Cost-effectiveness of COVID-19 vaccination in low- and middle-income countries

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ABSTRACT

Background

Despite the advent of safe and effective COVID-19 vaccines, pervasive inequities in global vaccination persist.

Methods

We projected health benefits and donor costs of delivering vaccines for up to 60% of the population in 91 low- and middle-income countries (LMICs). We modeled a highly contagious (R_e at model start=1.7), low-virulence (IFR=0.32%) “omicron-like” variant and a similarly contagious “severe” variant (IFR=0.59%) over 360 days, accounting for country-specific age structure and healthcare capacity. Costs included vaccination startup (US$630 million) and per-person procurement and delivery (US$12.46/person vaccinated).

Results

In the omicron-like scenario, increasing current vaccination coverage to achieve at least 15% in each of the 91 LMICs would prevent 11 million new infections and 120,000 deaths, at a cost of US$0.95 billion, for an incremental cost-effectiveness ratio (ICER) of US$670/year-of-life saved (YLS). Increases in vaccination coverage to 60% would additionally prevent up to 68 million infections and 160,000 deaths, with ICERs <US$8,000/YLS. ICERs were <US$4,000/YLS under the more severe variant scenario and generally robust to assumptions about vaccine effectiveness, uptake, and costs.

Conclusions

Funding expanded COVID-19 vaccine delivery in LMICs would save hundreds of thousands of lives, be similarly or more cost-effective than other donor-funded global aid programs, and improve health equity.

Key words: COVID-19, COVAX, health equity, vaccination, low and middle-income countries, cost-effectiveness

BACKGROUND

As of May 2022, approximately 60% of the 6 million global deaths attributed to COVID-19 occurred in low- and middle-income countries (LMICs) [1]. However, the World Health Organization (WHO) estimates that actual deaths may be 2.5-3.1 times higher [2]. Moreover, mortality alone does not account for the epidemic's secondary toll on economic productivity, healthcare access, and social wellbeing [3–5].

Although safe and effective vaccines offer a strategic path toward epidemic control, their benefits have largely been confined to high- and upper-middle-income countries. For example, as of May 2022, approximately 74% of individuals in high-income countries had received a primary COVID-19 vaccine course compared to under 40% of those in LMICs, with only 13% in low-income countries, specifically [6]. Ensuring global access to COVID-19 vaccines would reduce morbidity and mortality, stem economic losses from epidemic-related disruptions, and potentially reduce the risk of new variants emerging [7,8].

The COVAX Advance Market Commitment (AMC) program was designed to increase global vaccine equity by raising funds and delivering SARS-CoV-2 vaccines to 92 LMICs [9]. By April 2022, donors had committed over US$12.4 billion and secured vaccine supply for nearly 45% of the LMIC population [10]. Despite these achievements, delivery of and demand for vaccines have kept vaccination coverage low in and uneven between many LMICs [11–13]. Moreover, 45% vaccine supply is below the projected level needed to achieve epidemic control [14].

We sought to estimate: 1) the clinical impact and cost-effectiveness of increasing vaccination coverage from the status quo in May 2022 to at least 15% in 91 LMICs, and 2) the value of increasing coverage incrementally to at least 60% vaccination coverage in these countries.

METHODS

Analytic Overview

We used the Clinical and Economic Analysis of COVID-19 Interventions (CEACOV) model, a validated, dynamic microsimulation of the natural history of COVID-19 (Supplementary Methods and Supplementary Figure 1) [15], to simulate discrete epidemics in 91 COVAX AMC-eligible LMICs. We excluded India because of its plan to produce vaccines domestically [16]. We estimated country-specific outcomes over 360 days, including infections, deaths, and years of life lost attributable to COVID-19 mortality. We compared a counterfactual scenario in which LMICs had no vaccine supply to one in which estimated vaccination rates as of May 2022 (median 32%, range 0-86%, Supplementary Table 1) had been achieved to demonstrate the value of status quo vaccination for disease prevention in future waves [13]. We then modeled increases in vaccine supply such that all LMICs increased vaccination from the current status quo to at least 15%, 30%, 45%, and 60% coverage. Costs were from the donor perspective and included fixed costs and variable costs per person vaccinated (Table 1).

Because the contagiousness and severity of future SARS-CoV-2 variants are unknown, we modeled two epidemic scenarios. In the base case, we assumed an epidemic growth rate and infection fatality ratio (IFR) similar to that of an omicron-like variant. We then modeled a second variant with similar transmissibility as the omicron-like variant but with a higher IFR to reflect the severity of prior variants. In the base case, we assumed modest unboosted vaccine effectiveness as observed during the omicron era (Table 1, Supplementary Figure 2) [27,28]. We conducted sensitivity analyses among a subset of 12 countries to assess the robustness of estimates to assumptions about effective reproductive number (R_e), vaccine effectiveness, vaccine uptake, and vaccination program costs.

Model Structure

Disease states and progression

The CEACOV model is based on an SEIR framework, including susceptible, exposed, infectious, recovered, and deceased states (Supplementary Methods and Supplementary Figure 1). Susceptible individuals face a daily infection probability with SARS-CoV-2, while infected individuals face daily probabilities of disease progression through six COVID-19 states: pre-infectious latency, asymptomatic, mild/moderate, severe, critical, and recuperation (Supplementary Table 2). With severe disease, symptoms warrant inpatient management. With critical disease, individuals require ICU care to survive. Recovered individuals are assumed immune from reinfection for the duration of the modeled time horizon [30]. The model considers three age bands: 0-19, 20-59, and ≥60 years. Mortality from COVID-19 is dependent on age and availability of hospital and ICU beds (Supplementary Table 2).

Transmission

Individuals with SARS-CoV-2 infection transmit to susceptible individuals at health state-stratified rates (Table 1). All susceptible people face equal probabilities of contacting infected individuals and becoming infected (i.e., homogenous mixing). The daily number of projected infections depends on the prevalence of active disease and proportion of the population susceptible to infection. Transmission rates were calibrated to achieve the base case R_e–the average number of transmissions caused per infection at simulation onset. Practice of non-pharmaceutical interventions, such as mask mandates and physical distancing, are reflected in the R_e value.

Resource use, costs, and cost-effectiveness

In the model, vaccines are prioritized for those ≥60 years [31]. Remaining doses are next given to those 20-59 years, and finally to those <20 years. The model tallies hospital and ICU admissions for those with severe or critical disease, accounting for country-specific capacity constraints. Costs are from the donor perspective and are based on estimated COVAX AMC vaccination program costs [17,29]. The incremental cost-effectiveness ratios (ICERs) for strategies corresponding to different levels of population vaccination coverage are calculated by dividing the difference in costs by the difference in benefits (years of life saved or infections prevented) for each strategy compared to the next lower-cost strategy.

Input Parameters

Country characteristics

Country-specific population estimates and age structures were sourced from the United Nations 2019 World Population Prospects (Supplementary Table 1) [32]. Hospital and ICU bed capacities were derived from data published by the WHO, World Bank, and country-level health agencies, as well as from peer-reviewed literature (Supplementary Table 1). We assumed that the entirety of hospital and ICU capacity would potentially be available for COVID-19 cases but did not model expansions in healthcare capacity. The estimated COVID-19 vaccination coverage for each country as of May 2022 was derived from Our World in Data estimates (Supplementary Methods; Supplementary Table 1) [13].

Disease progression and transmission dynamics

The average duration of each COVID-19 state was derived from studies describing the clinical characteristics of COVID-19 cases in China and the US (Supplementary Methods and Supplementary Table 2) [21,22,24,25,33]. In the base case, we modeled an epidemic with an R_e

of 1.7 at model start, such that 47% of the population would become infected over the 360-day period in the 0% vaccination coverage scenario. We modeled this to correspond to published estimates of omicron's transmissibility [34], as well as data suggesting 20-30% increases in seroprevalence after the first 2-3 months of omicron waves [19,20]. In the omicron-like and severe variant scenarios, the IFR in the absence of vaccination was 0.32% and 0.59%, respectively, to approximate severity estimates of the omicron and delta variants [35–38]. To do so, we used published data from meta-analyses of population IFR during the pre-delta era [37] and calibrated our model such that the omicron-like variant would have 60% reduced probability of developing severe or critical disease in an exposed but unvaccinated population [39]. Both the R_e and IFR were chosen under the assumption that most people had exposure to a previous SARS-CoV-2 variant prior to model start. At simulation onset, we assumed 0.5% prevalence of active infection based on SARS-CoV-2 incidence observed during inter-wave periods (Supplementary Methods) [18].

Vaccine effectiveness against infection, mild/moderate disease, and severe/critical disease

We included three measures of vaccine effectiveness in the model: effectiveness against infection, effectiveness against mild/moderate disease, and effectiveness against severe or critical disease (Supplementary Methods). Since vaccine effectiveness against future variants is unknown, we based the estimates on the effectiveness of mRNA vaccines–which make up nearly half of all doses allocated by COVAX as of May 2022 [6]–against symptomatic infection and hospitalization caused by the omicron (B.1.1.529) variant. In the base case analysis, we modeled a vaccine with 10% effectiveness against infection and 15% effectiveness against mild/moderate disease, based on the observed effectiveness of 2 doses of BNT162b2 (Pfizer) and mRNA-1273

(Moderna) ≥25 weeks after vaccination against symptomatic infection caused by the omicron variant in the United Kingdom (8.8% and 14.9%, respectively) [27]. We assumed 55% effectiveness against severe or critical disease as a conservative estimate of effectiveness of a 2-dose mRNA vaccine against hospitalization caused by the omicron variant [28].

Vaccination costs

We derived vaccination program costs using the COVAX Working Group's February 2021 updated delivery cost estimates [29] and a list of COVAX AMC negotiated prices for COVID-19 vaccines in 2022 [17]. Fixed costs of vaccination programs in 91 LMICs—which included costs attributed to planning and coordination, training, social mobilization, cold chain equipment, pharmacovigilance, and hand hygiene—were estimated to be US$630 million (Table 1). We estimated that vaccinating each individual would incur additional costs associated with cold chain, logistics, storage, waste, transportation, and technical assistance equal to US$2.46/person vaccinated [29]. Finally, we included a vaccine cost of US$10/course, based on the average COVAX AMC prices weighted by the number of vaccines delivered per manufacturer to the 91 LMICs as of May 2022 [6,17]. In sensitivity analyses, we adjusted program costs to be 0.5-2.0x the base case values to account for the uncertainty in delivery costs and variability in per-unit vaccine costs.

Sensitivity Analyses

Selection of representative countries for sensitivity analyses

We performed sensitivity analyses in the 12 largest countries by population, which also represented a range of WHO regions, demographic distributions, and healthcare capacities: Bangladesh, Democratic Republic of the Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania, and Vietnam (combined population: 1.5 billion, or 61% of the overall population in the 91 LMICs) (Supplementary Methods).

Parameters varied in one-way sensitivity analyses

We independently varied the following parameters to evaluate their impact on outcomes: vaccine uptake (50-90%), vaccine effectiveness (5-30% effectiveness against infection, 10-50% effectiveness against mild/moderate disease, and 40-80% effectiveness against severe/critical disease), R_e at model start (1.7-2.1), and total vaccination program cost (0.5x-2.0x base case costs).

RESULTS

Benefits and costs of global vaccination

In the base case analysis of a future wave caused by an omicron-like variant, the current vaccination coverage in 91 LMICs would curtail infections by 11%, from 1.2 billion to 1.1 billion, and decrease projected COVID-19 deaths 42%, from 3.9 million to 2.3 million, saving 25 million years of life compared to the counterfactual 0% coverage scenario (Table 2; individual country and regional estimates Supplementary Table 3). Increasing vaccination coverage from the status quo in May 2022 to achieve at least 15% coverage in all LMICs would prevent an additional 11 million infections and 120,000 deaths, at an additional cost of US$953 million, resulting in an ICER of US$670/year of life saved (YLS) (Table 2; Figure 1). Increasing coverage further to at least 30% and at least 45% would prevent an additional 101,000 and 42,000 deaths, and result in ICERs of US$1,040/YLS and US$3,050/YLS, respectively. Increasing vaccination coverage to 60% would continue to reduce infections and deaths, although with diminishing efficiency at US$7,820/YLS.

The value of the vaccination program was significantly higher when modeling the more severe variant. Although the number of infections prevented by each coverage level would be similar to those prevented in an omicron-like wave, the number of deaths prevented would be 1.6-2.0x higher, with lower ICERs, ranging from $390/YLS for achieving at least 15% coverage to $3,680/YLS for achieving at least 60% coverage.

Impacts of vaccine and epidemic traits

In one-way sensitivity analyses, the cost-effectiveness of providing vaccinations to the 12 largest LMICs was most affected by program costs, and, to a lesser extent, R_e at model start, vaccine effectiveness, and vaccine uptake (Table 3; Figure 2). Nonetheless, aside from the scenario in which program costs were doubled or vaccine uptake was reduced to 50%, the ICER for strategies up to and including at least 45% coverage remained below US$4,000/YLS across a wide range of assumptions for omicron-like and the more severe variants (Table 3). Under the severe variant assumption, the ICERs would remain below US$8,000/YLS for achieving at least 60% coverage, except when vaccine uptake was 50%.

Varying R_e, vaccine effectiveness, and vaccine uptake across our tested ranges changed the number of deaths in each strategy by 6%-53% compared to the base case. For example, when vaccine effectiveness was reduced (i.e., 5% effectiveness against infection, 10% effectiveness against mild/moderate disease, and 40% effectiveness against severe/critical disease), the model-estimated number of deaths would increase by 22%-26% compared to the base case (Supplementary Table 7). However, even with lower vaccine effectiveness, expanding vaccination coverage to least 45% of each country’s population continued to hold value (ICER: $2,270/YLS under the omicron-like variant and $1,660/YLS under the severe variant, Supplementary Tables 3-7).

DISCUSSION

In this modeling analysis, we estimated the cost-effectiveness of COVID-19 vaccination in LMICs, across a range of vaccination coverage levels. Under the assumption of a circulating omicron-like variant, we found that investments into COVID-19 vaccine supply and distribution to LMICs sufficient to increase vaccination from rates in May 2022 to at least 15% coverage in all countries would prevent nearly 11 million additional infections and 120,000 deaths over a one-year period with an ICER of $670/YLS. Expanding vaccination further to achieve at least 60% coverage would save an additional 160,000 lives with ICERs <US$8,000/YLS. Should a more severe variant emerge, the cost effectiveness of achieving 15% coverage rates would be even greater ($390/YLS) and achieving 60% coverage would remain <US$4,000/YLS. These results demonstrate the substantial health benefits and value of supporting LMICs to vaccinate large proportions of their populations, and complement arguments focused on health equity, economic benefits, and pandemic control efforts [40–42].

While there is no universally accepted ICER threshold to determine value among donor countries investing on behalf of lower-income countries, the ICERs we estimate for funding vaccinations in 91 LMICs range from $670/YLS for achieving at least 15% coverage to $7,820/YLS for achieving at least 60% coverage in an omicron-like scenario. These ICERs are substantially lower than or comparable to other donor-financed public health measures in LMICs, such as the global delivery of antiretroviral therapy for HIV through the US President's Emergency Plan for AIDS Relief (PEPFAR) [43]. Between 2004-2013, PEPFAR was supported by approximately US$49.8 billion in US government funding and resulted in an estimated 11.6 million years of life saved, for an ICER of approximately US$4,310/YLS (see Supplementary Methods) [43]. To put the COVID-19 vaccination program investment into further context, the total estimated cost of funding at least 45% vaccine supply to the 91 countries is approximately US$18 billion, which represents about 0.4% of the estimated US$4.2 trillion US government investment in the domestic COVID-19 response to date [44].

Our results were generally robust to assumptions about vaccine effectiveness, vaccine uptake, and vaccination program costs. For example, the cost-effectiveness of obtaining at least 30% vaccination coverage in an omicron-like scenario would remain $\leq$\$2,050/YLS even with low vaccine effectiveness (40% effectiveness against severe disease), low vaccine uptake (50%), or higher costs (2x vaccination program costs), and <$3,500/YLS for all scenarios of at least 45% coverage except with doubled vaccination program costs (ICER $6,870/YLS) or lower uptake to 50%. Achieving at least 60% coverage would have ICERs <$8,000/YLS in all scenarios modeling the higher severity variant, except if vaccine uptake were below 50%.

The severity of future COVID-19 variants and the effectiveness of current vaccines against future variants are unknown. We modeled our base case average IFR in the absence of vaccines (0.32%) to be similar to that of an omicron-like variant circulating in a highly-exposed population. Even in this relatively low IFR scenario, achieving at least 15% vaccination coverage would have an ICER of US$670/YLS compared to current vaccination rates. To account for the substantial uncertainty in the characteristics of future waves, we also modeled a higher IFR (0.59%), which produced even greater value in vaccination delivery. If a more severe variant emerges, and our IFR estimates are too low, then successful vaccination programs would be even more cost-effective.

This analysis should be interpreted in the context of several assumptions. The analysis is intended to estimate the cost-effectiveness of vaccination across a range of scenarios related to vaccine effectiveness, cost, and epidemic scale across 91 countries but not to precisely predict the future of the epidemic or health outcomes. There are also several important limitations. First, the ICER estimates for the vaccination program correspond to costs from the donor perspective but do not consider the broader financial impact. For example, the focus on ICERs, in $/YLS, does not account for averted domestic healthcare costs within the recipient countries resulting from reduced infections and hospitalizations following vaccination. These savings could be substantial: for example, a vaccination program in South Africa with a 67% vaccine supply has been estimated to reduce net domestic health care costs by over US$400 million [45]. We also do not model the potential economic gains that are expected to be realized in donor countries if global vaccination is accomplished. In the absence of a successful global vaccination program, economic losses of up to US$9 trillion across different sectors are projected, as much as half of which are expected to be borne by high-income countries [41]. Second, the benefits in our model are restricted to the direct impacts from COVID-19 disease prevention over 360 days. We did not include the many potential secondary or longer-term health benefits of COVID-19 vaccination, or the costs or benefits associated with booster or annual vaccinations. The pandemic has also indirectly increased morbidity and mortality in LMICs by overwhelming health systems, worsening food insecurity, disrupting supply chains, infecting healthcare workers, and repurposing healthcare budgets [5,46]. Effective vaccination programs have the potential to mitigate each of these healthcare system challenges. We also did not account for potential longer-term secondary benefits of vaccination programs, such as preventing the emergence of viral variants, strengthening public health infrastructure in LMICs, or preventing long-term complications of COVID-19 [47]. Each of these considerations means that our analysis is conservative with respect to benefits, and that global vaccination would be even more cost-effective if they were included. Third, this model specifically addresses the shortfall in funding for and delivery of COVID-19 vaccines (or donations made in kind) but not other contributors to vaccine supply inequities, such as manufacturing constraints or intellectual property rights [48]. Estimates as of January 2022 suggest that global production capacity will allow for approximately 23 billion vaccines to be produced in 2022 [49], somewhat mitigating these concerns. Moreover, to achieve the modeled vaccination rates, additional funding might be needed beyond procurement and delivery. For example, programs to help combat vaccine misinformation and hesitancy at the individual, community, and national levels may be needed if low vaccine acceptance becomes a barrier to achieving vaccination coverage [12]. Costs of such information and health promotion campaigns are not included in this analysis. Fourth, we used natural history inputs derived from published literature (Table 1 and Supplementary Table 2), which might not be fully representative of COVID-19 disease in LMIC populations. However, we used country-specific age distribution and healthcare capacity inputs and calibrated IFR in our model to published meta-analyses of IFR across many settings [37]. We note that age is well-established as the greatest risk factor for COVID-19 mortality and, after accounting for age, additional co-morbidities have relatively little effect on mortality in LMICs [50]. Fifth, we chose to evaluate expanded primary vaccine course coverage instead of booster vaccination because only 13% of the population in low-income countries had received primary coverage as of May 2022 [6]. Therefore, our model was designed to evaluate primary vaccination coverage of at least 15% to 60%, which we believe to be more attainable targets in the near term. Future analyses should evaluate the value and health impact of booster doses as these initial targets are realized. Finally, the model utilizes data on vaccine effectiveness, hesitancy, and costs from published studies that are subject to uncertainty. For example, costs could decrease with increased distribution, or increase with interruptions in manufacturing or supply chains. Despite this, our findings were robust to plausible changes to vaccine effectiveness, hesitancy, and costs.

In summary, investing in COVID-19 vaccination to achieve at least 15% vaccination coverage in 91 LMICs would prevent nearly 11 million infections and 120,000 deaths over one year compared to current vaccination coverage and be highly cost-effective (US$670/YLS). Increasing coverage levels up to 60% would provide substantial additional benefits and remain cost-effective at thresholds below other donor aid programs [43]. These findings, in conjunction with the ethical, social, and economic benefits of global vaccination, support expanding vaccination programs in LMICs.

AUTHOR CONTRIBUTIONS

M.J.S. and K.A.F. conceived of the project. C.A., K.P.F., R.G., J.A.S., and F.S. contributed to data acquisition and analysis. M.J.S., K.A.F., A.C., K.P.R., C.A., K.P.F., and J.A.S. contributed to data interpretation. M.J.S. wrote the first draft of the manuscript. All authors contributed to significant revisions of the manuscript and approved the final version.

CONFLICT OF INTEREST

All authors have no competing interests to report.

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ADDITIONAL INFORMATION

Supplementary Information is available for this paper. Correspondence and requests for materials should be addressed to Mark J. Siedner, MD, MPH (address: 100 Cambridge Street, Suite 1600, Boston, MA 02114; telephone: 617-726-4686; fax: 617-724-1637; email: msiedner@mgh.harvard.edu).

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FIGURE LEGENDS

Figure 1. Cost-effectiveness of investing in COVID-19 vaccinations for low- and middle-income countries. Modeled outcomes are presented for donor investments into COVID-19 vaccinations for the 91 COVAX Advance Market Commitment (AMC) countries under an omicron-like (blue) and severe variant (red). For each vaccine supply strategy, the years of life saved (YLS) compared to the strategy in which no vaccine is administered are plotted against the total cost of the vaccination program. YLS are discounted at 3%/year; costs are undiscounted since they are an upfront investment from the donor perspective. The incremental cost-effectiveness ratio (ICER) of each strategy is represented by the inverse of the slope connecting two points and labeled next to each strategy, rounded to the nearest ten. Strategies that are dominated do not contribute to the cost-effectiveness frontier and are denoted by lighter shading.

Figure 2. One-way sensitivity analyses: influence of key parameters on the cost-effectiveness of COVID-19 vaccination in the 12 largest low- and middle-income countries. One-way sensitivity analyses for the 12 largest low- and middle-income countries: Bangladesh, Democratic Republic of the Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania, and Vietnam. These countries were chosen since they account for 61% of the population in the 91 low- and middle-income countries (LMICs) and reflect a range in global region, age structure, hospital bed capacity, intensive care unit (ICU) bed capacity, and current vaccination coverage (see Supplementary Methods). We independently varied effective reproductive number (R_e) at model start (Panel A), vaccine effectiveness (Panel B), vaccine uptake (Panel C), and program costs (Panel D) for the omicron-like (blue) and severe (red) variant scenarios. For each sensitivity analysis and vaccine supply strategy, years of life saved (YLS) compared to the strategy in which no vaccine is administered are plotted against the

total cost of the vaccination program. YLS are discounted at 3%/year; costs are undiscounted since they are an upfront investment from the donor perspective. Base case, high estimate, and low estimate sensitivity analysis outcomes are represented by solid, dashed, and dotted lines, respectively. Strategies that are dominated do not contribute to the cost-effectiveness frontier and are denoted by lighter shading. Base case vaccine effectiveness was 10% protection against infection (low-high sensitivity analysis: 5-30%), 15% protection against mild/moderate disease (10-50%), and 55% protection against severe/critical disease (40-80%).

Table 1. Input parameters for an analysis of COVID-19 vaccination strategies in COVAX AMC-eligible countries.

Parameter	Base case value (Range)	Source(s)
Initial state distributions		
Susceptible, %	99.5	Assumption based on [18], see Supplementary Methods
Infected, %	0.5	
Transmission dynamics		
R_e at model start	1.7 (1.7-2.1)	Assumption based on [19,20]
Rate of onward transmission by health state, transmissions per person-day[a]		[21–25]
Asymptomatic	0.1577	
Mild or moderate disease	0.1284	
Severe disease	0.0090	
Critical disease	0.0071	
Recuperation after critical disease	0.0090	
Vaccine specifications		
Uptake, % of population accepting vaccine	70 (50-90)	[26]
Effectiveness in preventing SARS-CoV-2 infection, %	10 (5-30)	Assumption
Effectiveness in preventing mild/moderate COVID-19, %	15 (10-50)	Assumptions based on [27]
Effectiveness in preventing severe or critical COVID-19, %	55 (40-80)	Assumption based on [28]
Costs of vaccine purchase and delivery		
Fixed costs, US$ millions	630 (315-1,260)	[29]
Variable costs, US$ per person vaccinated		
Variable delivery costs	2.46 (1.23-4.92)	[29]
Vaccine purchase	10.00 (5.00-20.00)	[6,17]

Abbreviations: AMC, Advance Market Commitment; R_e, effective reproductive number.

[a] Corresponds to R_e of 1.7 at model start.

Table 2. Clinical and cost outcomes of investing in COVID-19 vaccinations for 91 low- and middle-income countries.

Variant type/ modeled vaccine supply	Total population vaccinated	Total cost of vaccination (US$)	SARS-CoV-2 infections	COVID-19 deaths	Discounted total YLS	ICER (US$/infection prevented)	ICER (US$/YLS)
Omicron-like variant							
No vaccine	0	0	1,200,849,000	3,852,000	Reference	Reference	Reference
Status quo[a]	961,872,000	12,502,896,000	1,071,462,000	2,253,000	18,431,000	dominated	dominated
At least 15%	1,029,385,000	13,455,733,000	1,060,840,000	2,134,000	19,940,000	dominated	670
At least 30%	1,184,239,000	15,385,216,000	1,040,669,000	2,033,000	21,794,000	100	1,040
At least 45%	1,378,006,000	17,799,551,000	1,019,598,000	1,990,000	22,585,000	dominated	3,050
At least 60%	1,609,393,000	20,682,637,000	993,131,000	1,971,000	22,953,000	110	7,820
Severe variant (1.75x hospitalization need compared to omicron-like variant)							
No vaccine	0	0	1,197,105,000	7,081,000	Reference	Reference	Reference
Status quo[a]	961,872,000	12,502,896,000	1,067,859,000	4,287,000	31,911,000	dominated	dominated
At least 15%	1,029,385,000	13,455,733,000	1,057,737,000	4,096,000	34,344,000	100	390
At least 30%	1,184,239,000	15,385,216,000	1,038,046,000	3,894,000	37,984,000	100	530
At least 45%	1,378,006,000	17,799,551,000	1,016,440,000	3,811,000	39,462,000	110	1,630
At least 60%	1,609,393,000	20,682,637,000	990,769,000	3,777,000	40,245,000	110	3,680

Total population vaccinated, total cost of vaccination, COVID-19 infections, and total years of life saved (YLS) are rounded to the nearest thousand. Costs, which are from the donor perspective, are in US$ and undiscounted since they are an upfront investment. YLS are calculated compared to the 0% vaccine supply strategy and discounted at 3% per year. Incremental cost-effectiveness ratios (ICERs) are presented as dollars per infection prevented and dollars per YLS and are calculated using unrounded values and then rounded to the nearest ten dollars. All dominated strategies presented in this table are instances of extended dominance (i.e., the dominated strategy has a higher ICER than that of a strategy providing greater health benefits).

[a] The modeled vaccine supply in the status quo was based on country-specific primary course vaccination coverage estimated to have been achieved as of early May 2022 and is equivalent to 38% of the overall population in the 91 low- and middle-income countries (see Methods).

Table 3. Cost-effectiveness of COVID-19 vaccinations when key parameters are varied in the 12 largest low- and middle-income countries

Variant type/modeled vaccine supply	Incremental cost-effectiveness ratio (US$/year of life saved)										
	R_e at model start[a]		Vaccine effectiveness[b]			Vaccine uptake			Total vaccination cost		
	1.7[c]	2.1	Low	Base case	High	50%	70%[c]	90%	0.5x	1.0x[c]	2.0x
Omicron-like variant											
No vaccine	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Status quo	710	dom	dom	710	dom	810	710	650	350	710	1,410
At least 15%	710	dom	1,070	710	490	dom	710	670	360	710	1,420
At least 30%	1,020	620	1,590	1,020	680	1,210	1,020	1,010	510	1,020	2,050
At least 45%	3,440	1,950	2,270	3,440	1,840	dom	3,440	1,480	1,720	3,440	6,870
At least 60%	10,820	10,290	12,570	10,820	3,540	11,690	10,820	3,690	5,410	10,820	21,640
Severe variant											
No vaccine	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Status quo	420	dom	dom	420	260	440	420	350	210	420	840
At least 15%	420	340	570	420	300	540	420	430	210	420	840
At least 30%	530	350	770	530	350	700	530	480	270	530	1,060
At least 45%	1,930	1,520	1,660	1,930	1,120	3,310	1,930	800	960	1,930	3,860
At least 60%	3,990	3,100	7,850	3,990	1,510	DOM	3,990	2,400	2,000	3,990	7,980

One-way sensitivity analyses were conducted in the 12 largest low- and middle-income countries (LMICs): Bangladesh, Democratic Republic of the Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania, and Vietnam. These countries were chosen since they account for 61% of the population in the 91 LMICs and reflect a range in global region, age structure, hospital bed capacity, ICU bed capacity, and current vaccination coverage (see Supplementary Methods). Incremental cost-effectiveness ratios are presented as US$/infection prevented and US$/year of life saved (YLS) and rounded to the nearest ten. Costs to derive these estimates are from the donor perspective, are in US$ and undiscounted since they are an upfront investment. Dominated strategies are ones that provide fewer health benefits than a less costly strategy (strong dominance; DOM) or have a higher incremental cost-effectiveness ratio than that of a strategy providing greater health benefits (extended dominance; dom). In incremental scenarios resulting in relatively few additional infections or deaths, strategies with increased vaccine supply may appear to be dominated by those with lower vaccine supply due to stochastic variation. Total cost of the vaccination program included both fixed and variable costs.

Abbreviations: R_e, effective reproductive number; Ref, reference.

[a] An R_e of 1.7 and 2.1 resulted in 48% and 64% of an unvaccinated population being infected, respectively, during the 360-day modeled time horizon.

[b] Base case vaccine effectiveness was modeled as 10% protection against infection, 15% protection against mild/moderate disease, and 55% protection against severe/critical disease. The low vaccine effectiveness was modeled as 5% protection against infection, 10% protection against mild/moderate disease, and 40% protection against severe/critical disease. The high vaccine effectiveness was modeled as 30% protection against infection, 50% protection against mild/moderate disease, and 80% protection against severe/critical disease.

[c] Indicates the value used in the base case.

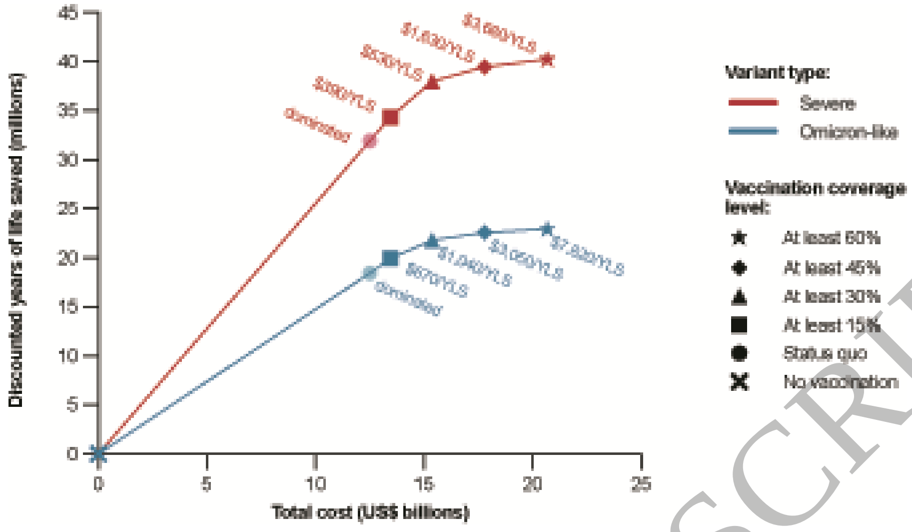

Figure 1

119x69 mm (.73 x DPI)

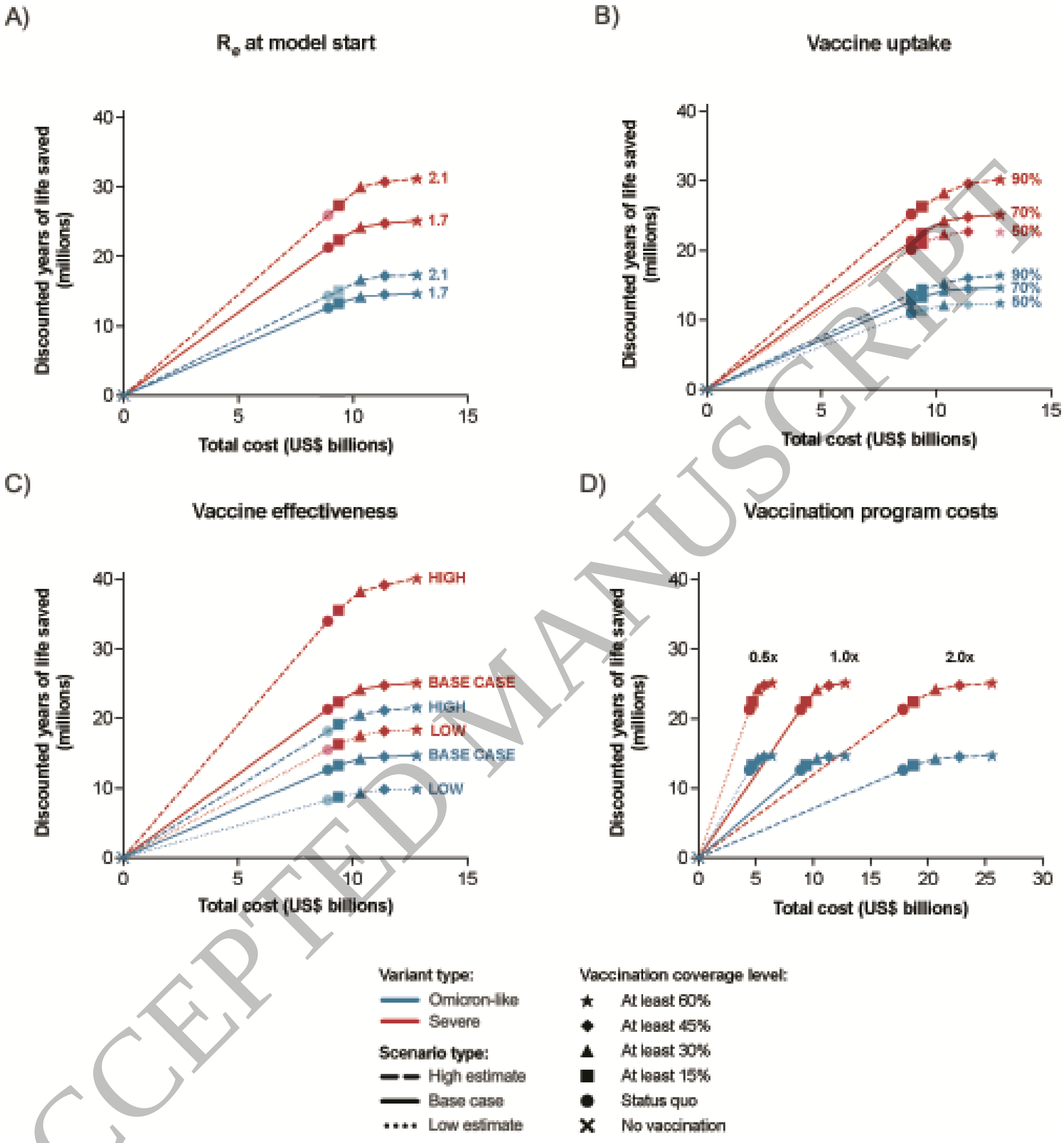

Figure 2

165x176 mm (.73 x DPI)