Impact of the 100 days mission for vaccines on COVID-19: a mathematical modelling study

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Summary

Background The COVID-19 pandemic has underscored the beneficial impact of vaccines. It also highlighted the need for future investments to expedite an equitable vaccine distribution. The 100 Days Mission aims to develop and make available a new vaccine against a future pathogen with pandemic potential within 100 days of that pathogen threat being recognised. We assessed the value of this mission by estimating the impact that it could have had on the COVID-19 pandemic.

Methods Using a previously published model of SARS-CoV-2 transmission dynamics fitted to excess mortality during the COVID-19 pandemic, we projected scenarios for three different investment strategies: rapid development and manufacture of a vaccine, increasing manufacturing capacity to eliminate supply constraints, and strengthening health systems to enable faster vaccine roll-outs and global equity. Each scenario was compared against the observed COVID-19 pandemic to estimate the public health and health-economic impacts of each scenario.

Findings If countries implemented non-pharmaceutical interventions (NPIs) as they did historically, the 100 Days Mission could have averted an estimated 8·33 million deaths (95% credible interval [CrI] 7·70–8·68) globally, mostly in lower-middle income countries. This corresponds to a monetary saving of US$14·35 trillion (95% CrI 12·96–17·87) based on the value of statistical life-years saved. Investment in manufacturing and health systems further increases deaths averted to 11·01 million (95% CrI 10·60–11·49). Under an alternative scenario whereby NPIs are lifted earlier on the basis of vaccine coverage, the 100 Days Mission alone could have reduced restrictions by 12 600 days (95% CrI 12 300–13 100) globally while still averting 5·76 million deaths (95% CrI 4·91–6·81).

Interpretation Our findings show the value of the 100 Days Mission and how these can be amplified through improvements in manufacturing and health systems equity. However, these investments must be enhanced by prioritising a more equitable global vaccine distribution.

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Introduction

The COVID-19 pandemic was the largest public health crisis the world has faced in over 100 years. Despite efforts to limit the spread of the virus and an unprecedented acceleration in vaccine development timelines, there have been over 750 million confirmed cases of COVID-19 and over 20 million excess deaths.[1] The economic impacts of the pandemic were also vast, triggering the largest global economic crisis in over a century.[2] Although COVID-19 vaccinations are estimated to have prevented almost 20 million deaths,[3] there is a need to understand the further health and economic benefits that could have been achieved with shorter vaccine development times and improved global equity in pandemic preparedness.

The Coalition for Epidemic Preparedness Innovations (CEPI) was an early investor and key player in the global COVID-19 response.[4] In 2021, CEPI articulated its so-called moonshot 100 Days Mission: an initiative to cut vaccine development time for new pathogens to 100 days,[5] about a third of the time it took the world to deliver the first COVID-19 vaccine. This mission has received support from the G7 and G20, establishing the International Pandemic Preparedness Secretariat[6] to support the implementation of the 100 Days Mission against a future unknown pandemic, or disease X. The availability of COVID-19 vaccines within 100 days would have substantially changed the pandemic; however, these benefits would be finite without enabling equitable access to vaccine products[7] through system equity. Despite the aims of WHO and the implementation of a fair-allocation system in the form of COVID-19 Vaccines Global Access (COVAX), the global COVID-19 vaccination programme was hampered by global inequities in vaccine access and roll-out.[8,9] Over 40 countries were unable to meet the COVAX target of 20% coverage and more than 90 were unable to meet the WHO target of 40% coverage by the end of 2021.[10] It has also been

Research in context

Evidence before this study

We searched PubMed from Dec 9, 2019 up to Aug 9, 2023, for the terms "vaccin* AND (100-day* OR '100 day*') AND (impact OR value) AND (COVID-19 OR SARS-CoV-2) AND (estimat* OR evaluat*)". We identified one study that estimated the impact on cases and mortality due to a delay in vaccination access. This study focused only on lower-income and middle-income countries via statistical modelling, restricting its ability to capture impacts of vaccination on transmission dynamics. We also identified a medRxiv preprint that estimated the impact of earlier vaccinations on the UK and USA only, using a mathematical model similar to our own.

Added value of this study

This mathematical modelling study helps to quantify the potential public health and economic impacts of the 100 Days Mission to respond to an emerging epidemic with a vaccine within 100 days. Using mathematical models fitted to the historic COVID-19 pandemic, we quantified the impact that the 100 Days Mission would have had by retrospectively estimating the deaths averted, economic savings in terms of the value of statistical life and value of statistical life-years, and time spent under restrictions. By doing a global analysis, this study is, to the best of our knowledge, the first to show the differential impact that earlier vaccination would have had across income groups.

Implications of all the available evidence

The results highlight the substantial benefit that earlier access to vaccinations would have had on the COVID-19 pandemic. They also highlight the additional benefits of investments in vaccine distribution and manufacturing, which lead to the largest improvements in lower-income and middle-income countries in terms of the number of deaths averted. Furthermore, the findings show the broader benefits that earlier vaccination would have in terms of allowing countries to relax non-pharmaceutical interventions and reopen schools earlier while still averting millions of deaths due to COVID-19. The public health and economic benefits that the 100 Days Mission would have enabled during the COVID-19 pandemic shows the necessity for improving global vaccine manufacturing capacity and health system infrastructure to prepare for future pandemic threats.

recognised that wider support beyond faster deployment of vaccine products will be needed to increase global vaccine uptake, and that vaccine manufacturing capacity will need to be expanded but also diversified to promote self-sufficiency and regional resilience.[7] Additionally, local supply chains and vaccination infrastructure must be scaled to ensure that the most efficacious mRNA vaccines that rely on cold-chain infrastructure are available worldwide in the event of a future pandemic.[11]

COVID-19 vaccinations changed the course of the pandemic, allowing the lifting of non-pharmaceutical interventions (NPIs) such as travel restrictions, stay-at-home orders, and school closures[12] that were relied on initially to reduce SARS-CoV-2 transmission. Although NPIs were effective in reducing the burden of COVID-19 disease, there remain concerns around the broader health[13] and social[14] costs of these measures, including long-term harms to education.[15,16] Several countries achieved high vaccination coverage during 2021 and used the protection that this conferred as an exit strategy from NPIs, including the UK,[17] Israel,[18] and Singapore.[19] However, several countries were unable to achieve high proportions of vaccination coverage before the arrival of the delta variant and either had to maintain NPIs to minimise the impacts of the more virulent variant such as in South Africa,[20] or suffered significant epidemic waves with high mortality, such as in India.[21]

See Online for appendix

We aimed to quantify the potential impact of the 100 Days Mission by retrospectively estimating the impact it would have had on the global COVID-19 pandemic. By quantifying the potential public health and economic gains, we provide evidence to support decision making surrounding future investments in vaccine research and development capabilities. We also aimed to quantify the impact of additional investments to overcome other limiting factors in the global vaccination campaign, including enhancements in global manufacturing capacity and health systems.

Methods

Transmission model

For all analyses presented here, we used an extended version of a previously published compartmental susceptible-exposed-infectious-recovered transmission model of COVID-19 vaccination with an explicit healthcare pathway (appendix pp 2–3).[3,22,23] We expanded the vaccination pathway to include booster vaccination alongside waning efficacy from the primary series. The new model captures the restoration of immunity via booster doses for all those previously vaccinated and subsequent top-up campaigns targeted at vulnerable age groups (appendix pp 3–6). This new vaccine pathway has been parameterised to match platform-specific vaccine efficacy data[3] and the duration of protection on the basis of modelled immune responses,[24] which is further described in the appendix (pp 7–8). Full model extensions, parameter values, and sources are detailed in the appendix (pp 2–13).

Fitting process

As in previous research,[3] we estimate country-specific profiles for the reproduction number in the absence of immunity and vaccination, R_t. This profile represents the transmissibility of the virus, population mixing, and government responses that impact mixing and behaviour. The values that we estimate thus represent the average number of secondary infections that would be caused in the absence of infection-induced and vaccine-induced protection. Profiles are inferred by fitting the epidemic model to estimated excess-mortality[1] over the duration of the global epidemic. This allows us to account for the widespread and globally heterogeneous under-reporting of COVID-19 infection and deaths.[25] Our model fitting methods are described fully in the appendix (pp 9–10). This analysis covered 180 countries and territories with a population greater than 100 000 as reported in World Population Prospects 2019,[26] which had at least 1 week of positive estimated excess mortality and had started COVID-19 vaccination before the end of 2021 (for all included regions and their model fits see appendix p 27). Lastly, we excluded China from our estimates because of its unique position as the origin of the detected epidemic and its large influence on estimates of deaths averted stemming from its population size.

100 Days Mission scenarios

We first modelled the impact of the 100 Days Mission by simulating a counterfactual scenario in which the global vaccination campaign started on April 20, 2020, 100 days after the full SARS-CoV-2 genome was first made public.[27] This scenario assumes that vaccinations in each country began 232 days earlier than they did in reality,[28] but with the same roll-out process.

Vaccine allocation scenarios

We explored two additional scenarios to reflect increased investment in vaccine research and delivery infrastructure. The Manufacturing scenario removes supply constraints, allowing vaccinations to start on April 20, 2020, in all countries, without stockouts. The removal of stockouts is modelled by altering the daily vaccination rates such that the weekly average number of vaccines administered does not decrease over time, which ensures that the vaccination rate is monotonically increasing. The infrastructure–equity scenario enhances both national health systems and global distribution networks, so that all countries achieve 40% vaccine coverage in the first year and 40% booster coverage in the second year. These scenarios

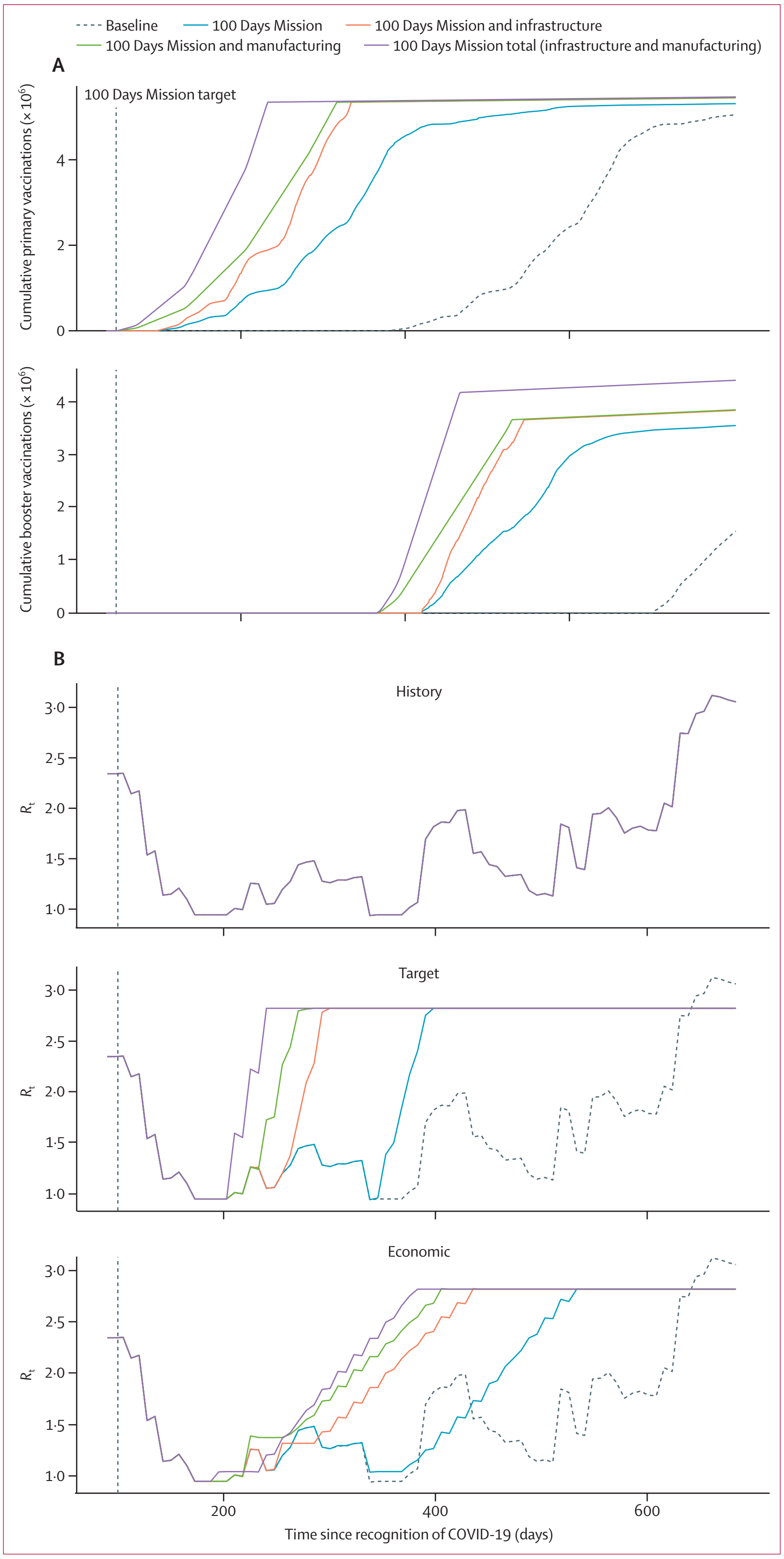

Figure 1: **Example primary (top row) and booster (bottom row) vaccine allocation scenarios (A) and example History (top row), Target (middle row), and Economic (bottom row) NPI scenarios (B)**

(A) The baseline (real world) scenario is shown with a black dashed line for comparison against the four vaccine allocation scenarios modelled indicated with different colours. The baseline (real world) scenario R_t is shown with a black dashed line for comparison against the different NPI scenarios in B. The earlier relaxation of NPIs is only observed under the Target and Economic scenarios, in which NPIs were assumed to be relaxed earlier in response to earlier vaccine availability. NPI=non-pharmaceutical intervention. R_t=reproduction number in the absence of both infection-induced and vaccine-derived immunity are considered both independently and in combination, but always in combination with the 100 Days Mission. Details are given in the appendix (pp 14–15) with an example shown in figure 1.

Non-pharmaceutical intervention changes

As vaccine roll-out improves, we expect countries might also relax NPIs earlier. Therefore, we simulated three scenarios for NPI relaxation speeds as vaccination coverage improves. The History scenario assumes no changes to NPIs, maintaining historical R_t trends. In contrast, the Target and Economic scenarios assume that NPIs were relaxed earlier. For each country, recalling that R_t reflects the change in transmission only due to NPIs and not due to infection-induced and vaccine-induced protection, we assumed that the R_t associated with all NPI restrictions removed was equal to the 90% quantile of the R_t profile after April 20, 2020, which

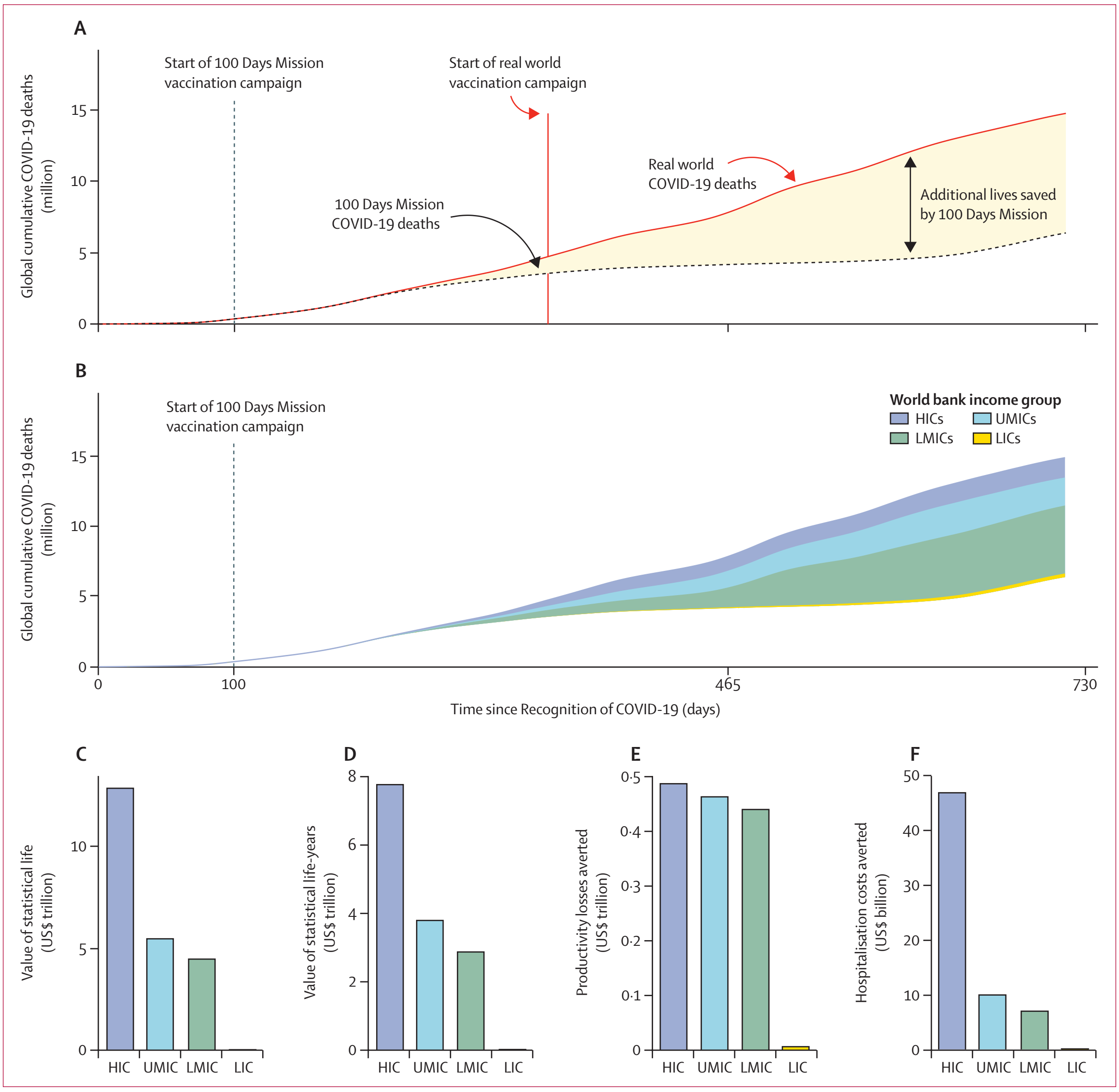

Figure 2: **Global impacts of the 100 Days Mission**

Cumulative COVID-19 deaths up to the end of 2021 (A), the cumulative deaths up to the end of 2021 (B), the global health economic impacts of the 100 Days Mission scenario calculated from deaths averted on the basis of value of a statistical life (C), value of a statistical life-year (D), the losses averted on the basis of productivity losses due to illness (E), and hospitalisation-associated costs (F). In panel A, the solid red line shows observed COVID-19 deaths during the pandemic and the black dashed line represents cumulative deaths in the 100 Days Mission vaccine allocation scenario and History NPI lifting scenarios. The gap between the red and black line indicates the deaths averted due to the modelled scenario. The vertical red line indicates the start of the COVID-19 vaccination campaign in 2020, which can be compared with the vertical blue dashed line, indicating when the vaccination campaign would have begun under the 100 Days Mission vaccine allocation scenario. In panel B, impacts are given by the World Bank income group: with coloured areas showing the contribution towards the total deaths from each World Bank income group averted due to the 100 Days Mission. The blue vertical dashed line indicates the start date of vaccination. HIC=high-income. UMIC=Upper-middle-income. LMIC=Lower-middle-income. LIC=Low-income.

we find is highly correlated with the average R_t profile value during periods with the lowest NPI as determined by the Oxford Government Response Tracker stringency index (appendix p 27). The Target scenario lifts all restrictions over 2 months after reaching more than 80% adult coverage in high-income countries or more than 80% coverage in those older than 60 years in other countries. The Economic scenario lifts NPIs more gradually after reaching the over-60 target, prioritising school reopening because of its significant economic impact, with the remaining NPIs lifted over the following 6 months. These scenarios are also evaluated independently and in combination with the 100 Days Mission. Details are given in the appendix (pp 14–15, 18–19) with an example shown in figure 1.

The economic benefits of earlier NPI relaxation are assessed by comparing reductions in NPI days and school closure durations against the UNESCO monitoring of school closures.[29] For countries not reaching vaccine targets, NPI lifting is based on median times from vaccine roll-out to NPI relaxation by other countries in the same income groups. NPI lifting is delayed during spikes in R_t until transmission decreases, as determined by a negative 28-day trend in daily infections, reflecting a more realistic government response. Details are given in the appendix (pp 14–15).

Outcomes

We evaluated the impact of each combination of R_t and vaccine scenarios by comparing against the historical COVID-19 epidemic that each country experienced. We quantified the impact of each scenario by calculating the difference in COVID-19 deaths, hospitalisations, and infections from the start of the epidemic to the end of 2021. For each country, we summarised the median and 95% quantiles from 100 sampled parameter sets. For global or across-country income group comparisons we randomly chose 100 combinations of parameter draws from each country, before combining these and summarising. For the Target and Economic scenarios, we estimated the impact that earlier vaccination had on reducing the length of NPIs as the additional number of days globally without NPIs in place and the number of weeks without school closures. This was calculated as the total number of days globally of openness (no NPIs implemented) gained relative to the Historic scenario, with a day considered fully open if R_t was greater than the 95% quantile of the profile.

Health economic analyses

We estimated health-care costs related to COVID-19 using data from the WHO-CHOICE programme,[30] which included country-specific unit costs adjusted to 2021 purchasing power parity values. Productivity losses were calculated on the basis of premature mortality of working age individuals, with an assumed retirement age of 64 years and valuing 1 year of productivity loss at the country's gross national income per capita. We used two approaches to estimate the monetary values associated with the number of lives saved: the number of lives saved multiplied by the country-specific monetary value of a statistical life (VSL) and multiplied by the value of a statistical life-year (VSLY). VSLY accounts for country-specific discounted life expectancy (appendix pp 16–17).

	Number of deaths averted, millions	Number of hospitalisations averted, millions	Number of infections averted, billions
Global	8·33 (7·70–8·68)	26·72 (22·26–34·72)	1·44 (1·16–1·75)
World Bank income group			
High-income countries	1·33 (1·23–1·61)	6·12 (5·07–7·54)	0·28 (0·24–0·32)
Upper-middle-income countries	1·94 (1·70–2·27)	5·59 (4·34–6·77)	0·25 (0·19–0·29)
Lower-middle-income countries	4·80 (4·24–5·00)	15·67 (10·27–21·27)	0·80 (0·57–1·30)
Low-income countries	0·26 (0·24–0·28)	0·91 (0·72–1·10)	0·06 (0·04–0·07)

Median estimates (95% credible interval) are presented. No changes in NPIs and each country has the same epidemic in terms of their historical trend in R_t. Impact is presented globally and in each World Bank income group. NPI=non-pharmaceutical intervention. R_t=reproduction number.

Table 1: **Estimated public-health impact of the 100 Days Mission in combination with the History NPI lifting scenario**

	Number of deaths averted per 1000 people	Number of hospitalisations averted per 1000 people	Number of infections averted per 1000 people
Global	1·32 (1·22–1·37)	4·23 (3·53–5·50)	227·47 (183·21–277·90)
World Bank income group			
High-income countries	1·10 (1·01–1·33)	5·06 (4·19–6·24)	230·85 (194·71–266·97)
Upper-middle-income countries	1·70 (1·49–1·98)	4·88 (3·79–5·91)	221·61 (166·93–251·79)
Lower-middle-income countries	1·44 (1·28–1·50)	4·71 (3·09–6·40)	239·24 (171·51–392·14)
Low-income countries	0·41 (0·37–0·45)	1·43 (1·13–1·74)	89·96 (68·49–109·01)

Median estimates (95% credible interval) are presented. No changes in NPIs and each country has the same epidemic in terms of their historical trend in R_t. Impact is presented globally and in each World Bank income group. NPI=non-pharmaceutical intervention. R_t=reproduction number.

Table 2: **Estimated public-health impact of the 100 Days Mission (per 1000 people) in combination with the History NPI lifting scenario**

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We estimate that the 100 Days Mission could have averted an additional 8·33 million deaths (95% credible interval [CrI] 7·70–8·68) due to COVID-19 by the end of 2021 (figure 2, table 1) in combination with the History NPI lifting scenario (no changes in NPIs and each country has the same epidemic in terms of their historical trend in R_t). In the same scenario, we estimate that 26·72 million severe cases (95% CrI 22·26–34·72) of COVID-19 requiring hospitalisation (table 1) and

	Value of statistical life, trillion US$	Value of statistical life-years, trillion US$	Productivity losses averted, trillion US$	Hospitalisation costs averted, billion US$
Worldwide	22·61 (20·77–26·93)	14·35 (12·96–17·87)	1·39 (1·20–1·69)	63·38 (57·03–73·30)
World Bank income group				
High-income countries	12·90 (11·58–16·63)	7·77 (6·87–10·74)	0·49 (0·41–0·77)	46·67 (38·51–56·25)
Upper-middle-income countries	5·48 (4·53–7·10)	3·79 (3·12–5·05)	0·46 (0·36–0·60)	9·91 (7·50–11·35)
Lower-middle-income countries	4·48 (3·84–4·77)	2·87 (2·44–3·18)	0·44 (0·36–0·50)	6·96 (4·93–9·84)
Low-income countries	0·019 (0·017–0·021)	0·011 (0·010–0·012)	0·0057 (0·0049–0·0064)	0·103 (0·078–0·125)

Median estimates (95% credible interval) are presented. No changes in NPIs and each country has the same epidemic in terms of their historical trend in R_t. Impact is presented globally and in each World Bank income group. NPI=non-pharmaceutical intervention. R_t=reproduction number.

Table 3: **Estimated health economic impacts of the 100 Days Mission globally in combination with the History NPI lifting scenario**

	Value of statistical life, million US$ per 1000 people	Value of statistical life-years, million US$ per 1000 people	Productivity losses averted, million US$ per 1000 people	Hospitalisation costs averted, thousand US$ per 1000 people
Worldwide	3·58 (3·29–4·27)	2·27 (2·05–2·83)	0·22 (0·19–0·27)	10·04 (9·03–11·61)
World Bank income group				
High-income countries	10·67 (9·57–13·75)	6·43 (5·68–8·88)	0·40 (0·34–0·64)	38·59 (31·85–46·52)
Upper-middle-income countries	4·79 (3·96–6·20)	3·31 (2·73–4·41)	0·40 (0·32–0·52)	8·66 (6·55–9·92)
Lower-middle-income countries	1·35 (1·15–1·44)	0·86 (0·73–0·96)	0·13 (0·11–0·15)	2·09 (1·48–2·96)
Low-income countries	0·030 (0·027–0·033)	0·017 (0·015–0·019)	0·009 (0·008–0·010)	0·162 (0·123–0·197)

Data are median (95% credible interval) are presented. No changes in NPIs and each country has the same epidemic in terms of their historical trend in R_t. Impact is presented globally and in each World Bank income group. NPI=non-pharmaceutical intervention. R_t=reproduction number.

Table 4: **Estimated health economic impacts of the 100 Days Mission globally (per 1000 people) in combination with the History NPI lifting scenario**

1·44 billion infections (95% CrI 1·16–1·75; table 1) would have been averted.

The majority of averted deaths, hospitalisations, and infections would have occurred in lower-middle-income countries (LMICs; figure 2, tables 1 and 2). This finding reflects both the larger population size living in LMICs (3·4 billion individuals in 2021)[31] and that the potential impact of the 100 Days Mission is concentrated in the countries that suffered high COVID-19 death tolls owing to low vaccination coverage. The majority of deaths that could have been averted by vaccinations in high-income countries (HICs) were averted in the Real World vaccination campaign, with over 8 million deaths estimated to have been averted in HICs.[3] However, countries with vaccination campaigns that arrived too late to prevent the large death toll associated with the delta wave in 2021 benefit more from the 100 Days Mission in comparison to countries that were already able to achieve high vaccination coverage before relaxing NPIs (see appendix p 20 for the modelled scenarios and impacts for all included regions). Earlier vaccination has a relatively low impact in low-income countries (figure 2), reflecting the smaller population size of these countries (665 million in 2021)[31] and that their younger demographics are less prone to disease and hospitalisation.

The estimated VSLs that could have been saved by the 100 Days Mission under the History scenario is US$22·61 trillion (95% CrI 20·77–26·93) globally. The comparable figure is $14·35 trillion (95% CrI 12·96–17·87) with the value of the statistical life-years (VSLY) averted (table 3). The lower value based on VSLY reflects the age gradient in the severity of COVID-19,[32] with the majority of deaths averted occurring in older individuals with fewer remaining years of life expectancy. Significantly smaller costs are averted owing to productivity losses ($1·39 trillion [95% CrI 1·20–1·69]) and hospitalisation costs ($63·38 billion (95% CrI 57·03–73·30]; table 3). Owing to the significantly higher VSL in HICs (appendix p 16), 57% of the global value of statistical life averted occurs in HICs (figure 2), despite the majority of deaths averted by the 100 Days Mission occurring in LMICs (figure 2).

Increased investment in both global manufacturing and health systems infrastructure further increases the number of deaths that could be averted and the associated health-economic savings. In the 100 Days Mission with both manufacturing and health systems investments, we estimate that 11·01 million deaths (95% CrI 10·60–11·49) could have been averted and a value of $31·29 trillion (95% CrI 28·66–33·72) in statistical lives saved. However, this scenario is unlikely to occur in reality, with the amounts of investment modelled and resultant improvements in vaccine coverage likely to precipitate countries relaxing NPIs earlier.

In all scenarios in which NPIs were relaxed earlier as a result of the earlier availability of vaccines from the

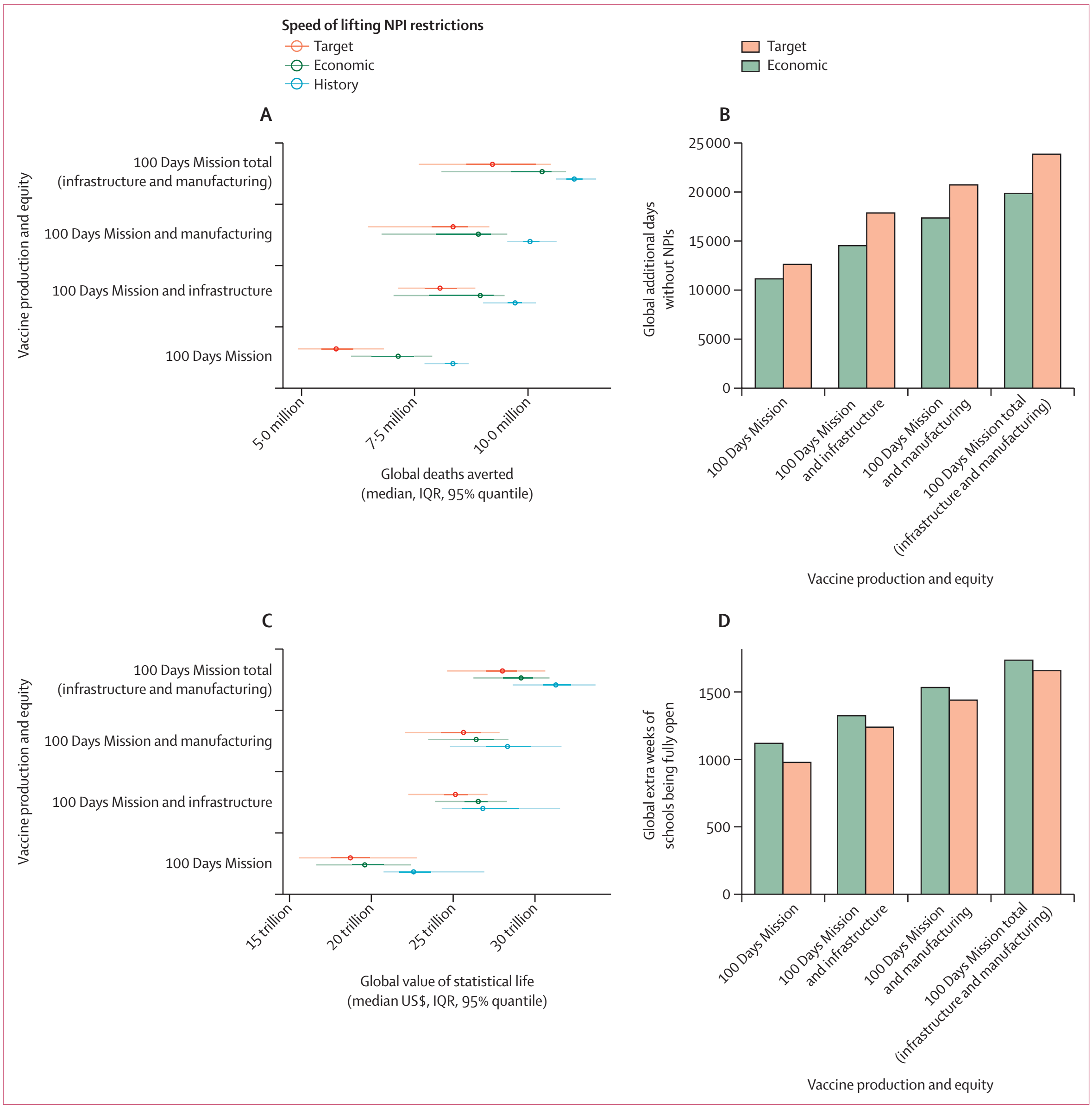

Figure 3: **Global impacts of the 100 Days Mission scenarios and on NPI duration**

The figure displays the global impact of the four vaccine allocation scenarios and three NPI lifting scenarios on: the total number of deaths averted (A), the financial value of the statistical lives saved (B), and the additional number of days without NPIs (C), and the additional number of weeks of schools being fully open (D). Additional days without NPIs and weeks of schools being fully open were estimated by comparing the Economic (green) and Target (orange) NPI lifting scenarios with the History (blue) scenario. The number of days without NPIs and weeks of schools being fully open increased with increasing speed of NPI lifting and as vaccine allocation equity increased. In parts (A) and (C), the median (point), 50% credible interval (dark horizontal bar), and 95% credible interval (light horizontal bar) are shown. NPI=non-pharmaceutical intervention.

100 Days Mission, we estimate that additional lives would have been saved relative to the baseline (figure 3). Under the Target NPI lifting scenario—where NPIs are lifted earlier in response to vaccination targets being reached—we estimate that 5·76 million deaths (95% CrI 4·91–6·81; 100 Days Mission alone) to 9·20 million deaths (95% CrI 7·58–10·49; 100 Days Mission with both manufacturing and infrastructure investments) could have been averted despite the earlier relaxation of NPIs. In these same scenarios, we estimate that 12 600 and 23 900 fewer days of NPIs would have been implemented globally (figure 3), or 70 days and 133 days on average per country. In these scenarios, we also estimate that there would have been an extra 980 weeks and 1660 weeks of schools being fully open (5 weeks and 9 weeks on average per country, respectively) and 2150 and 3180 extra weeks of schools being partly open worldwide (8 weeks and 19 weeks on average per country, respectively).

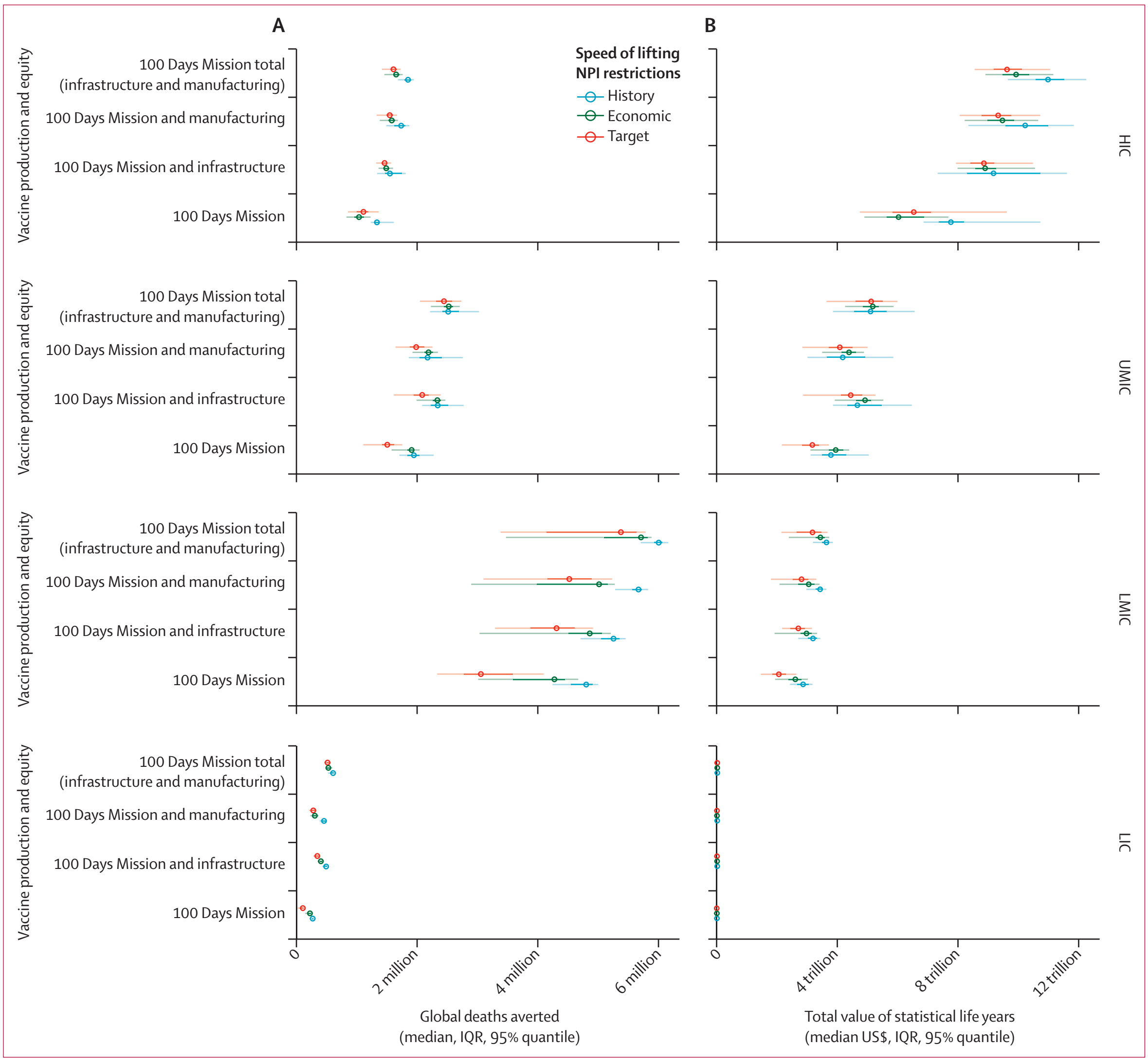

Figure 4: **Total number of deaths averted and value of statistical life-years saved**Total number of deaths averted (A) and value of statistical life-years saved (B) by the 100 Days Mission in each World Bank income group, across each set of NPI and vaccine scenarios. The median (point), 50% credible interval (dark horizontal bar), and 95% credible interval (light horizontal bar) are shown. NPI=non-pharmaceutical intervention.

Under the Economic scenario—where NPIs are lifted earlier but more slowly than under the Target scenario while ensuring school opening is prioritised—we observe similar trade-offs between public health and economic gains as a result of the earlier relaxation of NPIs. In all scenarios, we estimate that the public health and health economic outcomes would be greater than under the Target scenario but still lower than the History scenarios. We estimate that 7·12 million deaths (95% CrI 6·08–7·87; 100 Days Mission vaccination scenario) to 10·30 million deaths (95% CrI 8·08–10·83; 100 Days Mission vaccination scenario with both manufacturing and infrastructure investments) could have been averted. In these same Economic scenarios, we estimate that there could have been an additional 700 and 400 extra days of schools being fully open (an extra 4 days and 2 days on average per country, respectively) and 1700 and 550 extra days, respectively, of schools being partly open worldwide (an extra 9 days and 3 days on average per country) compared with under the Target scenarios. However, in these scenarios, we estimate that there would be 1500 and 4000 more days, respectively, with NPIs implemented globally (an extra 8 days and 22 days on average per country).

On the basis of VSLY, we find that under the Target NPI scenario, the 100 Days Mission alone would save $11·6 trillion (95% CrI 9·4–14·9). With additional investments in manufacturing and infrastructure, it would save $17·5 trillion (95% CrI 15·2–19·5). Under the Economic scenario, this rises to $12·4 trillion (95% CrI

10·3–14·6) and \$18·3 trillion (95% CrI 16·2–19·9), respectively. Under both scenarios the largest increase in savings from additional investment in manufacturing and infrastructure occurs in HICs (figure 4). However, the proportional increase in the total value of life-years saved from the additional investments is higher in upper-middle-income countries (UMICs; 61·3%) and LMICs (54·4%) than in HICs (47·4%) under the Target scenario. Under the Economic scenario, the proportional increase is higher in HICs (64·6%) than in UMICs (31·1%) and LMICs (31·8%). The difference between Economic and Target scenarios between income groups reflects that HICs were assumed to wait until 80% vaccination coverage is reached in all adults before relaxing NPIs in the Target scenario. In contrast, non-HICs relaxed NPIs once 80% coverage was reached in the 60-year age group. Consequently, the faster vaccine roll-out speeds assumed with additional investment are particularly beneficial for non-HICs under the Target scenario, given the shorter period over which NPIs are relaxed in the Target scenario (2 months) compared with the Economic scenario (6 months; see appendix p 20 for public health, health-economic, and NPI outputs for all scenarios).

Discussion

Earlier access to COVID-19 vaccines could have had substantial benefits. Under the 100 Days Mission, we estimate that 8·33 million deaths could have been prevented by the end of 2021, representing 57% of the global excess mortality during this period. This benefit is concentrated in LMICs, with an estimated 4·80 million deaths averted. Previous work estimated that real-life COVID-19 vaccination campaigns averted 7·4 million deaths in LMICs.[3] However, only 1·33 million additional deaths could have been averted in HICs, in contrast to the previously estimated 8 million deaths averted during the real-life vaccination campaign.[3] To fully benefit LMICs, investments in vaccine research must be supported by improvements to manufacturing and health system infrastructures to achieve equitable access and higher vaccine coverage.[7] With these additional investments, we estimate that globally 11 million deaths could have been prevented, representing a saving of \$18·3 trillion based on the value of statistical life-years. For comparison, WHO estimated that \$99 billion was spent on vaccinations in 2021,[33] with an additional €35 billion spent on private–public research and development investment and advance purchasing agreements.[34]

NPIs have been effective at reducing transmission but incur significant economic and societal costs,[12,35] notably impacting education owing to school closures. Studies show negative associations between school closures and learning,[13,36] with long-term economic impacts from lost schooling likely to augment social inequalities.[15,16] Consequently, one of the major benefits of earlier access to vaccination is the reduction in school closures. In our Economic scenario, prioritising school reopening could have averted 1120 weeks of full school closures and 2490 weeks of partial school closures, while still averting 7·12 million deaths worldwide and saving \$11·6 trillion. This represents, on average, an additional 6 weeks of fully open schools and 14 weeks of partly open schools per country. Although the benefits of prioritising schooling are evident, the impact on transmission rates (R_t) varied between countries, with higher-income countries having a greater increase in R_t, as observed in previous studies.[37] Consequently, reopening schools and relaxing NPIs safely will crucially require scaling up both vaccine delivery infrastructure and manufacturing. Without addressing both aspects, advancements in vaccine development speed might not translate into equitable benefits globally.

A limitation of our economic analysis is the lack of concrete estimates of the full disability costs associated with COVID-19. Post-COVID-19 condition (also known as long COVID) is widely documented and can represent a long-term disability,[38,39] but complete estimates of disability weights are still being developed, owing to the non-specific and complex nature of long COVID symptoms and high proportions of under-ascertainment of COVID-19 infections.[40–42] Consequently, we focused on costs of deaths, hospitalisations, and associated productivity losses. Further research is needed to generate appropriate disability weights to fully estimate the benefits of each strategy.

Considerable uncertainty exists in our modelled scenarios, particularly regarding how countries might have reacted differently with earlier vaccine access and knowledge of their impending availability. Countries might have implemented more stringent NPIs, potentially leading to greater health impacts, or reduced adherence to restrictions owing to perceptions of lower risk.[43] Decisions on relaxing NPIs are likely to account for hospitalisation burdens, variants of concern, the epidemiological situation in neighbouring countries, and intervention costs. Additionally, the impact of earlier vaccination differs between countries, especially where the majority of COVID-19 mortality occurred post-2021 (ie, zero-COVID countries such as New Zealand). Additionally, earlier and wider vaccination campaigns could have influenced the evolution of variants of concern, potentially reducing or accelerating antigenic evolution. Inequitable vaccinations in populations with low coverage might drive antigenic evolution,[44] so wider vaccination could mitigate this. Alternatively, variants with increased immune escape ability, such as omicron, might have evolved earlier, reducing indirect protection from vaccination campaigns. This would probably have decreased the deaths averted, as indirect protection was estimated to have averted one-fifth of the total deaths averted during the first year of the COVID-19 vaccination campaign.[3] Lastly, challenges in estimating vaccination impact with a counterfactual approach include uncertainties in model parameters and the actual number of COVID-19 deaths.[25] We used reported excess mortality and estimates from *The Economist* for countries not reporting excess mortality, which are broadly consistent with WHO estimates.[45] Despite these uncertainties, our results provide an extensive assessment of the potential impact of earlier vaccination.

These results show that investments in support of the 100 Days Mission—in tandem with broader support to enhance manufacturing and health systems—could play a key role in controlling a future potential pandemic. The estimates of the impact that these investments could have had retrospectively during the COVID-19 pandemic show the value that earlier vaccine roll-out could have had in saving lives, compounded by the impact of being able to lift NPIs more rapidly. Although valuing the economic impact of more rapid opening is challenging, there is a clear benefit both to health and the economy in these investments. The scenarios explored in our analysis highlight how significant economic gains can be achieved by prioritising vaccine development as a method of pandemic preparedness. Although prioritising public health agendas was often viewed as antithetical to the economy during the pandemic, counterfactual scenario planning exercises such as this highlight the economic impacts of public health decisions and are a key tool for policy makers. Despite the unknowns in how countries would respond if the 100 Days Mission succeeds, these findings show the significant public health and economic gains that the mission could have.

The 100 Days Mission is ambitious, requiring global innovation through creating vaccine libraries, clinical trial networks, accelerated immune response marker identification, rapid vaccine manufacturing, and strengthened global disease surveillance.[46] However, our study shows the clear benefits that these necessary improvements in global vaccine manufacturing capacity and health system infrastructure could provide in preparing for future pandemic threats.

Contributors

GB, OJW, and ACG conceived the study with input from DOM. GB led model development, with input from OJW on counterfactual simulation analyses. ABH and PW contributed to model development. OJW and DOM developed the health economic analysis with input from DGW and data from AAT. OJW and GB produced the first draft of the manuscript and have accessed and verified the underlying data. All authors read, contributed to, and approved the final draft. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

The Coalition for Epidemic Preparedness Innovations (CEPI) funded the investigation into the impact of the 100 Days Mission. The authors maintained full freedom when designing the study and deciding on additional scenarios to explore. ACG has received personal consultancy fees from HSBC, GlaxoSmithKline, Sanofi, and WHO related to COVID-19 epidemiology and from The Global Fund to Fight AIDS, Tuberculosis and Malaria for work unrelated to COVID-19. ACG was previously a non-remunerated member of a scientific advisory board for Moderna and is a non-remunerated member of the scientific advisory board for the Coalition for Epidemic Preparedness; has received personal consultancy fees from WHO for work related to malaria. OJW also received personal consultancy fees from WHO and the Clinton Health Access Initiative for work related to malaria. ABH has received personal consultancy fees from WHO for work related to COVID-19, and grant funding for COVID-19 work from WHO and NSW Ministry of Health, Australia; and is a member of the WHO Immunization and Vaccines Related Implementation Research Advisory Committee. AAT developed the allocation algorithm in collaboration with COVAX through funding from the Bill & Melinda Gates Foundation. All other authors declare no competing interests.

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