A Re-Analysis of EU's COVID-19 Vaccine Procurement Strategy in View of the An-Ticipated Cost-effectiveness of Vaccination

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Research Article

Keywords: European Union, COVID-19, vaccine, procurement, cost-effectiveness

Posted Date: November 18th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1034892/v1

Abstract

Aim

The EU has received criticism for being slow to secure COVID-19 vaccine contracts in 2020 before the approval of the first COVID-19 vaccine. The purpose of this study is to retrospectively analyze the EU's COVID-19 vaccine procurement strategy. To this end, the study retrospectively determines the minimum vaccine efficacy that made vaccination cost-effective from a societal perspective in Germany before the clinical trial announcements in late 2020. The result is compared against the expected vaccine efficacy before the announcements.

Methods

Two strategies were analyzed: vaccination followed by complete lifting of mitigation measures and a long-term mitigation strategy. A decision model was constructed using, e.g., information on age-specific fatality rates, intensive care unit costs and outcomes, and herd protection threshold. The base-case time horizon was 5 years. Cost-effectiveness of vaccination was determined in terms of costs per life year gained. The value of an additional life year was borrowed from new, innovative oncological drugs, as cancer reflects a condition with a similar morbidity and mortality burden in the general population in the short term as COVID-19.

Results

A vaccine with 50% efficacy against death due to COVID-19 was not clearly cost-effective compared to a long-term mitigation strategy if mitigation measures were planned to be lifted after vaccine rollout. The minimum vaccine efficacy to achieve cost-effectiveness was 40% in the base case. The sensitivity analysis shows considerable variation around the minimum vaccine efficacy, extending above 50% for some of the input variables.

Conclusions

This study shows that vaccine efficacy levels expected before clinical trial announcements did not clearly justify lifting mitigation measures from a cost-effectiveness standpoint. Hence, the sluggish EU's procurement strategy still appeared to be rational at the time of decision making.

Introduction

In November 2020, the pharmaceutical companies Pfizer/Biontech and Moderna independently announced that their vaccine candidates against SARS-CoV-2 have demonstrated evidence of efficacy against COVID-19 in participants without prior evidence of SARS-CoV-2 infection. The case splits between vaccinated individuals and those who received the placebo indicated a vaccine efficacy rate above 90% (FDA 2020, Polack 2020). The European Commission approved the Biontech-Pfizer and Moderna vaccines for use across

the 27 Member States on December 21, 2020 and January 6, 2021, respectively. The Commission has so far given the conditional marketing authorization for four vaccines.

On June 17, 2020, the European Union (EU) put forward a strategy that would see the European Commission centrally purchase a Covid-19 vaccine on behalf of all EU countries (European Commission 2020). Before the first approval, the EU Commission signed contracts with six vaccine manufacturers: BioNTech/Pfizer, Moderna, AstraZeneca, CureVac, Johnson & Johnson, and Sanofi. In total, she secured almost two billion doses of vaccine. That was basically enough for the 450 million inhabitants of the 27 EU member states - even if two doses per person have to be administered for almost all vaccines and not all vaccines would be approved. Nevertheless, the EU has received criticism for being slower than Israel, the United Kingdom, and the United States to secure vaccine contracts, thus slowing down the vaccine rollout (euronews 2021).

According to EU Commission spokesman Stefan De Keersmaecker, the EU wanted to position itself broadly. He argued that at that time there was no way of knowing which vaccine would be marketable first or at all (Eisele 2021).

The rather lower original order number of 200 million doses from BioNTech/Pfizer and 80 million doses from the U.S. company Moderna was partly due to their innovative technology and their high prices. The BioNTech vaccine also has to be cooled to minus 70 degrees Celsius and is therefore comparatively difficult to handle (Eisele 2021).

The purpose of this study is to re-analyze the appropriateness of the EU's vaccine procurement strategy. To this end, the study retrospectively determines the minimum efficacy of a vaccine that was necessary to obtain an acceptable cost-effectiveness ratio in the general German population before the announcements of the first phase III trial results. The estimated minimum efficacy allows a comparison with anticipated efficacy levels before the announcements. To serve this purpose, the study uses the best available data from the second half of 2020.

Methods

Conceptual approach

Cost-effectiveness

A new vaccine is considered to be cost-effective if its incremental cost-effectiveness ratio (ICER) versus a less effective treatment is smaller than or equal to the cost-effectiveness threshold λ:

$$\frac{c}{h} = \frac{v - s + b}{h} \leq \lambda, \qquad (1)$$

where c is incremental costs; h denotes incremental net health benefit including harm from side effects; v is the cost of the new vaccine including costs of vaccine administration, subsidies, establishing vaccination

centers, transportation, and managing side effects; s denotes savings from avoiding COVID-19-related morbidity; and b refers to the cost resulting from avoidance of COVID-19 death.

Minimum efficacy

As mentioned, this study took the perspective before the approval of the first COVID-19 vaccine. The aim was to determine the minimum vaccine efficacy against death due to COVID-19 that makes vaccination cost-effective. Replacing the unequal sign in Eq. (1) by an equal sign and rearranging Eq. (1) yields the minimum health benefit $h_{\min}$:

$$\frac{v - s + b}{\lambda} = h_{\min}. \qquad (2)$$

Next, $h_{\min}$ is converted into a minimum relative efficacy $\epsilon_{\min}$ compared to the maximum health benefit $h_{\max}$:

$$\varepsilon_{\min} = \frac{h_{\min}}{h_{\max}}. \qquad (3)$$

Comparators

As a comparator of a COVID-19 vaccine the study uses a mitigation strategy including a partial lockdown/shutdown, which had been the COVID-19 response strategy in Germany during the first pandemic wave. I did not assume a suppression of the pandemic, however, because the strategy chosen by the German government headed more towards mitigation than suppression. This mitigation strategy included compulsory face masks, physical distancing, and quarantine directives but also a shutdown of businesses such as nightclubs (in sum, a partial lockdown/shutdown).

Decision model

A decision model was constructed based on a previously developed and validated model (Gandjour 2020). The latter model determines the gain in life years of a strategy that is successful in 'squashing the curve' compared to the situation before the pandemic. It is based a life-table model that summarizes the age-specific mortality impact of the SARS-CoV-2 pandemic. The base-case calculation relies on an independence assumption, implying that individuals not dying from COVID 19 have the same probability of death as all individuals before the rise of the pandemic. Given that patients who die from COVID 19 tend to have more comorbidities (Wu 2020), I assumed a harvesting effect in a sensitivity analysis. This approach presumes that those who die from COVID-19 are sicker and would have died any-way. In this scenario, I assumed for age groups with excess mortality associated with COVID-19 (the difference between observed and pre-pandemic mortality rates) that except for COVID-19, there are no other causes of death in the forthcoming 12 months.

Given the absence of suppression, I did not assume that further pandemic waves are prevented. Hence, I adjusted the number of life years gained from 'squashing the curve' for the expected number of pandemic

waves and the resulting death toll under mitigation. To this end, I multiplied the death toll of the first pandemic wave in Germany (the termination was set to July 31, 2020) with the expected number of pandemic waves and deducted the resulting figure from the gain in life years by 'squashing the curve'. Given that some commentators predicted the second wave to be substantially worse than the first, I assumed a doubling of the death toll in a sensitivity analysis.

I did not further adjust the number of life years gained for a possible deferral of elective procedures, assuming that ICU capacity will be sufficient in future pandemic waves.

The time horizon (5 years in the base case) was set based on the expected duration of vaccine immunity. The transmission dynamics of SARS-CoV-2 were considered comparable to those of influenza (van Damme 2020), which typically causes epidemics in temperate climates every year during winter. In the absence of a vaccine, future SARS-CoV-2 pandemic waves were therefore assumed to peak in winter and return yearly.

Vaccine efficacy

Vaccine efficacy can be defined based on the attack rate (the proportion of individuals infected in the specific risk group over a nominated period) or the frequency of only severe cases (Préziosi 2003). The herd immunity threshold was calculated based on an inversely proportional relationship with vaccine efficacy (in terms of attack rate) (Chowell 2009):

$$\varphi = \frac{1}{\epsilon}\left(1 - \frac{1}{R_0}\right), \qquad (4)$$

where ϕ refers to the herd immunity threshold, ϵ is vaccine efficacy, and R_0 is the basic reproduction number of a disease.

Cost calculation

The study took a societal viewpoint, by including both direct medical costs and indirect/productivity costs. Whereas from the perspective of static efficiency the GDP drop associated with the lockdown/shutdown can be considered sunk at the time of decision-making, from the perspective of dynamic efficiency, which sets incentives for innovation (e.g., for vaccines in future pandemics), it is still relevant. As vaccine development and distribution in future pandemics is likely to occur only in conjunction with a shutdown strategy, considering the full shutdown cost avoids introducing excessive incentives for innovation. Therefore, a dynamic efficiency perspective was considered in the base case.

In the short term, a vaccination strategy must be regarded as an add-on to a mitigation strategy because vaccination of a large part of the population cannot be achieved immediately. However, in the mid- to long-term, vaccination avoids the costs of mitigation strategy, which is the contribution of the lockdown/shutdown to the total economic burden of the SARS-CoV-2 pandemic. In addition, vaccination avoids the deaths associated with mitigation strategy, which is not able to suppress the pandemic.

In terms of vaccination costs, I considered the costs of i) the vaccine itself, ii) the clinical administration, and, in agreement with a dynamic efficiency perspective, iii) scientific research failures. In terms of the costs of

the vaccine, I considered prices that do not include a markup above the marginal costs. This agrees with the economic principle that drug prices need to be adjusted for producer surplus, as it presents a gain in societal welfare (Garrison 2010). For the costs of scientific research failures, I considered the probability of success of clinical trials of vaccines.

Data

As mentioned in the introduction, the data used in the model and presented in the following are not the most recent ones. Nevertheless, they were relevant before the announcements of the COVID-19 vaccine results and hence are those that mattered for the EU vaccine procurement strategy.

Economic data

According to the European Economic Forecast by the European Commission in November 2020, GDP of Germany was set to contract by 5.5% in 2020. Second wave of infections was expected to dampen the rebound to 3.5% in 2021. Assuming there was no permanent damage to productive capacity, Germany's economy was projected to continue to grow above potential in 2022 at 2.5% and complete its recovery to the pre-crisis levels. As the 2021 GDP growth projection was revised down to 3.5% from 5.3% in the forecast of July 2020, the impact of the second wave is calculated to be a 1.8% contraction of GDP. This percentage was also applied to potential future waves. According to the European Economic Forecast, the total volume of the government measures "to fight the COVID-19 pandemic and stabilise the economy (…) amounts to 4.7% of GDP in 2020 and 2.1% in 2021". By subtracting the GDP contraction due to the second wave, I determined the GDP loss independent of the second wave.

However, the European Economic Forecast was conducted assuming the absence of a pandemic in the counterfactual scenario, without considering the voluntary restrictions such as social distancing that may take place in view of the rapid spread of the virus in the population (cf. Aum 2021). That is, individuals may take precautions even without the lockdown orders. Accounting for the latter would decrease the incremental cost of the lockdown/shutdown over no pandemic. In a sensitivity analysis I assumed the contribution of the lockdown/shutdown to the total loss of economic activities to be 10%, to account for the voluntary restrictions that may take place in the absence of a lockdown/shutdown. This estimate agrees with the one regarding the contribution of a shutdown to the loss of economic activities in Denmark, which was estimated to be 14% (=4%/29%) (Sheridan 2020).

To determine the productivity gains resulting from a vaccination compared to a mitigation strategy, I used the data sources reported in Table A1 of the Appendix.

The German federal government has been funding three vaccine developers with a total of 750 million euros. BioNTech from Mainz received 375 million euros and Curevac from Tübingen received 230 million euros through a special vaccine development program (Finkenzeller 2020). This subsidy was included in the analysis and related to one vaccinated individual.

Concerning the costs of the vaccine itself, I applied an estimate of US$10 per person (converted to euros), which represents the costs of the Johnson & Johnson vaccine (Dittmer 2020). Johnson & Johnson declared

not to strive for profits (Dittmer 2020). The costs of failures were based on a failure rate of 70%, representing a weighted average of industry-sponsored and non-industry-sponsored vaccine development programs with end dates after January 1, 2000, and start dates before January 7, 2020 (Wong 2020).

All costs are presented in euros, year 2020 values.

Clinical and epidemiological data

According to the United States Food and Drug Administration (FDA) (2020), the efficacy of the primary endpoint in a placebo-controlled efficacy trial should be at least 50%, to classify a widely deployed COVID-19 vaccine as effective, while ensuring safety. Hence, I took this estimate (50%) as the lower limit of the vaccine efficacy. As the FDA allows both SARS-CoV-2 infection and deaths associated with COVID-19 to be defined as primary endpoints, applying the 50% threshold to the life years gained as a measure of vaccine efficacy is still valid.

To calculate the per capita gain in life years through mitigation, I applied the COVID-19 infection fatality rate (IFR) of 0.75% (WHO 2020), which was estimated in summer 2020, to the previously developed model (Gandjour 2020). The IFR was adjusted upwards to account for the long-term mortality of ICU survivors. The per capita gain in life years accounts for the percentage of the population that must be immune in order to reach the herd immunity threshold. Furthermore, given that the IFR is lower than the case fatality rate (CFR) in Germany, I adjusted the percentage of patients admitted to the ICU accordingly because a lower CFR also implies a lower percentage of cases admitted to the ICU (Gandjour 2020).

In the base case, I assumed that a vaccine campaign was able to overcome the vaccine hesitancy by using strategies such as simple, easy-to-understand language (Volpp 2020). Thus, the campaign was projected to achieve an uptake that is sufficient to yield the herd immunity. Based on equation 4 and a herd immunity threshold of 70% for natural infection (Kwok 2020), the threshold is approximately 73% for a vaccine efficacy of 95%. For a vaccine efficacy of 50% I assumed the same uptake.

In a sensitivity analysis, I considered a vaccine uptake of 50% based on a survey of November 2020 in the German population (Kixmüller 2020). If herd immunity is not reached, local outbreaks may follow, necessitating local shutdowns/lockdowns. The economic costs of the latter were already accounted for by the economic projections in the absence of another pandemic wave, because the projections assumed continuous spreading of infections and only a “gradual lifting of containment measures” (European Commission 2020).

Immunity was assumed to last between one (Galanti 2020) and ten years. The latter estimate was based on the immunity status of the survivors of SARS, caused by another coronavirus, who still carry certain important immune cells 17 years after their recovery (Le Bert 2020). For comparison between vaccination and mitigation, the GDP drops associated with annual pandemic waves under mitigation were discounted at an annual rate of 3%, based on the social rate of time preference derived from the Ramsey equation (Ramsey 1928). For health benefits of mitigation, I applied a 2% discount rate, reflecting a 1% expected growth rate of the consumption value of health in Germany (cf. John 2019).

Willingness to pay (WTP)

The WTP for an additional life year (€101,493 per life year gained) based on the absolute rule was calculated by dividing the incremental costs of new, innovative cancer drugs (€39,751) by the incremental survival benefit (0.39 life years) (Gandjour 2020). As the WTP estimate does not account for life extension costs, the latter were not considered in calculating the cost-effectiveness of vaccination either (variable b in Eq. (2)).

Results

A future lockdown policy avoids productivity losses due to symptomatic infections and quarantines of contact persons that are associated with an uncontrolled spread of the pandemic. Based on the results reported in Table A2 of the Appendix, the avoided productivity loss is predicted to amount to 0.9% of the GDP.

Table 1 shows the input values and distributions used in the base case and sensitivity analysis. Vaccination with a vaccine with 50% efficacy followed by lifting of mitigation measures is less effective than a long-term mitigation strategy. Nevertheless, it is still cost-effective because savings are sufficiently large to pass the ICER threshold (Table 2). A vaccine needs to have an efficacy of at least 40% to be cost-effective in the base case. As shown in the sensitivity analysis (Figure 1), the range for the minimum efficacy of a vaccine lies between 6% and 88%. A small portion of the GDP loss attributable to the shutdown and a short duration of immunity have the largest impact on the minimum efficacy.

Table 1
Input values and distributions used in the base case and sensitivity analysis.

Input	Mean (range)	Reference
Epidemiological and clinical data		
Population size by age	see reference	Federal Office of Statistics 2020
IFR in Germany	0.0075 (0.005 – 0.01)	WHO 2020
CFR in Germany		Robert Koch Institut 2020
Total population	0.042	
0-9 years	0.00009	
10-19 years	0.00005	
20-29 years	0.00022	
30-39 years	0.00070	
40-49 years	0.0025	
50-59 years	0.0095	
60-69 years	0.048	
70-79 years	0.16	
80-89 years	0.28	
90+ years	0.33	
Probability of ICU indication	0.04 (0.04 – 0.08)	Robert Koch Institut 2020
False-positive ICU admissions	0.1 (0.1 – 0.2)	Abers 2014
CFR in the ICU	0.24 (0.23 – 0.25)	Robert Koch Institut 2020
CFR one year post ICU discharge	0.59 (0.47 – 0.73)	Damuth 2015
Herd protection threshold	0.70 (0.60 – 0.70)	Kwok 2020
Vaccine efficacy	0.5 – 1.0	FDA 2020
Immunity following one vaccination, years	5 (1 – 5)	Galanti 2020, Le Bert 2020
Cost data		

CFR = case fatality rate, ICU = intensive care unit, IFR = infection fatality rate

Input	Mean (range)	Reference
GDP reduction per pandemic wave, %	1.8	European Commission 2020
GDP reduction without a second wave, %	5.0	European Commission 2020
GDP drop attributable to shutdown versus voluntary restrictions, %	100 (10 – 100)	Estimate
German federal government subsidy for vaccine development	750,000,000	Finkenzeller 2020
Contribution of a shutdown to GDP reduction	30% (10 – 30)	Rathke 2020
Vaccine costs per individual	€8.47	Capital 2020
Vaccination costs per individual	€7.95	KV Nordrhein 2020
CFR = case fatality rate, ICU = intensive care unit, IFR = infection fatality rate		

Table 2
Incremental costs, effects, and cost-effectiveness of a vaccine with efficacy 50% compared to a mitigation strategy. All costs are in Euro. Costs and life years refer to one individual.

Lockdown costs	Subsidy	Vaccination costs	Total costs	Life years gained	ICER
-3,159.89	9.02	33.32	-3,117.55	-0.02	128,353.85
ICER = incremental cost-effectiveness ratio					

Discussion

This study shows that the minimum COVID-19 vaccine efficacy against death that makes complete lifting cost-effective is 40% in the base case. The relatively high level of efficacy needed to demonstrate cost-effectiveness is supported by the sensitivity analysis, which shows considerable uncertainty around the minimum efficacy. Hence, a vaccine efficacy level of 50% even against death does not clearly justify complete lifting of mitigation measures after vaccine rollout and may still require imposing lockdown measures even in the long-term (O'Donnell 2020).

The minimum efficacy needs to be compared against the anticipated efficacy before the announcements of the phase III trial results. Many experts were expecting a vaccine efficacy of only 50–70% (Zimmer 2020). Therefore, given that the level of vaccine efficacy predicted by many experts did not clearly imply that lifting mitigation measures is cost-effective, the EU's procurement strategy still appears to be rational at the time of decision making. This conclusion is supported by a UK field study from summer 2020 suggesting increased vaccine hesitancy in view of lower efficacy (McPhedran 2021). A more aggressive order strategy seems to have been only justifiable for a rather optimistic decision maker, who, in a state of ambiguity, prioritizes upside potential over downside potential, thus deemphasizing potentially catastrophic events.

As a word of caution, this decision-analytic study has several caveats. There are reasons why the study underestimates the health benefits and cost-effectiveness of a vaccine compared to a mitigation strategy and thus overestimates the minimum vaccine efficacy level. Some of these reasons were already captured in the sensitivity analysis and include a low IFR. First, the study does not consider the deaths and loss of health-related quality of life associated with the shutdown and social distancing, e.g., due to depressive or anxiety disorders, suicides, unemployment, domestic violence, and fewer emergency and regular visits to physicians for unrelated medical conditions. Nevertheless, official data on excess mortality in Germany (Federal Office of Statistics 2021) showed that both excess mortality and COVID-19 mortality peaked in the first half of April 2020, thus indicating that excess mortality was driven by COVID-19 and not by other causes. Second, unaffected individuals may experience a loss of personal freedom (Abele-Brehm 2020) and autonomy under lockdown. Third, under mitigation strategy elective procedures may need to be deferred if ICU capacity is expected to be insufficient. And forth, a vaccine may prevent COVID-19 infection with long-haul symptoms and save the direct (non-)medical costs and indirect costs associated with nonfatal COVID-19 cases.

Conversely, there are reasons to believe that the health benefits of mitigation and the minimum efficacy of a vaccine are underestimated. First, decreased economic activity can save lives, because it reduces air pollution, traffic accidents (Cornwall 2020), and accidents on construction sites (Deaton 2020). Second, social distancing may reduce deaths due to non-COVID-19 flu. Third, despite criticism on underinvestment in vaccine procurement, the number of COVID-19 vaccines ordered by the EU has exceeded the required quantity, thus resulting in oversupply. Given the lack of information on success rates of the various vaccines under development before the announcement of the first phase III trial result, an oversupply could not have been predicted with certainty. Accounting for excess supply, however, would decrease the cost-effectiveness of a vaccine and increase the minimum vaccine efficacy to demonstrate cost-effectiveness. Some of the biases listed in this and the previous paragraph may cancel each other out.

Finally, the number of life years as an outcome measure may be criticized for lacking a consideration of health-related quality of life. Quality-adjusted life years (QALYs) are able to capture an additional health benefit resulting from the avoidance of non-fatal COVID-19 cases and the associated loss in quality of life. On the other hand, QALYs diminish the health benefits obtained from additional survival time by accounting for a quality-of-life decrement. As the QALY metric thus discriminates against the elderly and the disabled, it has been considered ethically controversial (Ubel 1999). For this and other reasons, QALYs have not been used so far in Germany for the purpose of reimbursing and pricing new, innovative medicines (cf. IQWiG 2020). As another counterpoint, the public debate on COVID-19 in Germany before the trial announcement had been focusing mainly on mortality as an endpoint and the number of life years lost by the elderly who died from COVID-19. In sum, there is not a straightforward answer to the question of which outcome measure best reflects the value of a vaccine. Life years gained may serve as a compromise between the use of unweighted lives saved and QALYs gained.

In terms of the transferability and relevance of the results and conclusions of this study to other countries, the usual caveats apply. This holds in particular as the EU's procurement strategy was analyzed from a German perspective. The specific reasons for caution include between-country differences in clinical and

epidemiological data, costs, and the willingness to pay for health benefits. Hence, low levels of vaccine efficacy may still be acceptable from the viewpoint of other EU countries.

To summarize, this study shows that at least part of the criticism on EU's COVID-19 vaccine procurement strategy does not appear to be justifiable in view of cost-effectiveness considerations and vaccine efficacy expectations before the clinical trial announcements. As a complete lifting of mitigation measures in summer 2021 does not seem to be warranted in view of new mutational variants, the procurement strategy may not turn out to be a failure even from an ex-post perspective.

Declarations

- Ethics approval and consent to participate: Not applicable.
- Consent for publication: Not applicable
- Availability of data and material: All data are contained within the manuscript. The data sources are listed in Table 1 and are publicly available.
- Competing interests: The author declares that he has no competing interests.
- Funding: This article received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.
- Authors' contributions: AG is the sole author responsible for conception, drafting, and approving the submitted version.
- Acknowledgement: None

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Figures

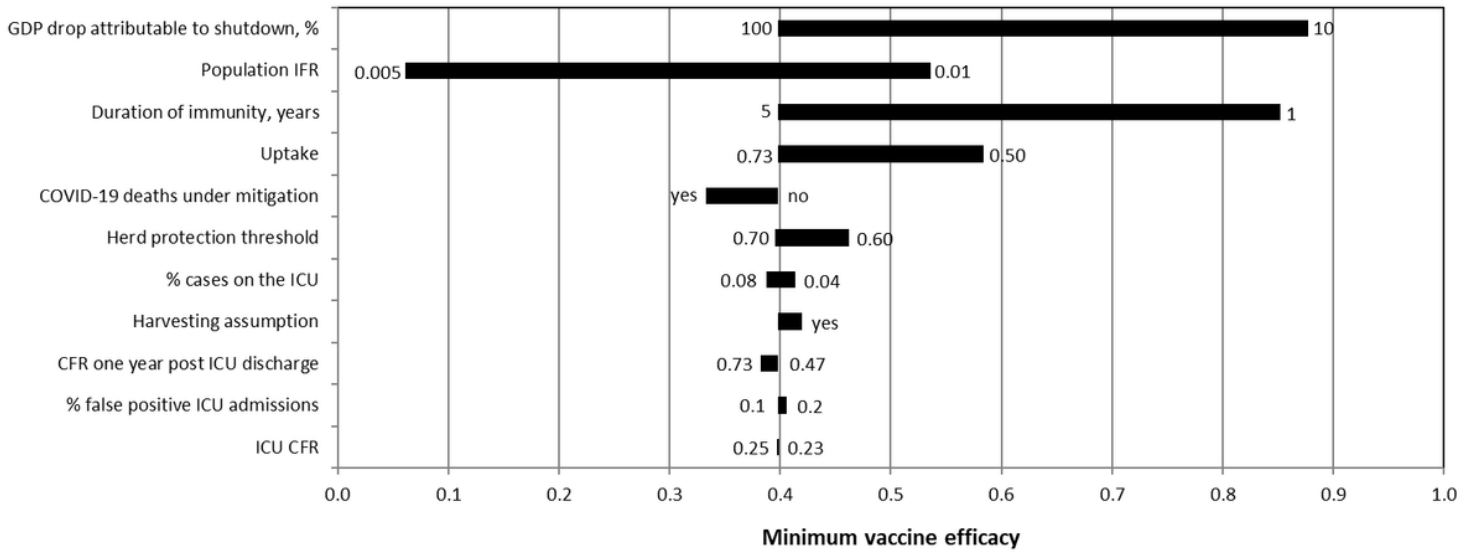

Figure 1

Tornado diagram demonstrating the results of the one-way sensitivity analysis. The variables are ordered by the impact on the minimum efficacy of a COVID-19 vaccine that makes vaccination cost-effective. The numbers indicate the upper and lower bounds.

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