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# Cost Utility of Vaccination Against COVID-19 in Brazil

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## ABSTRACT

*Objectives:* The objective of this study was to evaluate the cost-utility of the Oxford, CoronaVac, and Janssen COVID-19 vaccines from the perspective of the Brazilian public health system.

*Methods:* A total of 3 microsimulation models were constructed with individual data to evaluate the 3 vaccines. The simulation contains 7 transition states that are related to the natural history of the disease. The model with a daily cycle has a time horizon of 1 year and uses data from 289 days of the pandemic. The analysis was conducted from the perspective of the Brazilian public health system considering direct medical costs. For the model inputs, outpatient and hospital databases were used with information on treated patients stratified by age. Information on mortality was also stratified based on patients' age in the mortality database (SIM). The efficacy of vaccines to reduce the likelihood of patients becoming ill was evaluated independently for each vaccine. Information on the quality of life of patients in outpatient or hospital treatment and the sequelae resulting from the disease were extracted from the literature. The main outcome of the analysis was quality-adjusted life-years (QALYs).

*Results:* The vaccines showed incremental cost-utility ratios ranging from R$−23 161.3/QALY (Oxford) to R$17 757.85/QALY (CoronaVac). The older the population, the lower was the incremental cost-utility ratio. Given a willingness-to-pay threshold of R$17 586/QALY, all the vaccines were considered cost-effective in the probabilistic sensitivity analysis.

*Conclusions:* The results of the analysis by age group can help in the preparation of a vaccination prioritization plan.

*Keywords:* cost-utility analysis, COVID-19, health technology assessment, HTA, vaccines.

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## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, which causes COVID-19, is a single-stranded ribonucleic acid virus that was first identified in January 2020 in patients with viral pneumonia in Wuhan, China, and has rapidly spread around the world, leading to the World Health Organization (WHO) declaring it a pandemic on March 11, 2020.[1,2]

Transmission occurs through aerosol or respiratory droplets of those infected or contact with contaminated surfaces, and its clinical picture ranges from asymptomatic cases to more severe cases, requiring hospital care for 10% to 15% of those infected[3-5] and with mortality rates between 1.2% and 1.6%.[6] Age is the main risk factor for disease progression,[7] including in-hospital death.[8] According to the WHO, 118 529 397 cases of COVID-19 were confirmed worldwide by March 12, 2021, leading to the death of 2 630 678 individuals. In Brazil, there have been 11 363 380 cases and 275 105 deaths.[9,10] Nevertheless, the deficient testing capacity suggests that these numbers may be underestimated.[11]

Currently, the available preventive measures are not sufficient to contain the advance of the pandemic, and prophylactic vaccination is an important tool that stimulates the immune system by inducing the production of neutralizing antibodies capable of preventing or minimizing infection by the virus, in addition to stimulating the production of sufficient memory T lymphocytes to prevent viral replication, thus, avoiding the risks related to morbidity and mortality of this disease.[12]

The Oxford vaccine, developed by AstraZeneca, is based on a replication-deficient chimpanzee adenovirus vector containing the genetic sequence of the surface protein S of the SARS-CoV-2 virus, stimulating the immune system to recognize and fight the virus. In the phase III trials involving the Oxford vaccine, randomized, blind, placebo-controlled (meningococcal ACWY vaccine or saline solution) studies, with 11 636 participants from the United Kingdom, Brazil, and South Africa and a mean follow-up of 3 to 4 months (interquartile range 13-4.8), showed a mean overall efficacy after 2 doses of 70.4% (95.8% confidence interval [CI] 54.8%-80.6%). A total of 131 symptomatic cases of COVID-19 were confirmed in the study patients, with 30 (0.5%) cases in the vaccinated group and 101 (1.7%) in the control group.[13]

The CoronaVac vaccine, developed by SinoVac Life Sciences Co., contains the inactivated SARS-CoV-2 virus. In the phase III, randomized, multicenter, double-blind, placebo-controlled study of 12 123 health professionals in Brazil, the overall efficacy 14 days after the second dose of this vaccine was estimated at 50.38% (95% CI 35.26%-61.98%; $P$ = .0049). In that study, 85 (1.3%) participants in the vaccinated group developed a mild infection, according to the WHO classification, whereas in the placebo group, 159 (2.5%) participants had mild disease, 6 had moderate disease, and 1 had severe disease.[14]

The vaccine developed by Janssen Biotech is a replication-incompetent adenovirus type 26 vectored vaccine that contains the genetic sequence of the S protein of the SARS-CoV-2 virus. In their phase III, multicenter, randomized, double-blind, placebo-controlled study with 39 321 participants, with a mean follow-up of 2 months after vaccination, the overall efficacy was 66.1% (95% CI 55.0%-74.8%), with 66 (0.33%) cases of COVID-19 in the vaccinated group and 193 (0.98%) in the placebo group; thus far, this is the only vaccine provided in a single dose.[15]

The slow pace of obtaining vaccines and the uncertainties regarding their availability in Brazil[16] justify a cost-utility assessment among the available options, thus, allowing more effective guidance for investment. In the present study, the cost-utility of the Oxford, CoronaVac, and Janssen vaccines were evaluated.

### *Objectives*

The objective of this study was to evaluate the cost-utility of the Oxford, CoronaVac, and Janssen vaccines from the perspective of the Brazilian public health system.

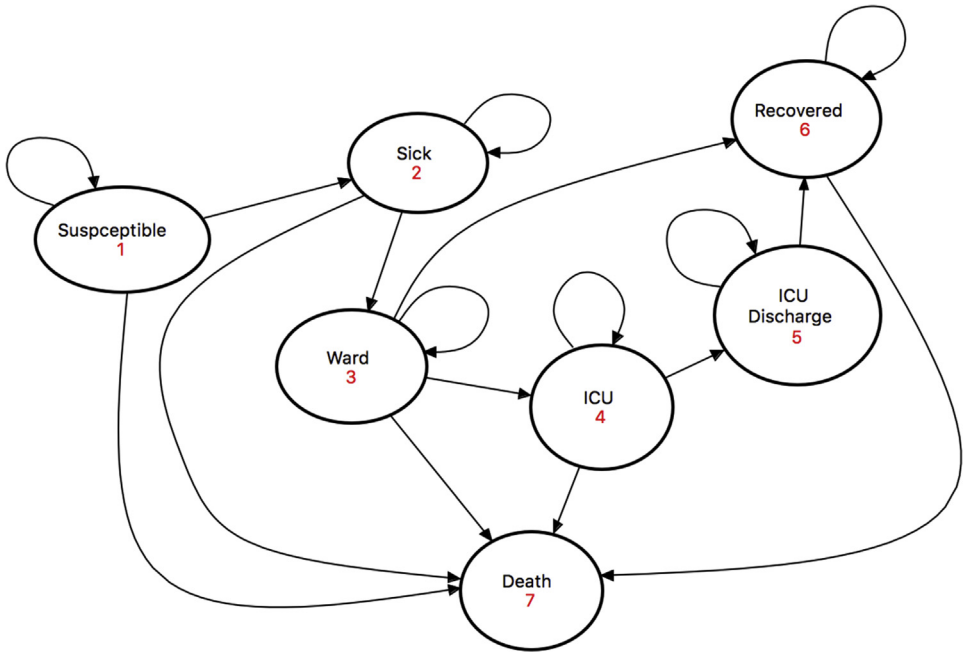
## Methods

A total of 3 Markov models were developed (one for each vaccine) with microsimulation of individual data, comparing each of the 3 hypothetical cohorts of 1 of the 3 vaccines (Oxford, CoronaVac, and Janssen) with a cohort of unvaccinated individuals. The model contains 7 transition states and considers patient age as a risk factor. For each patient who is included in the simulation, an age is randomly selected according to the age distribution of the susceptible individuals. Each individual starts the simulation in the susceptible state and may progress to "sick," "ward," intensive care unit ("ICU"), "ICU discharge" (from where the patient would return to the ward), and "recovered." In all states, the probability of death is considered, except at "ICU discharge." Patients were run in the simulation for a time horizon of 1 year in daily cycles (365 cycles). In this model, the efficacy of each vaccine influenced the probability of transition between the susceptible state and the "sick" state and reduced the probability of hospitalization and death. A reduction in transmission between individuals was not considered. At the time of the analysis, no data on reducing infection transmission were available because of the vaccine. In this case, the Markov model design was preferred considering only the prevention of sickness, hospitalizations, and death. The model was validated through face validity (peer review) and has been submitted to the public inquiry. The transition states and the relationships between them are outlined in Figure 1. The TreeAge Software (Williamstown, Massachusetts) was used for the analysis.

### *Assumptions*

The model was constructed from the perspective of the Brazilian Public Health System (SUS, for its acronym in Portuguese), and the direct medical costs involved in the care of outpatients hospitalized in the ward or the ICU were considered based on open-source data. In the time horizon of 1 year, no discount rate was applied in the simulation. Each vaccine (Janssen, CoronaVac, and Oxford), with its respective efficacy, were individually compared with the cohort that did not receive the intervention. After ICU discharge, patients returned to the ward in the state "ICU

**Figure 1.** Schematic representation of the transition states of the model.




ICU indicates intensive care unit.

discharge." No deaths were found in the data available in this state, and this possibility was not considered in the model.

### Data Sources

The e-SUS and SIVEP–Gripe (public health system databases) were used to extract data on the probability of transition between states and holding time in the states by age (continuous variable with annual intervals).[17,18] The e-SUS database contains records of patients undergoing outpatient treatment, and the SIVEP-Gripe database contains records of hospitalized patients. Cases of COVID-19 were selected from patients between 18 and 80 years of age. For data on the overall mortality rate of the population, the database of the Mortality Information System (SIM SUS, for its acronym in Portuguese) was used with data from 2019, when the pandemic did not yet exist in Brazil.[19]

Until the time of this analysis, with 289 days of the pandemic since the first case, Brazil had 5 665 089 reported infections. The beginning was considered the first case, with the end being the date of completion of the collection (December 9, 2020). From the databases, it was possible to extract beta distribution parameters for each age of individuals. These individual patient characteristics directly influenced the transition probabilities in the simulation.

In addition to the probabilities of hospitalization, the databases were also used to extract the mean holding time in the "sick," "ward," "ICU" and "ICU discharge" states. This information was included in the model, which considered the number of days that each patient remained in these states based on age.

### Costs

The SUS procedures table (SIGTAP) was the main source of information for estimating the cost of events in the model.[20] The values found were adjusted by a correction factor of 2.8, considering that the values in this table express only federal spending by the SUS. This calculation was based on the study Contas do SUS.[21] The adoption of this factor was agreed with the Ministry of Health. The Health Price Bank (BPS) database was also used to fund some items through federal purchasing information.[21,22] Direct medical costs included medical visits, diagnostic tests, hospital stay (ward and ICU), hemodialysis, laboratory tests, imaging tests, and the unit cost of each vaccine dose. The latter was influenced by the dollar exchange rate, which, in the analysis period, was quoted at R$5.34 per US dollar.[21] The cost per dose of the Oxford vaccine is U$3.16, and that of CoronaVac is U$10.31 (Table 1). The cost of the Janssen vaccine is U$10.00, in this case, simulated with only 1 dose, as recommended by the manufacturer.

It was assumed that each patient with the mild disease would only make 1 medical visit and that specific treatment for COVID-19 would not be prescribed. In cases requiring hospitalization, the daily costs of the ward or ICU were considered. A mean value for test frequency was adopted regardless of individual risk factors, being subdivided only between patients admitted to the ward or ICU and with the assumption of tests performed daily or performed only once per stay (Table 2).

The costs of imaging tests were differentiated into costs of tests when admitted to the ward or the ICU. The number of computed tomography scans per ward or ICU stay was estimated by the number of tests performed relative to the number of patients hospitalized for COVID-19 in the same period.[18] The number of x-rays for patients admitted to the ward was estimated by the number of tests performed relative to the number of patients hospitalized for COVID-19 in the same period.[18] In the ICU, the assumption was 1 x-ray per day. No information was found on the total number of echocardiograms, electrocardiograms, or lower limb venous Doppler ultrasounds. It was assumed that 30% and 70% of patients in the ward and ICU, respectively, would undergo

**Table 1.** Cost of vaccines and number of doses.

| Vaccines | Cost per dose (US$) | Doses |
|---|---|---|
| Oxford | 3.16 | 2 |
| CoronaVac | 10.31 | 2 |
| Janssen | 10 | 1 |

**Table 2.** Costs and use of resources included in the model.

| Care | SIGTAP (R$)* | Ward | ICU |
|---|---|---|---|
| Hemodialysis (COVID-19 complement) | 112.01 | 0.05 | 0.05 |
| Hemodialysis | 305.48 | 0.05 | 0.05 |
| Medical visit | 5.24 | single | single |
| Daily ward cost | 157.30 | daily | |
| Daily ICU cost | 838.95 | | daily |
| **Tests** | | | |
| Diagnostic test | 24.34 | single | single |
| Albumin | 1.52 | single | single |
| ALT (TGP) | 0.38 | single | single |
| AST (TGO) | 0.38 | single | single |
| Calcium | 0.35 | daily | daily |
| CK-MB | 0.77 | single | single |
| Creatinine | 0.35 | daily | daily |
| LDH | 0.69 | daily | daily |
| Ferritin | 2.92 | single | single |
| Gamma-GT | 0.66 | single | single |
| Blood gas analysis | 2.93 | daily | daily |
| Blood glucose | 0.35 | daily | daily |
| Blood culture | 2.15 | single | single |
| Hemogram | 0.77 | daily | daily |
| Magnesium | 0.38 | daily | daily |
| Potassium | 0.35 | daily | daily |
| Pro-BNP | 5.06 | single | single |
| C-reactive protein | 0.53 | daily | daily |
| Sodium | 0.35 | daily | daily |
| Troponin | 1.69 | single | single |
| Urea | 0.35 | daily | daily |
| Chest tomography | 25.54 | 0.3 | 0.3 |
| Echocardiogram | 7.48 | 0.3 | 0.7 |
| Chest x-ray | 1.78 | 0.7 | daily |
| Electrocardiogram | 0.96 | 0.3 | 0.3 |
| LL venous Doppler | 7.42 | 0.3 | 0.7 |

QALY indicates quality-adjusted life-year.
ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; CK-MB, creatine kinase; Daily, taken every day during the hospitalization; Gamma-GT, gamma glutamyl transferase; ICU, intensive care unit; LDH, lactic dehydrogenase; LL, lower limbs; Pro-BNP, pro-brain natriuretic peptide; SIGTAP, Sistema de Gerenciamento da Tabela de Procedimentos; Single, taken at the moment of hospitalization; TGO, transaminase oxalacética; TGP, transaminaza glutampiruvica.
*Values corrected with a factor of 2.8.

**Table 3.** Incremental cost-utility ratio with vaccine compared with placebo by age group.

| Incremental cost-utility ratio (R$/QALY) | | | |
|---|---|---|---|
| Age group | <59 years | 60-75 years | >75 years |
| Oxford | −8651.34 | −24 473.05 | −26 754.12 |
| CoronaVac | 117 982.49 | 5130.59 | −10 097.85 |
| Janssen | 71 787.10 | −5897.63 | −32 555.54 |

QALY indicates quality-adjusted life-year.
ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; CK-MB, creatine kinase; Daily, taken every day during the hospitalization; Gamma-GT, gamma glutamyl transferase; ICU, intensive care unit; LDH, lactic dehydrogenase; LL, lower limbs; Pro-BNP, pro-brain natriuretic peptide; SIGTAP, Sistema de Gerenciamento da Tabela de Procedimentos; Single, taken at the moment of hospitalization; TGO, transaminase oxalacética; TGP, transaminaza glutampiruvica.

echocardiograms, electrocardiograms, and venous Doppler ultrasounds, regardless of individual risk factors.

Dialysis was estimated to be required for 5% of hospitalized patients, regardless of whether they were admitted to a ward or the ICU based on a systematic review that showed the need for dialysis by acute kidney injury caused by the virus in that percent of patients.[23]

### *Utility*

The effectiveness of the model was measured in quality-adjusted life-years (QALYs). The impact on the quality of life and the utility of the different conditions caused by COVID-19 has not yet been published in the Brazilian population. For the model, utility values observed in the American population infected with SARS-CoV-2 were adopted and subdivided according to the symptoms. The mean utility of asymptomatic patients was considered to be equal to that of the general Brazilian population (0.88), progressively decreasing in patients with mild symptoms (0.833), hospitalized in the ward (0.5), hospitalized in the ICU (0.05), and dead (0.0).[24,25]

Currently, there is limited information on the impact and prevalence of post–COVID-19 symptoms after hospital discharge. In a sample of 100 survivors evaluated 4 to 8 weeks after discharge, using a 5-level version of EQ-5D telephone version in the United Kingdom, a reduction in quality of life was observed, with mean disutility values estimated at −0.061 and −0.155 for patients after discharge from the ward and ICU, respectively, showing a mean utility of 0.724 postward and 0.693 post–ICU.[25] These values were used in the model, assuming a disutility up to 6 months; from then on, the utility is again considered the mean utility of the Brazilian population.

### *Efficacy*

Data on vaccine efficacy were extracted from pivotal studies. The risks of illness were included in the model and are summarized in Table 3. For the Oxford vaccine, the results of the 2 cohorts showed that the standard dose and reduced dose followed by the standard dose were 62.1% (95% CI 41%-75.7%) and 90% (95% CI 67.4%-97%) effective, respectively. The weighted average of the 2 dosing regimens was 70.4% (95% CI 54.8%-80.6%). The overall efficacy of CoronaVac was 50.38% (95% CI 35.26%-61.98%; $P = .0049$), and that of the Janssen vaccine was 66.5% (95% CI 55.5%-75.1%) 28 days after vaccination. Each vaccine also influenced the probability of hospitalization and death according to the relative risks of 0.124, 0.15, and 0.182 to Oxford, CoronaVac, and Janssen, respectively.

Each vaccine influenced the probability of transition between the susceptible state and the “sick” state and reduced the probability of hospitalization and death. A reduction in transmission between individuals was not considered.

## Results

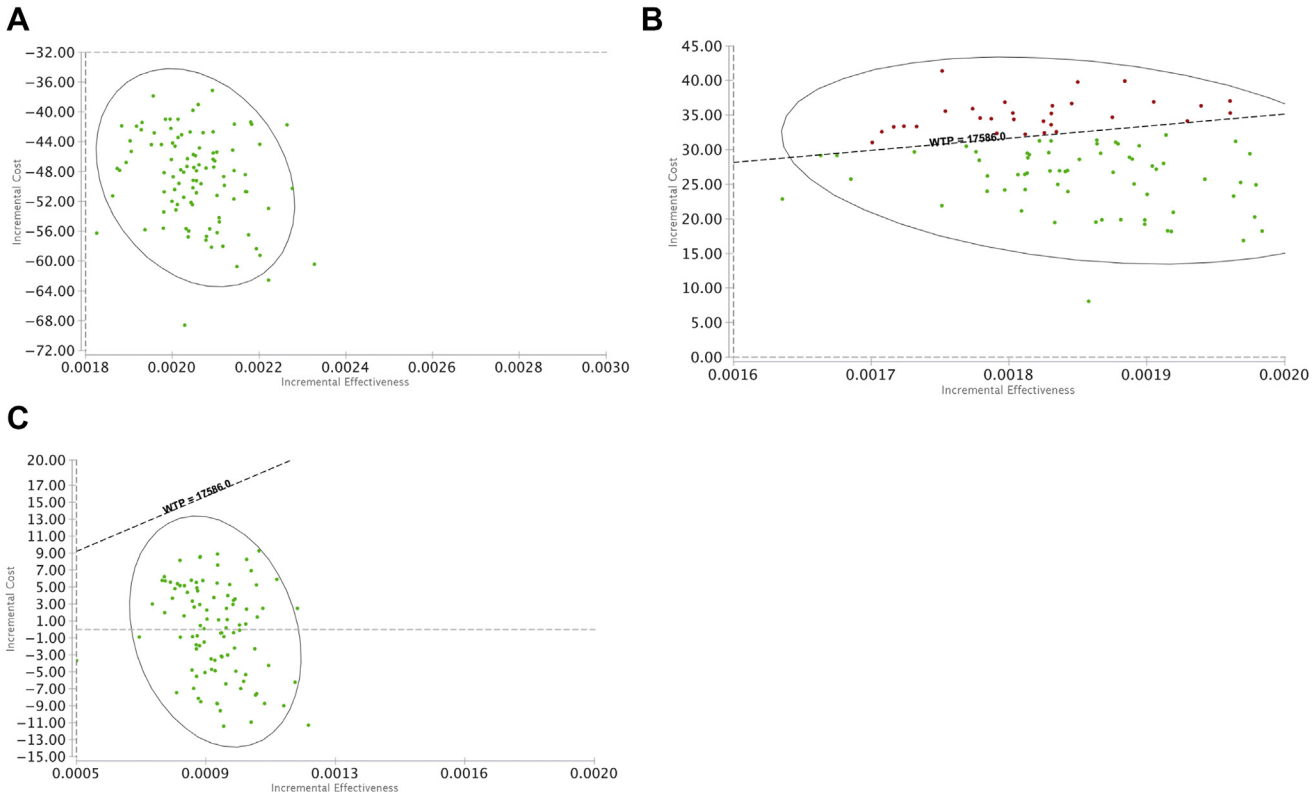
A total of 100 000 patients were simulated in first-order Monte Carlo simulations, which produced mean cost and effectiveness estimates for the cohorts with and without the vaccine. The use of the Oxford vaccine produced a mean incremental cost that generated savings of R$47.46 per patient, translating into incremental effectiveness of 0.00205 QALYs over a year and a dominant incremental cost-utility ratio of R$−23 161.3/QALY. For CoronaVac, the mean incremental cost produced an incremental cost of R$32.41 per patient, translating into incremental effectiveness of 0.0018 QALYs over a year and an incremental cost-utility ratio of R$17 757.86/QALY. The Janssen vaccine resulted in a mean incremental cost that generated savings of R$1.49 per patient with incremental effectiveness of 0.0008 QALYs over a year and a dominant incremental cost-utility ratio of R$−1690.83/QALY. The vaccines were not directly compared because of differences in outcome measurements. Table 4 summarizes these results.

**Table 4.** ICUR with vaccine compared with placebo.

| Technology | Cost of treatment (R$) | QALY | Incremental cost (R$) | Incremental effectiveness | ICUR (R$/QALY) |
|---|---|---|---|---|---|
| No Vaccine | 88.55 | 0.869 | | | |
| Oxford | 41.09 | 0.871 | −47.46 | 0.002 | −23 161.3 |
| No Vaccine | 88.55 | 0.869 | | | |
| CoronaVac | 120.97 | 0.87 | 32.41 | 0.0018 | 17 757.85 |
| No Vaccine | 88.56 | 0.869 | | | |
| Janssen | 77.79 | 0.87 | −17.77 | 0.0008 | −1690.83 |

ICUR indicates incremental cost-utility ratio; QALY, quality-adjusted life-year.

**Figure 2.** Scatter plot of the cost-utility analysis of the (A) Oxford vaccine, (B) CoronaVac, and (C) Janssen vaccine.




WTP indicates willingness to pay.

The probability distributions made it possible to perform a probabilistic sensitivity analysis where the model with 100 000 patients was simulated 100 times. The mean incremental cost-utility ratio (ICUR) resulting from these 100 simulations for the Oxford vaccine (Fig. 2A) was dominant at R$−23 792.3/QALY, the mean ICUR for CoronaVac (Fig. 2B) was R$15 331.13/QALY, and that for the Janssen vaccine (Fig. 2C) was dominant at R$−284.85/QALY.

The scatterplot shows 100% of the simulations with the Oxford, and 48% of Janssen vaccines in the lower right quadrant, representing a more effective intervention with lower cost (dominant). In contrast, 100% of the simulations with the CoronaVac are in the upper right quadrant, representing a more effective intervention with higher cost. A threshold of R$17 586/QALY, equivalent to 0.5 gross domestic product per capita/QALY, was considered to analyze the alternatives. All the simulations of the Janssen vaccine and 70% for the CoronaVac vaccine were below this threshold. All vaccines were considered cost-effective against this willingness-to-pay threshold. (Fig. 2).

Analyses of the ICUR by age group (<59, 60-75, and >75 years old) for the 3 alternatives were performed.

The data show that, with increasing age, the ICUR decreases. The vaccine with the best cost-utility ratio is the Oxford vaccine, which is dominant over all age groups. With respect to the proposed willingness-to-pay threshold, all vaccines were considered cost-effective for patients older than 60 years of age. CoronaVac and Janssen were not cost-effective in patients younger than 59 years old (Table 3).

## Discussion

A cost-utility model was constructed with data from 289 days of the pandemic in Brazil. These data are related to the first wave of the disease outbreak that hit the country. A susceptible-infected-recovered model was not constructed because data on the reduction in disease transmissibility by the vaccines studied were not available. Currently, there are robust data on the reduction in transmissibility for the Pfizer vaccine, which is not available in Brazil.[26] The use of the vaccine as prophylaxis against illness caused by the virus that causes COVID-19 was simulated. Studies on the 3 vaccines allowed us to evaluate which vaccine had the best cost-utility ratio.

The CoronaVac is the only vaccine that is not dominant and had higher costs and effectiveness than the nonvaccination strategy. The Oxford vaccine had the lowest ICUR, R$−23 161.3/QALY, followed by the Janssen vaccine that is also dominant, and then CoronaVac. All 3 manufacturers applied for emergency use approval; therefore, we chose to compare the ICUR of the alternatives to a conservative willingness-to-pay threshold of R$17 586/QALY. In the analysis by age group, all vaccines were considered cost-effective for individuals over 60 years of age. In the probabilistic sensitivity analysis, all vaccines were considered cost-effective in the general population.

Among the model's limitations was the lack of a susceptible-infected-recovered model design, which caused the simulation to fail to capture the natural dynamics of the pandemic and resulted in a simulation in which infections occurred uniformly

over time. In practice, the expected benefit from the reduction in secondary cases would be greater. In the study, a specific concentration of cases in a specific period of the time horizon was not simulated, as what occurs in the natural history of the disease. This prevents the model from being extrapolated beyond the stipulated time horizon and hinders long-term interpretations of the evolution of the pandemic.

Studies that have measured the efficacy of vaccines have different population stratifications. In addition to the outcomes being evaluated in a variety of ways, the time of the pandemic at which the evaluation was performed also differs among the 3 studies evaluated. The 3 vaccines will be used simultaneously in the population and are not mutually exclusive alternatives. For all these listed reasons, the study did not compare the alternatives among themselves, rather, all of them against a nonvaccination strategy. The study did not predict variants of the SARS-CoV-2 virus, and such a possibility with a possible decrease in vaccine efficacy was not simulated.

Another limitation is that the model assumes that everyone who requires ICU admission and tests has access to them, which, in practice, is not the case. Nevertheless, the model is conservative because impacts on the economy, individual incomes, and relatives who lost family members were not estimated by the adopted perspective.

This is the first cost-utility study of vaccines against COVID-19 from the perspective of the Brazilian public health system. The country has a universal health system and one of the most effective mass vaccination programs worldwide. The findings of this cost-utility analysis can help determine where to focus efforts and which vaccines will provide the greatest benefit.

## Article and Author Information

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*Drafting of the manuscript:* Fernandes, Magliano, Macedo, Padila, França, Braga
*Critical revision of the paper for important intellectual content:* Fernandes, Santos, Magliano, Tura
*Statistical analysis:* Tura, Macedo, Padila
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