverage.

Conflict of interest

None

Funding

This work did not receive any funding support from the public, not for profit, or commercial sectors.

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Supplementary materials

SECTION I:

Annualized changes in development assistance for immunization at defined time periods between 1990 and 2016

Time period	Gavi (change, 95%CI)	Non-Gavi (change, 95%CI)
Post Universal childhood immunization (1990-1999)	-	
Relative		-2.1% (4.3% to 0.1%)
Absolute		-7.7 (-15.8 to 42.3)
Gavi Phase I (2000-2005)		
Relative	53.9% (-2.8% to 110.7%)	21.0% (12.6% to 29.4%)
Absolute	73.8 (48.8 to 98.9)	143.5 (93.4 to 193.7)
Gavi Phase II (2005-2010)		
Relative	22.8% 2.1% to 43.6%)	-2.5% (-7.7% to 2.7%)
Absolute	131.9 (65.6 to 198.3)	-24.1 (-73.2 to 24.9)
Gavi Phase III (2010-2015)		
Relative	17.6% (14.6% to 20.4%)	8.5% (6.0% to 11.0%)
Absolute	208.9 (187.6 to 230.2)	117.5 (80.3 to 154.7)

Results from the primary model. A generalized linear model using a link log and family gamma combination to estimate the annualized change in relative terms, with link identity and family gamma combination to estimate the annual changes in absolute amounts. Absolute amounts are based on real currency expressed in 2017 USD

SECTION II:

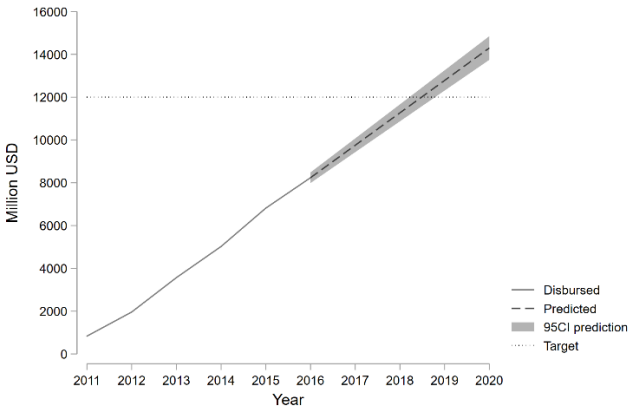
Annualized changes in development assistance for immunization at defined time periods between 1990 and 2016. A sensitivity analysis

Time period	Gavi (change, 95%CI)	Non-Gavi (change, 95%CI)
Post Universal childhood immunization (1990-1999)	-	
Relative		-1.9% (-3.9% to 0.0%)
Absolute		-7.4 (-14.8 to 3.7)
Gavi Phase I (2000-2005)		
Relative	31.3% (16.8% to 45.7%)	17.2% (8.9% to 25.4%)
Absolute	45.1 (32.0 to 58.2)	133.3 (81.2 to 185.5)
Gavi Phase II (2005-2010)		
Relative	14.2% (-0.7% to 29.3%)	-2.5% (-7.6% to 2.6%)
Absolute	95.8 (6.6 to 185.0)	-24.2 (-73.3 to 24.9)
Gavi Phase III (2010-2015)		
Relative	16.2% (13.0% to 19.3%)	8.4% (5.8% to 11.0%)
Absolute	210.3 (183.2 to 237.5)	116.5 (77.6 to 155.4)

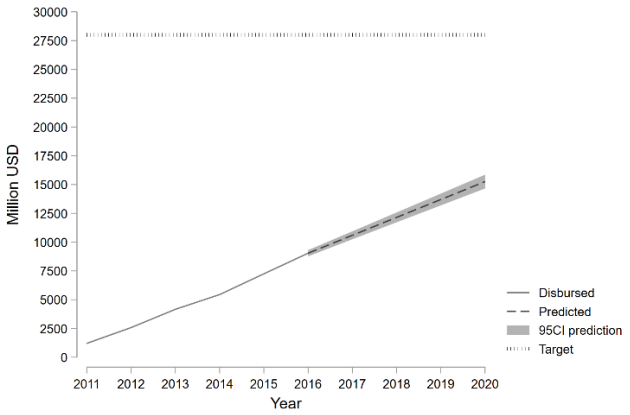
A generalized linear model using a link log and family gaussian combination to estimate the annualized change in relative terms, with link identity and family gaussian combination to estimate the annual changes in absolute amounts. Absolute amounts are based on real currency expressed in 2017 USD

SECTION III:

Figure illustrating cumulative amounts of development assistance for immunization starting from 2011 to 2020



Gavi



Non-Gavi

Chapter 2: Effect of donor funding for immunization from Gavi and other development assistance channels on vaccine coverage: evidence from 120 low and middle income recipient countries

Status (Submitted on 12/14/18 Reference JVAC-D-18-02016. *Under review*)

Abstract

Donor assistance for immunization has remained resilient with increased resource mobilization efforts in recent years to achieve current global coverage targets. As a result, more countries continue to introduce new vaccines while optimizing coverage for traditional vaccines. Gavi the Vaccine Alliance has been at the forefront of immunization support specifically among low income countries, alongside other channels of development assistance which continue to play a vital role in immunization.

Using available recipient country level data from 1996 to 2016, we estimate the impact of Gavi support for vaccines and health systems strengthening on vaccine coverage for DPT3, PCV3, Pentavalent3, Measles2 and Rotavirus2 vaccines. We investigate the same effects of total aid for immunization from other channels of development assistance. Standard time series cross sectional analysis methods are applied to investigate the effects of vaccine support controlling for country income, governance and population, and test for robustness of our analysis using different model specifications. Double counting was eliminated and results are presented in real 2017 US dollars.

We found significant positive effects of aid particularly among the newer vaccines. Using 2016 country specific disbursements and coverage levels as baseline, we estimate that among recipient countries below the universal target, additional DAH per capita required to reach 90%, ranged from 0.01USD to 4.33USD for PCV, 0.03USD to 9.06USD for pentavalent vaccine and 0.01USD to 2.57USD for rotavirus vaccine. The estimated number of children vaccinated

through 2016, attributable to Gavi support totaled 46.6million, 75.2million and 12.3million for PCV, pentavalent and rotavirus vaccines respectively.

Our analysis suggests substantial success both from a historical and prospective perspective in the implementation of global immunization initiatives thus far. As more vaccines are rolled out and countries transition from donor aid, strategies for fiscal sustainability and efficiency need to be strengthened in order to achieve universal immunization coverage.

Key words

Vaccine, Gavi, recipient countries, development assistance for health, GVAP, universal immunization coverage

Introduction

Global efforts towards achieving universal immunization coverage have increasingly been reinforced following the introduction of the Expanded Programme on Immunization in 1974 [1], an initiative of the World Health Organization (WHO). In 2000, the Global Alliance for Vaccines and Immunization, now Gavi, the Vaccine Alliance was created as a public private partnership aimed at improving access to new and underused vaccines for children living in the world's poorest countries [2]. Subsequent initiatives include the Global Immunization Vision and Strategy developed by WHO and UNICEF in 2006, and more recently, the Global Vaccine Action Plan (GVAP), a multi sectoral initiative launched in 2012 among others [3].

While Gavi, has remained the largest channel of donor assistance for immunization in recent years, other agencies have continued to channel substantial amounts of aid. Between 1990 and 2016, donor assistance for health (DAH) targeting immunization totaled $34.5 billion [4]. Of this, $12.4 billion was channeled through Gavi starting in 2000, while $22.1 billion was disbursed through the other DAH channels between 1990 and 2016. In 2016 alone, immunization DAH was estimated at $3.2 billion, of which $1.4 billion was from

Gavi and $1.8 billion from other channels. These include bilateral agencies, WHO, NGO's, Pan American Health Organization (PAHO), UNICEF, the Bill and Melinda Gates Foundation (BMGF), US foundations, the European Commission (EC), and development banks.

Funding from Gavi has historically been structured by program whereby eligible countries are encouraged to apply for support [5] within Gavi's portfolio that can be broadly categorized into new vaccine support and support targeting health systems strengthening (HSS). Since its inception in 2000, Gavi has supported the introduction and scale up of thirteen childhood vaccines including inactivated polio, Japanese encephalitis, measles and measles-rubella, meningitis A, oral cholera, pentavalent, pneumococcal, rotavirus, typhoid and yellow fever vaccines [6]. Other programs include HSS, cold chain optimization support, product switch grants, support for civil society organizations and more recently, graduation grants for countries transitioning from support.

Despite the absence of standardized reporting formats for all other channels for immunization aid as exists for Gavi, funding procedures for these have previously been characterized [7]. Available project level data show that eligibility for support follows a case by case basis given the different funding objectives and country needs at a specific time [8] .

Given the substantial amounts of aid from different channeling agencies for immunization, assessments measuring the potential impact on vaccine coverage are critical. In addition to quantifying the value for these investments, progress towards specific coverage targets at both global and domestic levels can be measured in order to guide subsequent resource mobilization and allocation. Relatedly, there is increasing interest among the donor community on the impact of aid as a result of existing flows and whether multilateral or bilateral funding structures offer any additional advantage over the other regarding effectiveness [9,10]. While the differences in effectiveness may result from the inherent processes by which the two channeling systems function, characterizing this phenomenon by the targeted outcomes would add onto available evidence to guide the ongoing debate. This is particularly critical in an era of overall DAH

stagnation [11] where accountability and results oriented procedures should inform future allocations. Previous assessments of immunization support have shown important positive impacts on vaccine coverage [12, 13], policy decisions regarding immunization and existing health systems [14]. However, following the growing commitment to optimize health systems through integrating support in more recent years, conflicting conclusions have emerged regarding aid effectiveness. Poor coordination and implementation have been cited as hindering factors and any observed success attributed to economic growth and good governance among others [15, 16].

With the increasing number of new vaccine introductions especially among developing countries, assessing the impact of aid using a wider array of childhood vaccines provides a more precise and yet comprehensive measure of effectiveness. We seek to evaluate the impact of both non-Gavi and Gavi DAH on DPT3 coverage, differentiating vaccine specific DAH effects from DAH for health systems strengthening. Furthermore, we quantify effects of vaccine specific DAH from Gavi on coverage for pentavalent3, rotavirus2, measles(MCV2) and pneumococcal3 (PCV3) vaccines.

Methodology

Data and definitions

The outcome measure is vaccination coverage defined as the proportion of children who have received vaccination for PCV3, MCV2, rotavirus2 and pentavalent3 vaccines under age 2 in a given birth cohort. Administrative estimates typically documented using through WHO/UNICEF [17], have previously been demonstrated as unreliable, with the direction and magnitude of this bias remaining unclear. While some studies have reported that administrative estimates of immunization are systematically higher than survey estimates [18], others have found that the direction of the bias, where present, is heterogeneous [19]. Additional bias from country membership in performance-based health systems, has also been documented such as the Gavi Immunization Services Support (ISS) program where administrative estimates from participant countries

were linearly correlated with the number of years of enrollment [12]. Improved data on coverage have as a result been estimated from multiple survey data sources by the Institute for Health Metrics and Evaluation (IHME). Major survey programs incorporated in the analysis include the Demographic and Health Surveys (DHS), the Multiple Indicator Cluster Surveys (MICS), the Reproductive Health Surveys (RHS), the Living Standards Measurement Studies, and the World Health Surveys (WHS). In addition, a comprehensive search was performed on websites of national ministries of health, to identify national surveys and smaller multi-country surveys. Methods by which these estimates and their uncertainty intervals are derived have been previously published [20] and are described in the appendix section V. We use vaccine coverage for each of the five vaccines as our dependent variable in order to evaluate the effect on both traditional and newly introduced vaccines. These include DPT3, PCV3, MCV2, Haemophilus Influenza-B3 (Hib3) as a proxy measure of pentavalent3, and rotavirus 2.

The main predictor variable is DAH from Gavi and other channels of development assistance for immunization. Gavi disbursements from 2000 to 2016 were disaggregated by program type [21], including cold chain equipment optimization platforms (CCEOP), civil society organizations (CSO), cash support, ebola EPI recovery plan, graduation grants, health systems strengthening (HSS), Injection safety support (INS), Immunization system strengthening (ISS), investment cases, new vaccine support (NVS), operational support, product switch grants, and vaccine introduction grants. Vaccine specific DAH was categorized as indicated for the different vaccines, including support for catch up campaigns targeting individual vaccines for example measles or measles-rubella vaccine.
Although Gavi specifies disbursements allocated to HSS programs, for the purposes of this analysis, we define health systems support (HSS) DAH as all disbursements targeted towards addressing existing health system constraints. Programs from which DAH was categorized as HSS included CCEOP, CSO, HSS, ISS, operational support, graduation grants, and epidemic recovery grants.

Disbursement data from non-Gavi funding channels were obtained from the development assistance for health (DAH) database [22] compiled by the Institute

for Health Metrics and Evaluation (IHME). We include channels that reported DAH specific for vaccines or immunization program activities which are WHO, NGO's, PAHO, UNICEF, BMGF, US foundations, World Bank International Development Association (WB-IDA), and development banks including the Asian Development Bank (ADB) and the Inter-American Development Bank (IDB). Due to the incomplete nature of project level data from these channels and lack of standardized descriptions for available projects, DAH from these was not further disaggregated by specific project within the immunization program as was done for Gavi DAH.

Development assistance from bilateral agencies excluded funds from other donor agencies transferred to any of these channels in order to avoid double-counting. Methods detailing this process have been detailed and published previously [4]. All DAH were real currency converted to 2017 USD which we further converted to per capita using the country year under one population for the years included in our time series.

We controlled for other potential socio-economic and demographic drivers of immunization coverage. Covariates included gross domestic product (GDP) per capita, maternal education, and the World Bank's rural population and governance effectiveness indicators (Appendix I).

The government effectiveness indicator captures perceptions of the quality of public services, civil service and degree of independence from political pressures, quality of policy formulation and implementation, and credibility of the government's commitment to such policies. This is one of the six worldwide governance indicators (WGIs) reported for over 200 countries [23] between 1996 and 2016. They are measured in units ranging from -2.5 to 2.5 with high values corresponding to better governance. One of the six WGI's, political stability and absence of violence has been shown to be predictive of aid effectiveness and vaccine coverage [13, 24]. We include the results from a sensitivity analysis using political stability and absence of violence as an alternative measure of the effect of governance on coverage in Appendix III.

Rural population is defined as a country's estimated population living in rural areas at mid-year as a percentage of the total mid-year population in a country according to the criteria used by that particular country.

Regarding maternal education, we used revised estimates from country level data based on publicly available censuses and nationally representative surveys of respondents' educational status. Sampling designs were taken into account to estimate the mean number of years of completed education. A detailed description of this methodology has been described and published previously [25].

Statistical Analysis

All outcome variables, DAH per capita, and GDP per capita were log transformed, while other variables were modelled as continuous. Our choice to use log transformed outcome variables was to allow for plausible interpretation of their respective coefficients [26]. We compare variations in coverage for each vaccine among recipient countries categorized by cumulative DAH, accounting for the time of introduction for different vaccines given the staggered introduction and scale up.

In order to investigate the effect of donor assistance for immunization on vaccination coverage, we used the system generalized method of moments(GMM) Arellano- Bover/Blundell-Bond(ABBB) model. This approach [27] has been suggested to remain robust to data structures with a dependent variable that is dynamic and contingent on its own past realizations such as vaccine coverage, independent variables that are not strictly exogenous potentially due to reverse causation, which is characteristic of our funding variables, fixed individual/country effects, and heteroscedasticity.

We ran five sets of models testing for the effect of each vaccine specifying exogenous and endogenous variables within our data set. All DAH variables were predetermined as endogenous, while governance, economic status, maternal education and rural population were specified as exogenous. We included one lag

for our dependent variable and applied the two-step sample finite sample correction for the standard errors. While this method may improve efficiency through introduction of more instruments, it on the other hand may likely result into overfitting of the model. We therefore tested the models for over identification of instruments using Hansen's test ($p<0.05$). In addition, we incorporated time dummies in our regression, but these were not significant and were consequently excluded from the final model.

To test the sensitivity of our findings from the system GMM approach, we ran the analyses using a fixed effects model with Huber-White standard errors.

Using our primary model, we evaluate the effect of aid from both Gavi and the other channels of assistance, demonstrating the potential improvements in coverage attributable to that support. For Gavi DAH that is further disaggregated by vaccine, we estimate the additional DAH per capita required to reach the 90% target among eligible countries that had started received support for a specific vaccine and still had coverage below 90% in 2016. In addition, we perform a counterfactual analysis accounting for the number of children that have been vaccinated as a result of Gavi support through 2016. Analyses were done using Stata (version 15.1) and R (version 3.2.2).

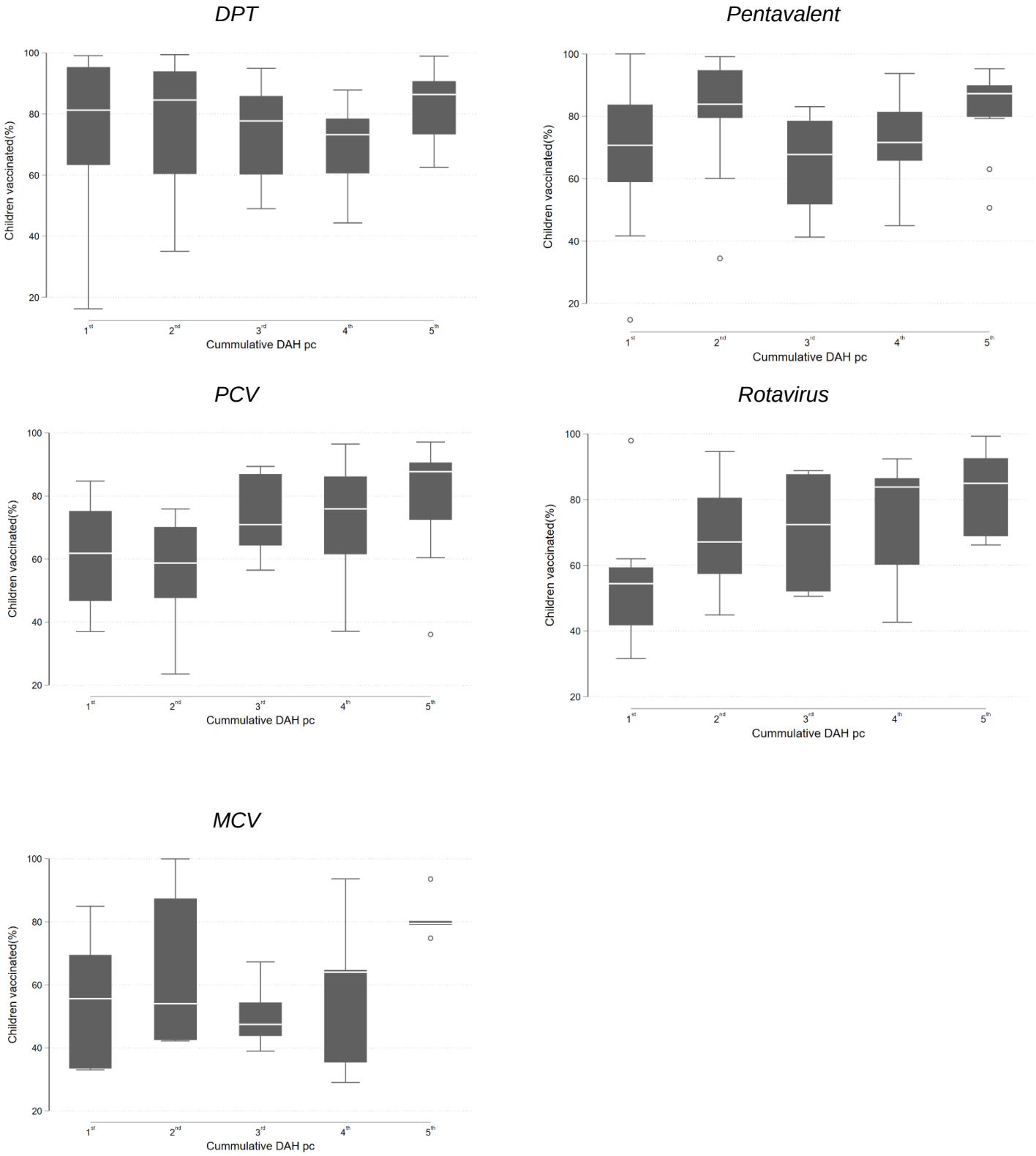
Results

A total of 120 low and middle income countries receiving DAH for immunization were included in our analysis with a time series ranging 1996 to 2016. While there have been great improvements in coverage with most countries reaching the historical global target of 80%, only 42 countries reached the currently stipulated GVAP target of 90% by 2015 (3)]. Some countries still recorded DPT3 coverage of less than 50% by 2015 including Equatorial Guinea, Angola, Chad, Central African Republic, Guinea, Nigeria, Somalia, South Sudan and Ukraine. The largest improvements were recorded in East Timor, Sierra Leone and Sudan all of which achieved at least 80% coverage by 2015 from a baseline level of less than 50%, at 28%, 40% and 46% respectively.

DAH for the different vaccines varied from country to country dependent on individual introduction and scale up processes, with the median DAH per capita amounts in 2016 standing at 15.59USD for total vaccine DAH, which ranged from 0.41USD for MCV, 3.41USD for rotavirus vaccine, 3.99USD for pentavalent vaccine and 10.40USD for PCV.

Figure 1 shows the crude relationship between cumulative vaccine specific DAH per capita categorized by quintile against coverage for the different vaccines. To account for the variability in time during which vaccine introductions were implemented, we include all years starting 2001 for DPT, 2005 for pentavalent, while the analyses for PCV, MCV and rotavirus were restricted to the period between 2010 and 2016 corresponding to the years during which these vaccines were introduced among majority of the recipient countries.

Figure 1: Relationship between vaccine DAH per capita and vaccine coverage



Median and overall range of vaccine coverage within each quartile of cumulative DAH per capita among Gavi recipient countries

For DPT3 vaccine, median coverage across all DAH categories of total vaccine spending fluctuated within a comparable interval ranging from 79.7% among countries with the least DAH to 86.4% among those that received the highest DAH.

Regarding pentavalent vaccine, we observed a positive correlation between DAH and coverage, more so between the 3rd and 5th quintiles with median coverage increasing from 67.7% to 87.3% among countries in these respective DAH categories. In addition, the distribution of coverage appeared more homogeneous among countries in the 5th quintile compared to those in all other DAH categories. This pattern becomes more pronounced in the relationship between DAH and coverage for PCV and rotavirus vaccines. For PCV, the median coverage increases progressively across the DAH groups starting from 61.8% in the 1st quintile, was slightly lower at 58.7% in the 2nd quintile, increasing to 70.9%, 75.9% and 87.7% among countries in the 3rd, 4th and 5th DAH quintiles respectively.

Among countries that received DAH for rotavirus vaccine, the median coverage increases from 54.4% in the 1st quintile to 67.1%, 72.4%, 83.8% and 84.9% among countries in the 2nd, 3rd, 4th, and 5th DAH quintiles respectively.

The relationship between DAH and coverage for MCV is noted to be less systematic compared to that for the newer vaccines, with the median coverage remaining comparable among countries in the 1st, 2nd and 3rd DAH quintiles while those that received the highest DAH recorded coverage of at least 75%.

In addition to the observed positive correlation between funding and coverage more particularly for pentavalent, PCV and rotavirus vaccines, this figure also demonstrates heterogeneity in coverage within groups of recipient countries receiving comparable amounts of DAH.

Table 1 summarizes the analysis exploring the main association of interest from the system GMM model. With exception of DPT3, increasing vaccine DAH per capita led to improvements in vaccine coverage with significant effects noted for PCV, pentavalent and rotavirus vaccines ($p<0.05$). For a 1% increase in vaccine

specific DAH, coverage for PCV was estimated to increase by 3.6% (95%CI: 1.1% to 6.1%), pentavalent by 0.9% (95%CI: 0.7% to 1.1%), and rotavirus by 2.3% (95%CI: 1.4% to 3.3%).

Similarly, a 1% increase in Non-Gavi DAH per capita would result in more moderate but significant increases in coverage for PCV by 1.6% (95%CI: 0.1% to 3.1%), pentavalent vaccine by 0.4% (95%CI: 0.2% to 0.6%), and rotavirus vaccine by 0.8% (95% CI: 0.3% to 1.3%).

For all vaccines, the one-year lag for coverage was significant indicating that coverage in the previous year influenced the level of coverage in the subsequent year. All models except that for pentavalent vaccine remained robust to over identification (Hansen's test p>0.05).

Table 1: Regression results with vaccine coverage as dependent variable from **system GMM**

	DPT3	**PCV3**	**Pentavalent3**	**MCV2**	**Rotavirus**
	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)
Gavi_vaccine DAH per capita	-0.071 (0.138)	**3.586* (1.261)**	**0.905* (0.113)**	1.457* (0.939)	**2.335* (0.478)**
Gavi_HSS DAH per capita	0.071 (0.108)	-0.045 (0.287)	0.030 (0.080)	0.032 (0.113)	0.002 (0.094)
Non-Gavi DAH per capita	0.006 (0.030)	**1.567* (0.786)**	**0.413* (0.106)**	0.299 (0.215)	**0.809* (0.218)**
GDP per capita	0.082 (0.176)	2.132 (2.044)	**0.947* (0.426)**	0.679 (0.756)	0.394 (0.933)
Governance effectiveness	0.144 (0.097)	-1.022 (1.809)	0.221 (0.364)	0.260 (0.702)	-0.684 (1.014)
Rural population	0.002 (0.006)	-0.070 (0.078)	-0.043 (0.017)	-0.016 (0.034)	-0.070 (0.049)
Maternal Education	-0.042 (0.114)	-0.277 (0.385)	0.018 (0.099)	0.195 (0.230)	0.218 (0.251)
Lag of 1 year	**0.968* (0.045)**	**0.887* (0.061)**	**0.713* (0.037)**	**0.886* (0.081)**	**0.887* (0.061)**
Number of observations	*2133*	*2133*	*2133*	*2133*	*2133*
Number of instruments	*65*	*65*	*65*	*65*	*65*
Hansen's test	*0.275*	*0.163*	*0.034*	*0.185*	*0.176*

***significant** at 0.05*
** significant at 0.1*
Vaccine DAH for DPT3 represents total vaccine spending while that for the other vaccines is specific to that vaccine
Gavi_vaccine DAH per capita, Gavi_HSS per capita, Non-Gavi DAH per capita, GDP per capita in log terms

We interpret these findings in absolute terms estimating the additional DAH for each vaccine required to improve coverage to the 90% target for each country in which the vaccine is already being administered. We restricted this analysis to vaccines for which we found significant effects which we applied only among countries that had already introduced the vaccine, received vaccine DAH in 2016, and had coverage of less than 90% in the same year.

Forty-three recipient countries were included for PCV and pentavalent vaccines, with coverage ranging from 22.2% to 89.7% and 14.3% to 87.4% respectively while twenty-seven countries were included for rotavirus vaccine with coverage ranging from 17.8% to 89.8%.

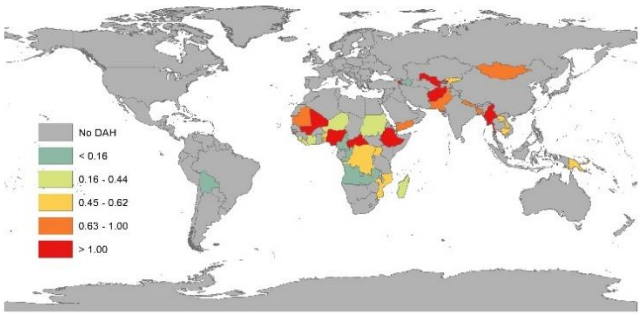
Among these countries, the median additional amount of DAH per capita for PCV relative to the observed DAH received in 2016 was 0.53USD ranging from 0.10USD to 4.33USD. The top five countries for which we estimated the highest amounts were Myanmar (4.33USD: 95%CI 2.53 to 13.3), Nigeria (2.91USD: 95%CI 1.70 to 8.95), Ethiopia (2.47USD: 95%CI 1.44 to 7.61), Uzbekistan (2.22USD: 95%CI 1.29 to 6.83) and Afghanistan (2.06USD: 95%CI 1.20 to 6.33).

For pentavalent, the median additional amount of DAH was 1.16USD ranging from 0.01USD to 9.06USD. Countries for which the highest amounts were estimated included Somalia (9.06USD: 95%CI 7.25 to 12.00), Kiribati (8.18USD: 95%CI 6.55 to 10.83), Nigeria (6.05USD: 95%CI 4.84 to 8.01), Chad (4.77USD: 95%CI 3.82 to 6.32) and Liberia (4.34 USD: 95%CI 3.48 to 5.75).

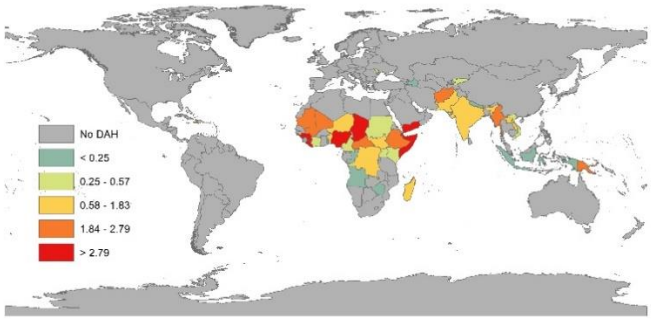
The median amount of additional DAH per capita required for rotavirus vaccine was 0.23USD ranging from less than 0.01USD to 2.57USD. Countries for which the highest amounts were estimated included Mali (2.57 USD: 95%CI 1.82 to 4.30), Kiribati (2.56USD: 95%CI 1.81 to 2.98), Liberia (1.65 USD: 95%CI 1.17 to 2.75), Sao Tome and Principe (1.46 USD: 95%CI 1.03 to 2.43), and Angola (1.18 USD: 95%CI 0.84 to 1.97). All countries are presented ranked by additional DAH needed in appendix section II. We present additional DAH by quintile for each of the three vaccines illustrating the distribution of additional investments required among recipient countries (Figure 2).

Figure 2: Distribution of estimated additional DAH per capita across recipient countries

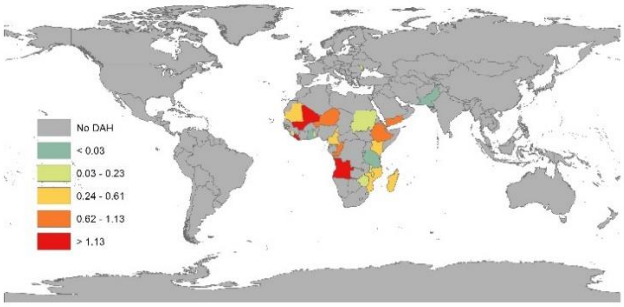
PCV
(43 countries)



Pentavalent
(43 countries)



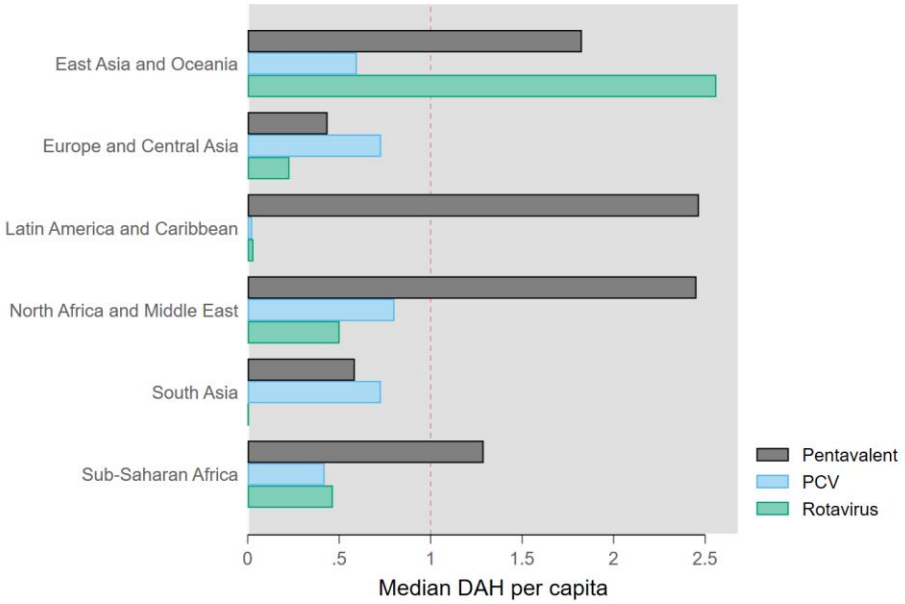
Rotavirus
(27 countries)



Additional amounts of vaccine specific DAH required among countries that had implemented vaccine introduction, received vaccine DAH, and had coverage of less than 90% in 2016. Includes 43 countries for PCV and pentavalent vaccine and 28 countries for rotavirus vaccine.

At regional level, a median additional amount of more than 1.0USD would be required among countries in East Asia and Oceania, Latin America and Caribbean, North Africa and Middle East and Sub-Saharan Africa regions for pentavalent vaccine, and East Asia and Oceania region for rotavirus vaccine (Figure 3).

Figure 3: Additional DAH per capita required by super region



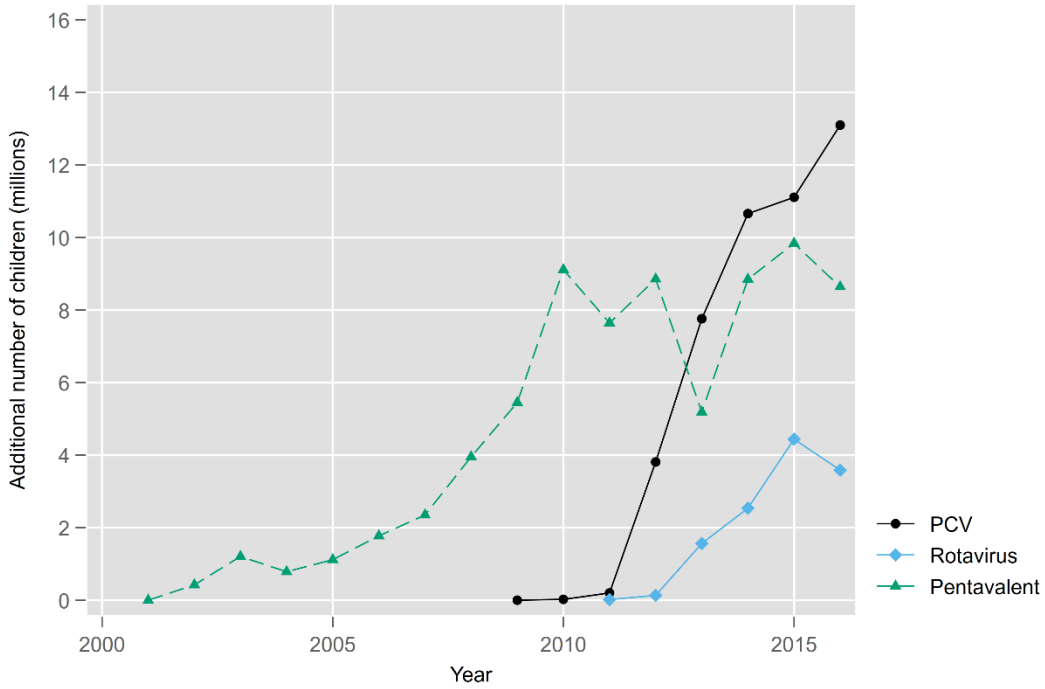
Additional amounts of vaccine specific DAH required by super region. Analysis includes low and middle income Gavi eligible countries that had implemented vaccine introduction, received vaccine DAH, and had coverage of less than 90% in 2016. Includes 43 countries for PCV and pentavalent vaccine and 27 countries for rotavirus vaccine.

Based on the disbursements made thus far, this analysis indicates substantial investments in PCV vaccine across different recipient countries with a potentially higher efficiency for future investments towards PCV and rotavirus vaccines relative to pentavalent vaccine.

Figure 4 shows results from our counterfactual analysis accounting for the number of children vaccinated as a result of Gavi support specifically for vaccines starting in 2002 for pentavalent, 2009 for PCV and 2011 for rotavirus. Our models predict that through 2016, the number of children who otherwise would not have been vaccinated sum up to 46.7million for PCV, 75.2million for pentavalent vaccine, and 12.3million for rotavirus vaccine. Between 2010 and 2016, we

observe a significant annualized growth with number of children covered doubling for both PCV at 2.31 (95%CI: 1.24 to 4.33) and rotavirus vaccine at 2.81(95%CI 1.39 to 5.65) compared to pentavalent vaccine at 1.03(95%CI: 0.33 to 1.73).

Figure 4: Additional number of children immunized as a result of Gavi DAH by vaccine



Using a fixed effects approach, we found comparable results, with a significant increase in coverage for all vaccines (Appendix IV). Effects of vaccine specific DAH on coverage for all vaccines remained positively significant but lower in magnitude relative to estimates from the system GMM. Similar to findings from the system GMM model, better governance impacted vaccine coverage positively, although in this case, we found significant effects for PCV, while higher maternal education was associated with improved coverage for PCV, pentavalent, measles, and rotavirus vaccines.

A sensitivity analysis using political stability as an alternative measure of governance also showed analogous results to our primary analysis qualitatively and quantitatively for both model specifications. Results of this analysis are presented in Appendix III in the supplementary materials.

Discussion

Our analysis shows that donor assistance for immunization from Gavi specifically targeting vaccines has contributed to improved coverage of the different vaccines within its portfolio including pentavalent, pneumococcal, measles and rotavirus vaccines. We observe a stronger effect for newer vaccines compared to traditional vaccines such as DPT. This may result from using an aggregated vaccine spending envelope compared to others for which individual vaccine specific amounts were applied. It may also be due to a shift in implementation of vaccination for DPT which has since been incorporated into pentavalent vaccine starting 2001 among Gavi recipient countries.

We estimate that the net number of children number of children immunized for pentavalent, pneumococcal and rotavirus vaccines totaled to 134.1million, with 25.3million vaccinated in 2016 only as a result of Gavi. This is line with evidence from Gavi's progress reports which suggest that a total of 690million children have been vaccinated overall since its inception, with 65million being vaccinated in 2017 alone [28]. We also show the accelerated increase in coverage for these vaccines after 2011 which reflects the Global Vaccine Action main objectives to bolster the number of new vaccine introductions among recipient countries while ensuring optimal coverage at both national and subnational levels [3].

In addition to the historical successes demonstrated, this assessment further illustrates the potential of Gavi DAH in the long term, providing a benchmark to guide quantification processes regarding the cost of immunization per child. In order to reach the 90% coverage target among recipient countries, we estimate additional resources required in order to close the coverage deficit assuming minimal heterogeneity in current funding implementation processes. Among the three vaccines, the highest amount of additional DAH was estimated for pentavalent vaccines relative to that for PCV and rotavirus vaccines. This is

attributable to a number of possible explanations. First, variations in vaccine prices may influence how much more DAH would be required for optimal coverage. As per the current UNICEF vaccine data, prices range from 3.0USD for PCV and rotavirus vaccine to at least 0.7USD for pentavalent vaccine depending on existing dose formulations [29]. However, even with comparable unit costs, greater investments have been made for PCV compared to other vaccines following the launch of unique global initiatives such as the Advance Market Commitment (AMC) through which funding for specific vaccines is secured allowing for increased availability among eligible recipient countries. On the other hand, operational costs for more affordable vaccines may lead to slow uptake particularly in countries with inadequate health systems. For example, injectable multi-dose vaccine vials such as pentavalent require additional vaccine supplies and different cold chain mechanisms without which potential bottlenecks in immunization delivery would result.

Further examination of countries with the highest amounts of additional DAH requirements suggest specific country characteristics which probably contributed to delayed roll out and uptake processes. Somalia, and Myanmar for which the highest estimated amounts of pentavalent vaccine and PCV DAH were required, have been characterized by political instability which have as a result led to programmatic challenges in essential health service provision [30, 31]. However, among sub Saharan countries such as Burkina Faso and Gambia with negligible additional amounts, existing health system policies have likely been a main driver of success in their respective immunization programs. For example, Burkina Faso has adopted legislations targeting equitable health protection for all citizens [32], while Gambia has implemented trekking clinics in addition to community health workers in a bid to reach more children [33].

Our results therefore provide evidence for success in terms of processes and outputs of a co-financing performance based system especially given that our coverage estimates are corrected for any reporting biases as earlier established to be associated with Gavi DAH [12]. The vaccine specific effects specifically suggest progress towards a potential decline in the burden of vaccine preventable diseases as indicated in the Gavi 2016-2020 strategy which lists hepatitis B,

rotavirus and measles among the disease dashboard indicators [34]. This also emphasizes the need for sustainability through catalytic funding or increased government health expenditure towards immunization particularly among recipient countries that are approaching or reached transition [5] from direct support.

Contrary to vaccine specific funding, Gavi HSS DAH did not have significant effects on vaccine coverage. This may appear concerning given the HSS mandate to address existing health system bottlenecks hindering optimal delivery and uptake of available vaccines. However, we attribute the lack of a demonstrable effect to a couple of possible circumstances. It is known that more resources targeting HSS are typically disbursed to countries lagging behind in meeting coverage targets in order to boost scale up of new and underused vaccines. The absence of significant effects from our primary model may also reflect contextual variations in the financial flows and resource implementation processes from country to country [35]. HSS applications are country led with countries making an investment case based on their prevailing health system bottlenecks overall. Moreover, given the lead time associated with funding cycles, actual implementation may be driven by changes in program priorities between the time of application and implementation, or resources used for wider system bottlenecks for which there may be no immediate or apparent effect on vaccination coverage. Comprehensive assessments of HSS resource effects could include intermediate program outputs such as health worker capacity, distribution systems, stakeholder partnerships and other system components [36] in order to provide a more robust understanding of any HSS resource effects.

Non- Gavi DAH has previously been characterized [7] using available project level data where resources have been previously categorized into funding specific towards vaccines, system strengthening activities and research and development activities. Even though vaccine spending from other channels tends to focus more on elimination and eradication efforts particularly after the initiation of Gavi, we found a smaller but significant impact on the newer vaccines. The keystone of

success for elimination and eradication of vaccine preventable diseases depends on ensuring adequate supplies, while essentially creating awareness and demand through community mobilization and tracking service delivery through surveillance. Also, it is not uncommon to integrate additional service delivery for primary health care during vaccination campaigns, the success of which has been documented [37, 38]. Immunization protocols in recipient countries are designed to ensure that children complete their initial vaccination schedule with different combinations including new and traditional vaccines given at pre-specified time points within the first year [39].

The impact of Non-Gavi DAH on newer vaccines therefore suggests a possible spill-over effect given that the interventions target a similar population demographic. For example, current polio eradication initiatives encourage exploiting the visibility and available infrastructure for supplemental immunization activities (SIAs) to strengthen routine immunization which in turn will mitigate the necessity of frequent SIAs [40]. Documented practices include identifying hard to reach populations, training health workers, facilitating cold chain capacity, and improving adverse events management [41]. With current elimination strategies against polio and measles [29], we expected a stronger effect on measles vaccine which together with polio vaccine have been described to form the bulk of vaccine specific spending from Non-Gavi DAH. However, given that we were unable to disaggregate this DAH as we did for Gavi, the actual effects of vaccine disbursements may have been masked as a result.

Our findings contribute to the existing evidence base characterizing the impact of donor aid on child health with a focus on vaccination coverage. This analysis is unique relative to others because we investigate the association between coverage and aid disaggregated by channel, further exploring any existing effects on both new and traditional vaccines. In addition, we use survey based coverage estimates that have been documented as superior to administrative estimates not only due to incorrect or incomplete recording, but also due to denominator inaccuracies within the recipient countries' points of care. Furthermore, we

employ methods that address the complexities associated with possible endogeneity in the relationship between our dependent and predictor variables thus offering a more robust representation of any existing effects.

Nonetheless, our study is prone to a number of limitations. Despite the fact that our coverage estimates are less biased compared to administrative data estimates, these are subject to other types of information bias and sampling error that are characteristic of survey data. Also, due to limited availability of data on program specific domestic health expenditure, we did not include government spending for immunization. As such, we are unable to evaluate the effects of aid relative to domestic expenditure, or whether any coverage improvements would have occurred regardless of existing aid mechanisms. Future evaluations should consider including a measure of domestic expenditure on immunization in order to provide insight on potential funding predictability and sustainability, and also assess for any program level fungibility [28].

An additional limitation of our top bottom assessment approach is based on the potential for aid leakage into less productive spending along disbursement chains [42] which would likely lead to an overestimation of observed effects. It is therefore imperative that the utility of financial reporting mechanisms such as the System of Health Accounts (SHA) continues to be standardized and strengthened more so in developing countries in order to allow for more robust and comprehensive evaluations of aid.

A number of global targets for equitable vaccine coverage and funding sustainability have recently been set as specified by the Global Vaccine Action Plan and Gavi's current strategic plan [43] among others. This calls for continued resource mobilization efforts towards immunization from both donors and governments alike. The direction of funding prospects in both the short and long term irrespective of the source is contingent not only on need, but also on the potential to achieve the intended health gains. Our analysis provides evidence of success from both a historical and forward looking perspective in the implementation of global immunization initiatives thus far, but even more

importantly underscores the significance of sustainability and efficiency in order to achieve universal immunization coverage.

Conflict of interest

None

Funding

This work did not receive any funding support from the public, not for profit, or commercial sectors.

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Supplementary materials

Appendix I

Data table

Covariate	Source	Metric	Timeframe	Log transformed specification (Y/N)
Donor assistance for immunization				
-Gavi	Gavi	DAH disbursed in 2017 USD	2000-2016	Y
-Non-Gavi	IHME	DAH disbursed in 2017 USD	1996-2016	Y
Vaccine coverage	IHME	Proportion of children	1996-2016	Y
GDP per capita	IHME	GDP per capita	1996-2016	Y
Under 1 population	IHME	Under 1 population	1996-2016	N
Rural population	World Bank	% rural residence at mid-year	1996-2016	N
Governance effectiveness	World Bank	Indicator ranging from -2.5 to 2.5	1996-2016	N
Political stability and absence of violence	World Bank	Indicator ranging from -2.5 to 2.5	1996-2016	N
Maternal education	IHME	Mean number of years	1996-2016	N

Sources
IHME: http://ghdx.healthdata.org/ihme_data
Gavi: https://www.gavi.org/results/disbursements/
World Bank: https://data.worldbank.org/indicator

Appendix II

Estimated additional DAH per capita required for pentavalent vaccine

Rank	Country	USD per capita	lower bound	upper bound
1	SOMALIA	9.062	7.257	12.001
2	KIRIBATI	8.185	6.554	10.838
3	NIGERIA	6.050	4.845	8.012
4	CHAD	4.775	3.824	6.323
5	LIBERIA	4.342	3.477	5.750
6	GUINEA	3.177	2.544	4.206
7	YEMEN	2.951	2.363	3.908
8	DJIBOUTI	2.916	2.335	3.861
9	MALI	2.796	2.239	3.703
10	ETHIOPIA	2.699	2.161	3.574
11	PAPUA NEW GUINEA	2.660	2.130	3.522
12	HAITI	2.466	1.975	3.266
13	AFGHANISTAN	2.452	1.964	3.248
14	MYANMAR	2.220	1.778	2.940
15	CENTRAL AFRICAN REPUBLIC	2.130	1.706	2.821
16	MAURITANIA	1.893	1.516	2.507
17	LAO DPR	1.826	1.463	2.419
18	PAKISTAN	1.621	1.298	2.146
19	SOUTH SUDAN	1.604	1.285	2.125
20	DEMOCRATIC REPUBLIC OF THE CONGO	1.551	1.242	2.054
21	MADAGASCAR	1.420	1.137	1.880
22	NIGER	1.160	0.929	1.536
23	BENIN	1.110	0.889	1.470
24	GUINEA BISSAU	0.687	0.550	0.909
25	INDIA	0.585	0.469	0.775

26	UGANDA	0.569	0.455	0.753
27	MOLDOVA	0.479	0.383	0.634
28	SUDAN	0.469	0.376	0.622
29	COTE DIVOIRE	0.449	0.359	0.594
30	KYRGYZSTAN	0.436	0.349	0.578
31	COMOROS	0.413	0.331	0.547
32	VIETNAM	0.405	0.324	0.537
33	CAMEROON	0.359	0.288	0.476
34	KENYA	0.270	0.217	0.358
35	SOLOMON ISLANDS	0.245	0.196	0.324
36	CONGO	0.219	0.176	0.290
37	SIERRA LEONE	0.119	0.095	0.157
38	ZIMBABWE	0.113	0.090	0.150
39	TOGO	0.095	0.076	0.126
40	ANGOLA	0.071	0.057	0.094
41	NEPAL	0.051	0.041	0.068
42	AZERBAIJAN	0.038	0.030	0.050
43	INDONESIA	0.004	0.003	0.005

Estimated additional DAH per capita required for pneumococcal vaccine(PCV)

Rank	Country	USD per capita	lower bound	upper bound
1	MYANMAR	4.333	2.528	13.312
2	NIGERIA	2.915	1.700	8.954
3	ETHIOPIA	2.476	1.444	7.607
4	UZBEKISTAN	2.221	1.295	6.823
5	AFGHANISTAN	2.063	1.204	6.339
6	ARMENIA	1.925	1.123	5.914
7	SOLOMON ISLANDS	1.720	1.003	5.284
8	CENTRAL AFRICAN REPUBLIC	1.555	0.907	4.776

9	MALI	1.085	0.633	3.332
10	NEPAL	0.953	0.556	2.928
11	GUINEA BISSAU	0.932	0.544	2.863
12	MONGOLIA	0.912	0.532	2.800
13	YEMEN	0.802	0.468	2.465
14	MAURITANIA	0.741	0.432	2.277
15	PAKISTAN	0.728	0.425	2.236
16	BANGLADESH	0.713	0.416	2.192
17	DEMOCRATIC REPUBLIC OF THE CONGO	0.615	0.359	1.889
18	LAO DPR	0.597	0.348	1.833
19	MOZAMBIQUE	0.561	0.327	1.723
20	KYRGYZSTAN	0.546	0.319	1.678
21	BENIN	0.535	0.312	1.643
22	UGANDA	0.520	0.303	1.596
23	PAPUA NEW GUINEA	0.511	0.298	1.571
24	CAMBODIA	0.475	0.277	1.459
25	SUDAN	0.445	0.259	1.366
26	COTE DIVOIRE	0.420	0.245	1.291
27	LIBERIA	0.420	0.245	1.290
28	NIGER	0.357	0.208	1.098
29	DJIBOUTI	0.301	0.175	0.924
30	TOGO	0.279	0.163	0.857
31	SIERRA LEONE	0.218	0.127	0.670
32	MADAGASCAR	0.208	0.121	0.639
33	LESOTHO	0.161	0.094	0.495
34	MOLDOVA	0.154	0.090	0.472
35	ANGOLA	0.087	0.051	0.267
36	GAMBIA	0.086	0.050	0.265
37	CAMEROON	0.080	0.047	0.245

38	ZAMBIA	0.034	0.020	0.104
39	AZERBAIJAN	0.032	0.019	0.099
40	CONGO	0.031	0.018	0.096
41	BOLIVIA	0.024	0.014	0.074
42	BURKINA FASO	0.010	0.006	0.030
43	INDONESIA	0.004	0.003	0.005

Estimated additional DAH per capita required for rotavirus vaccine

Rank	Country	USD per capita	lower bound	upper bound
1	MALI	2.574	1.828	4.300
2	KIRIBATI	2.562	1.820	4.279
3	LIBERIA	1.648	1.171	2.754
4	SAO TOME AND PRINCIPE	1.460	1.037	2.439
5	ANGOLA	1.183	0.840	1.976
6	DJIBOUTI	1.129	0.802	1.887
7	ETHIOPIA	1.006	0.715	1.681
8	CONGO	0.927	0.658	1.549
9	YEMEN	0.777	0.552	1.298
10	NIGER	0.631	0.448	1.055
11	MADAGASCAR	0.615	0.437	1.028
12	GUINEA BISSAU	0.578	0.410	0.965
13	MOZAMBIQUE	0.466	0.331	0.778
14	KENYA	0.236	0.168	0.395
15	CAMEROON	0.234	0.167	0.392
16	MAURITANIA	0.231	0.164	0.385

17	MOLDOVA	0.228	0.162	0.381
18	SUDAN	0.228	0.162	0.381
19	ZIMBABWE	0.147	0.105	0.246
20	SIERRA LEONE	0.131	0.093	0.220
21	TOGO	0.103	0.073	0.171
22	MALAWI	0.097	0.069	0.162
23	HAITI	0.031	0.022	0.052
24	GHANA	0.019	0.014	0.032
25	PAKISTAN	0.011	0.008	0.018
26	TANZANIA	0.003	0.002	0.004
27	GAMBIA	0.001	0.000	0.001

Appendix III

Regression results with vaccine coverage as dependent variable from both ABBB and fixed effects models using political instability as a measure of governance

	DPT3	**PCV3**	**Pentavalent3**	**MCV2**	**Rotavirus**
Model 1 (System GMM)					
	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)
Gavi_vaccine DAH per capita	-0.07 7(0.132)	**3.967* (1.159)**	**0.993* (0.107)**	1.935 (1.404)	**2.943* (0.632)**
Gavi_HSS DAH per capita	0.075 (0.105)	-0.473 (0.278)	-0.087 (0.079)	0.065 (0.163)	0.029 (0.137)
Non-Gavi DAH per capita	0.016 (0.035)	**0.948* (0.395)**	**0.487* (0.084)**	0.230 (0.183)	**0.595* (0.177)**
GDP per capita	0.135 (0.165)	1.562 (1.479)	**1.142* (0.378)**	1.444* (1.041)	1.584 (1.182)
Political stability	0.171 (0.187)	-3.426* (1.275)	0.563 (0.222**)**	-1.735 (1.056)	-2.410 (0.895)
Rural population	0.003 (0.005)	-0.047 (0.054)	-0.023 (0.016)	0.009 (0.032)	-0.033 (0.044)
Maternal Education	-0.045 (0.108)	0.169 (0.309)	0.131 (0.104)	0.243 (0.249)	0.224 (0.254)
Lag of 1 year	**0.967* (0.043)**	**0.885* (0.045)**	**0.763* (0.031)**	**0.919* (0.069)**	**0.877* (0.041)**
Number of observations	*2043*	*2043*	*2043*	*2043*	*2043*
Number of instruments	*83*	*83*	*83*	*83*	*83*
Hansen's test	*0.234*	*0.218*	*0.023*	*0.220*	*0.139*
Model 2 (Fixed Effects)					
	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)
Gavi_vaccine DAH per capita	**0.027* (0.005)**	**0.981* (0.059)**	**0.533* (0.033)**	**0.302* (0.056)**	**0.993* (0.058)**
Gavi_HSS DAH per capita	0.002* (0.001)	**-0.070* (0.017)**	**-0.054* (0.013)**	0.014 (0.016)	-0.035* (0.018)
Non-Gavi DAH per capita	-0.003 (0.002)	0.002 (0.027)	-0.025 (0.022)	0.007 (0.019)	0.030 (0.025)
GDP per capita	0.078 (0.054)	0.041 (0.462)	0.809* (0.463)	0.625* (0.374)	0.130 (0.361)
Political stability	**0.052* (0.021)**	0.106 (0.191)	0.150 (0.147)	0.021 (0.115)	0.169 (0.156)
Rural population	-0.006 (0.003)	-0.062 (0.051)	0.021 (0.037**)**	0.039 (0.032)	0.015 (0.039)
Maternal Education	0.008 (0.015)	**1.063* (0.215)**	**1.626* (0.137)**	**0.789* (0.158)**	**0.959* (0.187)**

**** significant** at 0.05*

**significant at 0.1*

Vaccine DAH for DPT3 represents total vaccine spending while that for the other vaccines is specific to that vaccine

Gavi_vaccine DAH per capita, Gavi_HSS per capita, Non-Gavi DAH per capita, GDP per capita in log terms

Data based on 115 countries for which data on political stability were available

Appendix IV

Table 2: Regression results with vaccine coverage as dependent variable from **fixed effects model**

	DPT3	PCV3	Pentavalent3	MCV2	Rotavirus
	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)	Coefficient(SE)
Gavi_vaccine DAH per capita	0.027* (0.005)	**0.919* (0.056)**	**0.508* (0.031)**	**0.301* (0.054)**	**0.928* (0.056)**
Gavi_HSS DAH per capita	0.002 (0.001)	**-0.067* (0.017)**	**-0.052 (0.012)**	0.011 (0.015)	**-0.037* (0.017)**
Non-Gavi DAH per capita	-0.002 (0.002)	-0.006 (0.027)	-0.023 (0.022)	0.009 (0.021)	0.015 (0.026)
GDP per capita	0.091* (0.051)	-0.095 (0.424)	0.698 (0.442)	0.440 (0.355)	0.138 (0.354)
Governance effectiveness	0.004 (0.025)	**0.666* (0.264)**	**0.508* (0.254)**	0.353 (0.230)	0.243 (0.231)
Rural population	-0.005* (0.003)	-0.071 (0.045)	0.017 (0.033)	0.031 (0.029)	0.003 (0.035)
Maternal Education	0.004 (0.015)	**1.016* (0.202)**	**1.548* (0.126)**	**0.785* (0.149)**	**0.876* (0.176)**
Number of observations	*2133*	*2133*	*2133*	*2133*	*2133*

**** significant** at the 0.05 level*

**significant at the 0.1 level*

Vaccine DAH for DPT3 represents total vaccine spending while that for the other vaccines is specific to that vaccine

Gavi_vaccine DAH per capita, Gavi_HSS per capita, Non-Gavi DAH per capita, GDP per capita in log terms

Appendix V

Vaccine Coverage

Definition

This modeling strategy pertains to the vaccine coverage measure (SDG Indicator 3.b.1), the proportion of the target population covered by seven key vaccines included in the national program, including: diphtheria-tetanus-pertussis (DTP, three doses), measles (one dose), polio (three doses), hepatitis B (three doses), *Haemophilus influenzae* type b (Hib, three doses), pneumococcal conjugate vaccine (PCV, three doses), and rotavirus vaccine (two or three doses). We use the geometric mean of coverage of these seven vaccines, based on their inclusion in the national vaccine schedule, to compute overall vaccine coverage of target populations.

We use data from household-level surveys as well as administrative reports of immunization coverage. Survey data which provided person-level information on immunization were identified and extracted. Major multi-country survey programs included in the analysis include the Demographic and Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS), Reproductive Health Surveys (RHS), Living Standards Measurement Study (LSMS) surveys, and World Health Surveys (WHS). We also conducted a comprehensive search of the Global Health Data Exchange (GHDx), as well as targeted internet searches and review of Ministry of Health websites, to identify national surveys and other multi-country survey programs.

Administrative estimates of immunization coverage were obtained from the Joint Reporting Process (JRF), through which the World Health Organization (WHO) and UNICEF collate annual estimates of immunization coverage reported by UN member states. These immunization coverage estimates are separate from those synthesized by WHO, and are calculated by dividing the number of doses of a given vaccine delivered to the target population (i.e., children aged 12 to 23) by the number of individuals in that target population.

We excluded all data sources that were not nationally representative or had high levels of missingness. We applied survey weights based on survey sampling frames whenever they were available to generate weighted national estimates of vaccination coverage accompanied by estimates of standard error (SE). Estimates of SE, as well as sample sizes, were used to calculate uncertainty, as described below. Any point estimates with sample sizes less than 50 were reviewed to ensure that were not substantive outliers and would otherwise have an undue influence on our analysis.

Data processing

Age splitting

Most household surveys collect information on maternal and child health (MCH) indicators for children under 5 and/or mothers who gave birth within five years prior to the time of survey. To maximize data use for our model, we included immunization data for children aged 12 to 59 at the time of survey. Children younger than 12 months of age were excluded to minimize the influence of potentially censored observations. For each vaccine, coverage estimates were assigned to birth-cohort years based on a child's age prior to the time of survey: we used responses recorded for children aged 12 to 23 months for immunization coverage for one year prior to the time of survey, children aged 24 to 35 months for coverage two years prior to the time of survey, and so forth.

Age-specific estimates are easily computed from individual-level microdata, but many published reports and survey summaries present data in broader age aggregates (e.g., DPT3 coverage for children aged 12 to 35 months). To standardize these age groups, we applied an age-splitting model used in the GBD study, as well as analyses that generated smoking and obesity prevalence by age group.

Using surveys with microdata as the reference, we used the following model to generate standardized age group-specific estimates of immunization coverage:

$$\tilde{P}_{a,c,t,k} = P_{a,c,t,k}^{a+x} \frac{P_{a,c,t,j}}{P_{a,c,t,j}^{a+x}}$$

where $\tilde{P}_{a,c,k}$ is the adjusted estimate of coverage for target age group a in country c and year t of survey k; and $P_{a,c,k}^{a+x}$ is coverage reported from survey k, for country c in year t for the age group spanning age a to age $(a + x)$. The ratio of coverage between the target age group and broader age group from a survey j with microdata from the same country-year was used to split data from survey k. Surveys to be split were ideally matched with DHS or MICS surveys. If microdata were not available for the same year, ratios within five years of the survey that required age-splitting were applied.

Administrative bias adjustment

Intervention coverage estimates based on administrative sources can be biased. Such biases may arise for a number of reasons, including discrepancies in the accurate reporting of services or interventions provided (e.g., number of vaccine doses administered) and target population (e.g., number of children in need of vaccines), as well as capturing these data in a timely manner from both public and private-sector facilities and health care providers. We implemented a vaccine-specific bias adjustment process to account for bias in administrative reports of immunization coverage in the JRF. Given that the magnitude, direction, and cause of such biases are heterogeneous across vaccine, space and time, a vaccine-specific, time-varying, all-location bias correction factor was used.

For immunization coverage, we view individual-level data collected through population health surveys as the most accurate and least biased source of information of vaccination coverage, particularly for geographies with incomplete health information systems. We thus compute administrative bias as the ratio between estimates of coverage from surveys (where available) and matched administrative coverage. We model this bias in a spatiotemporal Gaussian process regression (ST-GPR) framework, described further in the subsequent section of this appendix, using the Socio-demographic index (SDI) as a predictor. This method allows us to estimate vaccine-specific administrative bias factors for all geographies and years since 1980, even in places without survey data, by borrowing strength in data across space and time. The GPR framework properly estimates prediction errors in the data synthesis procedure by for uncertainty in

bias ratios when generating fitted values. In this framework, more weight is given to survey data with less uncertainty.

Vaccine-specific modeled estimates of administrative bias are then used to adjust administrative coverage data for over- or under-reporting to reflect observed survey coverage. Adjusted administrative data are used as inputs into the trend estimation process.

Trend estimation

We used a spatiotemporal Gaussian process regression (ST-GPR) to synthesize point estimates from multiple data sources and derive a complete time series for each vaccine. This method has been used extensively and accounts for uncertainty pertaining to each point estimate while borrowing strength across geographic space and time. Briefly, we assumed the Gaussian process was defined by a mean function *m*(•) and covariance function *Cov*(•).

We estimated the mean function using a two-step approach. Specifically, $m_c(t)$ can be expressed as:

$$m_c(t) = X\beta + h(r_{c,t})$$

where $X\beta$ is a linear model and $h(r_{c,t})$ is a smoothing function for the residuals; and $r_{c,t}$ is derived from the linear model. The following linear model was used to model DPT3, measles, BCG, polio coverage:

$$logit(P_{c,t}) = \beta_0 + \beta_1 \mathrm{HAQ}_{\mathrm{c,t}} + \alpha_c + \gamma_{R[c]} + \omega_{\mathrm{SR[c]}} + \varepsilon_{c,t}$$

where $P_{c,t}$ is vaccination coverage for country c year t; $HAQ_{c,t}$ is value of the Healthcare Access and Quality Index for country c and year t; α_c, $\gamma_{R[c]}$, and $\omega_{\mathrm{SR[c]}}$ are country, region, and super-region random intercepts, respectively. These estimates were then modeled through ST-GPR.

Given their recent introduction, there is limited coverage data for HepB, Hib, PCV, and rotavirus vaccines. To leverage the relatively data-rich DPT3 estimates, we

modeled the ramp-up of each vaccine by modeling their ratio with DPT3 coverage. We first calculated the ratio of each particular vaccine with DPT3 by survey-year. We then modeled the full time series of the ratio using ST-GPR and ultimately obtained estimates of coverage by multiplying the modeled ratio by the final estimated DPT3 coverage by location-year. The following linear model was used as the mean function for the HepB, Hib, PCV, and Rota ratio with DPT3:

$$logit(P_{c,i}) = \beta_0 + \beta_1 \mathrm{HAQ}_{\mathrm{c,i}} + \alpha_c + \gamma_{R[c]} + \omega_{\mathrm{SR[c]}} + \varepsilon_{c,i}$$

where $P_{c,i}$ is the coverage ratio for country c time since introduction i; $HAQ_{c,i}$ is value of the Healthcare Access and Quality Index for country c and time since introduction i; α_c, $\gamma_{R[c]}$, and $\omega_{\mathrm{SR[c]}}$ are country, region, and super-region random intercepts, respectively.

Random draws of 1,000 samples were obtained from the distributions above for every country for a given vaccine. Ninety-five percent uncertainty intervals were calculated by taking the ordinal 25th and 975th draws from the sample distribution.

To assess the accuracy of our modeled estimates, we performed cross-validation analyses using a knockout structure as previously described. ST-GPR hyper parameters were selected on models that minimized the overall root-mean squared error (RMSE) of the model across a set of 10 knockouts.

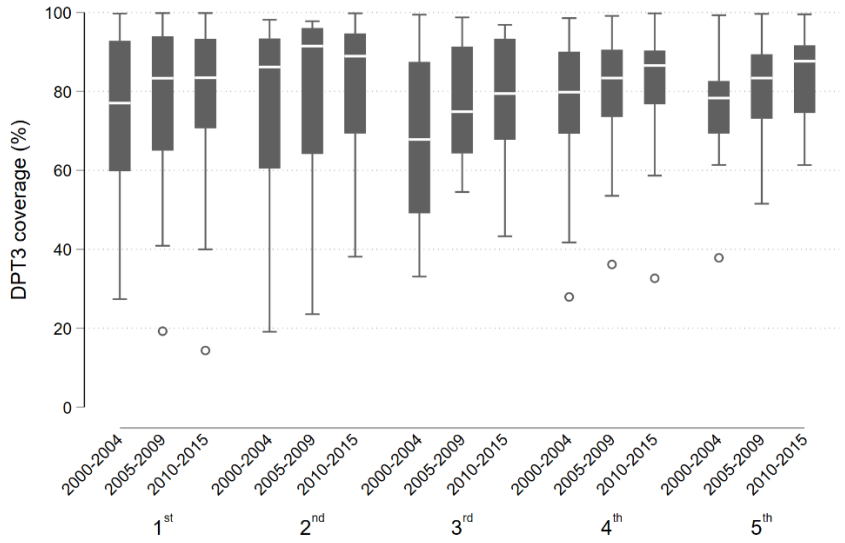
Full Coverage Indicator

To synthesize the full vaccination coverage indicator (SDG indicator 3.b.1), we calculated the geometric mean of the seven vaccines based on their inclusion in the national vaccine schedule for a given year. Newer-generation vaccinations such as PCV and Rota are introduced in the country-year's calculation only after the vaccine has been introduced into the national schedule. We included a three-year lag on introduction to reduce the possibility of sharp declines in full immunization coverage after a new vaccine is introduced into the schedule. National vaccine schedules and vaccine introduction dates were used as reported from WHO or from the country's Ministry of Health website where otherwise unavailable.

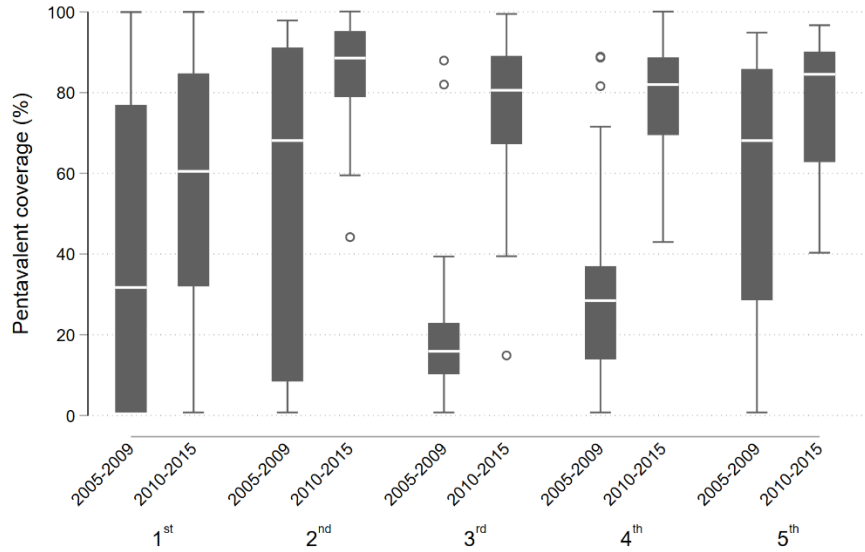
Additional materials

Relationship between mean coverage and cummulative DAH categories over the years post vaccine introduction

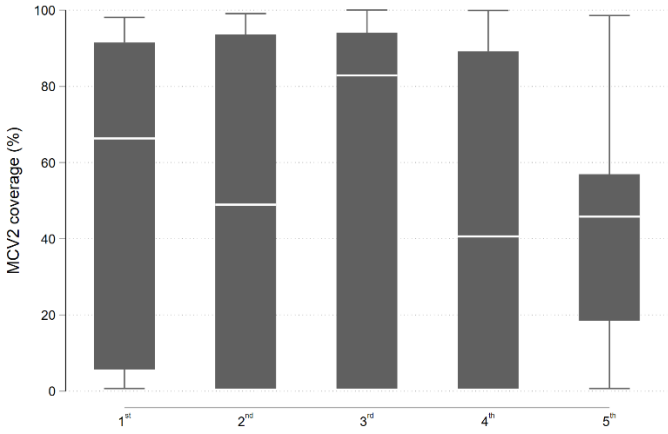
DPT3 vaccine (2000 to 2015)



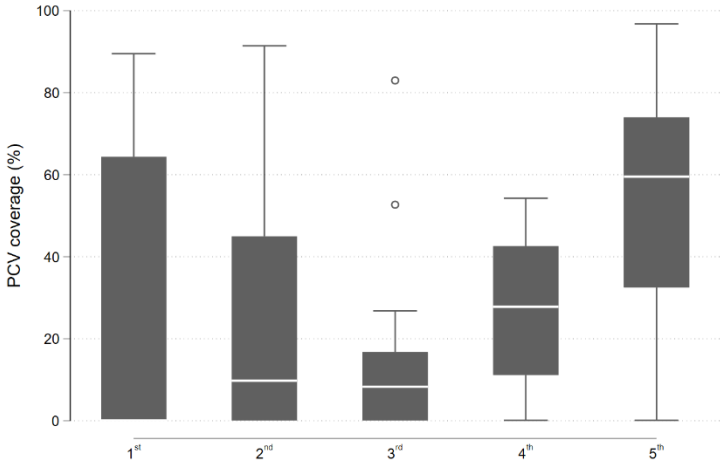
Pentavalent vaccine (2005 to 2015)



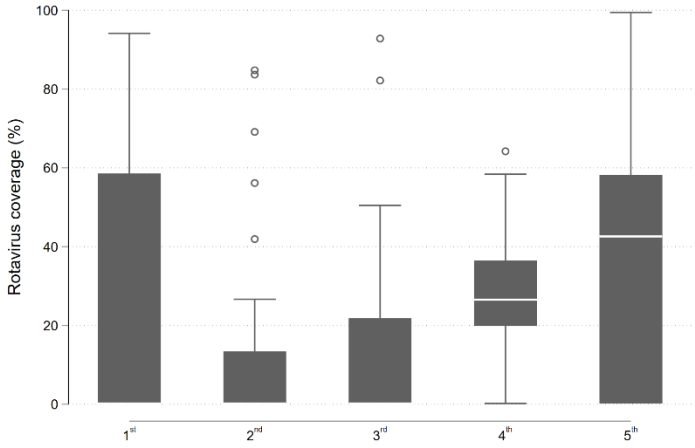
Measles vaccine 2010 to 2015



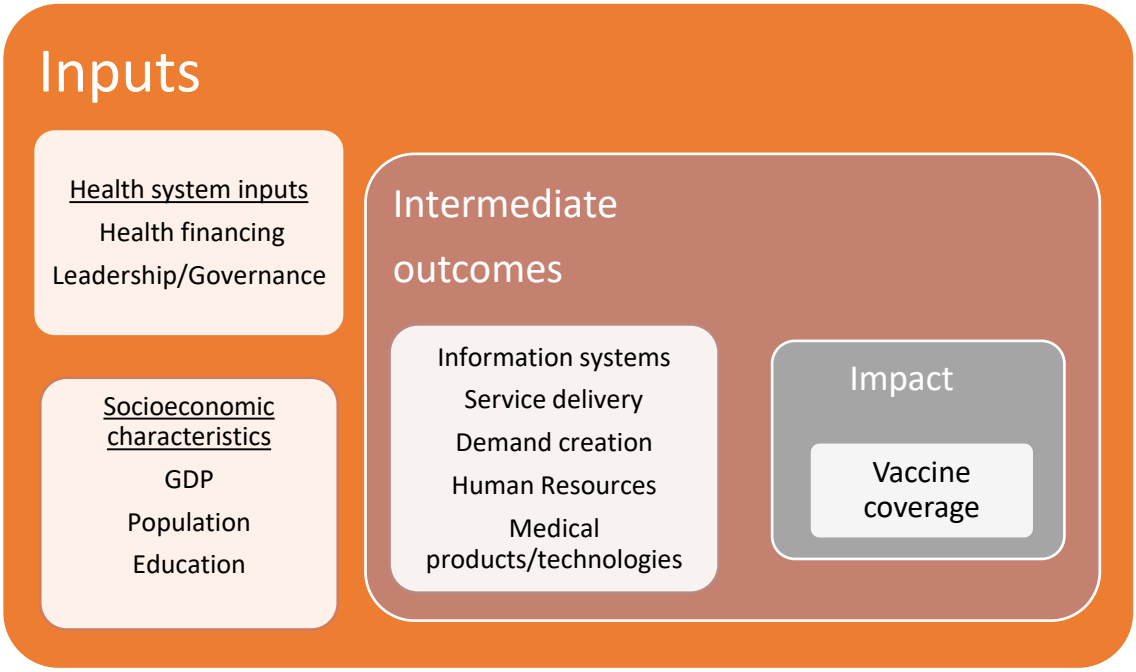
Pneumococcal vaccine (2010 to 2015)



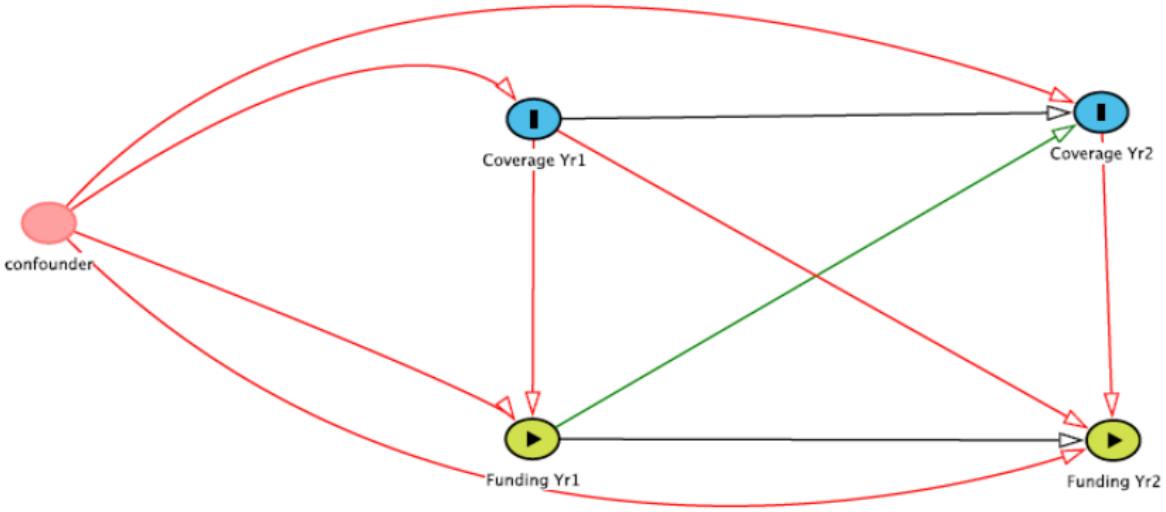
Rotavirus vaccine (2010 to 2015)



Conceptual model of factors influencing health outcomes at national level (partially adopted from the WHO Health Systems Framework):



A simplified dagitty illustration of the causal relationship between predictor and outcome at two time points from which the model choice was determined



The system GMM (ABBB) can be expressed as shown in the equations below:

1. Original/Level equation:

   $y = \rho y_{t-1} + \beta x_t + \vartheta j_t + \varepsilon$

   Corresponding IV's for RHS endogenous variables y_{t-1} *and* x_t *are*:

   Δy_{t-2} and Δx_{t-1}

   IV for exogenous variables classified by j: Δj_t

2. Orthogonal/differencing equation:

   $\Delta y = \rho \Delta y_{t-1} + \beta \Delta x_t + \vartheta \Delta j_t + \varepsilon$

   Corresponding IV's for RHS endogenous variables Δy_{t-1} *and* Δx_t *are:*

   y_{t-2} *and* x_{t-1}

   While IV for exogenous variables classified by Δj_t *:* j_t

Other assumptions include:

i) A dynamic process whereby current realizations of the dependent variable are influenced by the past
ii) Endogenous regressors
iii) Regressors for example the lagged dependent variable may be predetermined but not completely exogenous
iv) Random errors are uncorrelated across individuals and may demonstrate heteroskedasticity and serial correlation

Additional ABBB robustness tests implemented

	1st diff(AB) or system GMM	Orthogonal or original	2 step/1 step process(SE estimation)	Small sample corrections
Baseline	System	Orthogonal	2	Yes
Robust check1	1st diff	Orthogonal	2	Yes
Robust check 2	System	Original	2	Yes
Robust check 3	System	Orthogonal	1	Yes
Robust check 4	System	Orthogonal	2	No

Comparison of suggested approaches in relation to association under investigation

Approach	**Feasibility/Reason**	**Advantages**	**Disadvantages**
Matching	Poor- unmeasured confounding	-	-
Instrumental Variable analysis	Poor- Identification of a valid IV	-	-
Regression Discontinuity	Poor-No eligibility cut off for funding allocation	-	-
Ordinary Least Squares with panel corrected standard errors	Good	Auto correlation Heteroskedasticity Correction of SE	Not as efficient when serial correlation is high +LDV= attenuated effects of important predictors
First differences	Good	Endogeneity Auto correlation Heteroskedasticity	SE's may be biased downwards, magnifies gaps in unbalanced panels, complex
System GMM	Good	*Same as AB above** Resolves unbalanced panel problems SE finite correction	Highly sensitive to assumptions, prone to overfitting, complex

Chapter 3: Determinants of geographical inequalities for DPT3 vaccination coverage in sub-Saharan Africa.

Abstract

Childhood immunization is considered as one of the most effective health interventions, and as a result is a key indicator of progress towards universal health coverage. In the last decade, global improvements in achieving optimal levels of coverage have been made. However, despite substantial investments for immunization, the slowest progress has been documented in sub-Saharan Africa with considerable subnational variations. We explore potential drivers of equitable uptake of immunization based on subnational DPT3 coverage estimates.

Using vaccine coverage estimates at the 5km by 5 km area from 2000 to 2016, we quantify inequity using three measures. First, we assess the shortfall inequality which is a measure of the average deviation across subnational units from that with the highest coverage for each country. Secondly we estimate the threshold index which is the proportion of children below a globally set subnational coverage target, and lastly, a Gini coefficient which represents 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, with governance augmenting the observed relationship between development assistance and inequality. Results from this analysis also indicate that countries with the lowest coverage suffer the highest inequalities. We also highlight growing inequalities among countries which have since met national coverage targets such as South Africa and Kenya. In 2016, values for the shortfall inequality ranged from 1.24% to 43.36%, the threshold index from 0% to 100% and Gini coefficient from 0.01 to 0.37. Burundi, Comoros, Lesotho, Namibia, Rwanda, Sao Tome and Principe and Swaziland had the least shortfall inequality (<5%) while Angola, Ethiopia and Nigeria had values greater

that 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, mechanisms for resource implementation and accountability should be strengthened to maximize gains in vaccine coverage.

Introduction

Global health initiatives are increasingly emphasizing health equity as a key determinant to achieving universal health coverage. Specific to immunization, the Global Vaccine Action Plan (GVAP) endorsed by the 194 Member States of the World Health Assembly in 2012 promotes an equity based approach in setting vaccine coverage targets at both national and subnational levels. By 2015, the goal for all countries was to achieve 90% and 80% coverage of DPT3 vaccine at national and subnational levels respectively with the same targets for all vaccines included in routine immunization programs by 2020 (1). Given that vaccines are considered among the most effective interventions, equitable uptake of immunization remains an important pathway to achieving Universal Health Coverage (UHC), and as such, has been specified as a tracer indicator of progress (2).

Investments for the immunization program have continued to grow particularly through the efforts of the Gavi Alliance (3) that was launched in 2000 to foster equal access to vaccines for people living in the world's poorest countries. Gavi's 2016-2020 strategy comprises goals supporting the overall mission to save children's lives and protect people's health by increasing equitable use of vaccines in lower income countries. Their main objectives during this phase include increasing coverage and equity of immunization, while ensuring flexible responsiveness to the needs of children in fragile states (4).

In addition, evaluations quantifying the allocation of development assistance for vaccination by recipient, show that sub-Saharan Africa continues to be targeted more than other regions(5). These investments have led to significant improvements in vaccination coverage for both new and under used vaccines, however, progress remains heterogeneous across countries with the least progress in sub-Saharan Africa (SSA) (6) (7). Relatedly, national level gains in

coverage continue to occur against the backdrop of increasing or persistent inequality among sub populations within some of these countries (8) (9).

A number of initiatives have been undertaken to boost the absorption of immunization services to underserved or hard to reach populations within different contexts. For example, the World Health Organization (WHO), UNICEF and other development partners introduced the Reach Every District (RED) strategy in 2002 as an initial step towards more equitable access and coverage of vaccinations (10). This strategy subsequently evolved to Reach Every Child (REC) through existing partnerships at country level with the Centers for Disease Control (CDC) (11). The RED and REC approaches are largely country driven with multiple operational components, including building or strengthening outreach services, community engagement, providing supportive supervision, promoting surveillance mechanisms and data use, and building capacity at relevant subnational levels (12).

Impact assessments of these and other strategies have shown evidence of improvement both in delivery processes of immunization services and in vaccination coverage (13) (14). Beyond global remedial approaches, a number of countries have since implemented unique vaccine delivery mechanisms among existing primary health care interventions to expand access to their specific underserved or marginalized subpopulations (15) (16) (17).
Using available population based surveys, multiple studies have demonstrated disparities in vaccine coverage among populations of varying socioeconomic classes and the respective determinants (8) (18). Less frequently, the drivers of inequity in immunization coverage from a geographical standpoint have been evaluated among developing countries, with available evidence mostly comprising country specific assessments (19) (20) (21). Additional research comparing the differences in geographic and wealth priority health-related inequality conditions favor the use of the geographic dimensions as an initial step to assessing prevailing health inequality conditions, as it provides a more comprehensive profile which reflects the locality's specific characteristics (22). Characterizing geographical inequalities in vaccination outcomes is also critical in identifying

clusters if disadvantaged groups that represent high risk pockets due to lower herd immunity. Following this, socio-economic, political and demographic dimensions remain a fundamental next step in decomposing possible drivers of health specific to localities with the more severe outcomes (23) (24).

In this study, we estimate the magnitude of DPT3 vaccine coverage inequality using high spatial resolution estimates (5 by 5 kilometer area) among 45 sub-Saharan African countries and assess the relationship with different potential drivers. These include health spending from both domestic and foreign sources, governance, maternal education, economic status and rural population measured at country level.
Ensuring health and well-being for all is a main objective of the Sustainable Development Goals with a specific target towards vaccination (SDG 3.b.1) (25). In addition to identifying where the greatest coverage gaps exist, understanding possible drivers and determinants is key to this goal.

Methodology

Data and data sources

We use DPT3 coverage from 2000 to 2016 defined as the proportion of children aged under 2 years in a given birth cohort who have received vaccination to compute our measures of inequality. Despite the ongoing efforts to strengthen data quality at subnational health administrative units, unreliable estimates continue to persist. Misclassification due to poor quantification processes, inadequate denominator information and target population mobility across subnational borders has led to both over estimation or underestimation of subnational level coverage(6). In order to address this, geospatial-estimates of DPT3 coverage for every 5 by 5 km area in Africa have since been generated by the Institute for Health Metrics and Evaluation (IHME) using model-based geostatistics in which vaccine coverage survey data collected between 2000 and 2016 were combined with a collection of spatial covariates. A total of 183 subnational surveys encompassing nearly one million children aged 12 to 23 months were used in the modelling process, details of which have been published(26).

Data on country disbursements are extracted from the Gavi website for Gavi and IHME's development assistance for health (DAH) database for other immunization funding channels (27) .These included the World Health Organization(WHO), the Bill and Melinda Gates Foundation (BMGF), NGO's, PAHO, UNICEF, US foundations, the World Bank International Development Association (WB-IDA), and development banks. Double counting was excluded and all DAH converted to 2017 US Dollars. Methods detailing this process have been detailed and published previously(28).

Other covariates included gross domestic product (GDP) per capita, government health expenditure, rural population and governance indicators. Instead of using government health expenditure as an individual covariate, we converted this to a proportion of the economy (GDP) which provides an indication of the social and political choice on countries perception of how much should be spent on health relative to the overall government budget.

Government effectiveness is a composite indicator summarizing perceptions of the quality of public services, civil service and degree of independence from political pressures, quality of policy formulation and implementation, and credibility of the government's commitment to such policies (29). To allow for the different measures of governance, we included political stability as well which is a measure of citizens' perceptions of the likelihood that the government will be destabilized or overthrown by unconstitutional or violent means, including politically-motivated violence and terrorism. These are measured in units ranging from -2.5 to 2.5 with high values corresponding to better governance.

Rural population is defined as a country's estimated population living in rural areas at mid-year as a percentage of the total mid-year population in a country according to the criteria used by that particular country(29).

With exception of vaccination coverage, all other variables were measured at country level.

The choice of our variable set was informed by a conceptual framework corroborated by WHO's commission on social determinants of health (CSDH) framework capturing primary structural inputs that drive equity in health and well-being(30) in Appendix section III.

Definitions of inequality

Using 5 by 5 kilometer area coverage estimates, we quantify inequity in coverage for DPT3 vaccine for each SSA recipient country from 2000 to 2016. We use three corroborative measures of inequality for each country: 1) deviation from the subnational gold standard known as the shortfall inequality, 2) deviation from a global standard referred to as the threshold index and 3) the within-country spread of inequality (Gini coefficient).

The first measure, the *shortfall inequality*, defined as the weighted absolute mean difference from the best performing pixel or subgroup (31). To account for different population sizes, each difference is weighted by the size of the pixel. The weighted mean difference is calculated by taking the difference of each subgroup's coverage from that of the best performing subgroup and multiplying these differences by each pixel's population size. These are then summed and divided by the total population size in order to calculate the weighted mean difference. The highest performing sub-group as a reference point is that if inequalities were to be reduced, the goal would be to bring all subgroups up to the level of the best-performing subgroup. This approach further allows for within country benchmarking processes given the existing unique contextual factors attributed to the best performing sub-group.

Second, is a *threshold index* which is based on a global standard of coverage. For this, we use the GVAP subnational target of 80% (1). Using the DPT3 coverage value and population size within each subgroup, we compute the proportion of the target population that have not reached the global threshold for each country year. This approach quantifies how similar or dissimilar countries are based on an externally defined reference which allows for cross- country benchmarking using a standard measure which is particularly applicable for comparisons on a global perspective.

The third measure of inequality is the *Gini coefficient* (32) based on the Lorenz curve which demonstrates the proportion of the total of the population that cumulatively received vaccination for DPT3. This provides a measure of within country variation, with a unique characteristic of remaining robust to extreme ends of coverage unlike the shortfall inequality.

A higher value of the shortfall inequality or threshold index is indicative of worse inequality. The value of the Gini coefficients ranges from 0 signifying complete equality to 1 which would indicate complete inequality.

Table showing data used in this analysis and their respective sources:

Covariate	Indicator	Source
Total of Gavi and other immunization DAH	Total DAH disbursed per capita (2017 USD)	Gavi/IHME
Child vaccine target population	12-23 months of age	World pop/IHME
Governance/Stewardship	Government effectiveness Political stability	World Bank World Bank
GDP per capita	GDP/population	World Bank
GHE	Government expenditure on health	IHME
Rural population	% rural residence at mid-year	World Bank
Vaccine coverage - Shortfall inequality - Threshold index - Gini coefficient	DPT3 coverage at 5 by 5 km area/admin2	IHME

**Total DAH, GDP and GHE modelled as log transformed values*

Statistical analysis

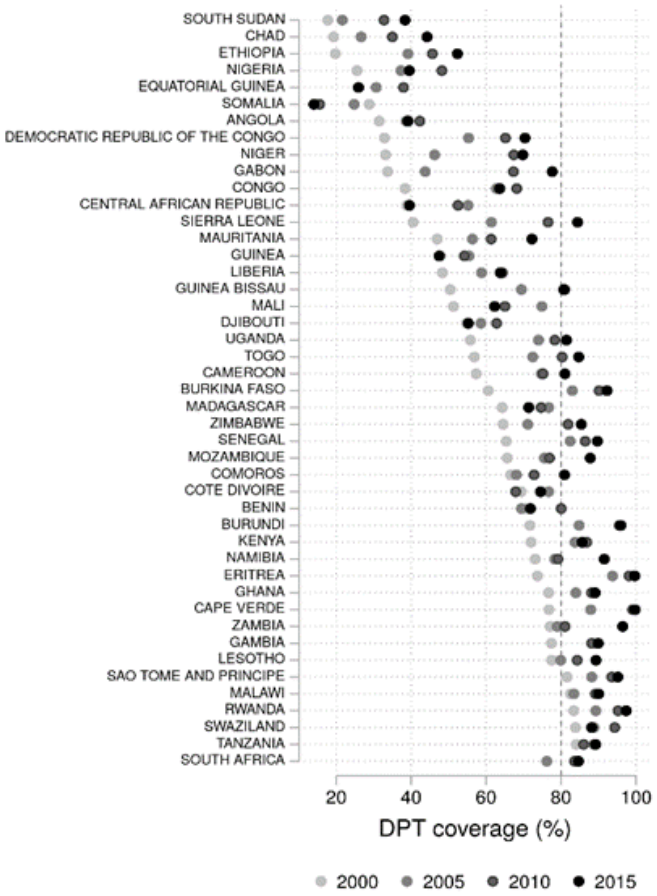
All measures of inequity, DAH per capita, government health expenditure and GDP per capita were log transformed, while other variables were modelled as continuous. Our choice to use log transformed variables was to allow for plausible interpretation of their respective coefficients. We demonstrate country specific distribution of coverage over time from 2000 to 2016 and plot the trends in inequality over time. We perform preliminary analyses determining the relationship between inequality and coverage and how inequality changes relative to DAH disbursements. In order to quantify existing associations with changes in inequality, we used both fixed effects with Huber White standard errors and random effects to estimate both within country and between country relationships with the given covariates. Interpretations for the shortfall inequality

and Gini coefficient are based off the fixed effects model to capture the within country associations, while the random effects formed the basis of interpretation for the threshold index to quantify country to country variation of any relationships between inequality and our given predictors (33) (34). All analyses were done using Stata (version 15.1).

Results

DPT3 coverage has increased by year during our study period, however, a substantial number of countries still fall short of the global target (Figure 1). Of the 45 countries included in our analysis, nearly half of the countries had not reached the 2015 GVAP target for DPT3. National level coverage in the most recent year (2016) varied from 13.9% to 99.7%, with ten countries reaching the current 90% GVAP target (Burundi, Burkina Faso, Cape Verde, Eritrea, Mozambique, Namibia, Rwanda, Sao Tome and Principe, Senegal and Rwanda). However, eight countries still had coverage of less than 50%; including Chad (48.4%), Guinea (47.1%), South Sudan (43.5%), Nigeria (42.2%), Central African Republic (41.3%), Angola (40.1%), Equatorial Guinea (26.9%), and Somalia (13.9%).

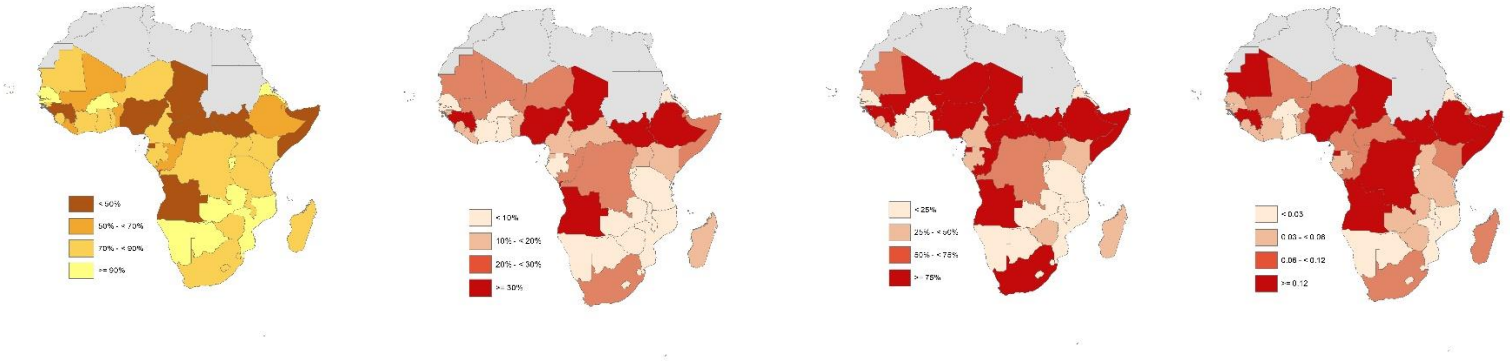
Figure 1. DPT3 coverage trend from 2000 to 2015 among sub-Saharan African countries



In 2016, values for within country shortfall inequality ranged from 1.24% signifying minimal variation across the subpopulations to 43.36%, the threshold index from 0% indicating that at least 80% of all the children under age 2 had received DPT3 vaccine to 100% and Gini coefficient from 0.01 to 0.37. Burundi, Comoros, Lesotho, Namibia, Rwanda, Sao Tome and Principe and Swaziland had the least shortfall inequality (<5%) while Angola, Ethiopia and Nigeria had values greater that 40%. A similar picture was noted for the other measures of inequality with Burundi, Cape Verde, Namibia and Rwanda scoring a threshold index of 0 while Central African Republic and Chad had the highest threshold index. The lowest Gini coefficients were estimated for Burundi, Lesotho, Rwanda and Swaziland (<0.01) and the highest for Ethiopia (0.20), Chad (0.23), Angola (0.24), and Nigeria (0.37).

Countries with the lowest coverage including Guinea, Nigeria, Angola, Chad, South Sudan, Central African Republic and Somalia demonstrated consistently high inequality levels as per the different measures as shown in Figure 2 below. However, countries including Zimbabwe, Uganda, Kenya, Sierra Leone, South Africa and Cameroon have since exceeded the 2015 GVAP target, yet still experience inequality with more than one quarter of their target population falling below 80% coverage in 2016.

Figure 2: Comparison between national DPT3 coverage and inequality-2016



Coverage *Shortfall inequality* *Threshold index* *Gini coefficient*

Country inequality time trends between 2000 and 2016, are illustrated in the three panels in Figure 3. Throughout the time series, the shortfall inequality peaks at 59.1%, the threshold index at 100% and Gini coefficient at 0.47. There was a strong inverse correlation between national level coverage and inequality at -0.81 for the shortfall inequality and -0.82 for both threshold index and Gini coefficient. Across the different dimensions, countries have varying baseline values with more dramatic patterns for the threshold index compared to their shortfall inequality and Gini coefficient trends. For these two, we observe subtler temporal patterns more so for the Gini values compared to shortfall inequality. There is higher within and between country variation in the threshold index with some countries experiencing steep gradients at a specific time point while six countries maintained a constant 100% throughout the entire time spectrum including Angola, Chad, Central African Republic, Somalia, South Sudan and Equatorial

Guinea. Quantifying a country's shortfall inequality values in comparison to the threshold index is critical as it allows for the additional dimension of the baseline coverage. For example, countries which score low on shortfall inequality with a high threshold value such as Benin, Guinea Bissau and Central African Republic in 2016, indicate overall poor performance while those with a contrasting picture such as Kenya with a low threshold index relative to the shortfall inequality indicate potential for interventions targeting isolated population pockets. Detailed country specific distribution of coverage over the years is presented in the Appendix section 1.

Table 1 summarizes the analysis exploring the potential determinants of inequality using within effects model for the shortfall inequality and Gini coefficient, and between effects for the threshold index. We found significant associations for development assistance, governance effectiveness and maternal education. For a 10% increase in DAH per capita, we estimated an associated reduction of 5.38% (95%CI: 0.02 to 10.74%), 25.16% (95%CI:7.6 to 42.68) and 5.51% (95%CI: 0.74% to 10.28%) for the shortfall inequality, threshold index and Gini coefficient respectively. A unit increase in governance effectiveness value was associated in a 3.55% (95%CI: 0.52% to 6.57%) reduction in the Gini coefficient. Similarly, an additional year of maternal education was associated with a 2.21% (95%CI: 0.36% to 4.06%) and 4.31% (95%CI: 1.95% to 6.67%) reduction in the Gini coefficient and 0 and threshold index respectively.

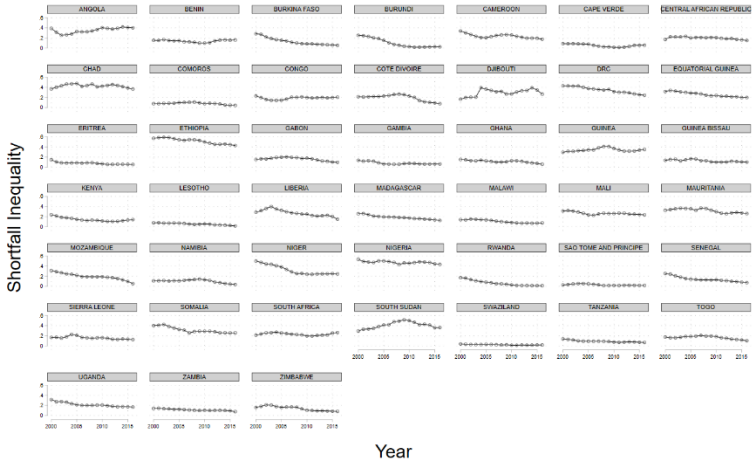
We further stratified countries by levels of governance to test for a possible differential effect of development assistance on inequality. The mean governance effectiveness value ranged from -2.20 in Somalia and South Sudan to 0.48 in South Africa, (median 0.81, IQR -1.23 to -0.53). Countries in the highest quintile of governance included Benin, Cape Verde, Ghana, Lesotho, Namibia, Rwanda, Senegal, South Africa and Uganda with mean governance effectiveness values of at least -0.5. The associations with development assistance increased two fold for the shortfall inequality, and four fold for the threshold index as shown in Table 2. A 10% increase in DAH per capita was associated with reductions in inequality by 11.78% (95%CI: 1.15% to 22.41%) and 87.98% (95%CI: 35.18% to 104.07%) for the

shortfall and threshold dimensions respectively. This finding suggests that countries with better governance may likely exercise more effective implementation of DAH, which in turn translates to higher gains in equity.

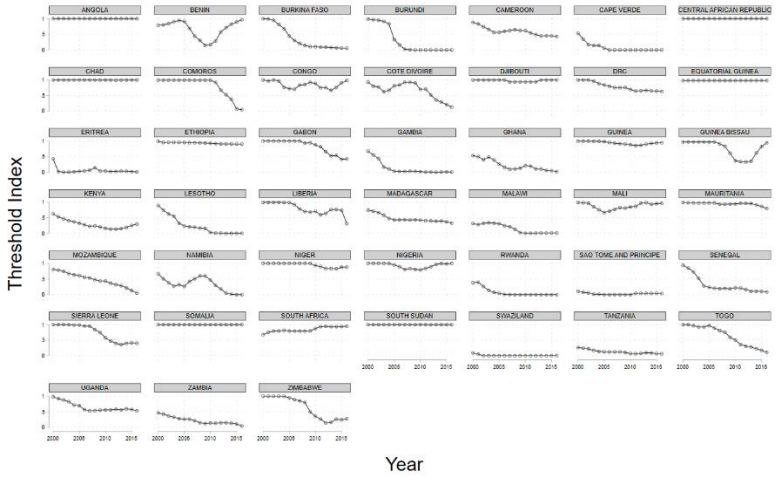
We replicated these analyses using district level estimates of DPT3 vaccine coverage which showed similar findings for DAH, governance and maternal education remaining as illustrated in Tables 3. Findings from the stratified analysis based on DPT3 coverage at admin 2 level are presented in Table 4 in the appendix section II.

A sensitivity analysis using political stability as an alternative measure of governance showed analogous results to our primary analysis. Results of this analysis are presented in Table 8 in the appendix section II.

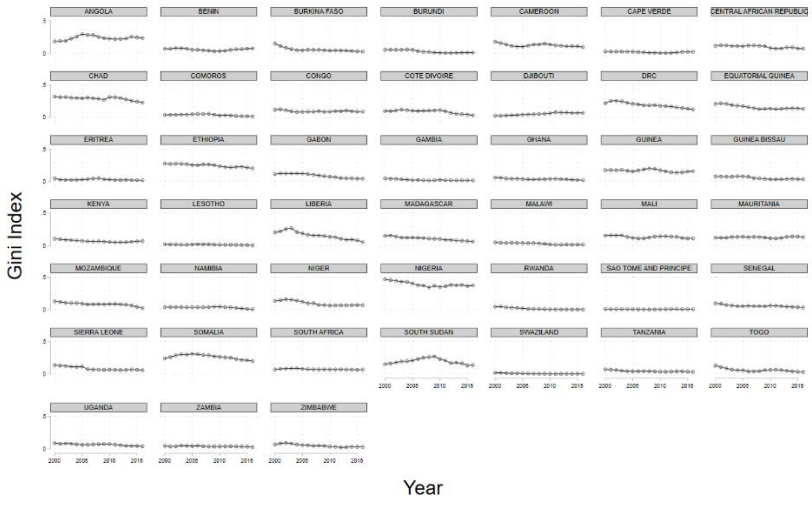
Figure 3: Country specific trends in inequality from 2000 to 2016



The shortfall inequality illustrates the weighted mean deviation from the best performing subnational unit



A country's threshold index quantifies the proportion of the population that remains short of the current global standard



Gini coefficient represents the degree of within country variation

Table 1: Regression results using within and between effects (5km by 5km *pixel* level coverage)

	Shortfall inequality	Threshold index	Gini coefficient
DAH per capita	-0.053 (0.026)**	-0.251 (0.089)**	-0.055 (0.023)**
GDP per capita	-0.006 (0.135)	0.120 (0.329)	0.101 (0.137)
GHE/GDP	-0.002 (0.076)	-0.136 (0.270)	-0.006 (0.080)
Governance effectiveness	-0.332 (0.169)*	-0.965 (0.565)*	-0.355 (0.150)**
Maternal Education	-0.135 (0.071)*	-0.431 (0.120)**	-0.221 (0.091)**
Rural population	0.034 (0.28)	0.006 (0.022)	0.019 (0.021)
Variance(rho/residual)	*0.930*	*0.642*	*0.919*
Number of observations	*705*	*705*	*705*

Results based on a fixed effects model for Shortfall inequality and Gini coefficient, and a random effects model for the threshold index
***significant at 0.05 level*
**significant at 0.1 level*
rho presented for shortfall inequality and Gini
residual variance for threshold index
Number of clusters = 45

Table 2: Regression results from a stratified analysis including countries with governance effectiveness values in the highest quintile (>-0.5)

	Shortfall inequality	Threshold index	Gini coefficient
DAH per capita	0.118 (0.045)**	-0.879 (0.290)**	0.090 (0.050)*
GDP per capita	-3.348 (1.541)	-4.366 (3.072)	-2.508 (1.608)
GHE/GDP	0.369 (0.352)	1.599 (1.147)	0.276 (0.273)
Governance effectiveness	-0.340 (0.300)	-1.438 (1.716)	-0.233 (0.254)
Maternal Education	0.225 (0.226)	-0.287 (0.361)	0.284 (0.189)
Rural population	0.028 (0.059)	0.059 (0.134)	0.012 (0.063)
Variance(rho/residual)	*0.982*	*0.684*	*0.980*
Number of observations	*144*	*144*	*144*

Results based on a fixed effects model for Shortfall inequality and Gini coefficient, and a random effects model for the threshold index
***significant at 0.05 level*
**significant at 0.1 level*
rho presented for shortfall inequality and Gini
residual variance for threshold index
Number of clusters = 9

Table 3: Regression results based on DPT3 vaccine coverage at *Admin2* level. A sensitivity analysis

	Shortfall inequality	Threshold index	Gini coefficient
DAH per capita	-0.018 (0.122)	-0.218 (0.082)**	-0.050 (0.024)**
GDP per capita	0.024 (0.135)	0.097 (0.361)	0.135 (0.148)
GHE/GDP	0.001 (0.077)	-0.366 (0.264)	0.003 (0.086)
Governance effectiveness	-0.317 (0.155)**	-0.931 (0.504)*	-0.349 (0.145)**
Maternal Education	-0.195 (0.094)**	-0.442 (0.129)**	-0.237 (0.102)**
Rural population	0.027 (0.022)	-0.021 (0.028)	0.025 (0.024)
Variance(rho/residual)	*0.915*	*0.725*	*0.928*
Number of observations	*705*	*705*	*705*

Results based on a fixed effects model for Shortfall inequality and Gini coefficient and a random effects model for the threshold index
***significant at 0.05 level*
**significant at 0.1 level*
rho presented for shortfall inequality and Gini
residual variance for threshold index
Number of clusters = 45

Discussion

We investigated the country level characteristics associated with three different dimensions of inequality for DPT3 vaccine coverage across 45 aid recipient sub-Saharan countries. Development assistance, governance, and maternal education were identified as important drivers of equitable uptake of immunization services. Our findings suggest an association between higher amounts of development assistance for immunization and improved equity for DPT3 vaccine coverage. These substantiate previous studies evaluating the relationship between development assistance for immunization and vaccination outcomes. For instance, previous evaluations of Gavi support have linked increasing investments to improvements in coverage for vaccines such as DPT3 vaccine, while vaccine specific DAH has also been associated with improvements for the different targeted vaccines. (35) (36). In addition, pilot evaluations of the Reach Every District (RED) approach supported through development assistance to maximize vaccine delivery particularly to underserved populations have shown substantial improvements in coverage following these strategies (13).

Good governance has been recognized as not only key to improving health care delivery, but as a necessary driver for Universal Health Coverage. Assessments linking governance to health have emphasized decentralization, stakeholder diversity, community engagement and social capital as crucial mechanisms through which health outcomes may be impacted (37). The role of governance in improving health has in fact been articulated through SDG 16 emphasizing the need to develop effective, accountable and transparent institutions and ensure responsive and inclusive decision making at all levels (38). Governance may also be a proxy for other services such as quality of health infrastructure, human resource capacity, human rights to education health and employment, and adoption of local values and needs which collectively translate to effective health service delivery (39).

Relatedly, we find that improvements in equity as a result of increased investments for immunization were augmented in the context of good governance. Indeed, even when resources are available, poor coordination and implementation have been associated with poor health outcomes among aid recipient countries (40). Better alignment in resource planning and coordination,

improving network relationships of interdependence through which service delivery is made and the use of timely evidence regarding health priorities all lead to better efficiency (41). These are key functions of governance which if strengthened, would yield effective health service delivery mechanisms and positive returns for investments.

Multiple studies have documented an inverse association between years of education attained mostly by women, and infant or child health outcomes. Possible pathways of this association include an increased uptake of both curative and preventive services such as vaccination, and better affordability for the needed services (42) (43). In addition to better health seeking practices overall, positive correlations have been documented between maternal education and complete immunization (44).

Using a complementary set of measures, our study adds onto available literature describing the landscape and potential drivers of health inequality in low resource settings. Isolated definitions of inequality offer an important but partial perspective on existing gaps, which makes this analysis a critical addition where we present a comprehensive picture from which countries can benchmark using their individual performance and at the same time evaluate progress against a global reference. Using the shortfall inequality measure countries can borrow and apply lessons from their best performing sub national units, while the threshold index can be used by development partners to make cross-country comparisons. The Gini coefficient is not sensitive to coverage extremes and is therefore a more standardized measure of within country variation which may be of value from a global perspective.

To our knowledge, this is the first study evaluating predictors of inequality based off high spatial resolution vaccine coverage estimates mitigating errors that arise due to masking of localized subpopulation patterns within traditional administrative subnational boundaries. Accuracy of the inequality measures may vary by geographical population distribution resulting into better precision in countries with larger spatial composition, such as Nigeria and Democratic Republic of the Congo compared to smaller countries like Rwanda or Burundi. However, our findings are supported using the sensitivity analysis based on vaccine coverage estimates at admin 2 level which also allow for subnational

policy decisions which are typically instituted at district level. By using DPT3 vaccine coverage, our inequality measures represent both access and retention of care within the childhood immunization program, nonetheless, subsequent evaluations on equity could consider multiple vaccines as more subnational coverage data become available.

There are a number of limitations to this study. Despite the fact that our coverage estimates are less biased compared to those from administrative sources, these are still subject to other types of information bias and sampling error that are characteristic of survey data. Relatedly, the accuracy of vaccination coverage estimates was dependent on availability of georeferenced data (26). Where these were lacking, administrative estimates were used which may have led to suppression of any local spatial variations. This calls for continued improvements in the quality of existing surveillance systems to allow for better precision in mapping health outcomes. Due to limited availability of program specific domestic health expenditure information, we did not include government spending allocated specifically to immunization, or other domestic spending such us out of pocket or private expenditures for immunization. An additional limitation of our top to bottom assessment approach for DAH is based on the potential for aid leakage into less productive spending along disbursement chains which would likely lead to an overestimation of the observed effects (45). Future assessments should consider the use of country led financial reporting mechanisms such as the System of Health Accounts (SHA) in order to allow for more robust and comprehensive evaluations of the different immunization program investments. The reliability of the World Bank's governance indicators has been challenged as these are based on subjective perceptions based on survey data that is prone to variability in composition and availability from country to country (46). While the aggregate indicators build on multiple data sources capturing the broad concepts of leadership, assessments highlighting the role of governance consequently provide an additional incentive to continue refining the construct validity of available metrics to allow for more robust evaluations of governance.

Our analysis is based on time series cross sectional approaches and therefore do not represent causal relationships between the given predictors and equity.

Despite these caveats, our findings provide an important starting point in the discussion of feasible causal theories in settings where the highest health inequalities have been documented.

Countries in sub-Saharan Africa bear a disproportionate distribution of vaccine preventable disease burden relative to the available resources required to address these (47). The global response to this burden has been substantial with a continued push for governments to prioritize funding for health to ensure sustainable health outcome improvements.

In order to realize the SDG agenda that is committed to leaving no one behind, resource impact evaluations should prioritize inequality from which lessons to address existing gaps can be drawn. This paper provides a critical policy message for both national and international audiences. The potential impact of immunization program investments on inequality is promising, yet, this can be undermined when mechanisms for resource implementation and accountability are weak. Therefore, it is essential that SSA countries continue to strengthen existing platforms to yield the most of inter-sectoral partnerships, and that development partners uphold requirements for accountability and efficiency in order to achieve universal vaccine coverage.

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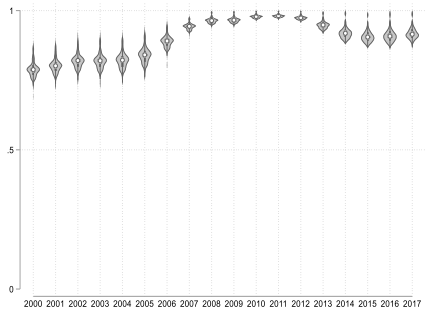
Supplementary materials

Appendix I

Cape Verde



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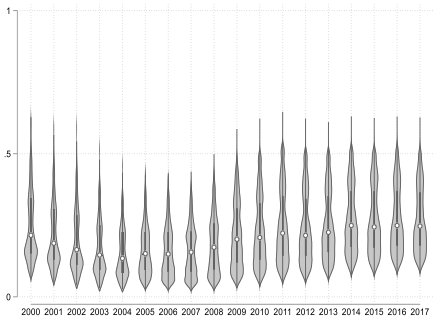

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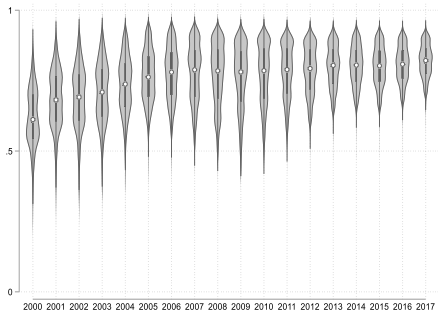

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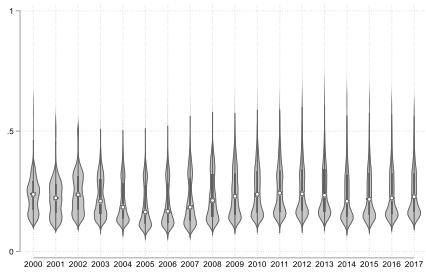

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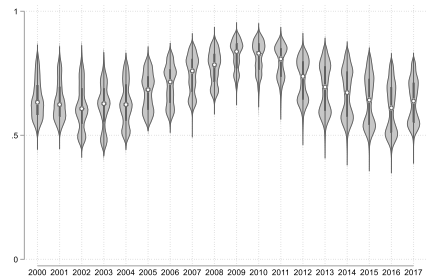

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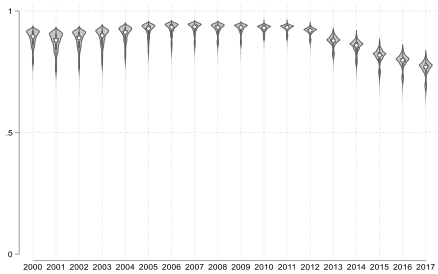

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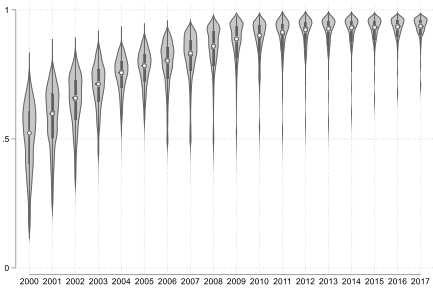

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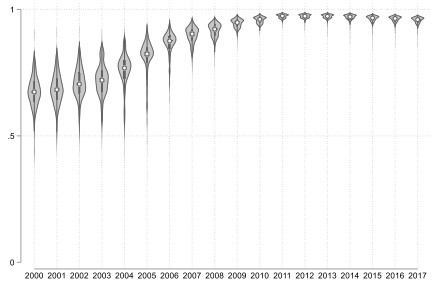

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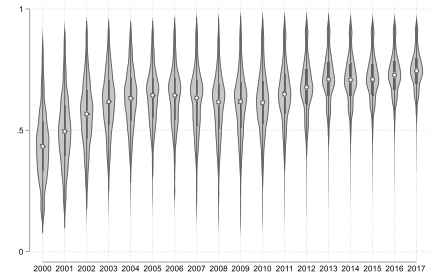

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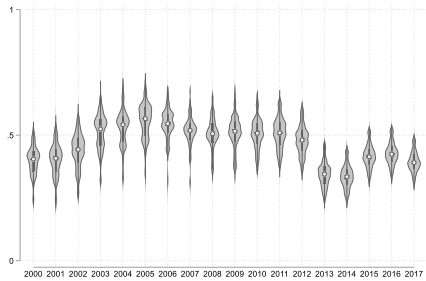

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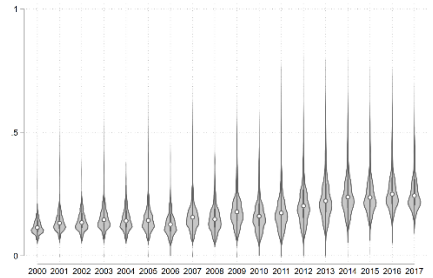

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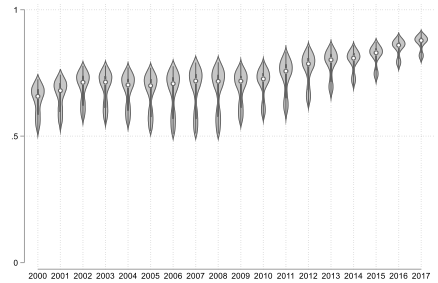

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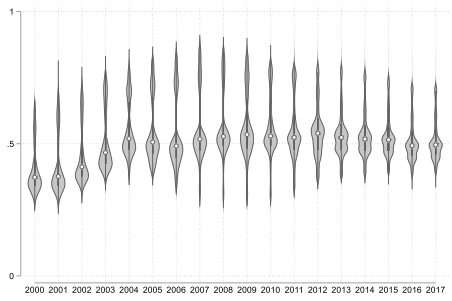

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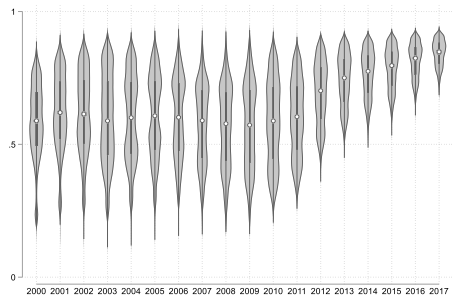

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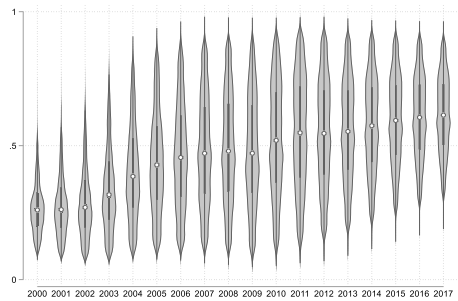

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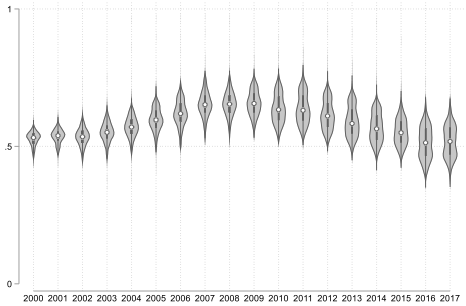

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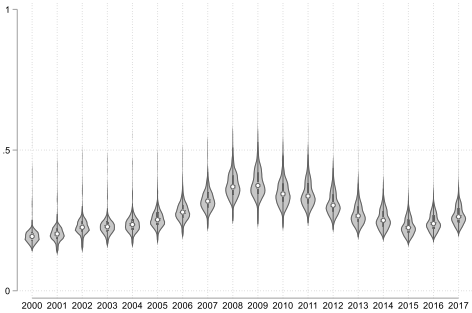

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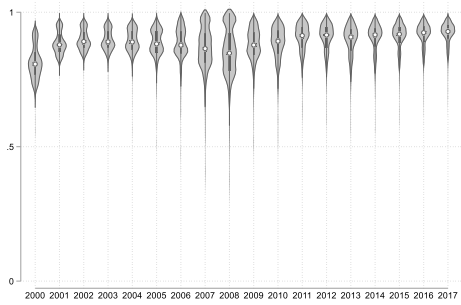

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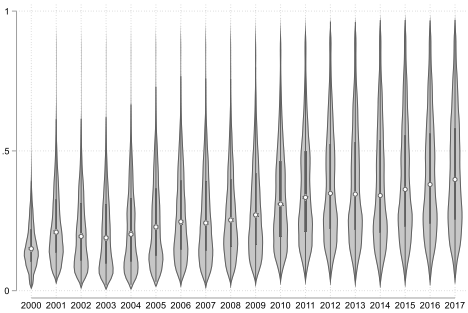

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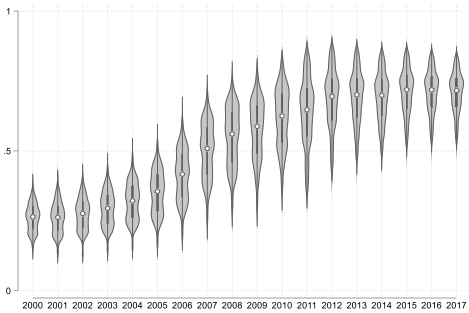

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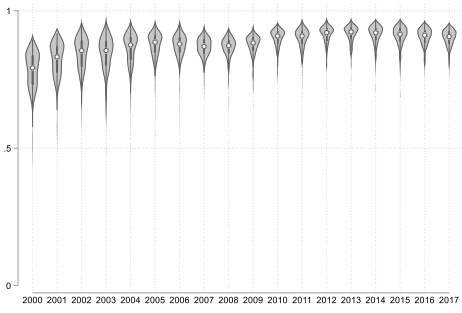

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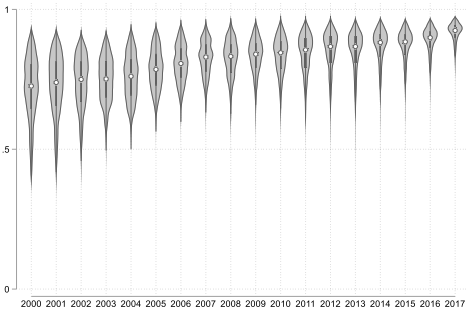

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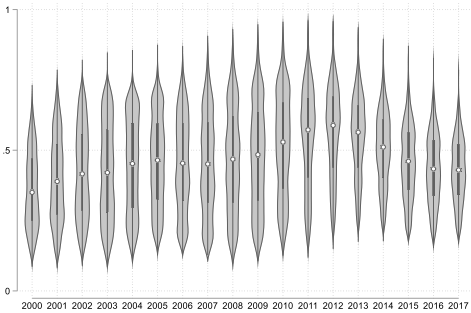

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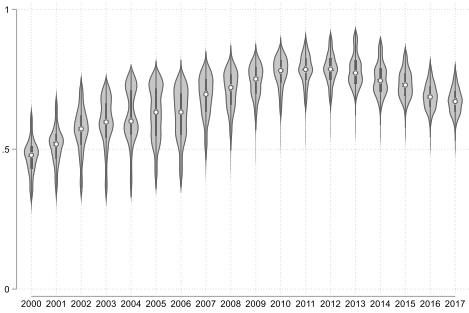

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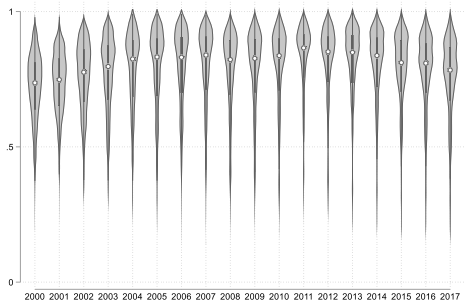

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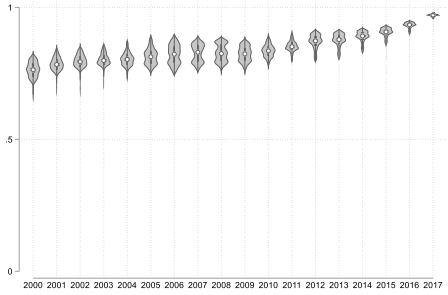

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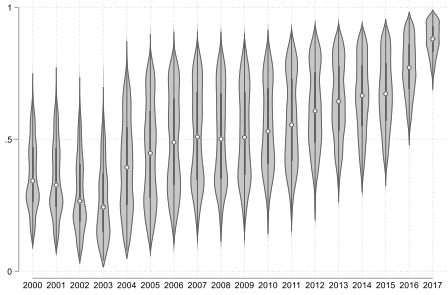
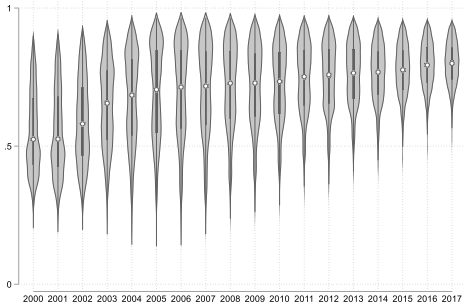
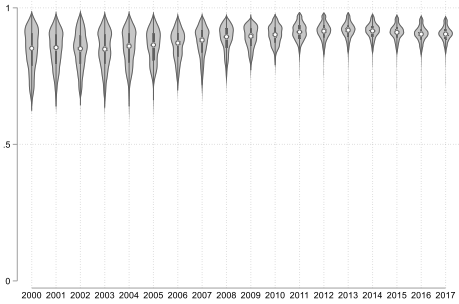


Madagascar



Malawi



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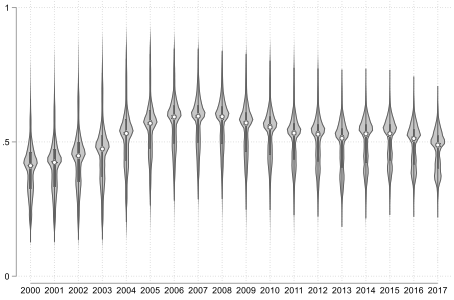

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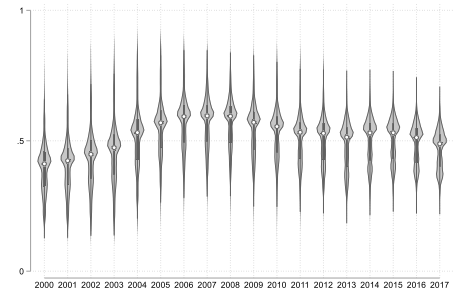

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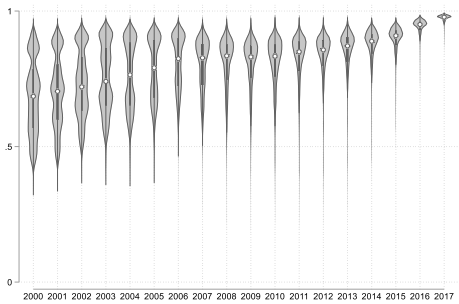

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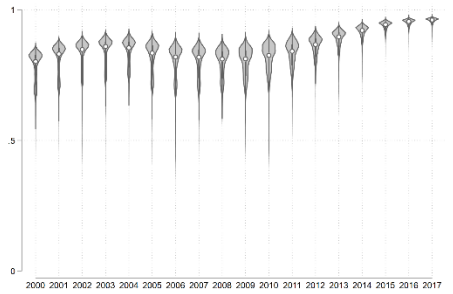

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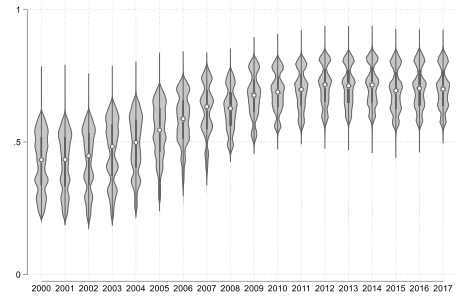

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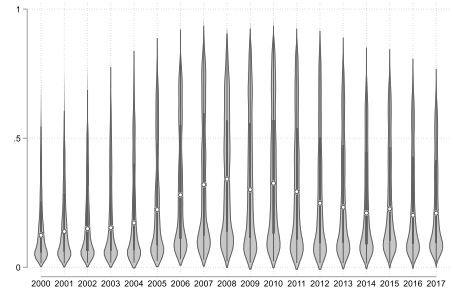

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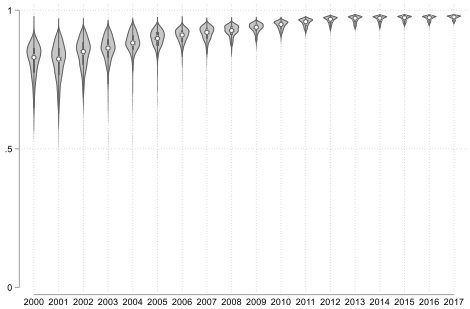

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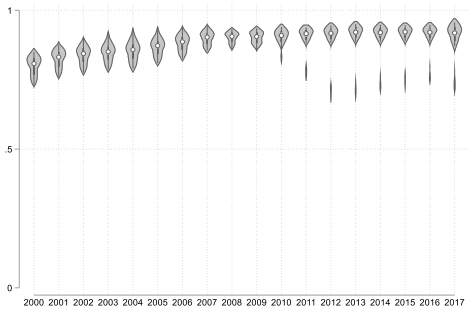

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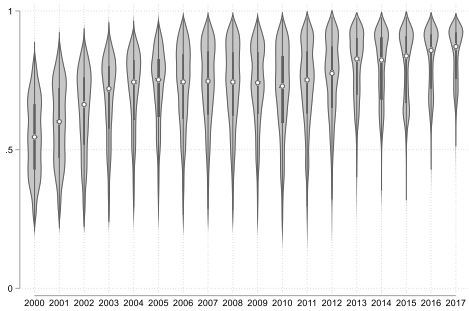

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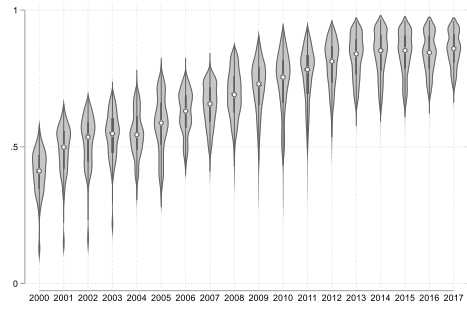

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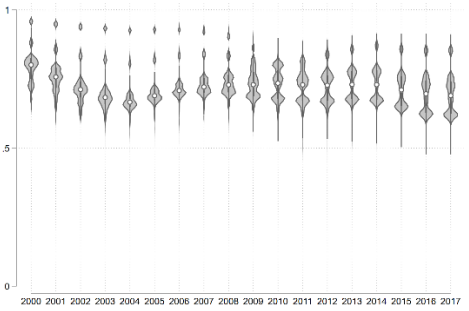

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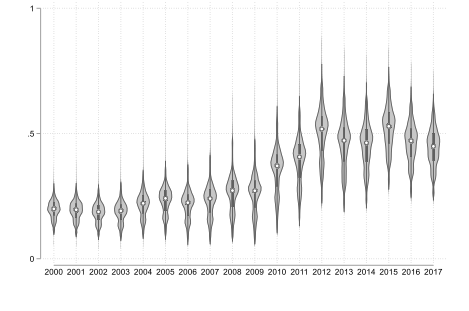

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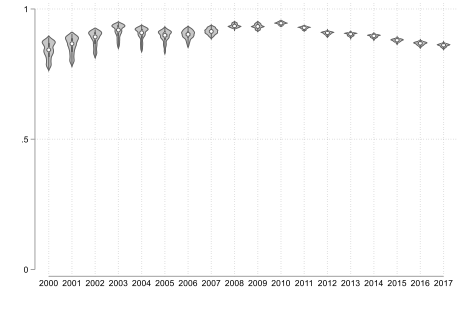

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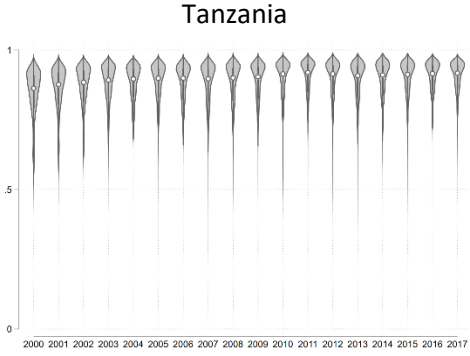

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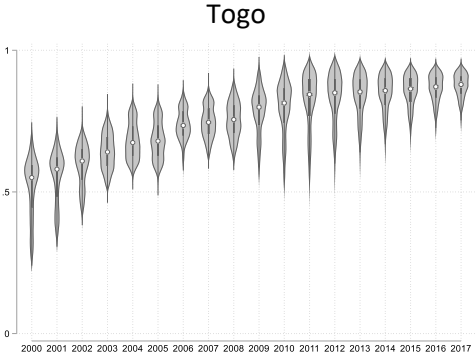

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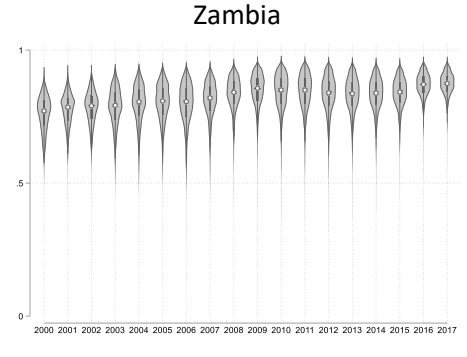

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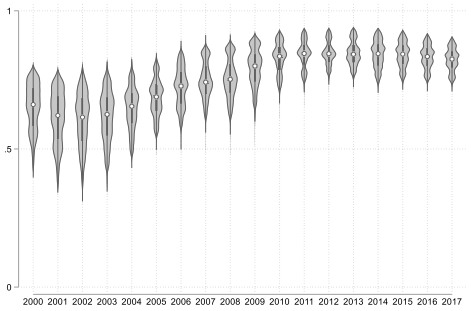

Appendix II

Table 4: Regression results from a stratified analysis including countries with governance effectiveness values in the highest quintile (>-0.5) using ADMIN 2 level DPT3 coverage

	Shortfall inequality	**Threshold index**	**Gini coefficient**
DAH per capita	0.104 (0.050)*	-0.757 (0.243)**	0.092 (0.050)*
GDP per capita	-2.587 (1.776)	-4.760 (3.375)	-2.833 (1.803)
GHE/GDP	0.277 (0.321)	1.829 (1.135)	0.197 (0.287)
Governance effectiveness	-0.226 (0.328)	-0.910 (1.452)	-0.281 (0.260)
Maternal Education	0.199 (0.225)	-0.217 (0.410)	0.228 (0.201)
Rural population	-0.003 (0.068)	0.048 (0.143)	0.022 (0.075)
Variance(rho/residual)	*0.979*	*0.738*	*0.980*
Number of observations	*144*	*144*	*144*

***significant at 0.05 level*
**significant at 0.1 level*
rho presented for shortfall inequality and Gini
residual variance for threshold index
Number of clusters = 9

Table 5: Regression results using **political stability** as an indicator for governance using DPT3 coverage at 5km by 5km pixel level. A sensitivity analysis

	Shortfall inequality	**Threshold index**	**Gini coefficient**
DAH per capita	-0.047 (0.026)*	-0.221 (0.082)**	-0.048 (0.172)**
GDP per capita	-0.097 (0.138)	-0.013 (0.321)	0.014 (0.131)
GHE/GDP	-0.025 (0.076)	-0.236 (0.242)	-0.031 (0.088)
Political stability	-0.054 (0.028)**	-0.237 (0.119)*	-0.079 (0.075)
Maternal Education	-0.109 (0.074)	-0.412 (0.117)	-0.192 (0.095)**
Rural population	0.038 (0.021)	0.003 (0.023)	0.019(0.023)
Variance(rho/residual)	*0.979*	*0.643*	*0.919*
Number of observations	*705*	*705*	*705*

***significant at 0.05 level*

**significant at 0.1 level*
rho presented for shortfall inequality and Gini
residual variance for threshold index
Number of clusters = 45

Appendix III

WHO's conceptual framework on the determinants of health equity