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COVID-19 impact on routine immunisations for vaccine-preventable diseases: Projecting the effect of different routes to recovery

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ABSTRACT

Over the past two decades, vaccination programmes for vaccine-preventable diseases (VPDs) have expanded across low- and middle-income countries (LMICs). However, the rise of COVID-19 resulted in global disruption to routine immunisation activities. Such disruptions could have a detrimental effect on public health, leading to more deaths from VPDs, particularly without mitigation efforts. Hence, as routine immunisation activities resume, it is important to estimate the effectiveness of different approaches for recovery. We apply an impact extrapolation method developed by the Vaccine Impact Modelling Consortium to estimate the impact of COVID-19-related disruptions with different recovery scenarios for ten VPDs across 112 LMICs. We focus on deaths averted due to routine immunisations occurring in the years 2020–2030 and investigate two recovery scenarios relative to a no-COVID-19 scenario. In the recovery scenarios, we assume a 10% COVID-19-related drop in routine immunisation coverage in the year 2020. We then linearly interpolate coverage to the year 2030 to investigate two routes to recovery, whereby the immunization agenda (IA2030) targets are reached by 2030 or fall short by 10%. We estimate that falling short of the IA2030 targets by 10% leads to 11.26% fewer fully vaccinated persons (FVPs) and 11.34% more deaths over the years 2020–2030 relative to the no-COVID-19 scenario, whereas, reaching the IA2030 targets reduces these proportions to 5% fewer FVPs and 5.22% more deaths. The impact of the disruption varies across the VPDs with diseases where coverage expands drastically in future years facing a smaller detrimental effect. Overall, our results show that drops in routine immunisation coverage could result in more deaths due to VPDs. As the impact of COVID-19-related disruptions is dependent on the vaccination coverage that is achieved over the coming years, the continued efforts of building up coverage and addressing gaps in immunity are vital in the road to recovery.

1. Introduction

The coronavirus disease-19 (COVID-19) pandemic has resulted in disruption to health services globally, including disruption of vaccination activities. Many low- and middle-income countries (LMICs) have faced drops in routine immunisation coverage, alongside delays in supplementary immunisation activities, such as campaigns [1,2].

In response to the evolving pandemic, early World Health Organization (WHO) guidance in March 2020 recommended temporary suspension of mass vaccination campaigns but continuation of

Abbreviations: LMICs, Low- and middle-income countries; VPDs, Vaccine-preventable diseases; FVPs, Fully vaccinated persons; IA2030, Immunization agenda 2030; WHO, World Health Organization; IHME, Institute for Health Metrics and Evaluation; VIMC, Vaccine Impact Modelling Consortium; NPIs, Non-pharmaceutical interventions.

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routine immunisation whilst maintaining prevention and control measures for COVID-19 [3]. Later, in May 2020, WHO interim guidance recommended consideration of vaccine preventable disease (VPD) outbreak risk when deciding whether to conduct campaigns [4]. The WHO's latest national pulse survey on the continuity of essential health services during the COVID-19 pandemic highlights that there has been a reduction in the number of countries (37% of 112 responding countries) reporting disruptions to immunisation services in 2021, compared to 62% of 129 countries reporting disruptions in 2020 [2].

The level of decline in vaccination coverage has been estimated throughout the pandemic. Early projections by the Institute for Health Metrics and Evaluation (IHME) estimated the disruption that had already occurred until July 2020 (based on various data sources, including survey data, monthly administrative data on health services and data on human mobility patterns) and projected what may occur for the remainder of 2020 [5]. This led to a prediction of a 7–17% drop in coverage of third diphtheria-tetanus-pertussis (DTP3) dose in 2020 [6]. Further modelling work by IHME used administrative data and reports from electronic immunisation systems, with mobility data as model input and estimated the global coverage in 2020 for DTP3 and the first dose of measles-containing vaccine (MCV1) to have fallen by 7.7% and 7.9%, respectively [7]. Notably, the level of disruption varies geographically with some areas more affected than others [7–8]. In Gavi-supported countries, coverage with a full course of pentavalent vaccine and MCV1 both decreased to 78% from 82% and 81%, respectively [8]. Despite disruptions, more children were vaccinated in December 2020 than in December 2019, showcasing the vast efforts made by countries and international organisations to bring vaccination programmes back on track [8].

Prior to the pandemic, vaccination coverage for VPDs had been increasing, significantly reducing morbidity and mortality related to VPDs across LMICs [9]. In LMICs, the immense progress made has been in part due to Gavi, the Vaccine Alliance, which was created in 2000 with a goal of providing vaccines to save lives and protect people's health. Over 2000–2020, Gavi has supported vaccination for over 888 million children through routine programmes and over 1.19 billion vaccinations through preventive vaccination campaigns, preventing over 15 million future deaths [10].

The beneficial population-level effects of vaccination programmes cannot be assessed directly as the counterfactual, i.e., the situation without vaccination, cannot be observed. Advantageously, mathematical models enable us to quantify the impact of vaccination in terms of cases, deaths and disability-adjusted life years averted. The Vaccine Impact Modelling Consortium (VIMC), established in 2016, consists of multiple independent modelling groups with the aim of estimating the impact of vaccination programmes for 12 VPDs over 112 LMICs [11]. Recently, the VIMC estimated that without COVID-19-related disruptions to vaccination coverage, 47 (95% CI[39, 56]) million deaths would be averted due to vaccination activities over 2020–2030 for 10 VPDs across 112 LMICs [9].

Furthermore, a study conducted to inform the Immunization Agenda (IA2030) estimated that 51.0 million (95% CI[48.5, 53.7]) deaths would be averted due to vaccinations administered between the years 2021 and 2030 for 14 pathogens in 194 countries [12]. IA2030 is based on aspirational country-specific DTP3 2030 targets. The study assumed 2019 coverage levels remained constant through 2021.

A previous study assessing the impact of COVID-19 disruptions on VPDs, estimated the health impact of 50% reduced routine immunisation coverage in 2020 and delay of campaign vaccination from 2020 to 2021 for measles, *Neisseria meningitidis* serogroup A and yellow fever showing risks of increased disease burden and measles outbreaks [13].

It is important to estimate the long-term impact of different routes to recovery to determine their effectiveness. In this study, we investigate the impact of COVID-19-related disruptions with different recovery scenarios for ten VPDs, namely, *Haemophilus influenzae* type b (Hib), hepatitis B (HepB), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), rotavirus (Rota), rubella, *Streptococcus pneumoniae* (PCV) and yellow fever (YF). We use an impact extrapolation method developed by the VIMC to estimate the effect of routine immunisation coverage changes. Impact is attributed to the year in which the routine immunisation activity occurred [14]. Based on IHME and Gavi estimates of coverage declines, we examine a 10% drop in coverage in the year 2020 and linearly project different routes to recovery over the years 2021 to 2030 i.e., reaching IA2030 targets in the year 2030 or falling 10% short (with the 10% drops being absolute, not relative to existing coverage). Comparing this to a scenario with no COVID-19-related disruptions, we estimate the effectiveness of the different routes to recovery.

2. Methods

To estimate the effect of coverage changes to routine immunisation, we use the impact extrapolation method developed by the VIMC (Fig. 1) [14]. This method is computationally and time efficient as it allows us to take the impact ratio (impact attributable per fully vaccinated person) from previous VIMC work and apply it to a new coverage scenario in order to extrapolate the impact calculation to the new coverage estimates. More specifically, for each country, the new number of fully vaccinated persons (FVPs) is first calculated by multiplying the new coverage with the country's target population size where the target population is the number of people eligible for vaccination with a particular activity. Then to calculate the updated impact of vaccination per country and per year, we multiply previously estimated country- and year-specific impact ratios associated with routine immunisations [9] with the corresponding new number of FVPs (Fig. 1). These impact numbers are then summed across all countries and years to calculate the total impact of vaccination.

As the impact extrapolation method is primarily a linear interpolation of previous vaccine impact estimates with new coverage estimates, it may not capture any outbreaks or existing population immunity that may occur for the outbreak prone VPDs with dynamic models (Table 1) [14]. Furthermore, any expected changes in transmission due to non-pharmaceutical interventions (NPIs) that have been employed during the COVID-19 pandemic, such as mask-wearing, lockdowns and social distancing, would not be captured within this analysis (Table 1).

Impact is attributed to the year in which the vaccination activity took place (year of vaccination activity stratification method) [14]. For routine immunisation, the impact ratio ρ for a specific country, c, is given by: $\rho(c) = \frac{\sum_{y-a\in Y_V - A_V} D(a,c,y)}{\sum_{y\in Y_V} FVP(c,y)}$, where a is age, y is year, D is the impact in terms of deaths averted, and Y_V-A_V are cohorts receiving vaccinations in years Y_V. The impact by year of vaccination for a specific country and year, D(c,y), is then given by: $D(c,y) = \rho(c) \times FVP(c,y)$, where FVP(c,y) are FVPs vaccinated through routine immunisation and the impact ratio is the same across all age groups. This method estimates the long-term impact of vaccination due to routine immunisation that occurs in a particular year. Hence, we capture the impact for pathogens where the mortality occurs later in life, such as HepB and HPV. Here, we focus on impact in terms of deaths averted due to routine immunisation that occurs over the years 2020 to 2030. Using the impact extrapolation with the year of vaccination activity stratification method,

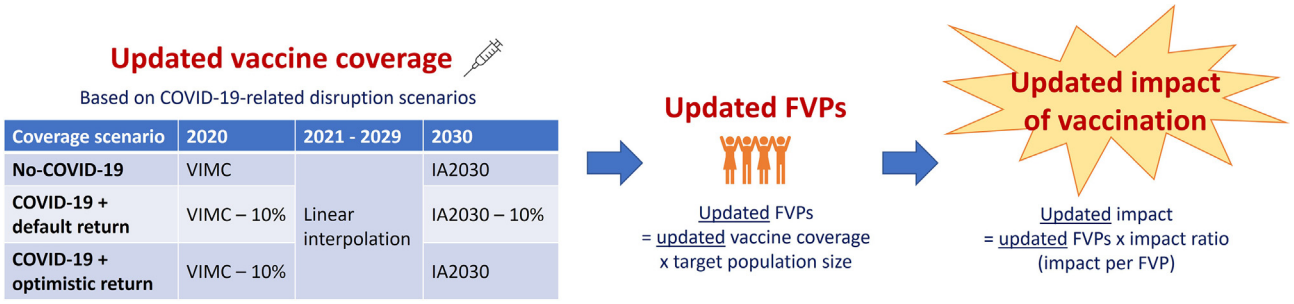

Fig. 1. Schematic of the impact extrapolation method and coverage scenarios over the years 2020 to 2030. VIMC coverage corresponds to coverage used for previous Vaccine Impact Modelling Consortium work [9] and IA2030 coverage corresponds to the immunization agenda coverage [12].

Table 1
For the ten vaccine-preventable diseases analysed: number of countries with routine immunisation activities over the years 2020 to 2030; type of model(s) used by the Vaccine Impact Modelling Consortium; type of vaccination activities (routine immunisation and/or supplementary immunisation activities); risk of outbreaks occurring and expected changes in transmission due to non-pharmaceutical interventions (NPIs).

Disease	Number of countries	Model type(s)	Activity type(s)	Outbreak risk	Expected changes in transmission due to NPIs
Haemophilus influenzae type b (Hib)	2020–2021: 110, 2022–2030: 112	2 static	Routine immunisation	Minimal	NPIs may lead to a reduction in transmission
Hepatitis B (HepB)	2020–2030: 112	2 dynamic + 1 static	Routine immunisation	Some	NPIs expected to cause short term disruption but minimal effect over timespan of disease
Human papillomavirus (HPV)	2020–2022: 17, 2023–2030: 110	2 static	Routine immunisation + Supplementary immunisation activities	Minimal	NPIs expected to cause short term disruption but minimal effect over timespan of disease
Japanese encephalitis (JE)	2020–2022: 8, 2023–2030: 17	1 dynamic + 1 static	Routine immunisation + Supplementary immunisation activities	Minimal	No/minimal changes expected
Measles	2020–2030: 112	2 dynamic	Routine immunisation + Supplementary immunisation activities	Yes	NPIs may lead to a reduction in transmission
Neisseria meningitidis serogroup A (MenA)	2020–2030: 26	2 dynamic	Routine immunisation + Supplementary immunisation activities	Yes	NPIs may lead to a reduction in transmission
Rotavirus (Rota)	2020–2021: 64, 2022–2030: 112	1 dynamic + 1 static	Routine immunisation	Yes	NPIs may lead to a reduction in transmission
Rubella	2020–2022: 88, 2023–2030: 112	2 dynamic	Routine immunisation + Supplementary immunisation activities	Yes	NPIs may lead to a reduction in transmission
Streptococcus pneumoniae (PCV)	2020–2030: 112	2 static	Routine immunisation	Minimal	NPIs may lead to a reduction in transmission
Yellow fever (YF)	2020–2023: 25, 2024–2030: 36	2 static	Routine immunisation + Supplementary immunisation activities	Yes	No/minimal changes expected

the effect of coverage improvements is averaged over the whole time period [14]. The updated impact, D*, is given by: $D^*(c,y) = \rho(c) \times FVP^*(c,y)$.

In the previous VIMC model runs, twenty-one mathematical models were used to inform the estimates with two models per pathogen (except HepB which has three models) thereby increasing robustness as the models differ in their underlying assumptions and modelling frameworks. All VIMC models are reviewed against predefined minimum standards, including the model generating the required outputs (deaths, cases and disability-adjusted life years), the use of standardised demographic data provided by VIMC and the availability of comprehensive model documentation with details of model parameterisation or fitting. In addition, there are desirable criteria including rigorous fitting to epidemiological data, although the out-of-sample validation sets may consist of simulated data or output produced by alternative models rather than representative surveillance data from the target populations. The DynaMICE model for measles is a notable example that has not been validated with out-of-sample population data but a recent paper [15] explored the model's sensitivity to changes in a range of key determinants and compared its incidence estimates to those from alternative models. Supplementary Appendix 2 of [9] also describes the VIMC model review process.

Previous VIMC estimates did not include COVID-19-related disruptions to coverage. Model estimates focused on 112 countries, including 73 currently and formerly Gavi supported countries and 39 other countries that are of interest due to high burden and/or potential vaccine introduction [9]. Pathogens endemic only in certain regions such as JE, MenA, and YF have estimates for 17, 26 and 36 countries, respectively (Table 1). Standardised, national-level, age-stratified demographic data were provided to all modellers from the 2019 United Nations World Population Prospects (UNWPP) for years 2000 to 2100 [16]. Detailed model descriptions are provided in [9] (HepB [17], HPV [18–19], Hib [20–21], JE [22],Measles [23–24], MenA [25–26], PCV [20–21], Rota [27–28], Rubella [29–30], YF [31]).

Coverage estimates for 2020 are based on the previous VIMC estimates which are modelled using historical WUENIC (WHO/

Table 2
Fully vaccinated persons (FVPs) and deaths averted due to routine immunisation activities over the years 2020–2030 for each disease and in total across all ten diseases (*Haemophilus influenzae* type b (Hib), hepatitis B (HepB), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), rotavirus (Rota), rubella, *Streptococcus pneumoniae* (PCV) and yellow fever (YF)). Relative change (%) in FVPs and deaths averted in comparison to the no-COVID-19 scenario also shown where relative change is given by 100*(COVID-19 scenario - no-COVID-19 scenario)/no-COVID-19 scenario. See Fig. 1 for more detail on the coverage scenarios.

Coverage scenario	Disease	FVPs in millions (Relative change (%))	Deaths averted in millions (Relative change (%))
No-COVID-19	HepB	1890.67	12.55
2020: VIMC	Hib	1037.56	2.45
2021–2029: Linear interpolation	HPV	322.28	3.84
2030: IA2030	JE	261.37	0.12
	Measles	2111.43	19.32
	MenA	225.48	0.19
	PCV	917.14	2.10
	Rota	853.42	0.66
	Rubella	2014.30	0.65
	YF	243.99	1.84
	Total	9877.65	43.72
COVID-19 + default return	HepB	1683.16 (-10.98)	11.14 (-11.21)
2020: VIMC – 10%	Hib	923.25 (-11.02)	2.16 (-11.73)
2021–2029: Linear interpolation	HPV	299.37 (-7.11)	3.55 (-7.50)
2030: IA2030 – 10%	JE	216.20 (-17.28)	0.10 (-15.61)
	Measles	1876.60 (-11.12)	17.03 (-11.86)
	MenA	190.44 (-15.54)	0.16 (-15.03)
	PCV	792.56 (-13.58)	1.83 (-13.16)
	Rota	759.96 (-10.95)	0.59 (-10.98)
	Rubella	1811.87 (-10.05)	0.59 (-9.93)
	YF	211.70 (-13.23)	1.61 (-12.33)
	Total	8765.12 (-11.26)	38.76 (-11.34)
COVID-19 + IA2030 return	HepB	1795.86 (-5.02)	11.86 (-5.49)
2020: VIMC – 10%	Hib	984.18 (-5.14)	2.31 (-5.66)
2021–2029: Linear interpolation	HPV	321.13 (-0.36)	3.82 (-0.70)
2030: IA2030	JE	243.78 (-6.73)	0.12 (-5.99)
	Measles	1999.97 (-5.28)	18.21 (-5.73)
	MenA	208.50 (-7.53)	0.17 (-7.30)
	PCV	855.04 (-6.77)	1.97 (-6.48)
	Rota	817.68 (-4.19)	0.64 (-3.93)
	Rubella	1926.59 (-4.35)	0.63 (-4.25)
	YF	230.46 (-5.55)	1.73 (-5.82)
	Total	9383.19 (-5)	41.44 (-5.22)

UNICEF) coverage for existing routine immunisation programmes [9]. For countries that had not introduced a specific vaccine by 2018, the same future introduction year was assumed based on accelerated failure time model projections. Coverage estimates for 2030 are based on the IA2030 aspirational targets [12]. Hence, country-specific DTP3 endpoints were used as the 2030 coverage for Hib, HepB, JE, measles, MenA, Rota, Rubella, PCV and YF. For JE and YF, for countries with subnational introduction, the current coverage rate and population were used. For HPV, 90% coverage was used for all countries in 2030.

We investigate three scenarios: one with no COVID-19-related disruptions and two with COVID-19-related disruptions (Fig. 1). For the no-COVID-19 scenario, we assume no drop in routine immunisation coverage in the year 2020 and linearly interpolate coverage over 2021 to 2029, assuming that the IA2030 targets are reached in the year 2030. For the disruption scenarios, we assume a 10% absolute drop in routine immunisation coverage in the year 2020 then linearly interpolate coverage over 2021 to 2029, assuming that coverage in 2030 either reaches the IA2030 targets (IA2030 return scenario) or reaches the IA2030 targets with a 10% absolute reduction (default return scenario) [12].

Across all scenarios, we assume vaccine introduction years remain the same. Where routine immunisations were introduced later than 2020, we keep the coverage the same as it was expected to be in the year of introduction and linearly interpolate to the scenario-specific 2030 endpoint.

To compare the disruption scenarios to the no-COVID-19 scenario, we estimate the change in FVPs and deaths averted for each disease. More specifically, we show the proportional decrease in FVPs and increase in deaths in the COVID-19 scenarios relative to the no-COVID-19 scenario. We also estimate the impact (deaths averted) and FVPs attributable to each year's routine immunisation activities over the years 2020–2030. Note that the death terms in the COVID-19 scenarios do not include deaths due to COVID-19, only deaths attributable to the ten VPDs analysed.

3. Results

In the default return scenario over 2020–2030, we estimate that a COVID-19 drop in coverage leads to 11.26% fewer FVPs and 11.34% more deaths relative to the no-COVID-19 scenario. With the IA2030 return scenario over 2020–2030, these proportions decline to 5% fewer FVPs and 5.22% more deaths (Table 2). The impact of the COVID-19-related disruption varies across the diseases with some diseases able to recover more FVPs and thus deaths averted.

In both recovery scenarios, HPV is estimated to face the lowest effect due to disruption relative to the other VPDs. More specifically, HPV has a 0.36% or 7.11% reduction in FVPs and 0.7% or 7.5% more deaths with the IA2030 or default return, respectively (Table 2 and Fig. 2). HPV routine immunisation activities are introduced into many countries in 2023 (Table 1); prior to that routine immunisation is only present in 17 countries.

On the other hand, we estimate that JE and MenA face the largest relative effects due to disruption. Similar to HPV, JE only has routine immunisations in 8 countries in 2020; however, JE routine immunisation activities remain in relatively fewer (17) countries

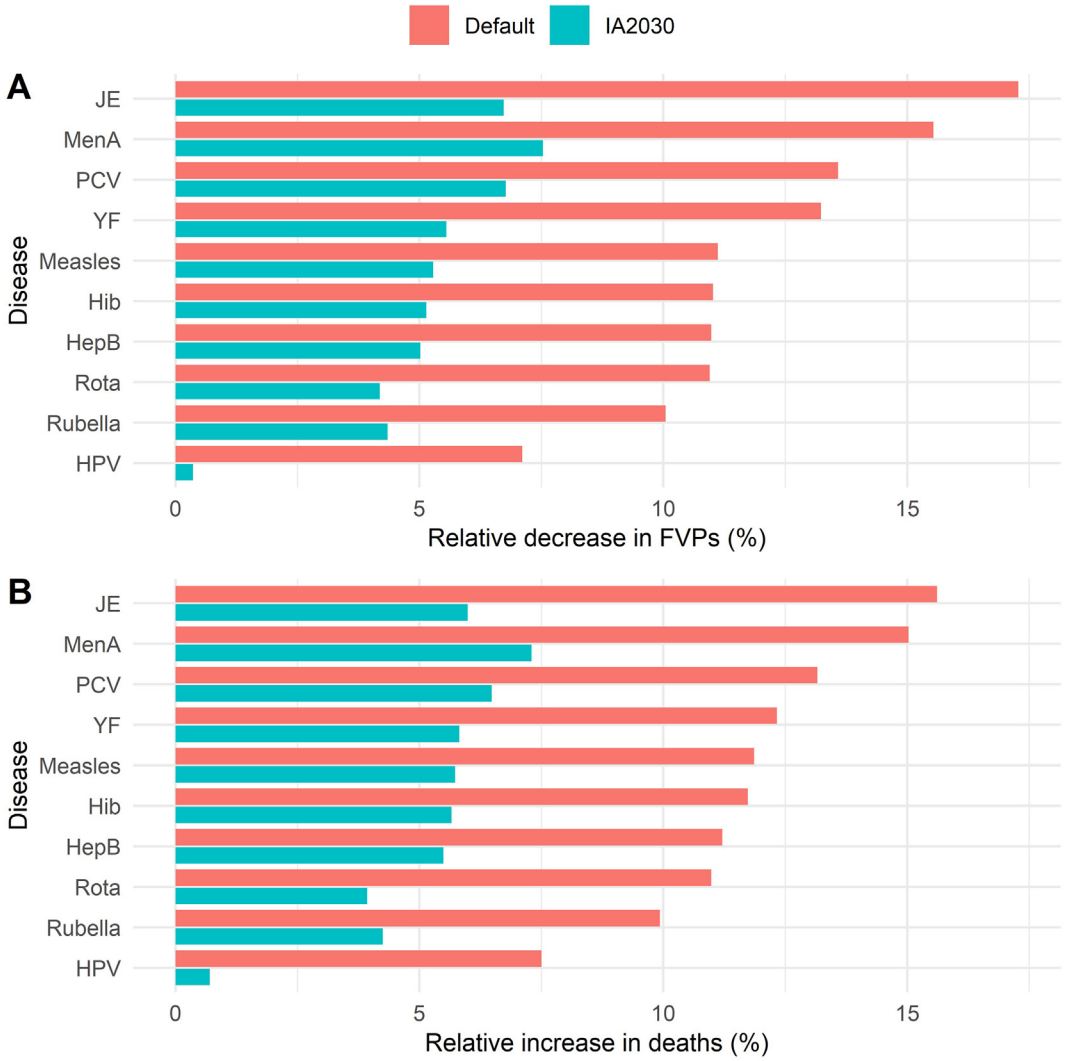

Fig. 2. Change over the years 2020–2030 for each disease in (A) fully vaccinated persons (FVPs) and (B) deaths in the default and IA2030 scenarios relative to the no-COVID-19 scenario. Disease abbreviations: *Haemophilus influenzae* type b (Hib), hepatitis B (HepB), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), rotavirus (Rota), rubella, *Streptococcus pneumoniae* (PCV) and yellow fever (YF). See Table 2 for more detailed information.

by 2030. MenA routine immunisation activities are also present in relatively fewer (26) countries over the years 2020 to 2030. The estimated impact attributable to each year of routine immunisation is similar for MenA and JE as it increases from 4.94% and 5.69% of deaths averted attributable to routine immunisation in 2020 to 12.68% and 12.95% of deaths averted attributable to routine immunisation in 2030, respectively (Fig. 3). With the default return, MenA and JE have the largest estimated impacts due to disruption with 15.54% and 17.28% drops in FVPs and 15.03% and 15.61% more deaths, respectively (Table 2). As JE and MenA routine immunisations in the year 2030 contribute to a large proportion of the estimated deaths averted over 2020–2030, the shortfall of 10% in the default return scenario has a large impact. Moving to the IA2030 return, the drop in FVPs declines to 6.73% and 7.53% with 5.99% and 7.30% more deaths for JE and MenA, respectively (Table 2 and Fig. 2).

We estimate that, relative to the other VPDs, PCV and YF face a moderate impact due to COVID-19-related disruptions. They have a similar pattern of the proportion of FVPs achieved and deaths averted attributable to each year of routine immunisation, with the proportion of deaths averted increasing stably from 7.16% (PCV) and 7.66% (YF) attributable to 2020 routine immunisation to 10.61% (YF) and 11.05% (PCV) attributable to 2030 routine immunisation (Fig. 3). With the default return, YF and PCV have an estimated 13.23% and 13.58% drop in FVPs and an estimated 12.33% and 13.16% increase in deaths relative to the no-COVID-19 scenario, respectively. With the IA2030 return, these estimates decline to a 5.55% and 6.77% drop in FVPs and a 5.82% and 6.48% increase in deaths for YF and PCV, respectively (Table 2 and Fig. 2). Note that this does not capture any YF outbreaks.

For the VPDs that have routine immunisations over a large number of countries from the years 2020 to 2030, i.e. HepB, Hib and measles, the estimated impact of the COVID-19-related disruption is similar (Table 1). For these VPDs, the estimated FVPs achieved and deaths averted attributable to each year's routine immunisations over 2020–2030 is more evenly distributed (with proportion of deaths averted ranging from 7.99–8.5% attributable to 2020 routine immunisation to 9.83–10.15% attributable to 2030 routine immunisation; Fig. 3). With the default return, HepB, Hib and measles are estimated to have a 10.98%, 11.02% and 11.12% drop in FVPs and a 11.21%, 11.73% and 11.86% increase in deaths relative to the no-COVID-19 scenario, respectively. With

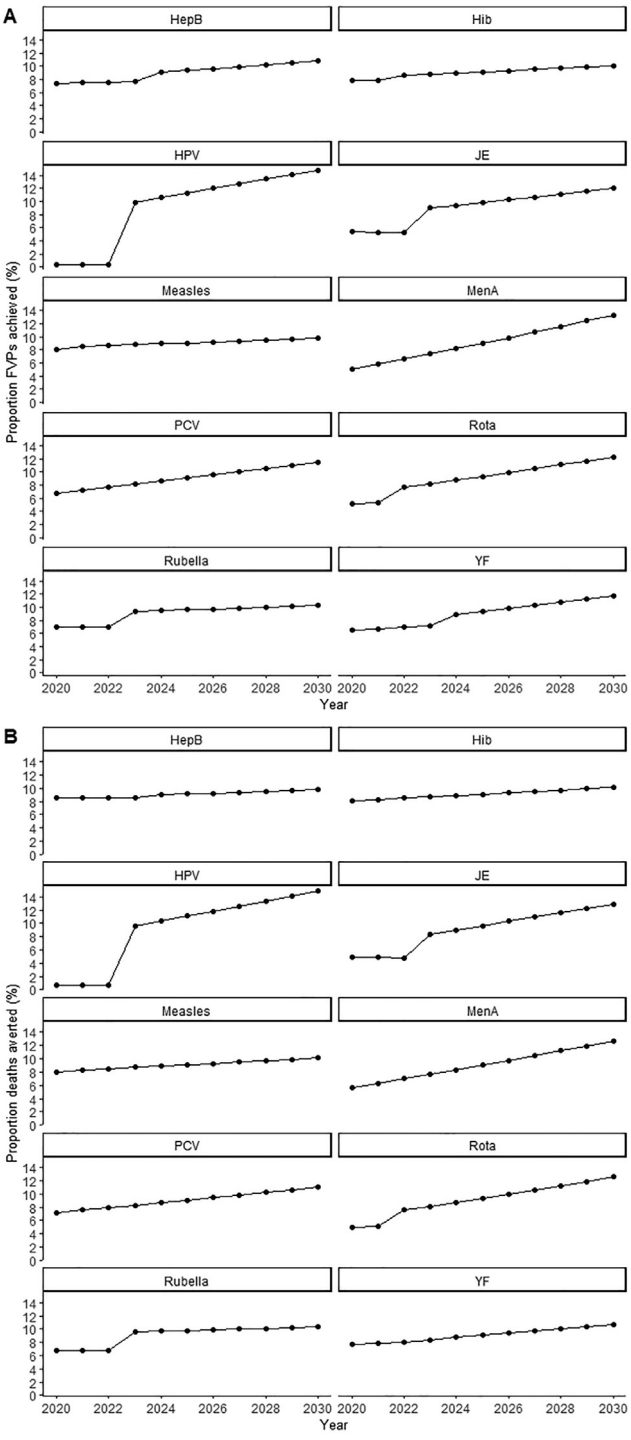

Fig. 3. Proportional (A) fully vaccinated persons (FVPs) and (B) impact (in terms of deaths averted) attributable to each year's routine immunisation activities in the no-COVID-19 scenario for *Haemophilus influenzae* type b (Hib), hepatitis B (HepB), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), rotavirus (Rota), rubella, *Streptococcus pneumoniae* (PCV) and yellow fever (YF).

the IA2030 return, these decline to a 5.02%, 5.14% and 5.28% drop in FVPs and a 5.49%, 5.66% and 5.73% increase in deaths for HepB, Hib and measles, respectively (Table 2 and Fig. 2).

Rota and rubella also have coverage in all 112 countries by 2030, highlighted by the increase in proportional FVPs and impact attributable to each year of routine immunisation (4.89% (Rota) and 6.78% (rubella) deaths averted in 2020, and 10.34% (Rota) and 12.53% (rubella) deaths averted in 2030; Table 1 and Fig. 3). With the default return, rubella and Rota show a 10.05% and 10.95% drop in FVPs and a 9.93% and 10.98% increase in deaths relative to the no-COVID-19 scenario, respectively. With the IA2030 return, these decline to a 4.19% and 4.35% drop in FVPs and a 3.93% and 4.25% increase in deaths for Rota and rubella, respectively (Table 2 and Fig. 2).

3.1. Outbreak-prone VPDs: comparison to previous VIMC work

As the impact extrapolation method risks not capturing any outbreaks for some of the VPDs (Table 1), we compare the results of our impact extrapolation analysis to modelling work carried out by VIMC members for measles, MenA and YF [13]. We note that both VIMC models for YF are static so even with new model estimates, YF outbreaks may not be captured. The model estimates for measles showed that the risk of an outbreak due to delayed campaigns varied by country, with those that had high pre-existing immunity facing lower risks of outbreaks. For MenA, in areas where there have been recent introductory campaigns capturing a wide range of ages (ages 1 to 29), there is more persistence of direct and indirect benefits which mitigate the impact of disruptions. Similarly for YF, strong existing herd immunity in areas where there have been recent campaigns aids in reducing the impact of disruptions [13].

4. Discussion

When interpreting the results, whose accuracy depends on the impact extrapolation method, we recommend considering each disease separately and consulting Table 1 to provide critical modelling context to use side-by-side with the quantitative summaries. We view these results as approximations in which our confidence is highest for diseases where the model type is static, outbreak risk is minimal, and expected transmission changes due to NPIs are minimal over the lifespan of the disease. For example, we may feel more confident in the impact estimates for Hib, HPV and PCV relative to estimates for measles, MenA and Rubella.

Overall, the IA2030 return scenario reduces the estimated impact of COVID-19-related disruptions for each of the VPDs. Our estimates suggest that the impact of the disruption varies by VPD, with HPV facing the lowest impact (0.7% increase in deaths with the IA2030 return). For HPV, routine immunisation activities occurring in 2020 contribute to less than 1% of the FVPs and deaths averted over the years 2020 to 2030 (Fig. 3). Hence, as a larger proportion of impact due to HPV routine immunisation occurs post-2022, the COVID-19-related decline in coverage in the year 2020 has a relatively low impact. Routine immunisation in the year 2030 contributes to the largest proportion of impact, 14.91% of estimated deaths averted, for HPV; that is, the later improvements in coverage are being averaged out over the whole time period. Hence, the beneficial effects of earlier HPV routine immunisation may be artificially inflated, thereby contributing to the low estimate of disruption impact. This is dependent on drastic expansions in coverage which face a risk of vaccine introduction delays or cancellations.

The other VPDs aside from HPV face a moderate to high projected impact, with JE and MenA estimated to have relatively higher impacts particularly if the IA2030 targets are not reached as for these VPDs the year 2030 is attributable to a relatively high proportion of deaths averted over the years 2020 to 2030 (15.61% and 15.03% more deaths in the default return reduced to 5.99% and 7.30% more deaths in the IA2030 return, respectively). In areas where there is existing immunity from earlier vaccination activi-

ties, these disruption impacts may be lower than estimated, particularly as our analysis is not accounting for any impact attributable to earlier campaigns that may have occurred.

Due to the impact extrapolation methodology used, we have focused on proportional changes in FVPs and deaths for each of the VPDs analysed. However, a specific proportional change is not equivalent across the VPDs as the baseline numbers are different. For example, a 1% increase in deaths attributable to measles corresponds to a larger number of deaths than a 1% increase in deaths attributable to a VPD across fewer countries, such as JE (baseline numbers shown in Table 2).

The VIMC validation exercise described in [14] suggests the impact extrapolation method is least accurate for dynamic models and diseases which are prone to outbreaks, but otherwise performs well for estimating impact under coverage changes of up to 10%. For larger changes to coverage, including when large supplementary immunisation activities are delayed or cancelled, accuracy of the approximation is likely compromised. In light of the global response to COVID-19, we also expect impact extrapolation to be less accurate for diseases whose transmission is sensitive to NPIs, and we acknowledge that our understanding of this limitation is still evolving. To reduce inaccuracies in our analysis, we have limited coverage changes to 10% in routine immunisation-only activities. In future work, new model estimates would be required to more accurately assess larger changes to coverage for both routine immunisation and supplementary immunisation activities, to account for herd effects and to capture possible outbreaks.

Notably, for the outbreak-prone VPDs (measles, MenA, Rota, Rubella and YF), the impact extrapolation method may be overestimating the impact of COVID-19-related disruptions for areas where there is existing immunity from earlier vaccination activities. Conversely, the impact extrapolation method risks not capturing any outbreaks that may have occurred. With larger delays to activities, the risks of not capturing such outbreaks increases.

Six of the VPDs assessed in our study (HPV, JE, measles, MenA, rubella and YF) have supplementary immunisation activities in addition to routine immunisation activities which have not been incorporated here. A previous study showed that delaying campaigns may increase the risk of measles outbreaks and the disease burden for YF [13]. With declines in vaccination coverage and in outbreak detection and control (which were reported as disrupted by 41% of 123 countries in 2020 [2]), the risk of outbreaks increased for the outbreak prone VPDs. By June 2020, Gavi reported that 30 Gavi eligible countries had reported VPD outbreaks, particularly for measles [32]. In August 2020, the death toll from a measles outbreak in the Democratic Republic of the Congo surpassed 7,000 (the world's worst) [33].

Importantly, a study promoting continuation of campaigns during the pandemic showed that personal protective equipment and symptomatic screening can reduce COVID-19 transmission [34]. Hence, catch-up campaigns for these VPDs where delays or cancellations have occurred may aid in reducing immunity gaps and limiting the impact of COVID-19-related disruptions [35]. In the latest WHO pulse survey, catch-up campaigns were reported by 31% of 112 countries as a mitigation strategy [2]. Although we assume a linear increase in vaccination coverage over time for the future years, realistically this may not be a true reflection of coverage changes seen over time, particularly in future analyses where campaigns are also included.

In our scenarios, we have assumed the same level of disruption to coverage for all countries and VPDs examined. However, levels of disruption are likely to vary across countries and diseases. For example, the most severe reductions in DTP3 and MCV1 coverage in 2020 were seen in north Africa and the Middle East, south Asia, Latin America and the Caribbean, with the lowest reductions in sub-Saharan Africa [7].

With global disruptions to vaccination programmes, there is evidence that the population of zero-dose children, i.e., children who have not received any dose of DTP, has increased. WHO and United Nations Children's Fund (UNICEF) estimates indicate that the number of children who did not complete the 3-dose DTP series worldwide increased by 20% to 22.7 million from 2019 to 2020. Of these children, 17.1 million (75%) are estimated to be zero-dose children [36]. To address such immunity gaps caused by disruptions, catch-ups and monitoring are important, e.g., through catch-up campaigns, expanding to reach age groups that may have aged out of the targeted ages and screening children in schools/health facilities for vaccination status [36].

Furthermore, the COVID-19 pandemic has had widespread impacts on other aspects of society, such as school closures. In May 2020, the World Bank highlighted that schools had closed in 180 countries, with 85% of students worldwide out of school [37]. Due to this, vaccines such as HPV, which are heavily reliant on delivery in schools, may be more negatively affected than assumed in our analysis. Conversely, there is also evidence that the rise in NPIs may reduce the transmission of certain pathogens, such as those that cause bacterial meningitis [38]. Overall, the expected changes in current and future transmission, and downstream changes, due to NPIs remain unclear but are likely to vary across the diseases analysed, for example, JE and YF are unlikely to be affected to the same extent as measles. Variation is also likely across countries as NPIs used have varied substantially in both timing and stringency [39]. Furthermore, despite short-term reductions in transmission, recent studies have highlighted the risks of resurgence and outbreaks following the relaxation of NPIs [40–42]. Further work and data are required to assess the full effects of these interventions.

As there has been immense progress to bring vaccination programmes back on track [8], we have only considered disruption in the year 2020 but this may be prolonged in some countries. It is still difficult to envisage the level of disruption in 2021 onward that countries may face due to the ongoing pandemic. Despite this uncertainty, it remains clear that building up coverage and addressing immunity gaps will be vital over the coming years.

5. Conclusions

Our study shows the importance of building up coverage as vaccination programmes recover from disruptions caused by the COVID-19 pandemic. This will enable the achievement of more vaccinated individuals and reduce morbidity and mortality caused by VPDs over future years.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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