Global effects of COVID-19 on routine childhood immunizations

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A thesis

Submitted in partial fulfillment of the

Requirements for the degree of

Master of Public Health

University of Washington

2020

Committee:

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Program Authorized to Offer Degree:

Global Health

University of Washington

Abstract

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In 2020 the COVID-19 pandemic and policies to reduce social contact have impacted health service delivery across the world. Interruptions in routine childhood immunizations without catch-up vaccination are likely to lead to outbreaks of vaccine-preventable diseases. We estimated the short-term effects of COVID-19 on vaccine coverage for the first does of measles-containing-vaccine (MCV1) and the third dose of diphtheria-tetanus-pertussis (DTP3) in 2020 in 204 countries and territories.

Utilizing mobility data from mobile phone users as a proxy for COVID-19 disruptions and various sources of vaccine coverage data including caregiver surveys, administrative data, and electronic medical records, we implemented a 2-stage spline modelling approach. For the second half of 2020 we generated estimates of vaccine disruptions based on projections of the COVID-19 pandemic and continued mobility reductions. Paired with estimates of expected 2020 vaccine coverage in the absence of COVID-19, we calculated the estimated 2020 coverage of DTP3 and MCV1 among 1-year-olds.

In the absence of COVID-19, we estimated that 83.9% and 86.3% of children under 1 would receive vaccinations for DTP3 and MCV1; we expect COVID-19 related health-delivery interruptions to decrease 2020 global coverage to 72.7% (95% UI 69.1 – 74.7) and 72.7% (95% UI 69.2 – 74.8) for each of these antigens, far below the 2020 Global Vaccine Action Plan goal of 90% coverage. Disruptions are nearly universal, affecting nearly every country, with the highest disruptions in South Asia, Latin American and Caribbean, and High-income countries.

In order to prevent outbreaks of measles and other vaccine-preventable diseases, national governments must act quickly to restore routine immunization programs for children and perform catch-up vaccinations for those missing vaccines including adapting data information systems to capture these efforts.

Introduction

On March 11, 2020, the World Health Organization (WHO) declared the first pandemic caused by a coronavirus.[1] By August 13, 2020, the world had seen over 20.4 million confirmed cases and 744,000 total deaths from COVID-19.[2] This pandemic has challenged every country of the world with impacts on economic, social, and political life for years to come. National policies and recommendations have encouraged individuals to stay home, minimize contact with others, and remain socially distanced. COVID-19 has been particularly challenging for health-systems, as leaders around the world work to ensure that health facilities have sufficient resources to handle COVID-19 cases in addition to caring for other patients and health challenges.

Global health and development experts are particularly worried about disruptions to routine childhood immunizations and the potential for future outbreaks among cohorts of unvaccinated children. During the 2014 Ebola virus outbreak in West Africa, interruptions in routine vaccinations lead outbreaks of measles in Guinea,[3] Sierra Leone,[4] and Liberia.[5] In March, the WHO released guidelines recommending the temporary suspension of mass immunization campaigns to protect against the spread of COVID-19 while countries continue the provision of routine immunizations whenever possible.[6] Research has emphasized the importance of continuing routine immunization, estimating that for every one COVID-19 death attributable to time spent in clinics for routine vaccinations, 84 (95% U.I. 14 – 247) childhood deaths could be prevented if routine childhood immunization efforts are continued in 54 African countries.[7]

Qualitative evidence suggests many countries have seen interruptions in their immunization programs. To understand the magnitude of these disruptions, a partnership of several key decision-makers conducted an immunization pulse poll of 260 health experts in 82 countries. In May, 85% of countries responding reported that vaccination levels were lower than January and February before the impacts of the pandemic.[8]

COVID-19 has led to interruptions in routine vaccinations because families are often unable or unwilling to travel to health facilities due to travel restrictions, limited public transportation, social distancing policies, and fear of exposure. Additionally, health resources including personal protective equipment and the workforce have been stretched and redirected. The supply of vaccines has been interrupted by travel and trade restrictions. COVID-19 has led many to leave cities for more rural areas with insufficient health system capacity and has generated increased feelings of distrust of health information.[8, 9,10]

In this paper, we estimated the short-term effects of COVID-19 on national coverage for the first does of measles-containing-vaccine (MCV1) and the third dose of diphtheria-tetanus-pertussis (DTP3) in 2020 in 204 countries and territories.

Methods

Data

Vaccine Coverage Data

To estimate reference vaccine coverage we used forecasted estimates from the Global Burden of Disease project of vaccination coverage for DTP3 and MCV1 among 1-year-olds in 2020. This

analysis uses similar methodology with additional data as formerly published research.[11] Baseline coverage results were available for 195 of the 204 countries estimated (Supplementary Results Table 1).

The sources used to estimate the level of vaccine coverage interruption during the pandemic period (March – July 2020) included data based on caregiver surveys, administrative reports, and electronic medical records (Table 1). These sources came from informal searches in PubMed, news platforms such as Google News, and general internet searches with a variety of terms combining the topics of COVID-19, disruption, and immunization coverage. We also received sources through professional collaborations with Gavi, the Vaccine Alliance; WHO; and the Bill and Melinda Gates Foundation.

Survey data

The Premise smart phone app-based platform offers micro-payments to respondents for completing tasks.[12] We conducted a survey of 7,230 caregivers of children under 2 in 76 countries during the month of July. We used the following survey questions to evaluate vaccine delivery interruptions during the COVID-19 pandemic:

- How old is your youngest child in months?
- During December-February, did your youngest child receive any vaccines?
- (IF NO) What were the reason(s) that your youngest child did not receive vaccines during December-February? (Option one or more choices from the following list.)
    - Shortage of vaccines or vaccines out of stock
    - I did not want my child to be vaccinated
    - Health facility closed
    - Turned away from health facility
    - No transportation
    - Lack of money
    - Partner or family does not approve
    - My child was not due for any vaccines during this time
    - I was sick and could not take my child
    - My child was sick
    - Other
    - Decline to respond
- Since March, has your youngest child received any vaccines?
- (IF NO) What were the reason(s) that your youngest child did not receive vaccines since March? (Option to select one or more answers from the same choices as above)

Using these five questions, for each country, we calculated indicators of vaccine coverage for the reference (December – February) and pandemic (March – July) periods. We included all youngest children who were 0-18 months at any time during the specified period and excluded children whose caregiver responded that they did not receive any vaccines because, “my child was not due for any vaccines during this time.” This resulted in 2,900 and 4,413 children in 74 countries in the reference and pandemic periods (Figure 1). We calculated the prevalence of receiving any vaccine among 0-18 month olds who were due for one in each period by taking the

number of children who received any vaccines during the given period over the total number of children eligible period. We calculated the disruption ratio and the standard error of the log ratio in country, *i*, with the following 2x2 table and formulas:

	Received vaccine	**Did not receive vaccine**	**Total**
Pandemic	*a*	*b*	n_p
Reference	*c*	*d*	n_r

$$Ratio_i = \frac{a_i/n_{pi}}{c_i/n_{ri}}$$

$$SE(\ln(Ratio_i) = \sqrt{\frac{1}{a_i} + \frac{1}{c_i} - \frac{1}{n_{pi}} - \frac{1}{n_{ri}}}$$

To account for zeroes, for any countries where *a*, *b*, *c*, or *d* were zero but not $a = c = 0$ or $b = d = 0$, we utilized the common protocol of adding 0.5 to all cells for calculations.[13] We excluded countries where the sum of eligible children in the reference and pandemic periods was less than 25, resulting in ratios from 56 countries to be included in the analysis.

In a sensitivity analysis, we used GBD estimates of reference 2020 DTP3 and MCV1 coverage in the denominator when calculating the disruption ratios for the Premise survey data. For both antigens in a paired samples t-tests, we found no statistically significant difference between the means calculated using the Premise reference period and the GBD estimated national coverage (p-value = 0.67 for DTP3 and 0.40 for MCV1). There were differences in the estimated ratios, especially in those with a small number of individuals sampled (Supplementary Figure 1). We chose to use the estimates from the Premise survey reference period because the sample was among the same population as the pandemic period disruption estimate.

Administrative data from the World Health Organization

The World Health Organization asked member states to report total DTP3 and MCV1 vaccination doses administered in each month from January through May of 2019 and 2020, receiving results from 82 countries for March, 43 for April, and 3 for May capturing over 91 million doses administered (Figure 2).[14] We calculated the interruption as a ratio of ratios by comparing the ratio of doses in March – May 2020 and the same month in 2019 to the ratio of doses administered in January and February of 2020 and the same months in 2019.

We used additional qualitative data shared by WHO including two sets of pulse poll results,[8] essential health services (EHS) polls, and additional data collected by the WHO regional offices to validate the quantitative interruption ratios calculated from the administrative data. Often, these polls suggested a disruption, whereas the admin data did not because, for example, a country may have experienced stockouts in early 2020. Based on discrepancies we excluded the administrative data for both antigens from Afghanistan, Bangladesh, Chad, Guatemala, Madagascar, Nepal, Venezuela, and Yemen; DTP3 from Haiti; and MCV1 from Kenya, Lesotho, Namibia, Senegal, Somalia, Tanzania, and Uruguay.

In locations with both Premise survey data and WHO administrative data, we compared the two sources of data. In 31 locations with DTP3, we found a Pearson's correlation coefficient of 0.35 and a Lin's concordance correlation coefficient of 0.33 (95% C.I. -0.01 – 0.59). In 27 locations with MCV1, we found a Pearson's correlation coefficient of 0.41 and a Lin's concordance correlation coefficient of 0.33 (95% C.I. 0.02 – 0.59).

Other sources of vaccine coverage data

We also used data from the Population Council KAP survey in Bihar and Uttar Pradesh. The study team uses phone-based surveys of an existing prospective cohort study to sample women ages 19-23 every month about knowledge, attitudes, and practices related to COVID-19. In the first survey, April 3 – 21, 2020, among 385 women in Bihar and 989 women in Uttar Pradesh, 42.6% and 32.6% stated demand for child immunization services, yet only 1.0% were able to receive services. In the second survey, May 13 – June 1, 2020, among 91 and 63 women in Bihar and Uttar Pradesh with demand for services, 20.8% and 19.0% successfully received vaccinations for their child.[15] We compared these coverage numbers to the GBD estimates of DTP3 and MCV1 2019 coverage to calculate disruption ratios for each state and time period.[16]

Additional available sources of data to quantify vaccine coverage interruption came from two United States Morbidity and Mortality Weekly Reports (MMWR),[17,18] the Nigerian National Health Management Information System (NHMIS) data tool,[19] research of electronic medical record data in England published in EuroSurveillance,[20] and media articles referencing administrative data in the United States and South Africa.[21,9] Each of the sources provided data in a different format, with variable time periods, target age groups, antigens, and populations. We included any vaccination in children under two that was a measles-containing-vaccine (MCV, MCV1, MCV2, and MMR) or covered diphtheria, tetanus, and pertussis (DTP3, Hexavalent, PENTA3). We included estimates of vaccine delivery or coverage. Whenever provided, we used 2019 as a control period to capture existing trends in the eligible population and underlying coverage patterns. More details for each source are provided in Table 1.

Imputation of Missing Antigens

For locations where we had estimates for one of the two antigens (2 countries missing DTP3 and 7 countries missing MCV1), we imputed the other antigen based on the global average ratio of disruption between DTP3 and MCV1, weighted by the sum of the inverse variance of both ratios. Based on 127 pairs in 70 countries where we had overlapping time points of data for both antigens, the average interruption for MCV1 was 0.97 times that of DTP3.

Mobility Data

As a proxy to estimate the impact of COVID-19 on health service delivery, we used mobility estimates generated by the Institute for Health Metrics and Evaluation for the COVID-19 projections.[22] Briefly, we synthesize daily cell-phone mobility data from Descartes Labs,[23] Facebook,[24] Google,[25] and Safegraph[26] from 131 of 204 countries and territories; many countries have state or province-level data available. In countries where data is not available, we imputed the regional average for full geographic coverage. Mobility data covered January through mid-July.

We employed a linear mixed effects model to estimate location-specific effects of five social distancing policies – school closures, restrictions on gathering, full and partial business closures, and stay at home orders – on human mobility patterns based on dates in which governments imposed and relaxed these policies. As governments began to relax mandates, we assumed that all countries would continue to follow general trends of relaxing mandates unless they reach a threshold of 8 per million daily COVID-19 deaths, at which point political actors would reestablish mandates and mobility would drop to minimum levels for a period of 6 weeks. Using this strategy and forecasts of the COVID-19 pandemic, we estimated expected mobility through 2021. The most recent IHME COVID-19 research publication provides the detailed methodology.[22]

For each estimate of vaccine coverage disruption in the model, we calculated the average COVID-19-related mobility decrease for the given location and time-period. For data from Michigan, Alabama, Bihar, and Uttar Pradesh, we used the state specific mobility values, and for all other data, we used national values. Mobility was calculated as the average percent reduction in mobility on a scale from 0 (no reduction) to 1 (100% reduction in mobility).

Analysis

We modeled the relationship between human mobility as a proxy for COVID-19-related health systems interruptions and the decrease in DTP3 and MCV1 vaccine coverage with a 2-stage random spline model with the Meta-Regression Bayesian, Regularized, Trimmed tool (MR-BRT) with the following set of equations:[27]

Stage 1 Global model	$\log\left(vaccine\ ratio_{t,a}\right) \sim spline\left(avg\ mobility_{t,a}\right) * \beta_{t,a}$
Stage 2 Location-specific model	$\log\left(vaccine\ ratio_{t,a,c}\right) \sim spline\left(avg\ mobility_{t,a,c}\right) * \beta_{t,a,c}$ $\beta_{t,a,c} \sim N(\beta_{t,a}, \sigma^2)$

For each data point, we assigned a weight in the model equal to the inverse variance of the log ratio. Estimates calculated based on administrative data in large population countries had implausibly small variance due to the high number of vaccines administered. We set a cap on the variance at $5.35 * 10^{-4}$, equal to 4 times that ce of the most certain estimate from the premise survey data; therefore, no estimate could have more than 4 times the weight of the most certain Premise estimate in the model. This cap affected the variance of 182 data points from WHO administrative data,[14] England EuroSurveillance data,[20] and NHMIS data.[19] For estimates without sample size or sufficient information to calculate the variance (N = 21), [9, 17,18,21] we imputed the median variance ($1.16 * 10^{-2}$) from the Premise Survey data to use as the weight in the model.

For each antigen, in stage 1 we fit a global model to all available ratios. We fit a cubic spline with knots at mobility reductions of 20%, 40%, and 60% to the log ratio. We did not include an intercept, forcing the spline to intersect 1, no disruption in vaccine coverage, at a mobility value of 0, no change from baseline mobility; we also implemented a monotonicity prior, not

permitting the vaccine coverage to increase as mobility decreased. This fit with the expected relationship and allowed our future projections to return to expected coverage once mobility returned to normal.

In 101 countries where we had data we fit a stage 2 spline using the global spline as a prior; therefore, the spline only varied from the shape and magnitude of the global model if there was sufficient evidence to suggest a diversion.

To calculate uncertainty intervals of disruption rates, we generated 1000 splines for each location. For the global model, we sampled 1000 estimates with replacement from the 101 country-specific maximum-likelihood estimate models. For the stage 2 splines, we used a fit-refit strategy, generating a posterior set of 1000 splines with a parametric bootstrap strategy. Based on these 1000 draws, we generated estimates based on the mean and provided 95% uncertainty intervals.

From this set of splines, we calculated the disruption for the observed pandemic period, March – June 2020, from daily observed mobility and estimated the disruption for 2020 based on observed and projected mobility. We multiplied these disruption ratios by the reference scenario 2020 vaccine coverage assuming no COVID-19 to produce the estimated coverage for each of these periods.

Results

Figures 1 and 2 include data coverage maps for the Premise survey and WHO administrative data respectively. 101 of 204 countries and territories have at least one source of data, including 8 of the 10 countries with the highest number of reported COVID-19 deaths.[28] Iran and France are not represented. Notably, France did not meet the threshold of 25 valid responses to the Premise survey for inclusion. The WHO administrative dataset includes reports from regions with lower reference vaccine coverage including South and Southeast Asia, Sub-Saharan Africa, and Latin America and the Caribbean.

Global stage 1 models for both DTP3 and MCV1 showed steep declines in vaccine coverage at initial mobility decreases and a secondary decrease for DTP3 at extremely low levels of mobility. Data suggested vaccination disruptions even at low levels of mobility reduction. In addition to the global models, Figure 3 also includes stage 2 location-specific splines for India, Nigeria, the United Kingdom, and the United States, the four locations with the most data.

In India, the PC KAP study suggested large disruptions in vaccine delivery during a period of high mobility reduction. In Nigeria, vaccine disruptions were less severe than would be expected based on the observed mobility, but in the United States, the effects are stronger.

In the United Kingdom we found small effects on MCV1 coverage and almost no interruption in DTP3 coverage, consistent with the conclusions of research on administrative data in England.[20]. Across all super-regions, COVID-19 had a marginally larger impact on MCV1 (Table 2).

One consideration is whether mobility will continue to be a good predictor of vaccine coverage interruptions as governments relax social distancing policies and mobility increases. Nigeria

provided the longest temporal trend with data from NHMIS through June of 2020.[19] For both DTP3 and MCV1 the decline in mobility is consistent with the pattern of vaccine disruption shown in the NHMIS, WHO, and Premise data (Figure 4). Importantly, data in Nigeria in June suggests that as mobility increases the relationship with vaccine coverage has remained similar to that of early in the pandemic.

Globally, in the absence of COVID-19, we estimated that 83.9% and 86.3% of children under 1 would receive vaccinations for DTP3 and MCV1 in 2020. During March-June of 2020, however, we estimated that vaccine coverage dropped to 86.9% (95% UI 83.1 – 89.0) and 84.7% (95% UI 81.0 – 86.9) of baseline for DTP3 and MCV1 respectively leading to 2020 global coverage estimates of 72.7% (95% UI 69.1 – 74.7) and 72.7% (95% UI 69.2 – 74.8). Of seven super-regions, Sub-Saharan Africa had the lowest expected vaccine coverage in the no-COVID-19 reference scenario and the smallest disruptions in vaccine delivery, driven in part by minimal mobility disruptions. Meanwhile, South Asia experienced the largest disruptions in vaccine delivery leading to an estimated 2020 coverage of 77.5% (95% UI 74.6 – 80.5) and 73.6% (95% UI 71.5 – 75.4) for DTP3 and MCV1 followed by Latin America and Caribbean and High-income countries (Table 2).

In the absence of COVID-19, we estimated that the United States would achieve 92.9% coverage for both DTP3 and MCV1 in 2020. Due to pandemic-related disruptions in routine immunizations, we expect only 73.0% (95% UI 68.7 – 78.1) coverage for DTP3 and 72% (95% UI 67.5 – 77.2) coverage for MCV1. In the UK, where there were minimal disruptions we expect that DTP3 coverage will drop from 95.8% in the absence of COVID-19 to 95.4% (95% UI 94.3, 95.8), and MCV1 will drop from 93.5% to 88.5% (95% UI (87.0, 90.1) coverage. Notably, the US and the UK experienced similar disruptions in mobility with average disruptions of 21.7% and 27.5% respectively (Figure 5, Supplementary Results Table 1).

In India, there were large disruptions in mobility, annual average of 40% of baseline, and large disruptions to routine immunizations. We estimated that coverage will decrease from 90.0% to 69.1% (95% UI 64.1 – 72.8) for DTP3 and from 94.2% to 65.2% (95% UI 62.6 – 67.2) for MCV1 due to COVID-19 related disruptions. In Nigeria, disruptions to mobility and vaccine coverage were both minimal. While non-COVID-19 2020 coverage was expected to be 53.9% and 60.6%, we expect coverage of 50.7% (95% UI 50.1, 51.3) and 56.3% (95% UI 55.7 – 56.9) for DTP3 and MCV1 (Figure 5, Supplementary Results Table 1).

The Global Vaccine Action plan set a target of 90% national coverage for all vaccines in the national schedule by 2020.[29] Based on past coverage trends, 3 super-regions and 98 countries representing 36.8% of the world's 1-year-olds were expected to achieve that target for DTP3, and 4 super-regions and 117 countries representing 57.4% of the world's 1-year-olds were expected to achieve that target for MCV1 in 2020 (Table 1, Figure 5, Supplementary Table 1). During March – June of 2020, mean estimated disruptions ranged from 52.8% to 99.9% of baseline coverage with a global disruption of 81.7% (95% UI 75.7 – 85.1) for DTP3 and 79.2 % (95% UI 73.1 – 82.8) for MCV1. If disruptions continue and COVID-19 progresses as projected, we expect that 0 super-regions and 26 countries will achieve 90% coverage for DTP3, and 0 super-regions and 17 countries will achieve 90% coverage for MCV1. According to these

estimates, only 16.7% and 2.8% of 1-year-olds in 2020 will live in countries meeting this target for DTP3 and MCV1 respectively.

Discussion

This analysis combined 9 data sources covering 101 countries to provide estimates of COVID-19's impact on vaccine delivery across the globe. We additionally validated this quantitative data with qualitative reports from national experts. These results could be used to determine which countries are at highest risk of outbreaks of measles or other vaccine-preventable diseases to focus funding and future disease prevention efforts.

Cell phone based mobility data had high spatio-temporal coverage and served as a proxy for the pandemic-related disruptions to the economy and health service delivery. We forecasted mobility based on social distancing policies; in this way, political actors can estimate how various policies in response to COVID-19 may affect mobility and disrupt health services, quantitatively evaluating the impact on vaccine delivery.

Mobility was an imperfect proxy for COVID-19 impact, and the relationship between mobility and vaccine delivery varied between locations. At a 40% reduction in mobility, DTP3 vaccine disruption estimates across locations ranged from 35.2% of baseline to no disruption with a standard deviation of 13.6. For MCV1, disruption estimates ranged from 32.2% of baseline to no disruption with a standard deviation of 13.5. Though both the UK and the US are locations with high baseline coverage, large COVID-19 epidemics, and similar reductions in mobility, the UK experienced smaller disruptions to routine childhood immunization programs. One reason may be that the UK emphasized the importance of maintaining the immunization program. In mid-April the Joint Committee for Immunisation and Vaccination released a statement encouraging the continuation of national immunization services,[30] proceeding two weeks of increased vaccine delivery in England.[20] In the US, fear of COVID-19 exposure during well-child visits is likely driving disruptions in coverage.[31]

Disruptions due to COVID-19 are likely the most widespread interruptions in vaccine delivery in the modern era of immunizations. The disruptions experienced by many countries during COVID-19 are comparable in magnitude to disruptions seen in Ukraine due to distrust of vaccines and health system failures, where MCV2 coverage dropped from 77% in 2012 to 29% in 2016, leading to a large measles outbreak in 2018 and 2019. [32,16] The WHO reports that this will be the first drop in DTP3 coverage within and across countries in 28 years.[33] While this analysis estimated the magnitude of interruptions and the impact on coverage, we forecasted the return to routine vaccinations without considering the "catch-up" vaccination that must occur. Ensuring that cohorts of children who missed routine vaccinations are caught up will be crucial for preventing deadly outbreaks of measles, diphtheria, tetanus, pertussis, and other vaccine preventable diseases.

Catch-up can be done through two primary strategies—mass vaccination campaigns or periodic intensification of the routine immunization program. In the Pulse poll, three fourths of respondents from 86 countries stated that there are country-plans for catch-up vaccinations.[8] Some countries have defaulter tracing information systems, which enable health workers to find

and vaccinate children who missed vaccines. Current data systems, however, are typically not structured to capture vaccinations outside of the target age group or during campaigns in which it can be difficult to determine whether children had been previously vaccinated. When the vaccinations are captured in data systems, the capacity to distinguish between children receiving vaccines on a traditional schedule and children catching up is variable across countries. In order to determine cohort-specific coverage it will be crucial to prioritize rapidly adapting data systems to capture both routine vaccinations and efforts to catch-up children who missed doses. As countries reopen and rebuild health systems, it will be important to focus on sustainable development, strategic investment in health care capacity and information systems, and health equity among those most impacted by COVID-19 and interruptions to the economy and health systems.

This analysis had many limitations. We did not have vaccine interruption data in all locations. Where we did have data, the Premise survey data covered a small portion of the population and was biased toward higher-educated individuals in urban areas. Respondents were expected to remember their child's vaccination schedule over a 7-month window, and it may have been especially difficult to remember vaccinations happening in the pre-pandemic period. In this survey, the pandemic period covered a long time window of March – June, but we would expect various degrees of service interruption during this time; however, we could not get finer temporal resolution from this survey. While the WHO administrative data was not subject to the same biases and provided monthly resolution, stockouts and booster campaigns resulting in uncharacteristic counts during reference months could have result in misleading disruption effects. Additionally, the pandemic and strains on the health system may have reduced the data quality, interfering with the health system's ability to record doses. We were unable to capture the non-sampling variance in the administrative data and chose to define an arbitrary variance cap on these estimates in the model. In future work, we could examine the variability of administrative data over time relative to trends in other data sources such as survey data to capture the location-specific non-sampling error in this type of data.

In a sensitivity analysis comparing two different strategies of calculating disruption ratios from the Premise survey data (using the survey responses in the reference period versus using GBD estimates of national coverage in the absence of COVID-19 for the denominator), though there were not statistically significant differences, it was clear that different strategies yielded different ratios (Supplementary Results Figure 1). Small survey sample sizes are a large driver of the differences. In addition, recall bias could have led the Premise reference coverage to be smaller than the GBD estimated coverage, and an urban population that is higher in educational attainment would have lead Premise reference coverage to be greater than the GBD estimated coverage. In future work, it will be important to ensure large sample sizes and sampling to ensure representation across strata of socioeconomic status, geography, and age.

Additionally, estimated disruptions for the second half of 2020 relied on projections of COVID-19 cases and deaths, which are uncertain and depend on many political and individual decision-makers. Most of our vaccine coverage data came from the period when mobility was low and decreasing, the time in which COVID-19 had the largest impact on economic, social, political,

and institutional life. We did not have sufficient data to determine if the relationship between mobility and vaccine delivery would stay the same as the pandemic progressed. If countries focus on reopening health facilities and dedicate resources to vaccination programs, health systems may adapt to reductions in mobility, and vaccine delivery may return to baseline levels faster than overall mobility. Additionally, as mobility returns to baseline levels, coverage data will likely include catch-up vaccinations.

As more data becomes available, it will be important to use out of sample validation to verify the relationship between vaccination coverage and mobility over time. If the relationship with mobility changes with reopening, it will be illustrative to examine which countries are able to recover and return to routine immunizations more quickly than expected and examine the policies utilized to do so. In addition, the model could be improved by leveraging additional information across geography. While we used a two-stage modeling strategy, we could gain additional information by modelling in multiple stages along the geographic hierarchy, borrowing strength from countries in the same super-region and region.

We examined the effect of total number of COVID-19 deaths and cases, the sociodemographic index, and the health access and quality index, but did not find any meaningful relationships to help explain differences in disruption across countries. As countries re-open, these factors or other determinants may be important to consider in modelling.

Conclusion

The COVID-19 pandemic and social distancing policies to ensure its control have led to nearly universal disruptions in routine vaccination programs across the globe. As a result, many countries will no longer meet the 2020 Global Vaccine Action Plan target of 90% coverage of routine vaccinations for both DTP3 and MCV1. As countries begin to reopen and restore health services, it is crucial that health systems resume routine vaccinations and catch up among children who missed doses to prevent outbreaks of vaccine preventable diseases. In doing so, nations must adapt data systems to capture both routine and catch-up vaccination.

Table 1: Sources of Vaccine Coverage Data

Source	Data points	Sample size	Antigen(s)	Age (months)	Location(s)	Data source	Reference period	Reference value	Pandemic period	Pandemic value
Eurosurveillance[20]	16	271,834 doses administered	Hexavalent MMR	0 – 6 12 – 18	England	Doses administered from electronic patient records	Jan – Feb 2020	Ratio of doses administered in Jan – Feb 2020 and doses administered in Jan – Feb 2019	Weekly; Mar – Apr 24, 2020	Ratio of weekly doses administered and doses administered in the same week of 2019
MMWR: Michigan[17]	1	9,269/9,539 children in 2019/2020	MCV1	0 – 16	Michigan, USA	Vaccine coverage from the electronic immunization registry	May 2019	Vaccine coverage	May 2020	Vaccine coverage
MMWR: United States[18]	7	27,410 doses administered	MCV	0 – 23	USA	Doses administered from electronic medical records	Jan – Feb 2020	Average weekly doses administered in Jan – Feb 2020	Weekly; Mar – Apr 18, 2020	Weekly doses administered
NHMIS[19]	8	14,790,429 doses administered	MCV1 Penta3	–	Nigeria	Doses administered from administrative data	Jan – Feb 2020	Ratio of doses administered in Jan – Feb 2020 and doses administered in Jan – Feb 2019	Monthly; Mar – Jun 2020	Ratio of monthly doses administered and doses administered in the same month of 2019
Population Council KAP Study[15]	8	486/154 young women with demand for immunization services for a child under 2 in first/second survey	Any	0 – 23	Bihar and Uttar Pradesh, India	Survey of young women (19-23)	2019	GBD 2019 vaccine coverage (MCV1, DTP3) for each state	2 survey periods; Apr 3 – Apr 22 and May 13 – June 1, 2020	Percent of women with demand for childhood vaccination services who were able to receive vaccines for their child
Premise survey[12]	74	2,900/4,413 eligible children in reference/ pandemic periods	Any	0 – 18	74 countries (Figure 1)	Survey of Caregivers	Dec 2019 – Feb 2020	Proportion of children due for vaccines receiving any vaccines	Mar – Jul 2020	Proportion of children due for vaccines receiving any vaccines

Source	Data points	Sample size	Antigen(s)	Age (months)	Location(s)	Data source	Reference period	Reference value	Pandemic period	Pandemic value
Scientific American[21]	2	–	MMR	0 – 23	Alabama, USA	Monthly vaccinations as a percentage of total 2018 monthly vaccinations from state health department	Jan – Feb 2020	Ratio of Jan – Feb 2020 monthly vaccinations as a percent of Jan – Feb 2018 and Jan – Feb 2019 monthly vaccinations as a percent of Jan – Feb 2018	Monthly; Mar – Apr 2020	Ratio of 2020 monthly vaccinations as a percent of the same month of 2018 and 2019 monthly vaccinations as a percent of the same month of 2018
Spotlight[9]	1	–	MCV2	–	South Africa	Vaccine coverage from administrative data	April 2019	Vaccine coverage	April 2020	Vaccine coverage
WHO[14]	256	91,103,745 doses administered	MCV1 DTP3	–	82 countries (Figure 2)	Total monthly vaccinations from national governments reported to the WHO	Jan – Feb 2020	Ratio of doses administered in Jan – Feb 2020 and doses administered in Jan – Feb 2019	Monthly; Mar – May 2020	Ratio of monthly doses administered and doses administered in the same month of 2019

Figure 1: Data coverage for Premise survey

The map depicts the sum of valid responses from the reference (December – February) and pandemic (March – July) periods in each country. Data from countries in red with less than 25 total valid responses were not included in the analysis. ATG=Antigua and Barbuda. BRB=Barbados. COM=Comoros. DMA=Dominica. E Med.=Eastern Mediterranean. FJI=Fiji. FSM=Federated States of Micronesia. GRD=Grenada. KIR=Kiribati. LCA=Saint Lucia. MDV=Maldives. MHL=Marshall Islands. MLT=Malta. MUS=Mauritius. SGP=Singapore. SLB=Solomon Islands. SYC=Seychelles. TLS=Timor-Leste. TON=Tonga. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines. VUT=Vanuatu. WSM=Samoa.

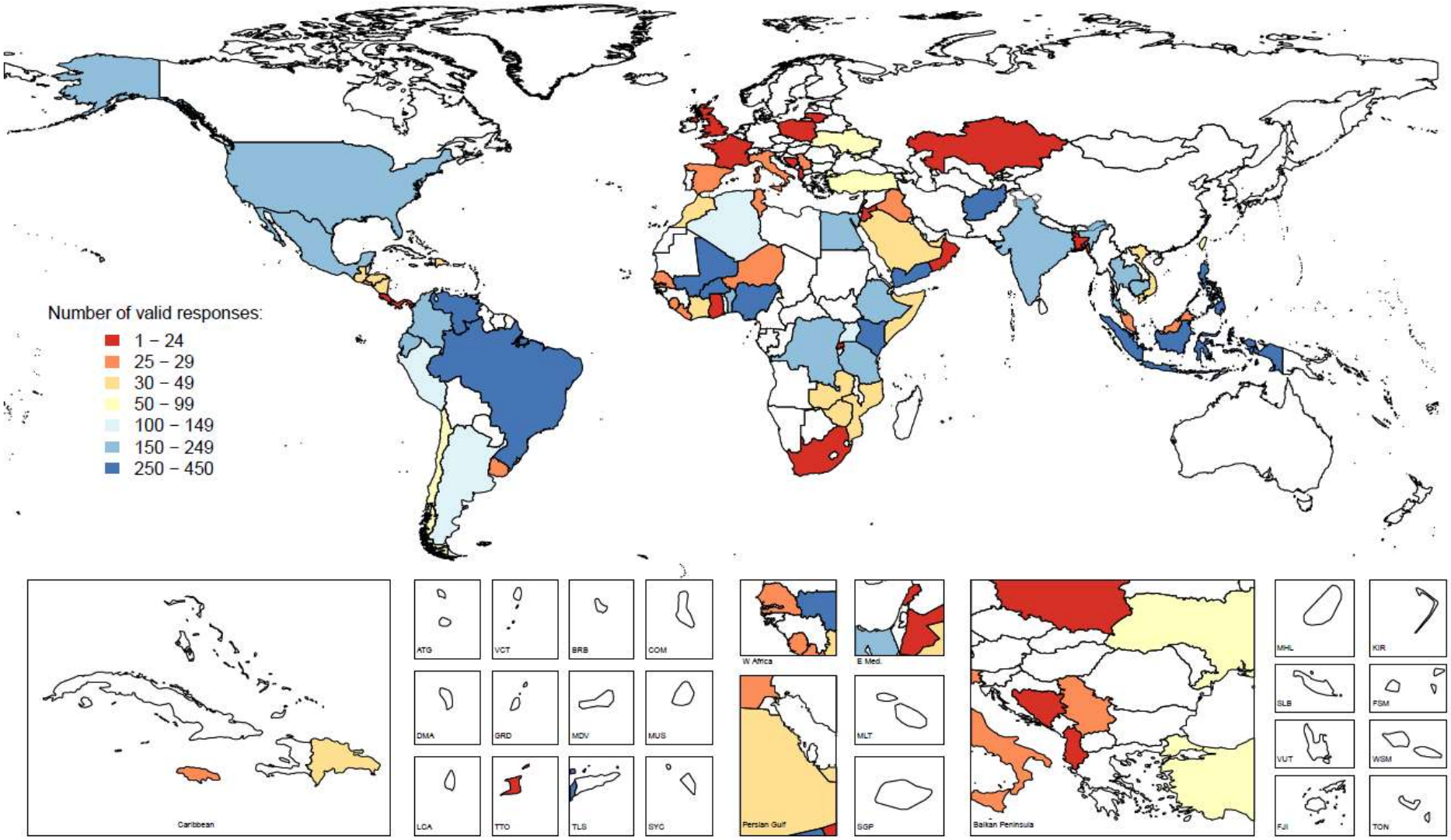


Figure 2: Data coverage for WHO administrative data

The map depicts countries for which we received administrative vaccine delivery data from the WHO for March, April, and May. We excluded data from Afghanistan, Bangladesh, Chad, Guatemala, Haiti, Kenya, Lesotho, Madagascar, Namibia, Nepal, Senegal, Somalia, Tanzania, Uruguay, Venezuela, and Yemen because it did not align with qualitative data from Pulse polls, essential health services polls, and additional qualitative data collected by the WHO regional offices. ATG=Antigua and Barbuda. BRB=Barbados. COM=Comoros. DMA=Dominica. E Med.=Eastern Mediterranean. FJI=Fiji. FSM=Federated States of Micronesia. GRD=Grenada. KIR=Kiribati. LCA=Saint Lucia. MDV=Maldives. MHL=Marshall Islands. MLT=Malta. MUS=Mauritius. SGP=Singapore. SLB=Solomon Islands. SYC=Seychelles. TLS=Timor-Leste. TON=Tonga. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines. VUT=Vanuatu. WSM=Samoa.

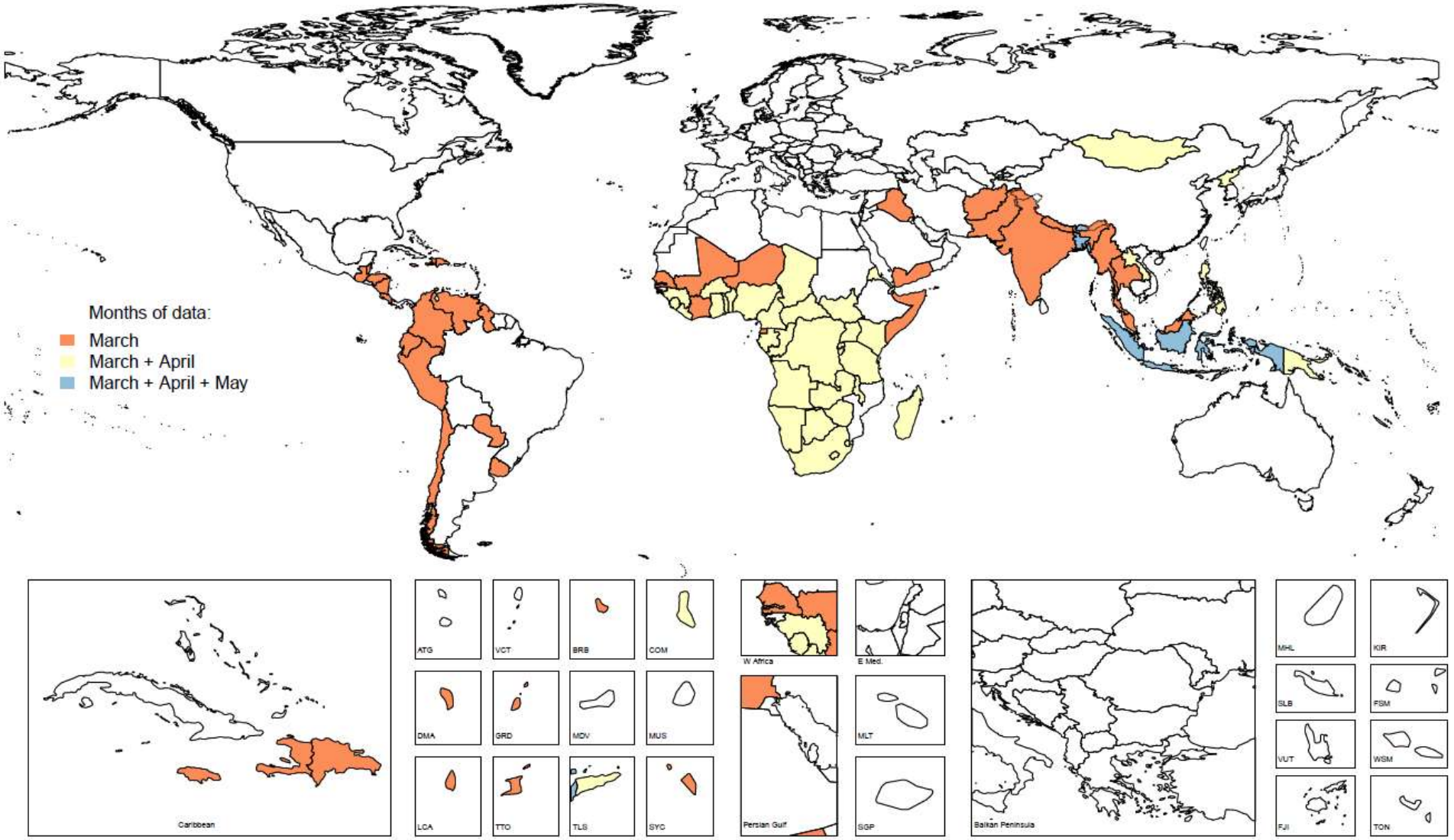


Figure 3: Spline fits for DTP3 and MCV1 vaccine coverage—global model and select countries, 2020

The panels show A) DTP3 and B) MCV1 coverage disruptions relative to reductions in mobility. Plots depict the stage 1 global model and 4 selected stage 2 location-specific models. Each spline spans the domain of daily observed mobility for a given location. The area of each point is relative to the inverse variance and weight in the model. Data points for each of the selected countries have been highligted in the correcsponding country color. The shaded area covers the 95% uncertainty interval around the estimate while the line depicts the mean estimate.

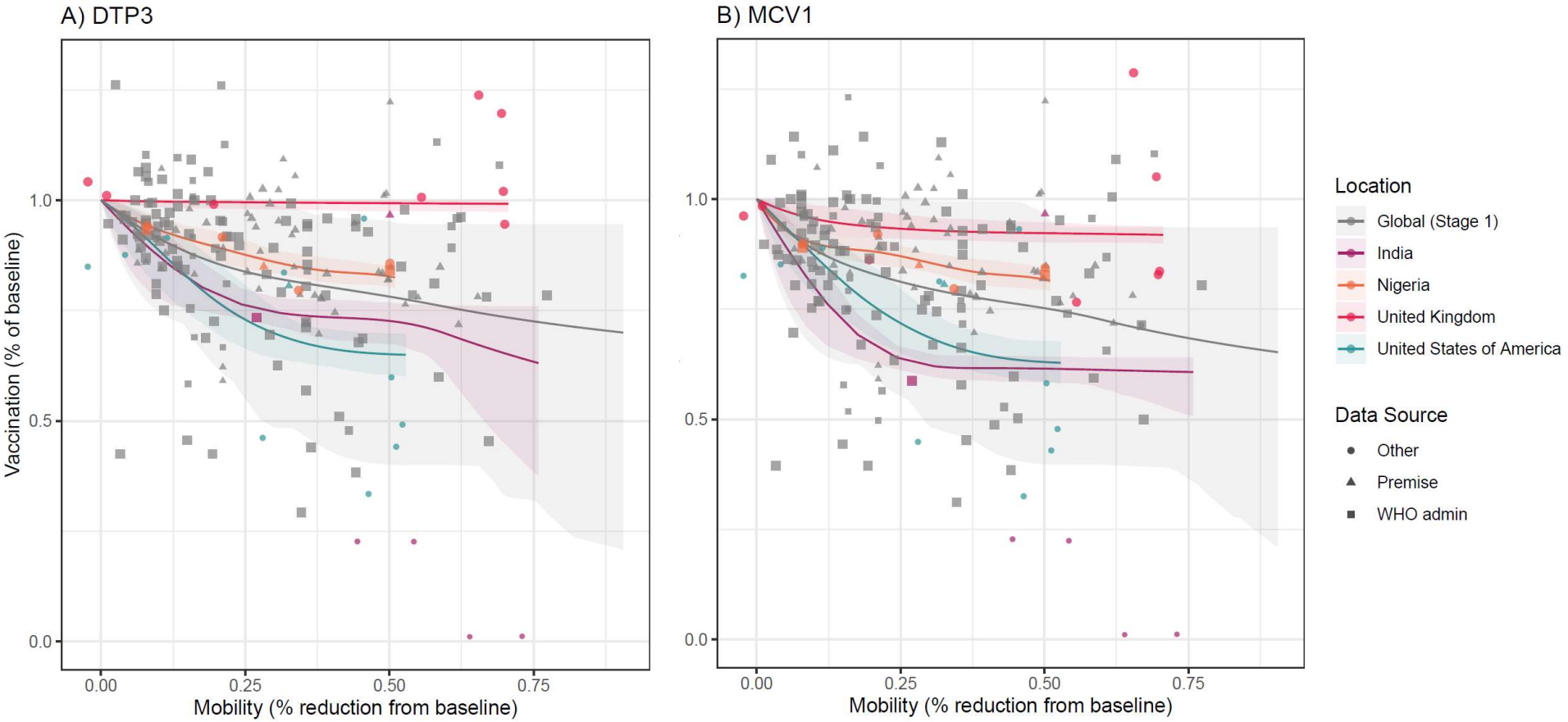


Figure 4: DTP3 and MCV1 vaccine interruption in Nigeria and mobility change from baseline, 2020

The upper panel displays estimated vaccine disruption for MCV1 and DTP3 in Nigeria with the data. Each point includes a vertical bar to demonstrate the 95% confidence interval around the data and a horizontal bar to show the time coverage of a data source. The Premise survey data (triangle) covered a time period of March through June; because it was not antigen-specific, we included it in both models. The solid line span the first half of 2020 for which we have vaccine coverage data. The dotted line provides the projection of coverage for the second half of 2020 based on the observed relationship with mobility, forecasted COVID-19 disease rates, and forecasted mobility. The lower panel displays the observed (solid) and projected (dotted) mobility for 2020 based on mobile phone data. The shaded area in the top panel covers the 95% uncertainty interval around the estimate while the line depicts the mean estimate.

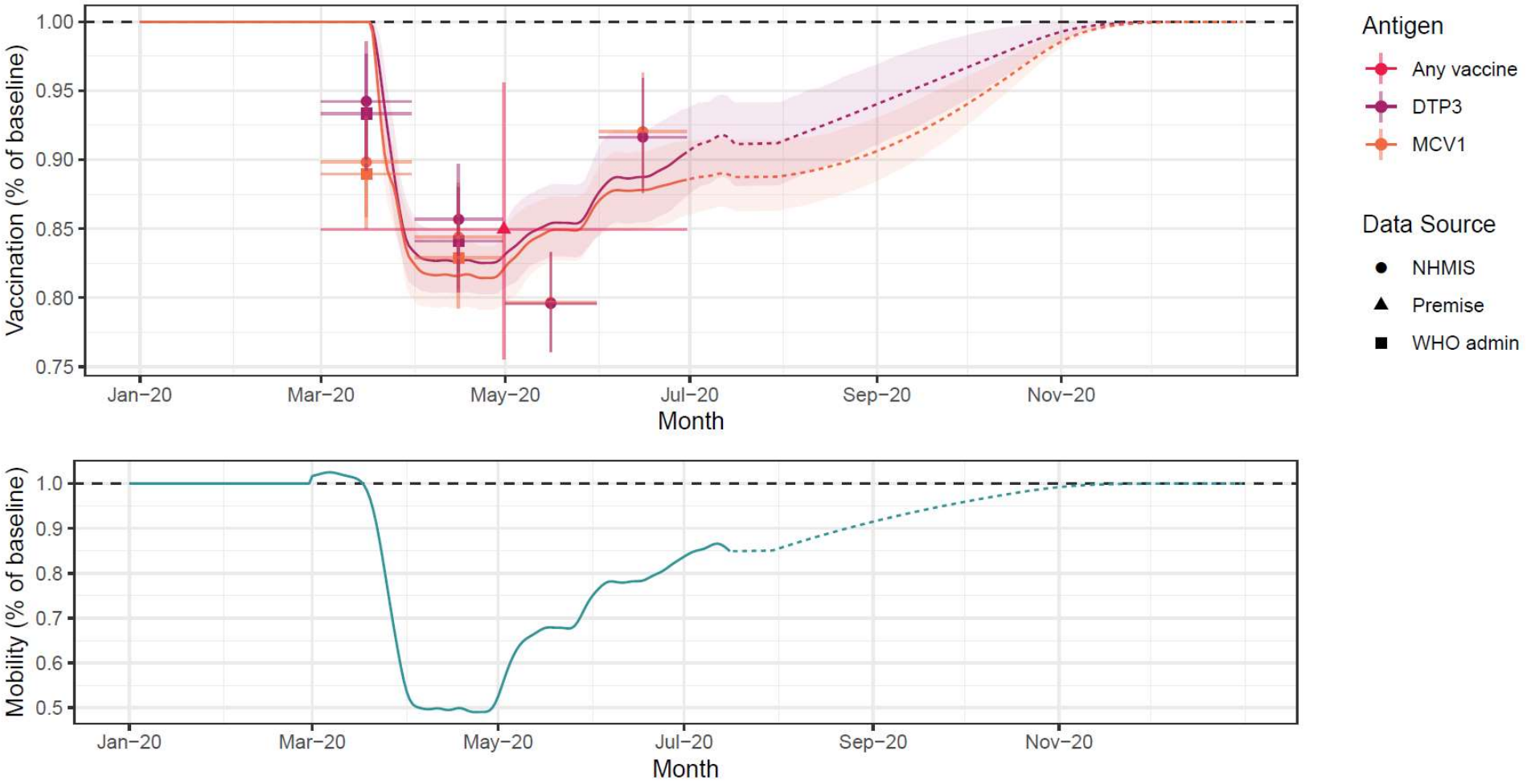


Table 2: Vaccine coverage and interruption for DTP3 and MCV1, Super-regions and global, non-COVID-19 2020 reference value, observed pandemic period, and 2020 projections

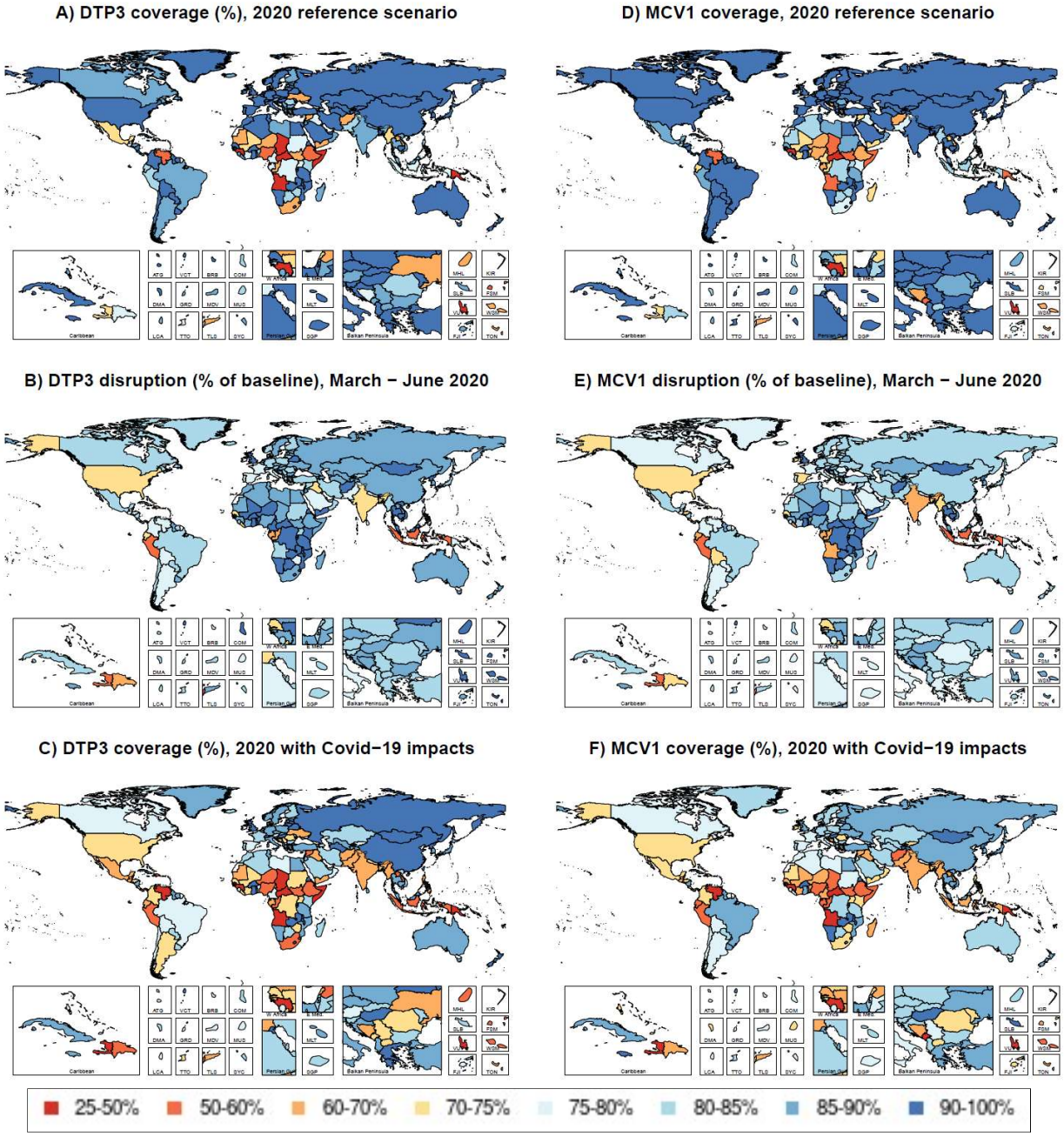
The reference coverage is the estimated value that would have been achieved for each antigen in the absence of COVID-19 based on past trends and vaccine coverage estimates. The interruption is the estimated percent of baseline delivery achieved during the given period. Coverage represents the proportion of infants receiving the vaccine during the specified period. Interruption and coverage results are provided for March – June of 2020 and for the entire year. March-June is the period for which we have data on both vaccine delivery and human mobility. Percentages in parentheses represent the 95% uncertainty interval of the estimate.

	DTP3					MCV1				
	Reference Coverage (%)	March – June 2020		2020*		Reference Coverage (%)	March – June 2020		2020*	
Location		Interruption (% of baseline)	Coverage (%)	Interruption (% of baseline)	Coverage (%)		Interruption (% of baseline)	Coverage (%)	Interruption (% of baseline)	Coverage (%)
High-income	94.3	79.9 (67.1, 86.4)	75.4 (63.1, 81.6)	85.7 (77.4, 90.3)	80.9 (73, 85.3)	93.9	77.3 (65, 83.8)	72.6 (60.9, 78.8)	83.6 (75.4, 88.8)	78.6 (70.8, 83.5)
Central Europe, Eastern Europe, and Central Asia	93.5	85.8 (61.1, 95.7)	80.2 (56.6, 9.6)	90.5 (74.9, 97.4)	84.7 (69.7, 91.2)	95.1	83.3 (61.2, 96.7)	79.2 (58.3, 92)	88.5 (74.8, 97)	84.2 (71.2, 92.2)
Sub-Saharan Africa	69.9	89.7 (88.3, 90.9)	63 (62.1, 63.8)	94.3 (93.3, 95.1)	66.1 (65.4, 66.6)	73.4	87.7 (86.1, 89)	64.6 (63.5, 65.5)	92.9 (91.6, 93.7)	68.3 (67.4, 68.9)
North Africa and Middle East	86.3	85.3 (76.8, 90)	73.5 (66, 77.6)	90.2 (84.6, 93.2)	77.6 (72.7, 80.4)	86.5	83.7 (75.7, 89)	72.1 (64.8, 76.8)	89 (83.4, 92.5)	76.8 (71.5, 80)
South Asia	88.3	73.2 (66.6, 77.6)	64.6 (58.6, 68.5)	77.5 (73.6, 80.5)	68.4 (64.9, 71.1)	90.5	69.4 (66.4, 71.7)	62.4 (59.6, 64.4)	73.6 (71.5, 75.4)	66.1 (64.2, 67.8)
Southeast Asia, East Asia, and Oceania	90.9	80.8 (65.5, 87.9)	74.2 (58.9, 81.4)	88.3 (79.2, 92.5)	80.7 (71.5, 85)	92.4	78.8 (64.9, 88)	73.3 (59.7, 82.3)	86.8 (78.7, 91.1)	80.4 (72.5, 84.7)
Latin America and Caribbean	82.2	78.5 (75.7, 81)	64.6 (62.2, 66.8)	81.9 (79.4, 84.3)	67.4 (65.3, 69.3)	89.9	76.3 (73.5, 78.7)	69 (66.3, 71.3)	80.1 (77.8, 82.5)	72.4 (70.2, 74.5)
Global	**83.9**	**81.7 (75.7, 85.1)**	**68.4 (62.8, 71.6)**	**86.9 (83.1, 89)**	**72.7 (69.1, 74.7)**	**86.3**	**79.2 (73.1, 82.8)**	**68.1 (62.3, 71.4)**	**84.7 (81, 86.9)**	**72.7 (69.2, 74.8)**

* Projections based on COVID-19 disease forecasts and the current relationship between decreased mobility and vaccine delivery.

Figure 5: Global maps of DTP3 and MCV1 reference coverage levels, COVID-19 disruptions, and expected coverage for 2020

Panels include A) DTP3 coverage estimated in 2020 in the absence of COVID-19, B) DTP3 disruption in Mar-June of 2020, C) estimated DTP3 coverage in 2020, D) MCV1 coverage estimated in 2020 in the absence of COVID-19, E) MCV1 disruption in Mar-June of 2020, and F) estimated MCV1 coverage in 2020. ATG=Antigua and Barbuda. BRB=Barbados. COM=Comoros. DMA=Dominica. E Med.=Eastern Mediterranean. FJI=Fiji. FSM=Federated States of Micronesia. GRD=Grenada. KIR=Kiribati. LCA=Saint Lucia. MDV=Maldives. MHL=Marshall Islands. MLT=Malta. MUS=Mauritius. SGP=Singapore. SLB=Solomon Islands. SYC=Seychelles. TLS=Timor-Leste. TON=Tonga. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines. VUT=Vanuatu. WSM=Samoa.



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