POPULATION HEALTH INITIATIVE
UNIVERSITY of WASHINGTON

Targeting Key Factors to Realizing Improved Global Vaccination Coverage: Final Report

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Authorship and Funder

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Acronyms

VIP	Vaccine Improvement Potential
SDI	Socio-demographic Index
MOV	Missed opportunities for vaccination
DTP1	Diphtheria-tetanus-pertussis vaccine, first dose
WHO	World Health Organization
UNICEF	United Nations Children's Fund
SAGE	Strategic Advisory Group of Experts on Immunization
MMR	Measles-mumps-rubella vaccine
GDP	Gross Domestic Product
DHS	Demographic and Health Survey
HAQI	Healthcare Access and Quality Index
IHME	Institute for Health Metrics and Evaluation
DAH	Development Assistance for Health
MCV1	Measles-containing vaccine, first dose
DALYs	Disability-adjusted life years
CAR	Central African Republic
NSTOP	National Stop Transmission of Polio program
NPHCDA	National Primary Health Care Development Agency
NFELTP	Nigeria Field Epidemiology and Laboratory Training Program
CDC	Centers for Disease Control and Prevention
OR	Odds Ratio
BCG	Bacillus Calmette–Guérin vaccine
HepB3	Hepatitis B vaccine, third dose
Hib3	Haemophilus influenzae type B vaccine, third-dose
MCV2	Measles-containing vaccine, second dose
PCV3	Pneumococcal conjugate vaccine, third dose
Pol3	Polio vaccine, third dose
RCV1	Rubella-containing vaccine, first dose
RotaC	Rotavirus series completed, two or three doses

Executive Summary

This study sought to create a composite measure – the "Vaccination Improvement Potential" (VIP) index – that summarized the relationship between increased immunization coverage and a few key factors and variables. The project team was successful in its work and has now published the VIP Index, which for the first time ever organizes data regarding key indicators and trends into a single index. The comprehensive nature of this index will allow key stakeholders to make easy comparison between locations and across time to better target efforts to improve and/or maintain vaccination coverage levels in a country or region.

To create the VIP Index, the project team first identified countries that showed above-average improvement in vaccination coverage over the past decade. We also investigated the extent to which missed opportunities to vaccinate children (MOV) have been addressed in these high performing countries. We next conducted a literature review to identify the most important factors that contributed to vaccination coverage improvements in different regions of the world and across different socio-demographic ranges. We organized 13 different data sources associated with improved immunization rates for more than 200 countries across 30 variables. These variables included measurements of national health expenditure, development assistance for health, characteristics of the health system, socio-demographic attributes, and the public's trust in vaccines.

To further validate the effectiveness of the VIP Index, we conducted a counterfactual analysis of vaccination coverage and disease burden in which we modeled the result of the worst performing country from the low SDI group achieving the VIP Index value of the best performing country in the low SDI group. The counterfactual analysis demonstrated that improvements to the VIP Index in the lowest-performing country could lead to almost a three-fold improvement in vaccination coverage and reduced disease burden.

We found there were regional patterns in VIP Index changes over time. Consistent high performers included countries in Western Europe and high-income North American and Asian countries. There were also important differences in subcomponents of the Index between regions. For example, increased vaccine hesitancy in recent years was found to pose a risk to high vaccine coverage in Western Europe and several regions of Asia. In addition, lower levels of health spending per capita and development assistance could jeopardize ongoing improvements in coverage in several areas of sub-Saharan Africa.

The results of this study informed the creation of a web-based dashboard that allows users to explore the results of our VIP Index and other historical trends related to vaccination coverage and mortality data associated with vaccine-preventable diseases. This web-based portal also highlights key reflections from the study to offer users both a data driven and narrative overview of the project.

The VIP index is a first-of-its-kind tool for understanding the capacity that exists in a country to realize improved immunization rates. It creates a new resource that can guide researchers, policymakers, and health officials to more effectively deploy resources to realize improvements in vaccination coverage, assess the impact of those improvements, and identify countries that might require additional support to improve vaccine coverage.

Background

Recent Trends in Global Immunization

Childhood immunizations coverage has increased in many areas of the world in the last 40 years.[1] For example, global coverage of the diphtheria-tetanus-and-pertussis vaccine (DTP) vaccine increased from 39.9% to 64.2% between 1980 and 1990.[1] Most recently, however, improvements in global vaccination rates have been plateauing.[2] Some regions have experienced stalled or decreased vaccination rates between 2010 and 2019 for certain immunizations such as DTP, measles (MCV), and polio (Pol).[1] Increasing the rate of childhood immunizations continues to be a key goal of the World Health Organization (WHO) as recent estimates suggest there remain roughly 20 million children who are unvaccinated or under-vaccinated across different regions of the world.[2]

Existing Frameworks to Predict Immunization Improvement Potential

Global vaccination rates can be affected by disparate issues, such as healthcare system characteristics, socio-economic and demographic circumstances, and psychological or attitudinal barriers. Several of these factors can vary across time, place, and vaccine type, further complicating efforts at understanding them at a global scale.[3–5]

There are several conceptual frameworks that researchers have developed to group factors related to vaccination coverage. One review of 43 studies related to non-socio-demographic determinants of vaccination coverage identified 23 determinants of vaccination uptake.[6] These were synthesized in a framework that includes five domains: Access, Affordability, Awareness, Acceptance, and Activation. A different systematic review led to a framework that included three types of factors: 1) Intent to Vaccinate, 2) Community Access, and 3) Health Facility Readiness.[7] Further, the WHO has also developed a framework called SAGE for factors related to vaccine hesitancy that includes 23 different factors.[4]

Demographic and Socioeconomic Factors Impacting Vaccination Coverage

Many studies have identified demographic and socioeconomic factors associated with vaccination coverage or uptake. The effect of some of these factors on vaccination uptake and coverage are modified by income or levels of development. A systematic review in Europe of MMR vaccine uptake found associations between ethnicity, low income and education levels, higher number of children, and irregular marital status with lower MMR vaccine uptake.[8]

In lower income countries, studies of demographic factors commonly reported sociodemographic characteristics such as urban vs. rural, gender of children, number of children, maternal age, religious beliefs, and minority group membership as indicators of vaccine uptake. Young maternal age, number of children, large family size, and low parental education have also been identified in multiple studies to be inversely associated with childhood vaccine uptake in lower income countries.[9–11]

A 2018 study of Chinese vaccination rates found that male children, minority children, those born at home, those who immigrated from an adjacent county, and those living in urban-rural fringe areas or mountainous areas had significantly increased odds of not being fully immunized.[12] The number of children in a family and migration status were also implicated with low vaccine uptake in sub–Saharan Africa by a 2020 systematic review.[13] The educational level of a child's caretaker has been shown to be related to vaccine uptake in many studies, with lower levels of education being associated with lower levels of uptake.[8–12,14–17] The vaccination status of the caregiver as well as their occupation has also been associated with vaccine uptake.[9,13,14,16] Finally, low family income and other financial barriers have been associated with levels of vaccine uptake in multiple studies. [3,8,11,13–15,17]

The Anti-vaccination Movement

The anti-vaccination movement is a social and cultural phenomena influenced by an array of complex factors that are having an increasingly strong impact on attitudes surrounding vaccine hesitancy.[18] Although anti-vaccine sentiments have existed since the invention of vaccines, the modern popularity of the "anti-vax" movement has its roots in a retracted paper that incorrectly related the MMR vaccine with autism in 1998. The incorrect association was repeated across media and by various high-profile celebrities that led to the movement gaining greater prominence in the United States.[18] Through the widened accessibility of the internet in the years following this publication, the anti-vax movement has used this medium to widely and rapidly disseminate their ideas. Recent evidence suggests that confidence in the importance, safety, and effectiveness has been decreasing in numerous countries around the world, including Azerbaijan, Indonesia, Nigeria, Pakistan, and Serbia.[19]

The Covid-19 pandemic offered a unique opportunity for researchers to study how the proliferation of vaccine misinformation spreads online and to what degree people from different demographic backgrounds engage with its content. Multiple studies have analyzed the spread of vaccine misinformation on popular social media sites.[20–23] For example, a randomized control trial aiming to estimate the impact of exposure to misinformation on participants' intent to get vaccinated was conducted in the United Kingdom and the United States during September 2020. This study found that exposure to misinformation lowers the intent of an individual to accept a Covid-19 vaccine among those who had previously reported that they would "definitely" accept such a vaccine. Additionally, misinformation that made use of scientific jargon induced a greater drop in intent to accept vaccination among participants. Not all demographics were shown to be equally impacted by misinformation: lower income groups in both countries were less likely to lower their intent to vaccinate than higher income groups.[24] Although higher income levels are frequently seen in studies to be associated with higher vaccine uptake, a study in California of clusters of children who received nonmedical exemptions from mandated vaccines showed clusters are more likely to contain families who are white, highly educated, and of higher income.[25] The association of parents who intentionally delay vaccination with higher incomes has also been identified and discussed in the review by Dubé et al.[18] The authors propose that this may be in part a result of the success of previous vaccination programs that have given parents less exposure to the dangers of vaccine preventable diseases, thus affording a parent's fear of vaccine side effects to surpass the fear of the diseases themselves.

There are also related political and ideological factors at play in parents who delay childhood vaccination. Although the complexity of ideologically-based factors makes them harder to quantify, they remain an important feature of the anti-vax movement worth further investigation. In an article published in Gender and Society, the author conducted qualitative interviews of parents who have delayed childhood vaccinations. The common themes in participant answers showed that Neoliberal cultural frames of individual choice emphasizing the mother's sole focus on their own children and a disregard for community health serve as an ideological basis for vaccine exemption. The author stated these attitudes are largely a reproduction of cultural values centered on individualism and class-based privilege of those living in wealthy communities.[26]

The "anti-vax" movement is a complex interaction of ideological, political, and social factors influenced by loosely connected organizations and individuals. Through social media platforms anti-vax actors have been able to communicate to wide audiences, and impact intentions to become vaccinated. Due to the heterogeneous nature of the movement, intervention and fact-checking campaigns will need to be specifically tailored to combat different styles of misinformation based on delivery method, target audience, and ideological basis.

Structural Factors Impacting Vaccination Coverage

The economic and political domains of a country or region interact with and shape individual and population health outcomes, including vaccination rates. Many studies have examined the impact of government spending on healthcare, healthcare infrastructure, and policies related to vaccination programs. For example, a 2021 study explored the relationship between economic growth and healthcare spending in low-income countries, finding that government healthcare spending per capita and per birth on routine immunizations were significant positive predictors of vaccination coverage. In contrast, it was found that Gross Domestic Product (GDP) per capita and aggregated development assistance for healthcare per capita were not significantly associated with vaccination outcomes in low-income countries. This indicates that a focus on growth in GDP per capita and healthcare development assistance alone may not be enough to increase vaccine coverage in low-income countries.

At the global level, a 2016 analysis found the proportion of births attended by healthcare staff correlated significantly with immunization coverage across multiple regions. [3] For example, a study in Afghanistan found that delivery in a healthcare facility and having a healthcare facility visit in the last 12 months were strong indicators of individual vaccine status.[9] Similarly, a study in India found that vaccination status was closely related with antenatal care visits, non-institutional delivery, and maternal tetanus vaccine status.[10]

Missed Opportunities to Vaccinate Children

One promising approach to increase childhood vaccination rates is addressing missed opportunities for vaccinations (MOV). MOV refer to instances when children who are of an appropriate age to receive a vaccine during a visit to a health facility, but do not receive the necessary vaccine. Past studies have found childhood and family characteristics are strong predictors of MOV. Factors such as a child's age, sex, and birth order as well as maternal age, mother's education attainment, and family income were all significantly associated with MOV in studies conducted in Africa.[27]

The Use of Modeling and Counterfactual Analyses in Vaccination Coverage

Previous research has helped establish the link between national vaccination coverage and disease burden. For instance, a 2013 article established that there was a relationship between vaccination coverage and disease burden in 29 countries in Europe that showed a significant association between disability adjusted life years and vaccination coverage.[28] A historical analysis of mortality burden in the Netherlands showed strong negative association with mass vaccination campaigns drastically reducing childhood mortality due to vaccine preventable diseases.[29] Investigations into seasonal influenza and rotavirus disease burden have also shown reductions in disease related mortality associated with greater vaccine uptake.[30, 31]

Research Objectives and Approach

Our project had four main objectives that sequentially built upon each other.

Objective 1:

- Identify the factors that influenced vaccination coverage improvement among countries with a low socio-demographic index.
- Approach: Analyze global trends in vaccination coverage and review the published literature for select locations.

Objective 2.

- Identify the extent of missed opportunities to vaccinate children (MOV) in select high-performing countries.
- Approach: Utilize survey data on vaccine coverage and family characteristics over multiple time points to understand patterns and trends in missed opportunities.

Objective 3.

- Develop an index of "Vaccine Improvement Potential" (VIP) in each country between the periods of 1990 to 2019 to summarize the capacity that exists in each location to realize improved immunization rates.
- Approach: Organize publicly available data on the most important factors leading to improved vaccination coverage and combine into a single summary measure.

Objective 4.

- Demonstrate a potential application of the VIP index to model alternate scenarios of index improvement and immunization coverage on disease burden.
- Approach: Model the impacts of the worst performing country in the low SDI group achieving the same VIP Index value as the best performing country on immunization coverage. Also conduct a counterfactual analysis of disease burden for different levels of immunization coverage in this low performing country.

Methods

Objective 1. Methodology to Identify Factors Influencing Coverage Improvement

We calculated the percent change in childhood immunization coverage between 2014 and 2019 for 11 vaccines in more than 200 countries using 2020 Global Burden of Disease Data.[32],[1] We used the Socio-Demographic Index (SDI) value of each country in 2019 to create low SDI (≤0.579), middle SDI (0.58–0.742), and high SDI (>0.743) groupings to make appropriate comparisons between locations.[33] Any country that showed improvement that was 1.5 times the interquartile range above the third quartile was identified as a "high performer." We then conducted a thorough review of scientific literature regarding vaccination coverage and improvements in the top three high-performers to identify the most important factors that helped explain the greater-than-expected improvements.

Objective 2. Methodology to Assess Missed Opportunities to Vaccinate

We used data from the Demographic and Health Survey (DHS) in Nigeria[34,35] and Liberia[36,37] to assess whether high-performing countries in the low-SDI group had addressed missed opportunities for vaccination (MOV) in children. Exact details on the way we calculated MOV have been described in a prior publication.[17] For each child, we calculated missed opportunities for DPT and MCV vaccinations using data on child's age, vaccine records included in the survey, and each country's recommended vaccine schedule. In each country we fit a logistic regression model with missed opportunity as a binary outcome and predictor variables that included certain characteristics of the mother, such as age, education, literacy, marital status, occupation, and other household characteristics, such as household size, assets, urban/rural surrounding, and subnational region. We used a 0.05 significance level to identify which factors were most associated with MOV. We also included a term for the year in which the data was collected in order to evaluate whether MOV probabilities have changed over time. For variables found to be significantly associated with MOV, we calculated the predicted probability of having an MOV within different strata of that variable.

Objective 3. Methodology to Develop Vaccine Improvement Potential Index

Thirteen different indicators associated with improved immunization rates were combined to create a single composite measure of vaccination improvement potential (Table 1). The indicators were selected after reviewing the literature on key factors related to improving vaccination coverage globally and among the countries identified as part of Objective 1. Two indicators came from the latest available Global Burden of Disease estimates: the socio-demographic index (SDI)[33] and the Healthcare Access and Quality Index (HAQI)[38]. Three indicators came from the 2017 IHME Financing Global Health Report[39,40]: total health spending, government health spending, and development assistance for health. Public trust in government was obtained from the World Values Survey.[41] Perceptions of government corruption came from Transparency Intl.[42] Three indicators came from the United Nations: births attended by skilled health workers[43], immigrant population[44], and urban population.[45] Three variables related to the public's belief that vaccines are safe, important, and effective came from the Vaccine Confidence Project.[19]

We used the geometric mean to combine information from several indicators together. This method was chosen in part because of its simplicity and because it has been successfully used to construct several health-related indices.[33, 46] Data sources that were uniformly available for multiple regions and years were prioritized.

Table 1. Variables and their range in years and locations that were used to construct the VIP Index.

	Indicator	**Years**	**Geographies Represented**
1	Socio-demographic Index	1990 – 2019	204
2	Total health spending per person	1995 – 2018	204
3	Government health spending per total spent	1995 – 2018	204
4	Development assistance for health per person	1995 – 2018	204
5	Healthcare Access and Quality Index	1990 – 2016	195
6	Corruptions Perception Index	2012 – 2020	178
7	Trust in Government	1990 - 2020	101
8	Births attended by skilled healthcare staff	2000 – 2020	196
9	Immigrant population proportion	1990 – 2020	203
10	Urban population proportion	1950 – 2020	204
11	Vaccines considered safe	2015 – 2020	145
12	Vaccines considered important	2015 – 2020	145
13	Vaccines considered effective	2015 – 2020	145

We ensured that all data satisfied the following conditions in order to calculate the geometric mean for each year and location: (1) all predictor variables were continuous, (2) there were no negative numbers, (3) there were no values of zero, (4) all numbers were either positively or negatively associated with the outcome being measured, (5) all variables were normally distributed or could be transformed to approximate a normal distribution, and (6) there were no missing values.

The only variable with zero as a potential value was Development Assistance for Health (DAH) since in some instances countries might not be eligible to receive funds due to their high-income status. DAH was only included as a component in the index for locations that were eligible to receive such funds each year. DAH eligibility was determined yearly for each location using eligibility criteria that is based on country income level as determined by the World Bank.[47] High-income countries and upper middle-income countries were deemed not eligible for development assistance and low-income countries were marked as eligible. Middle income and lower middle-income countries were considered eligible only for all years in which they received funds. All locations had a constant of 1 added to avoid zero values for countries that were determined to be eligible for DAH for a given year but still received no donations.

Some indicators are not available for all years (e.g., immigrant population size is estimated every five years) and some responses were missing for some locations. To address, we fit a regression with year as a predictor in each country to ensure the following variables had a complete time series: SDI, total health spending, development assistance, government health spending, HAQI, births attended by skilled, immigrant population size, urban population, and trust in government. The regression model depended on the outcome variable: we used linear regression for monetary variables (such as total health spending, and development assistance for health) and logistic regression for variables that range between 0 and 1 (all other variables). Although variables such as those related to vaccine confidence and corruption perception had some missing data as well (see Table 1), we did not use regression to complete these values to avoid extrapolating beyond the observable data. We included these variables in our analyses for years and locations in which they are available for a particular country.

The complement of two variables – Trust in Government and Immigrant Population Size – were used since the literature suggests that in these cases a higher number is associated with lower vaccination improvements. Each of these variables was subtracted from 100 to obtain the complement value.

Total health spending and development assistance for health were log-transformed in order to approximate a normal distribution. In addition, these two variables were also re-scaled into a number that ranged from 0 to 1 using the following normalization formula:

$$Variable\ index\ value = \frac{actual\ value - minimum\ value}{maximum\ value - minimum\ value}$$

To validate our newly constructed index, we fit a logistic regression model in which the index results were the independent variable and the first dose of DTP and MCV coverage was the dependent variable, controlling for region and year. We used a random subset of 80% of the complete dataset, excluding the year 2019 to fit the model (training data set). We then used the model to predict vaccination coverage in the remaining 20% of the dataset (the testing data set) as well as in 2019, the most recent year in which vaccination coverage data was available. We then calculated a Brier Score for each set of predictions to evaluate the success of our models which used index result to predict vaccination coverage.

Objective 4. Methodology to Demonstrate Potential VIP Application

Model impacts of worst-performer becoming best performer in low-SDI group

We used a logistic regression model to predict vaccination coverage in 2019 if the country with the lowest score on the VIP Index was able to raise its value to that of the country with the highest score. Both countries of comparison were drawn from the low-SDI category. We used the logistic regression previously used in Objective 3 in which measles vaccination coverage was the dependent variable and the VIP Index was the independent variable, while controlling for year and geographic region. Additionally, we repeated our analysis with diphtheria vaccination coverage being the dependent variable.

Counterfactual analysis of disease burden for different scenarios of immunization coverage

We fit a log-linear model to predict disease burden in our low-performing country under different levels of vaccination coverage. The outcome of interest in our model was the burden of measles and diphtheria measured in disability-adjusted life years (DALYs) per 100,000 people. The main predictor variable was the percentage of children immunized against measles or diphtheria.

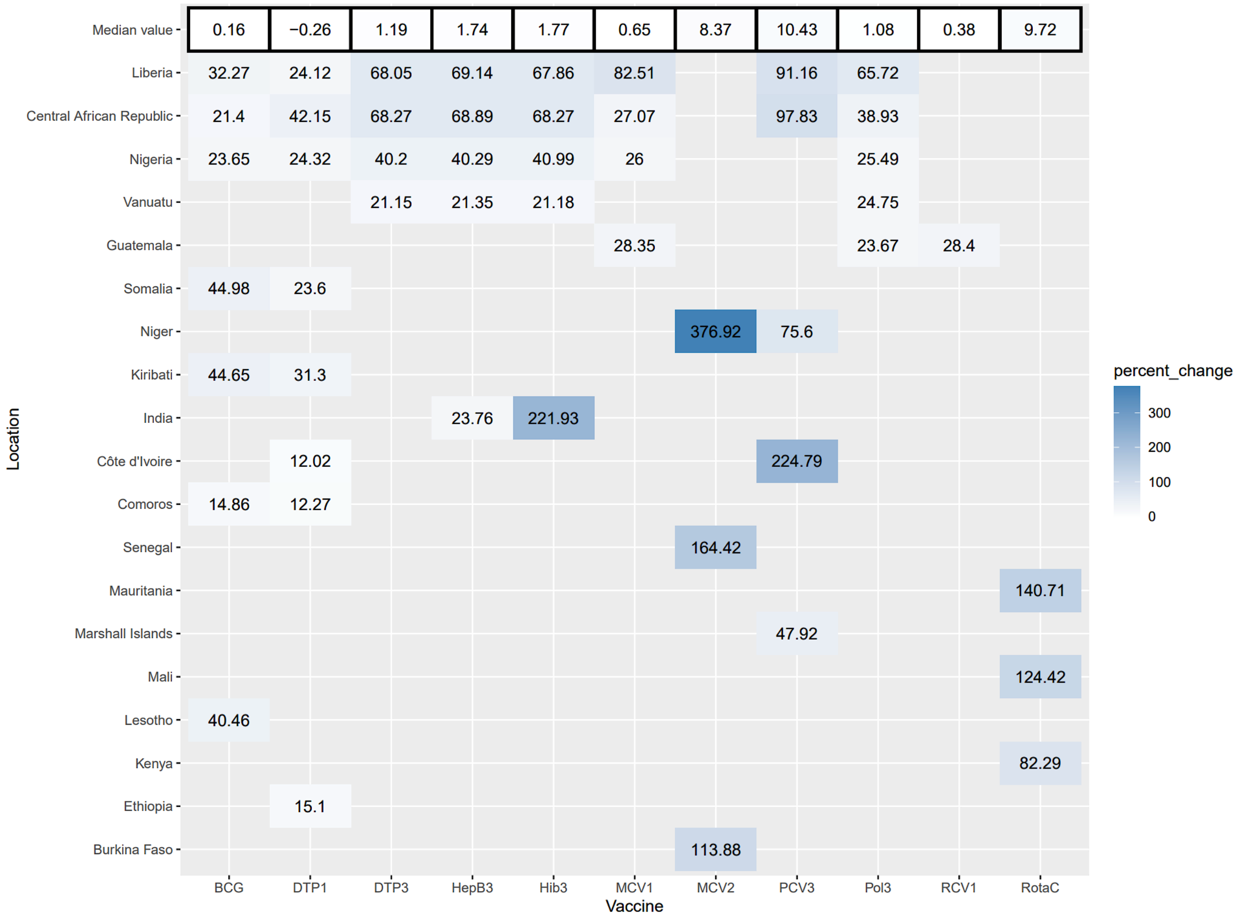
Results

Objective 1. Results of Identifying Factors Influencing Coverage Improvement

Identification of high-performing locations

Between 2014 and 2019, a few low-SDI countries were very successful at improving their vaccination coverage. For instance, measles vaccination coverage saw a median increase of 0.65% between 2014 and 2019 among all low-SDI countries. However, during this same period Liberia, the Central African Republic (CAR), and Nigeria saw an 83%, 27%, and 26% increase, respectively. Additionally, each of these countries exceeded the global median percent change for seven or more different vaccines during this time (see **Figure 1**).

Figure 1. Percent change in vaccination coverage for low-SDI countries with above average improvement in vaccine coverage between the years 2014 – 2019. Darker shading indicates much better-than average improvement for vaccine coverage during this period. Blank cells mean the location was not considered high-performing for that vaccine.



Despite key geographic, political, and historical differences between Liberia, the Central African Republic, and Nigeria, there were a few key similarities that likely influenced their above-average improvements. During these years, each of these locations experienced public health emergencies that severely impacted health services, including routine immunizations. For instance, the Ebola epidemic in Liberia in 2014 impacted primary care services, including routine immunizations.[48] Internal armed conflict in CAR between 2012 and 2015 led to a disruption of the cold chain necessary for vaccine storage, closure of health facilities, and weakening of disease surveillance systems. [49] Similarly, barriers to vaccination in Nigeria between 2005 and 2009 included structural issues including lack of security and armed conflict [50] as well as cultural and religious beliefs affecting vaccine acceptability.[51]

During these crises, increased attention to the issue of childhood immunization coverage led to increased technical assistance and funding by multilateral organizations and other international donors. The need to address these emergencies often led to scaled-up efforts to vaccinate children, investments in new technologies to identify high need populations, and implementation of new strategies to reach low-uptake communities.

In Liberia, the Ebola epidemic highlighted the need to further strengthen the country's outbreak surveillance system, and between 2015 and 2017, Liberia implemented an integrated electronic disease surveillance and response system.[52] The country also launched nationwide vaccination campaigns in response to disease outbreaks that resulted from disruptions caused by the Ebola outbreak.[53, 54] In the Central African Republic, a mass vaccination campaign was implemented in 2015-2016 leading to the large improvements seen in vaccine coverage. The campaign's success could be attributed to its prioritization of routine vaccines for both infants as well all children under 5 who were missing vaccines.[49] Thus, despite ongoing public health emergencies, greater need was met by increased efforts to vaccinate a larger number of children.

Nigeria was one of three countries in the world in 2013 with endemic polio, and it continued struggling to improve polio vaccine coverage.[55] The urgency of stagnating or worsening coverage in this key location resulted in many international donors and bilateral organizations contributing resources to address the polio vaccination gap in the country, which directly and indirectly benefited other vaccines. Examples of these newly-funded efforts include the use in 2011 of geographic information systems to assist in microplanning and tracking of vaccination teams in regions with high polio transmission and low vaccine coverage.[50] In 2012, the National Stop Transmission of Polio (NSTOP) program was launched as a collaboration between the National Primary Health Care Development Agency (NPHCDA), the Nigeria Field Epidemiology and Laboratory Training Program (NFELTP), and U.S. Centers for Disease Control and Prevention (CDC).[56]

Objective 2. Results of Assessing Missed Opportunities to Vaccinate

Nigeria

There were a few variables in our analysis that were statistically significant predictors of missed opportunities for DPT vaccination in Nigeria (**Figure 2**). These included the mother's education level (p-value = 0.0034), mother's literacy status (p-value = 0.01), and family wealth index (p-value < 0.01). Children with mothers that had no primary education had 18% higher odds of missed opportunity compared to mothers that received a primary education (Odds Ratio (OR) = 1.18, 95% CI [1.01, 1.38]. Children with mothers who were illiterate had 23% higher odds of having a MOV than children with mothers who were literate (OR = 1.23, 95% CI [1.05, 1.44]). Children in the highest family wealth quintile had 23% lower odds of having an MOV for DPT compared to children in the lowest quintile (OR = 0.77, 95% CI [0.64, 0.92]). The year in which the data was collected was also a strong predictor of MOV (p-value < 0.001). Children in 2013 had over double the odds of having a MOV as children in 2018 (OR = 2.12, 95% CI [1.92, 2.35]).

Variables that were statistically significant predictors of missed opportunities for measles vaccination included the family's wealth index (p-value < 0.01) and urban/ rural residence (p-value < 0.001) in Nigeria (**Figure 3**). Children in the highest wealth quintile had 52% lower odds of MOVs compared to children in the lowest quintile (OR = 0.48, 95% CI [0.35, 0.65]). Children in rural households had 45% lower odds of MOV compared to children living in urban areas (OR = 0.55, 95% CI [0.46, 0.65]). We also found that year was a statistically significant predictor of measles MOV in Nigeria (p-value < 0.001). Children in 2013 had 65% higher odds of MOV than children in 2018 (OR = 1.65, 95% CI [1.39, 1.97]).

Liberia

Mother's education level (p-value = 0.011), the total number of children born (p-value = 0.035), and the mother's marital status (p-value = 0.031) were statistically significant predictors of missed opportunities for DPT vaccination in Liberia (**see Figure 4**). Children of mothers with no education had 39% lower odds of having a MOV compared to participants with at least a secondary level of education (OR = 0.61, 95% CI [0.42, 0.88]). Children that had no siblings had 35% lower odds of MOV compared to children in families with six or more children (OR = 0.65, 95% CI [0.43, 0.97]). Children with mothers that were single also had 25% lower odds of having a MOV as children whose parents were in a union (OR = 0.75, 95% CI [0.56, 1.00]). The year of survey administration was also a significant predictor of MOV (p-value = 0.003). Children in 2019 had 33% increase in odds of MOV compared to children in 2013 (OR = 1.33, 95% CI [1.11, 1.61]).

Variables that were statistically significant predictors of missed opportunities for measles vaccination in Liberia included the mother's literacy status (p-value = 0.01), family wealth index (p-value < 0.01), and rurality of residence (p-value < 0.001). Children of mothers who were illiterate had 46% lower odds of MOV compared to children of mothers that were literate (OR = 0.54, 95% CI [0.32, 0.88]). Participants in the highest wealth quintile had 63% lower odds of having MOV (OR = 0.38, 95% CI [0.17, 0.74]). Children living in rural areas had 52% lower odds of having MOV compared to children living in urban areas (OR = 0.48, 95% CI [0.33, 0.69]). We did not find that the year of data collection was a statistically significant predictor of measles MOV in Liberia (p-value = 0.55).

Figure 2. Factors related to missed opportunity for vaccination (MOV) in Nigeria for DPT vaccine.

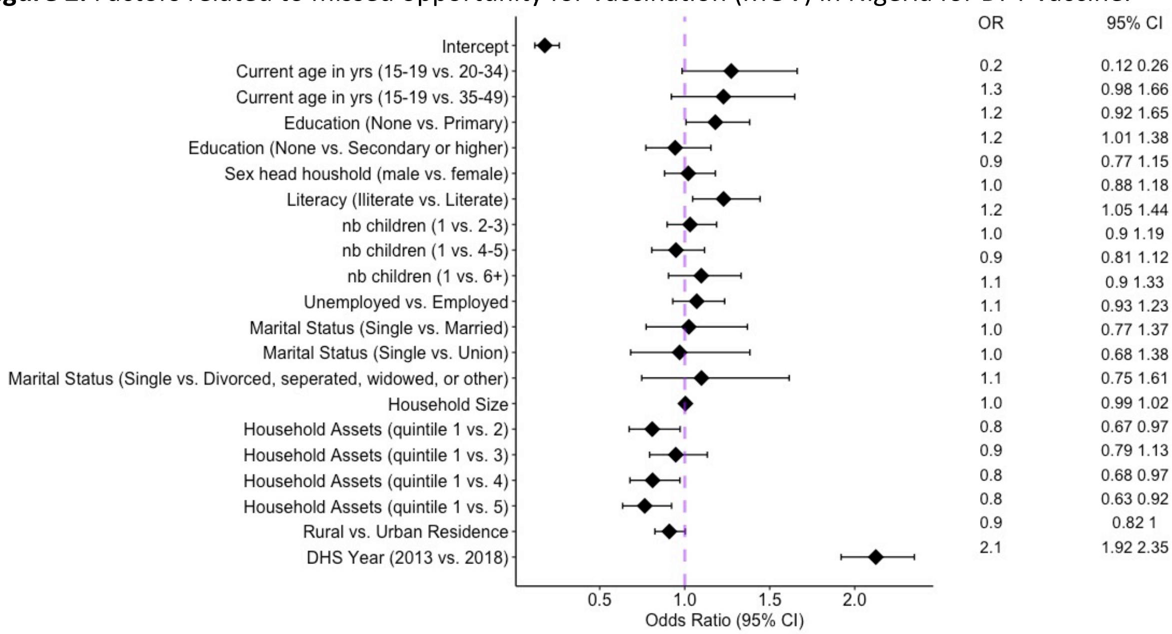


Figure 3. Factors related to missed opportunity for vaccination (MOV) in Nigeria for measles vaccine.

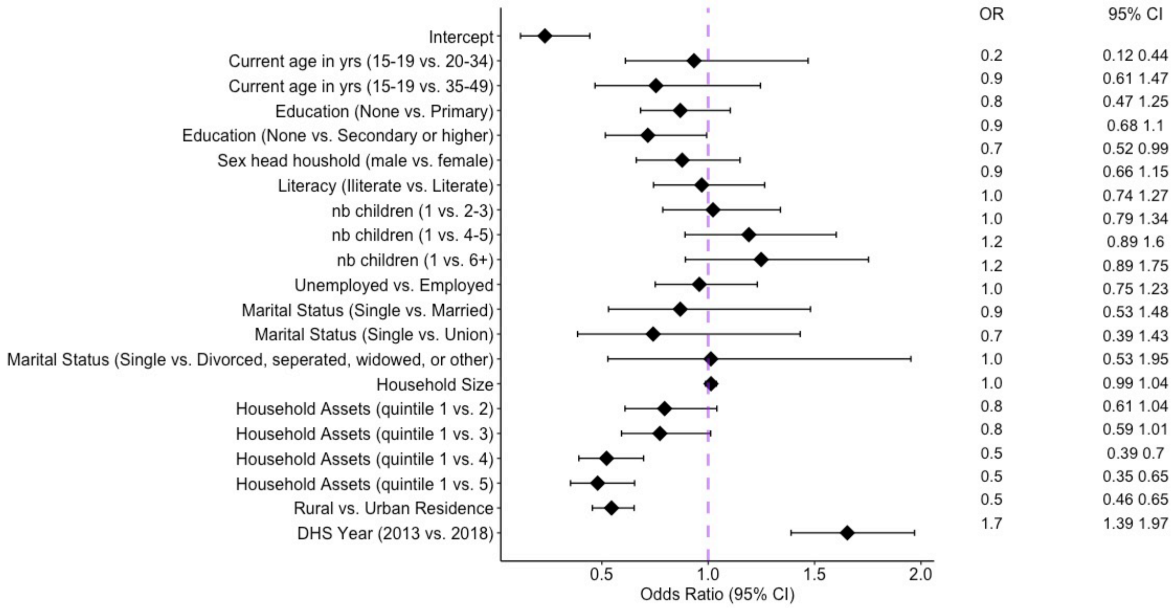


Figure 4. Factors related to missed opportunity for vaccination (MOV) in Liberia for DPT vaccine.

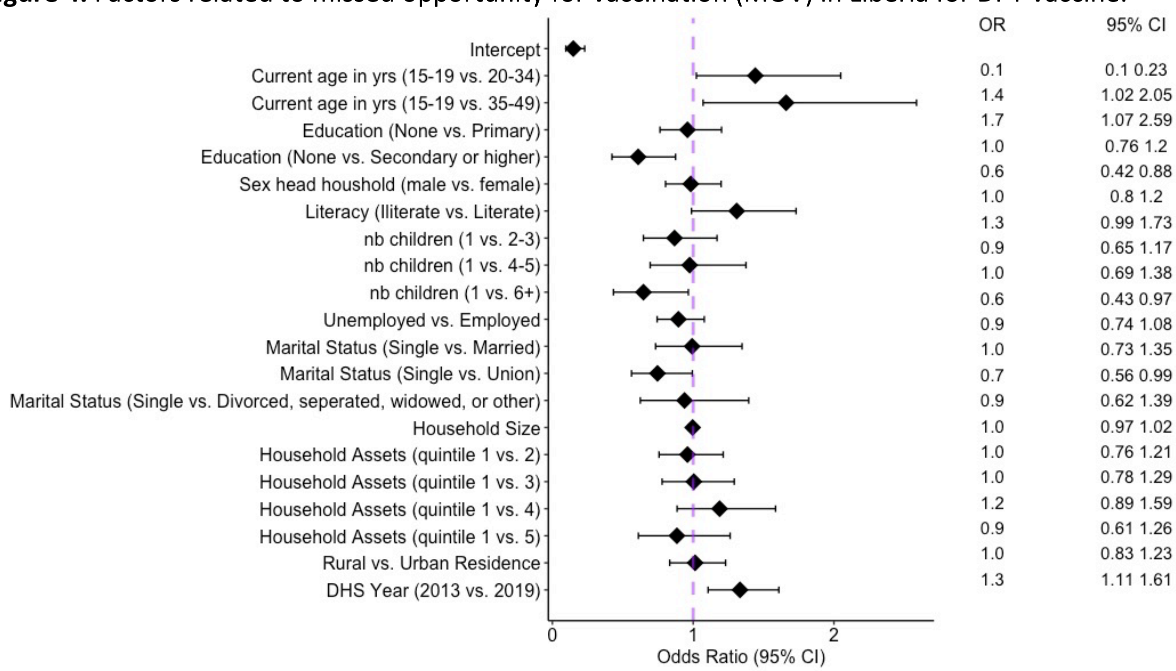
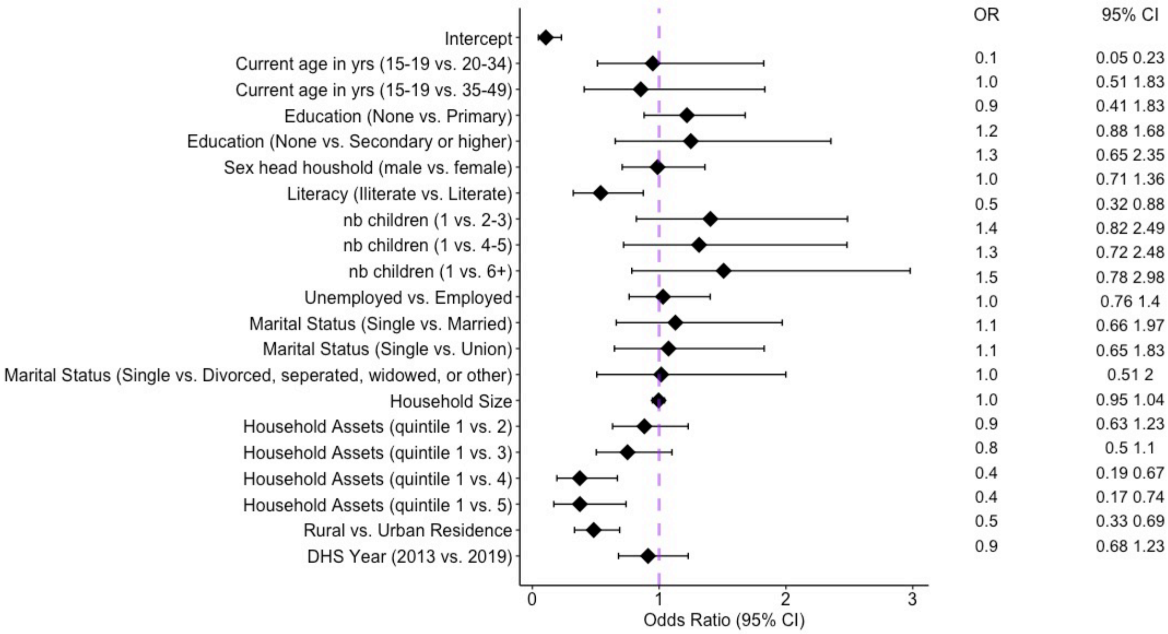


Figure 5. Factors related to missed opportunity for vaccination (MOV) in Liberia for measles vaccine.



Objective 3. Results of Developing Vaccine Improvement Potential Index

VIP index results were produced for 204 countries for each year between 1990 and 2019. In 1990, the mean vaccine index potential value was 0.49, ranging from 0.13 to 0.86 across all areas. In 2019, the mean vaccine index value was 0.59, ranging from 0.25 to 0.84. The difference between the highest and lowest scoring countries was smaller in 2019 (0.58) compared to 1990 (0.72). On average the lowest scores were found in several regions in sub-Saharan Africa and South Asia in both 1990 and 2019 (**Figure 6**). In 1990, Myanmar, Somalia, Afghanistan, Ethiopia, and the Democratic Republic of the Congo had the lowest scores. By 2019 most of the lowest ranked countries in 1990 saw an improvement in VIP except Somalia, which had a very similar rank order (204th vs. 203rd) over the 20-year period. Regions with a high score in 1990 included Western Europe, North America, and Australasia (**Figure 8**). These regions generally continued to have higher scores on average in 2019, although there were some distinct decreases in some of these regions as well.

There were some regional patterns in subcomponents of the index that at times contributed to decreased scores. For instance, for many countries in Western Europe, such as France, Switzerland, Sweden, Italy, and the United Kingdom, the incorporation of data on vaccine confidence lowered the overall VIP index results in these locations in recent years. These and many other countries in the region have reported relatively low rates of public trust in the safety and effectiveness of vaccines. Similar trends in vaccine confidence occurred in several East and Southeast Asian countries such as Japan, the Republic of Korea, Singapore, Vietnam, and the Philippines. Countries in sub-Saharan Africa, in contrast, reported relatively high levels of trust in vaccination safety and effectiveness. Countries in this region, however, reported generally low levels of overall health-related expenditures and government spending on health, as well as low-levels of births attended by skilled health workers, which affected their index results. Countries in South Asia also had relatively low values on the Socio-Demographic Index as well as low levels of health-related expenditures, government-spending on health, and development assistance for health which resulted in lower VIP index results.

We also assessed the relationships between the VIP Index and Socio-demographic Index. There was a stronger relationship between the index and SDI among countries in the low-SDI category compared to the middle- and high-SDI groupings. Among the low-SDI group **(Figure 7**), VIP Index values increase linearly, with some noticeable outliers such as South Sudan, Eritrea, and Central African Republic which have a lower VIP Index for their SDI value. Among the middle-SDI group (**Figure 10**), the trend line was much flatter, suggesting that SDI was not as strongly associated with index value. However, there were some outliers in this grouping as well, such as Tokelau and Tuvalu, which differ greatly from other countries of a similar SDI. There was also less of a trend between VIP index and SDI among high-SDI countries (**Figure 11**); however, some countries appeared to be outliers such as Greenland and Russia, which performed better and worse than expected for their SDI.

In our validation models, the vaccine index was strongly associated with vaccination coverage after controlling for year and geographic region. For DTP1, a one point increase in the vaccine index was associated with a 4.61% increase in vaccination coverage. For MCV1, a one point increase in the vaccine index was associated with a 3.83% increase in vaccination coverage. The index result was fairly successful in predicting vaccine coverage levels for both MCV1 and DTP3 vaccination coverage among the testing data set and for the year 2019 (Table 2).

Table 2. Predictive success of each model used.

Prediction	**Brier Score**
MCV1 coverage in testing data	0.12
DTP3 coverage in testing data	0.13
MCV1 coverage in 2019	0.09
DTP3 coverage in 2019	0.11

Figure 6. Average VIP Index is shown for each region for years 1990-2019, each graph shows all regions in grey with the labeled region being highlighted.

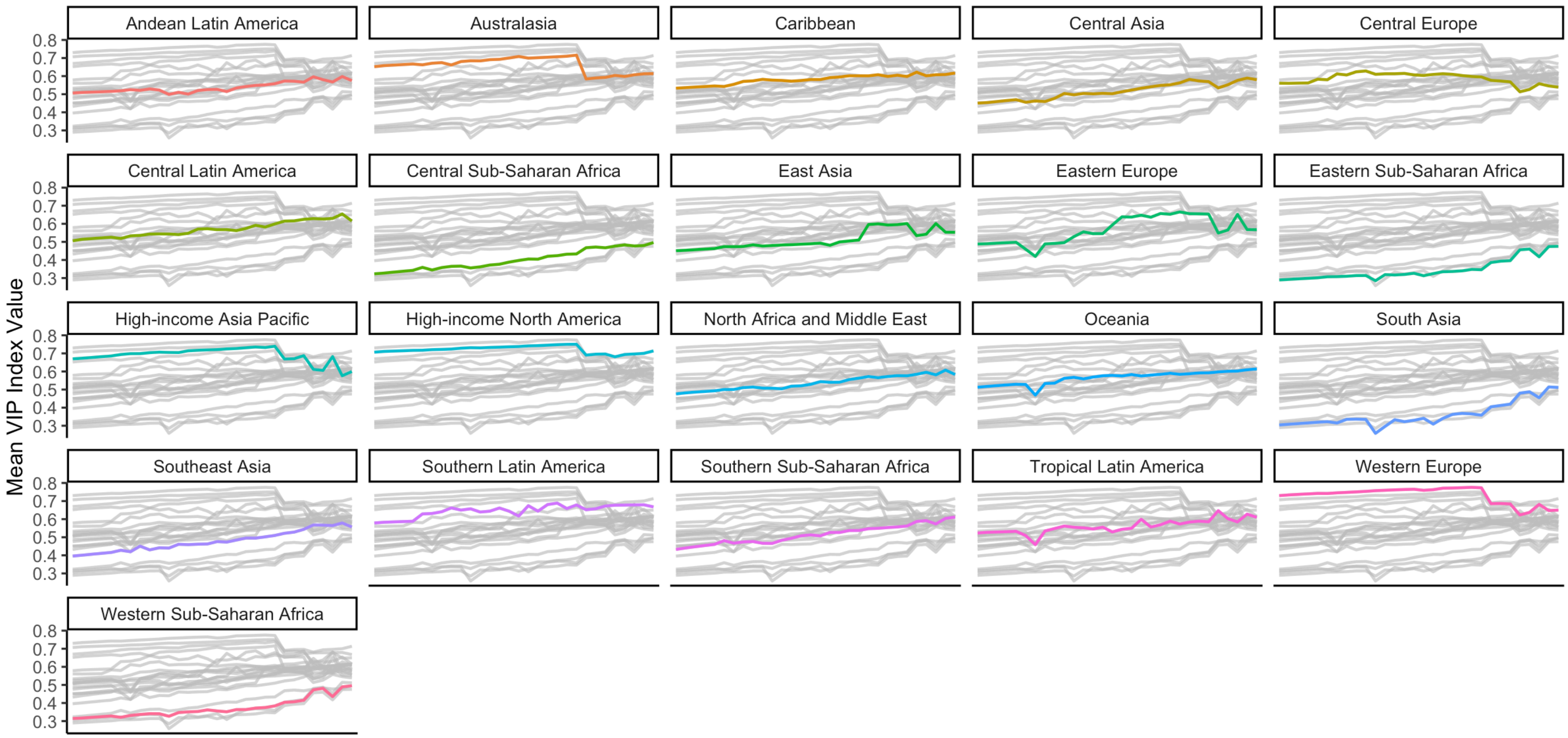


Figure 7. 2019 VIP Index values for each country in the low SDI group plotted against their SDI value in 2019 with a best fit general linear model line.

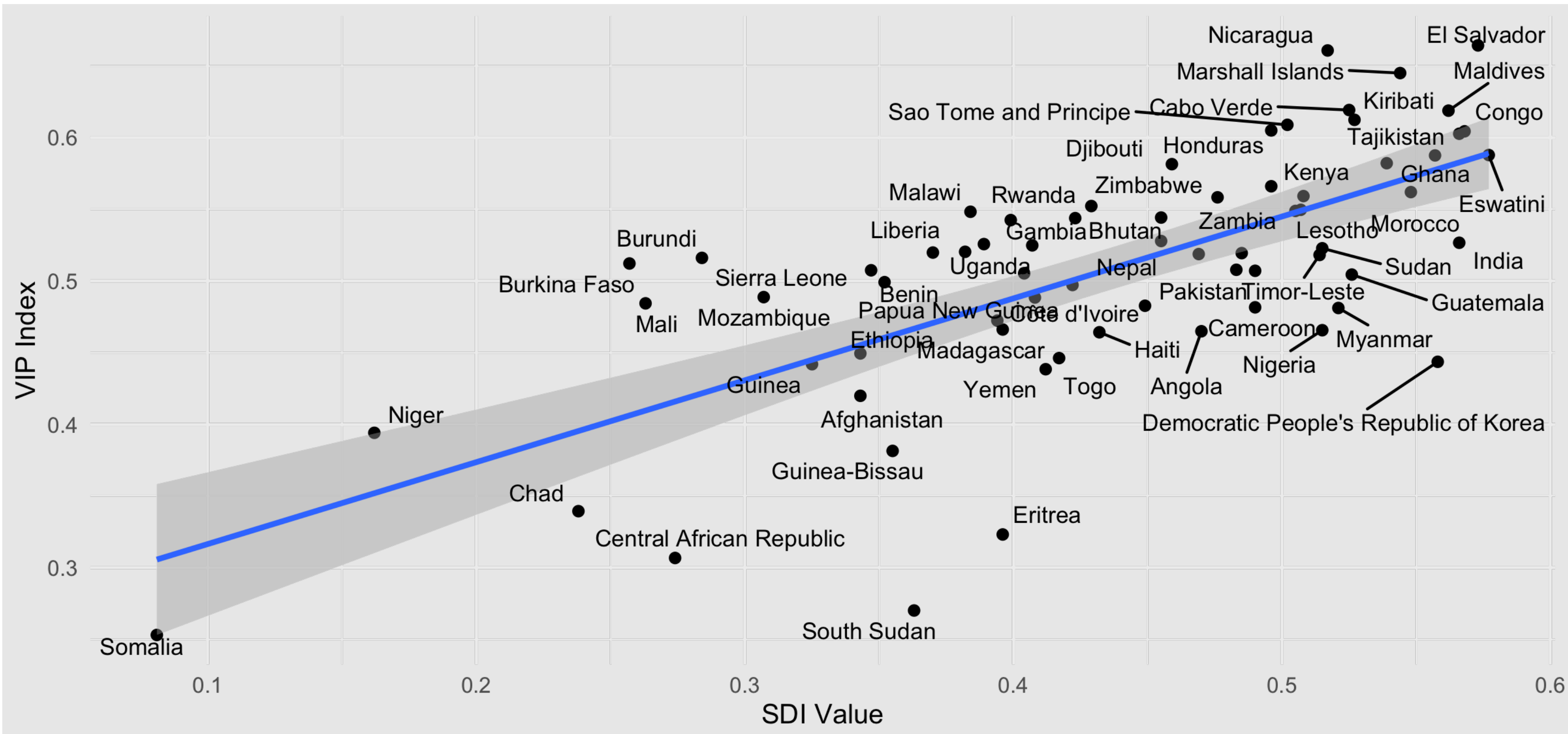


Figure 8. 2019 VIP Index values for each country in the medium SDI group plotted against their SDI value with a best fit general linear model line.

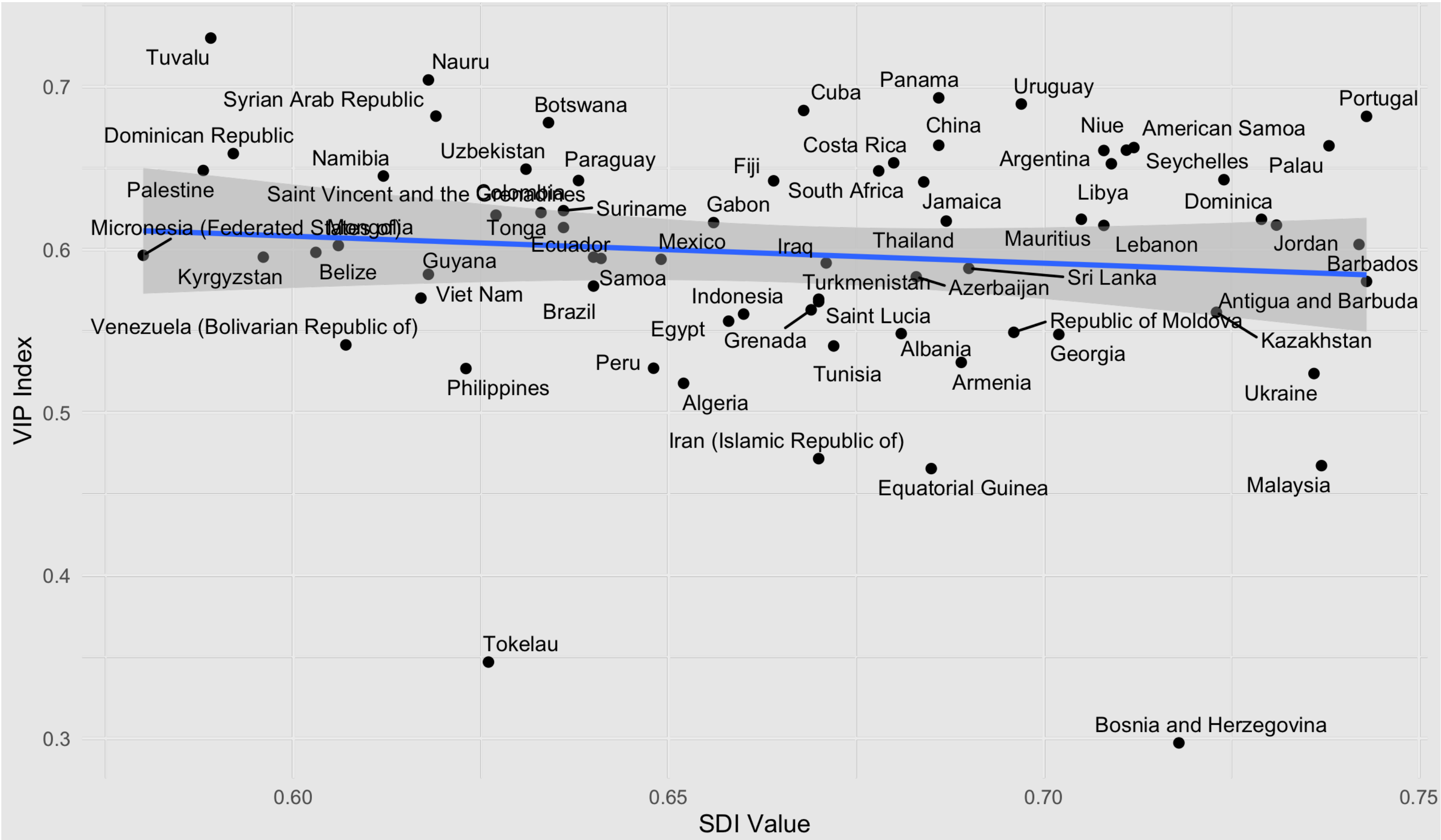
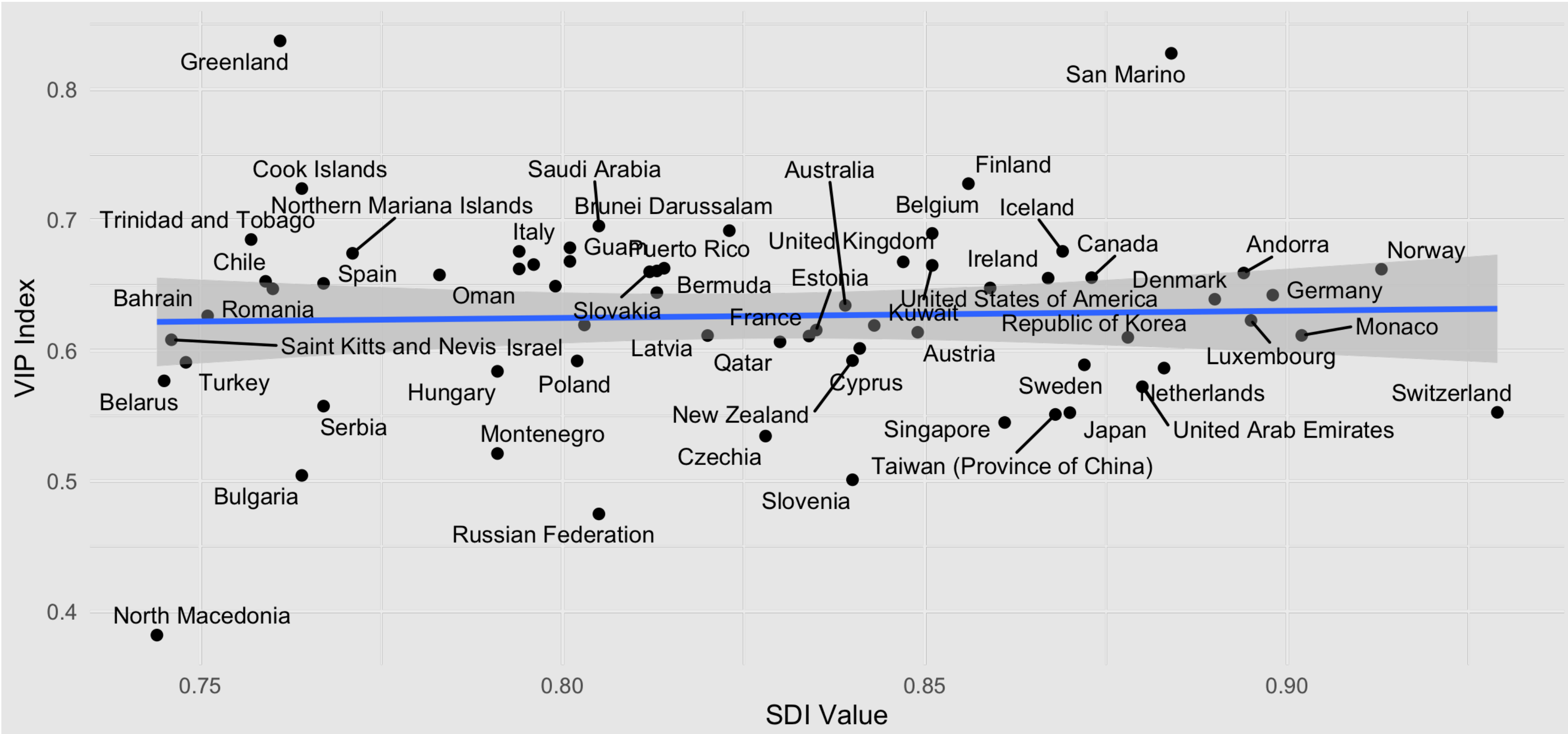


Figure 9. 2019 VIP Index values for each country in the high SDI group plotted against their SDI value with a best fit general linear model line.



Objective 4. Results of Demonstrating Potential VIP Application

Part I: model impacts of worst-performer becoming best performer in low-SDI group

The country with the lowest VIP Index in the low-SDI group in 2019 was Somalia (0.25) and the country with highest index scores was El Salvador (.57). If Somalia were to raise its index score to the same level as that as El Salvador, its measles immunization coverage is predicted to increase almost three-fold, from 25% to 91%, and its three dosage DTP immunization coverage is predicted to increase from 15% to 89%.

Part II: Counterfactual analysis of disease burden for different scenarios of immunization coverage

Somalia should see a reduction in the burden of measles and diphtheria in the country if both measles and DTP vaccine coverage were to improve and reach the value predicted in Part I of our analysis. These counterfactuals are shown in Tables 3 and 4.

Table 3. Measles disease burden predicted under different levels of immunization coverage in Somalia in 2019.

Measles vaccine coverage %	**Measles burden (DALYs rate per 100,000)**
24.5	15,577
37.66	11,696
50.82	8,778
63.98	6,590
77.14	4,947
90.3	3,713

Table 4. Diphtheria disease burden predicted under different levels of immunization coverage in Somalia in 2019.

DTP3 vaccine coverage %	**Diphtheria burden (DALYs rate per 100,000)**
24.5	381
37.66	204
50.82	109
63.98	58
77.14	31
90.3	16

Discussion

We created a summary index of the vaccination potential for more than 200 countries for the past three decades using publicly available data on factors related to vaccination improvement. We found distinct geographic patterns in our analyses, with countries in sub-Saharan Africa and South Asia having the lowest VIP index values and high-income countries in Western Europe and North America showing greater values. We validated the index results using data on childhood vaccination rates between 1990 and 2019 and found that the index was fairly successful at predicting vaccination rates. We also demonstrated the predictive capability of the VIP Index by using the index results with other data sources on vaccine-preventable diseases and immunization coverage.

Previous studies have identified numerous factors that influence vaccination rates, ranging from the sociodemographic, structural, and behavioral. This study is the first attempt to organize distinct indicators from each of the various categories into a composite index. Having a single summary measure for each country and year can simplify efforts to track change for a given country, evaluate national interventions, compare within and between regions, and identify positive outliers worthy of further investigation. Increased data availability in the future could result in an even greater predictive power of the index. Similarly, future versions of the VIP index could include subnational analyses to identify specific areas within countries that are showing unique patterns of vaccine improvement potential, or locations that are falling behind and struggling to improve.

Our findings are in accordance with past research showing that concentrated efforts can lead to a demonstrable improvement in vaccination coverage. Nigeria has been the subject of much research and international attention due to its large population of unvaccinated children and being one of the few locations with endemic polio. Vaccination coverage data over the past decade showed that Nigeria, Liberia, and the Central African Republic exceeded the average improvement in childhood immunizations seen in other low-SDI countries. These countries were able to overcome challenging public health emergencies that ranged from armed conflict to the outbreak of novel diseases such as Ebola that disrupted the immunization system. The interventions used to respond to these included increased funding, modernizing public health technology, novel outreach strategies, new public health care services, and addressing factors related to vaccine misinformation and hesitancy. Secondary data analysis showed that the occurrence of missed opportunities for vaccination was associated with certain demographic variables such as maternal education, marital status, maternal literacy, and family wealth in Liberia and in Nigeria. We found some evidence that MOV have improved in Nigeria over the past decade, but less so in Liberia. Additional research should examine interventions and recent changes that might have had direct and indirect effects on MOVs in order to understand how they might be replicated in other locations.

Our study findings also highlight how quickly routine childhood immunizations are impacted during emergencies. There are many ways that routine immunization can be disrupted and unforeseen barriers can emerge. The Covid-19 pandemic is just one of many recent examples. The development of vaccines to help prevent Covid-19 brought renewed attention to the role that vaccines play in public health. Yet it has also underscored the challenge of making vaccines widely. The pandemic and our study highlight the important of addressing mistrust of vaccinations to prevent outbreaks of vaccine-preventable diseases. They also highlight the role of global investments in countries that need support with funding health services, disease surveillance, and designing local interventions to address misinformation.

Our study had a few limitations. First, we used publicly available data to conduct secondary analyses and reviewed the literature to understand the context among high-performing countries. Since we did not collect data ourselves, we are only able to uncover that which has been published and is available in the peer-reviewed literature. Additionally, there exist multiple potential methods to construct an index such as ours with each having different strengths and limitations. One feature of the index construction method that we used is that it does not allow for the inclusion of structural zeros in the data, which in some cases are accurate.

Conclusion

This project successfully created a first-of-its-kind global Vaccination Improvement Potential (VIP) Index that summarizes important variables related to vaccine improvement potential for every country in the world. This accomplishment was achieved by identifying key factors within low socio-demographic index scoring countries that influenced the improvement of vaccination coverage.

Countries such as Nigeria, Liberia, and the Central African Republic emerged as interesting case studies for their success in improving their vaccine coverage. Despite key geographic, political, and historical differences between these countries, they each in turn had to face public health emergencies to achieve above-average improvements. We utilized survey data on vaccine coverage and family and household characteristics over multiple time points to understand patterns and trends in missed opportunities in some of these countries. There seemed to be a few significant variables that were associated with MOV such as mother's education level, mother's literacy status, and family wealth.

We also validated the usefulness of the VIP index by conducting a counterfactual analysis showing the possible impact of a low preforming country achieving a higher VIP index, which showed an estimated three-fold increase in vaccine coverage and reduced disease burden. Further, we found there were distinct regional patterns in Index results and also among the subcomponents of the Index related to health spending, sociodemographic characteristics, and vaccine confidence. These results collectively represent areas for key stakeholders to target for potential intervention to improve and maintain high levels of vaccination coverage.

Dissemination

We have created a public-facing microsite to support dissemination of the results of this report. The site's dashboard allows users to interact with the results of the VIP Index as well as vaccine trends and mortality data across time and geographic region through maps and graphs. The dashboard also allows users to explore the data used to create the VIP Index and to download their own data if desired. The site can be visited at: https://rsc.csde.washington.edu/vaccinationimprovementpotential/.

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