

Real-world Evidence of COVID-19 Vaccines Effectiveness in Solid-organ Transplant Recipient Population in Colombia: A Study Nested in the Esperanza Cohort

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Background. Solid-organ transplant recipients (SOTRs) have a higher risk of coronavirus disease 2019 (COVID-19) complications and death and a less powerful and lasting response to vaccines and to natural infection. In Colombia, this population was prioritized in the National Vaccination Plan against COVID-19 and received vaccines from different platforms. The aim of this study was to estimate the effectiveness of the complete vaccination schedule and of the vaccine booster for COVID-19 administered to SOTRs in Colombia. **Methods.** A nested-cohort was assembled within the population-based ESPERANZA cohort and included the subset of 16 y and older SOTRs (n = 6963); the follow-up period spanned March 11, 2021, to May 11, 2022. The vaccine effectiveness was estimated with Cox proportional-hazards models so that the overall effectiveness of the complete vaccination schedule, the vaccine booster, each used vaccine, and the homologous and heterologous schedules were estimated, adjusting by the main confounders. **Results.** The overall effectiveness of being fully vaccinated was 73.7% (95% confidence interval [CI], 68.9%-77.0%) to prevent COVID-19 infection, 83.7% (95% CI, 78.7%-87.5%) to prevent hospitalization, and 92.1% (95% CI, 88.8%-94.4%) to prevent death due to COVID-19. Similarly, the effectiveness of the vaccine booster was 76.7% (95% CI, 70.6%-81.5%), 86.9% (95% CI, 79.4%-91.6%), and 94.5% (95% CI, 89.8%-97.1%) to prevent confirmed COVID-19 infection, hospitalization, and death due to COVID-19, respectively. In both cases, there were no statistically significant differences across age groups. **Conclusions.** Findings from this work show a high protection of vaccination against infection, hospitalization, and death due to COVID-19 in SOTRs, which increases with the vaccine booster.

(*Transplantation* 2023;107: 216–224).

INTRODUCTION

Infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the coronavirus disease 2019 (COVID-19), was declared a pandemic on March 11, 2020, by the World Health Organization.¹ The first confirmed infection case in the Colombian territory

was reported on March 6, 2020, which prompted the declaration of the health emergency on March 12, 2020.²

When the Colombian government began immunization for COVID-19, it acquired 5 vaccine types: ChAdOx1 nCoV-19 (AstraZeneca), CoronaVac (Sinovac), Ad26.COV2.S (Janssen), mRNA-1273 (Moderna), and BNT162b2

Received 18 July 2022. Revision received 23 August 2022.

Accepted 9 September 2022.

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This study was conducted using financial and economic resources provided by the Ministry of Health and Social Protection of Colombia (Ministerio de Salud y Protección Social).

M.P.A., J.F.N., L.A.C., and M.R.B. did design and statistical analysis conceptualization. J.F.N., L.A.C., and A.F.P. did data acquisition. M.P.A., J.F.N., L.A.C., M.R.B., A.F.P., and M.G.P. did data verification. M.P.A. and A.F.P. did dataset construction. M.P.A., J.F.N., and A.F.P. did statistical analysis. M.P.A.,

J.F.N., L.A.C., and M.R.B. drafted of the article. M.P.A., J.F.N., L.A.C., M.R.B., A.F.P., M.G.P., and F.R.G. did critical revision and discussion of the article.

J.F.N., L.A.C., and F.R.G. were members of the Colombian COVID-19 vaccine advisory committee. All other authors declare no competing interests.

This manuscript has been previously submitted to Social Science Research Network as a preprint; https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4166380.

Supplemental Visual Abstract; <http://links.lww.com/TP/C616>.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

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ISSN: 0041-1337/20/1071-216

DOI: 10.1097/TP.0000000000004411

(Pfizer-BioNTech). Given the global and national scarcity context, the National Vaccination Plan against COVID-19 assigned the first vaccines to people who were more likely to develop complications or die because of COVID-19.

The prioritization process of the National Vaccination Plan in Colombia was determined by an ethical framework and based on the existing best epidemiological evidence at that time.³ This defined the order of equitable access to biologicals based on the population's risk, through 5 phases. Phase 1 included adults over 80 y of age and health workers in COVID-19 areas; Phase 2 included people between 60 and 79 y old and other health workers; Phase 3 included people between 50 and 59 y old, patients with selected underlying diseases, including solid-organ transplant recipients (SOTRs) and other people who, because of their occupation, presented a higher risk of infection, complication, or death from COVID-19; Phase 4 included people between 40 and 49 y old, and people who were in places with risk of outbreaks; and Phase 5 included the population between 3 and 39 y old, which was not previously prioritized.³ It is worth noting that all 5 vaccines were used in the SOTR population because no specific vaccine platform was determined for them.⁴

SOTRs are more prone to a SARS-CoV-2 infection because of their immunosuppression and their lower likelihood to develop an effective immune response to vaccination⁵⁻¹¹ because their immune response to natural infection is also less powerful and lasting, rendering them more vulnerable to reinfections.¹² Additionally, chronic immunosuppression might reduce the infectious dose necessary to cause COVID-19 and hinder the immune control once the infection has been established, which increases the risk of severe infection and complications.¹³ Furthermore, it is hypothesized that SOTRs could shed higher viral loads for longer periods than healthy hosts, which could increase their chances to spread the infection to other people.¹²

Similarly, previous studies have found that both humoral and cellular immune responses to vaccines and natural infection are weaker in SOTRs, whereby boosters and additional doses are required^{5-7,14,15} to maintain the protection against COVID-19 infection and severe disease.¹⁴ Additionally, immunosuppression has also been identified to be caused by the use of certain substances, such as anti-metabolites, calcineurin inhibitors, and monoclonal antibodies, which explains the insufficient immune responses to current COVID-19 vaccination schemes in SOTRs.^{5,7-9,16,17}

Knowing the effectiveness of vaccination in real-life conditions will allow us to evaluate the impact of prioritization in countries where SOTRs were prioritized, to wholly estimate the impact of vaccination, and to adjust the vaccination schedules in this risk group. Therefore, the aim of this study was to estimate the effectiveness of the complete vaccination schedule and of the vaccine booster for COVID-19 administered to SOTRs in Colombia.

MATERIALS AND METHODS

Design and Population Study

A nested-cohort was assembled within the ESPERANZA cohort, which is a population-based cohort made up of all Colombian residents who were eligible to receive a COVID-19 vaccine and has methodology that has been described elsewhere.¹⁸ Our nested-cohort included all SOTRs aged 16 and older that were registered in Red

data—the National Health Institute (NHI) database. The follow-up period went from March 11, 2021, when the first individuals completed their vaccination schedule, to May 11, 2022, which corresponds to the latest update on the national statistics.

Data Sources

All data were obtained from the Integrated Social Protection Information System (in Spanish, Sistema Integrado de Información de la Protección Social), which is the official health statistics data source in Colombia. Information from it included people who were cross-referenced in 8 Social Protection Information System data records by using an individual anonymized number that is encrypted and automatically generated by the information system to protect the person's identity: (1) Red data include all SOTRs who reside in Colombia; (2) MIVACUNA contains sociodemographic data from vaccine candidates who were later vaccinated against COVID-19, according to the National Vaccination Plan against COVID-19; (3) PAIWEB registers people who have received any vaccine in Colombia and the basic vaccine information, such as dose, vaccine type, date, and vaccine location; (4) SEGCOVID contains information about confirmed COVID-19 cases; (5) SISMUESTRAS stores the results from polymerase chain reaction (PCR) and antigen tests conducted in Colombia; (6) Single Registry of Affiliates to the Social Protection System—Births and Deaths (Registro Único de Afiliados al Sistema de la Protección Social—Nacimientos y Defunciones, in Spanish) records death causes in Colombia; (7) the high-cost disease registry (Cuenta de Alto Costo, in Spanish) includes data about people with diseases that require a larger budget, that is, chronic kidney disease (CKD), high blood pressure (HBP), diabetes mellitus (DM), cancer, and HIV infection; and (8) unique affiliate database (Base de Datos Única de Afiliados, in Spanish) provides information regarding the affiliation regime to the health system. The listed databases are public, although they have restricted access and are currently available to the Ministry of Health and Social Protection.

Inclusion and Exclusion Criteria

This study first included male and female SOTRs aged 16 and older residing in Colombia, regardless of their vaccination status. Subsequently, individuals were excluded if they (1) had a history of confirmed COVID-19 infection, (2) had an incomplete vaccination schedule, or (3) reported inconsistencies in their vaccination records (ie, implausible vaccine dates or doses). Definitions of a complete vaccination schedule were those originally established by the manufacturer and adopted by the HSPM.¹⁹ Figure 1 shows the complete selection process.

Exposure Groups

Three groups were formed based on the subjects' vaccination status: unvaccinated, fully vaccinated, and vaccinated with booster. Unvaccinated individuals were those who did not receive any vaccine during the study period. The definition of fully vaccinated people depended on the administered vaccine; hence, for AstraZeneca, Pfizer, Moderna, and Sinovac, 2 doses with a 28-d period (21 d for Pfizer) between doses was considered to be a complete schedule. It is worth noting that in the case of longer periods between doses because of

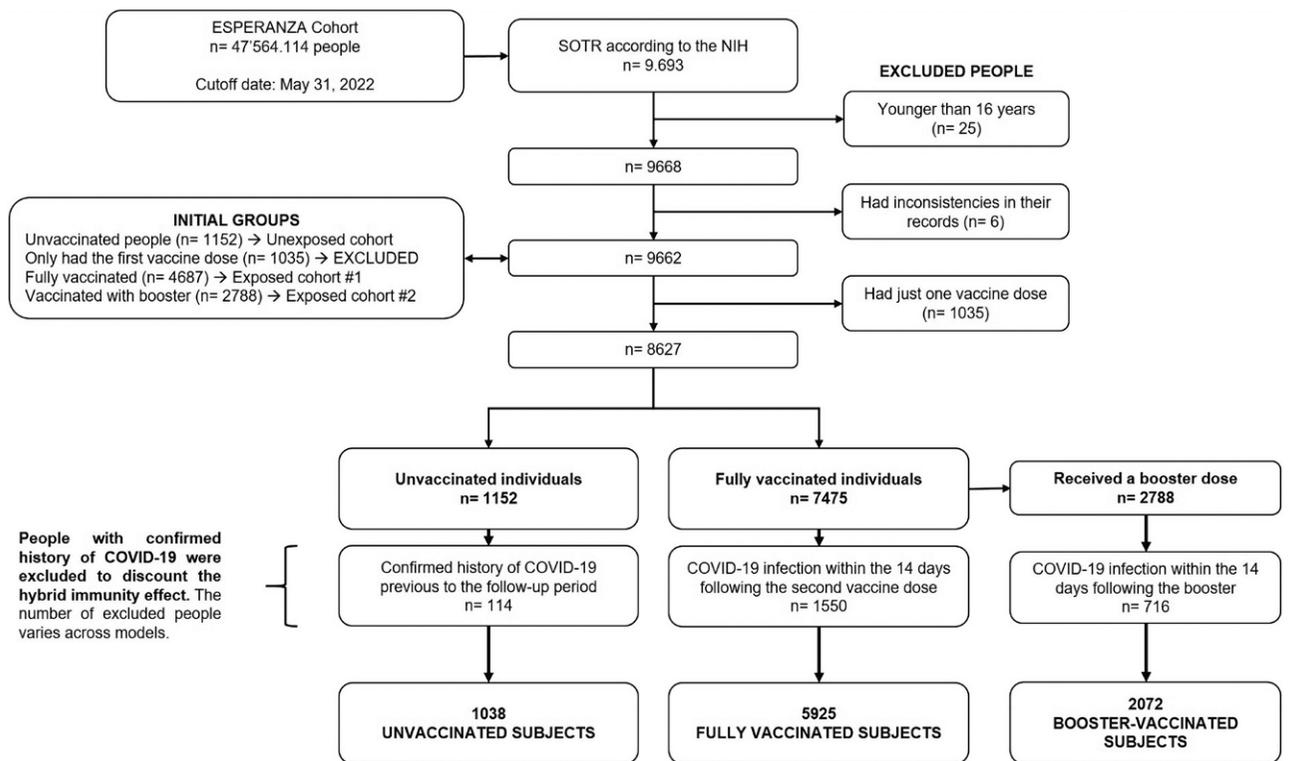


FIGURE 1. Flowchart of the selection process of the analytic sample. The fully vaccinated group includes 2788 people who later received at least one booster dose. COVID-19, coronavirus disease 2019; SOTR, solid-organ transplant recipient; NHI, National Health Institute of Colombia.

any cause, people could complete their vaccination schedule without recommending it, unless they had received a vaccine unavailable in Colombia. For the Janssen vaccine, a sole dose was deemed a complete vaccination scheme. Vaccinated with booster was defined as people who received at least 1 additional vaccine dose from the same or from a different platform; SOTRs were allowed to get a booster 1 mo after completing the vaccination schedule.²⁰ Allocation to either the fully vaccinated or vaccinated with booster groups was done 15 d after completing the vaccination schedule or receiving the first booster, respectively. In Colombia, heterologous vaccination was used for both the booster, from September 15, 2021,²⁰ and the initial vaccination schedule, from March 18, 2022.²¹

Outcomes

The study outcomes were (1) COVID-19 infection, defined as a COVID-19 diagnosis confirmed by PCR or antigen tests (these tests had to be validated by the NHI in Colombia) and registered in SISMUESTRAS; (2) hospitalization due to COVID-19, defined as having entered the general hospitalization service or the intensive care unit and having COVID-19 as one of the hospitalization causes at any moment of the hospital stay, as registered in SEGCOVID; and (3) confirmed death because of COVID-19, defined as having a confirmed COVID-19 diagnosis as the basic cause of death in the death certificate, as consulted in the Single Registry of Affiliates to the Social. Suspected deaths were not included in this study.

Covariates

Additional variables that have been deemed as relevant confounders in previous studies were also measured to

include them in the analysis: age (y); sex (male versus female); affiliation regime to the health system (contributory versus subsidized); municipality of residence; comorbidities diagnosis (yes versus no), such as CKD, cancer, DM, HBP, and HIV infection; and the prevalent SARS-CoV-2 variant at the time of the COVID-19 infection (this information was taken from www.covariants.org).

Statistical Analysis

Categorical variables were described with absolute frequencies and proportions, whereas quantitative variables were described with central tendency (medians) and dispersion (range and interquartile range [IQR]) measures. Subjects' characteristics were compared across exposure groups.

To estimate the overall vaccination effectiveness, a survival analysis was performed by using Cox proportional-hazards models to estimate the reduction in the risk of death, hospitalization, and infection in fully vaccinated individuals and in people vaccinated with booster. These models were adjusted for the confounders listed as covariates; the prevalent SARS-CoV-2 variant at the time of infection was adjusted for in the models to control the transmission risk. For those unvaccinated who did not develop any of the study outcomes, the infection risk given by a specific variant was randomly assigned proportional to its dominance during the study period. Additionally, all the time-to-event from the unvaccinated subjects during the study period was considered in the models.

Multiple types of right-censoring could occur, given by people who died by nonrelated COVID-19 causes, fully vaccinated individuals who received a booster or subjects

who finished the follow-up period without developing any of the study outcomes. These censoring were considered while constructing the models. The statistical analysis was carried out by using *R* (4.2.0 version) and its *survival* (3.3.1 version) and *ggplot2* (3.3.6 version) packages to perform the survival analysis and to create the graphs, respectively.

Ethics

This study used secondary data sources from public information systems. The research team did not have access to personal data from the participants at any moment and all used information was anonymized. Given that this study is classified as a research without risk according to the Colombian legislation,²² an approval from an Ethics Committee was not required.

RESULTS

The inclusion and exclusion criteria yielded a sample of 6963 SOTRs during the study period (March 11, 2021–May 11, 2022), from which 85% (n = 5925) were fully vaccinated (this figure includes 2072 individuals vaccinated

with booster) and 15% (n = 1038) remained unvaccinated throughout the whole follow-up. Out of the 6963 SOTRs, 42.1% were female, and the median age was 52 y (IQR: 39–62; range: 16–97), whereas the median age of the unvaccinated group was 44 y (IQR: 33–56). Additionally, 76.7% of the participants belonged to the contributory health regime and 82.4% had at least 1 comorbidity, in which CKD (72.3%) and HBP (70.3%) were the most frequent diagnosis. Table 1 describes the main characteristics of the study individuals by exposure group.

In the fully vaccinated group, the most frequently used vaccines were Pfizer (52.7%), Sinovac (24.0%), AstraZeneca (11.8%), Janssen (7.4%), and Moderna (4.1%). Furthermore, most subjects received a homologous schedule (n = 3425) in this group, with mainly Pfizer being administered (n = 1720), followed by Sinovac (n = 785), AstraZeneca (n = 407), Jansen (n = 349), and Moderna (n = 164). Regarding the vaccinated with booster group who had a homologous schedule (ie, 3 doses from the same manufacturer), Pfizer (61.7%), Sinovac (20.2%), and AstraZeneca (11.4%) were the most used. In the case of heterologous

TABLE 1.
Solid-organ transplant recipients' sociodemographic and clinical characteristics, ESPERANZA cohort

Variable	Unvaccinated (n = 1038) n (%)	Fully vaccinated ^a (n = 5925) n (%)	Vaccine booster (n = 2072) n (%)	Total (n = 6963) n (%)
Age (y)				
Median (IQR)	44 (33–56)	53 (40–63)	56 (44–65)	52 (39–62)
Range	16–97	16–90	16–90	16–97
16–59	859 (82.8)	3987 (67.3)	1257 (60.7)	4846 (69.6)
60 and older	179 (17.2)	1938 (32.7)	815 (39.3)	2117 (30.4)
Sex				
Female	460 (44.3)	2469 (41.7)	865 (41.7)	2929 (42.1)
Male	578 (55.7)	3456 (58.3)	1207 (58.3)	4034 (57.9)
Health system affiliation regime				
Contributory	638 (61.5)	4704 (79.4)	1763 (85.1)	5342 (76.7)
Subsidized	400 (38.5)	1221 (20.6)	309 (14.9)	1621 (23.3)
Comorbidities				
None	224 (21.6)	999 (16.9)	381 (18.4)	1223 (17.6)
≥1 comorbidity	814 (78.4)	4926 (83.1)	1691 (81.6)	5740 (82.4)
Cancer	21 (2.0)	183 (3.1)	77 (3.7)	204 (2.9)
Diabetes mellitus	123 (11.8)	1052 (17.8)	413 (19.9)	1175 (16.9)
Chronic kidney disease	710 (68.4)	4327 (73.0)	1453 (70.1)	5037 (72.3)
High blood pressure	700 (67.4)	4194 (70.8)	1413 (68.2)	4894 (70.3)
HIV infection	5 (0.5)	17 (0.3)	9 (0.4)	22 (0.3)
Prevalent SARS-CoV-2 variant at the time of infection				
Delta	113 (10.9)	960 (16.2)	624 (30.1)	1.073 (15.4)
Delta/Mu	90 (8.7)	312 (5.3)	0 (0.0)	402 (5.8)
Mu	519 (50.0)	2581 (43.6)	0 (0.0)	3100 (44.5)
Omicron	316 (30.4)	2072 (35)	1448 (69.9)	2388 (34.3)
Initial vaccine schedule manufacturer ^b				
AstraZeneca	NA	671 (11.8)	214 (11.4)	671 (11.8)
Janssen	NA	421 (7.4)	68 (3.6)	421 (7.4)
Moderna	NA	234 (4.1)	44 (2.4)	234 (4.1)
Pfizer	NA	2996 (52.7)	1056 (56.4)	2996 (52.7)
Sinovac	NA	1362 (24)	489 (26.1)	1362 (24)

^aThis group includes people with full schedule, which is made up of 2 subgroups: 1) those who completed the schedule and did not receive any booster during the entire study period and 2) those who completed the schedule and had a booster but were included analytically in the period before receiving the booster (censored booster doses).

^bRefers to the initial schedule's manufacturer. The additional dose is not considered for the group that received a booster, because this information is described in detail in Table 2. IQR, interquartile range; NA, not applicable; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 2.
Complete vaccination schedule and booster in solid-organ transplant recipients in Colombia, by manufacturer, ESPERANZA cohort

Vaccination schedule	Homologous (n = 947)	
	n	%
Pfizer	584	61.7
AstraZeneca (AZ)	108	11.4
Moderna	11	1.2
Sinovac	192	20.2
Janssen	52	5.5
	Heterologous (n = 990)	
	n	%
2 AZ + Pfizer	67	6.8
2 AZ + Moderna	37	3.7
2 AZ + Janssen	4	0.4
2 Pfizer + AZ	216	21.8
2 Pfizer + Moderna/Pfizer	289	29.1
2 Pfizer + Janssen	9	1.0
2 Moderna + AZ	5	0.5
2 Moderna + Pfizer/Moderna	27	2.7
2 Moderna + Janssen	1	0.1
2 Sinovac + AZ	73	7.4
2 Sinovac + Pfizer/Moderna	226	22.8
2 Sinovac + Janssen	7	0.7
Other combinations	29	3.0

Records that did not specify the manufacturer of the vaccination schedule were excluded from this table

schedule in those who had a booster, the main combinations were Pfizer/Moderna (29.1%), Pfizer/AstraZeneca (21.8%), and Sinovac/Pfizer (22.8%). The complete description of all combinations is shown in Table 2.

As to the outcomes occurrence in the exposure groups, the risk of COVID-19 infection, hospitalization, and death due to COVID-19 was 26.4%, 9.6%, and 7.5%, respectively, in the unvaccinated group. On the other hand, figures were significantly lower in the fully vaccinated group, so that the risk of COVID-19 infection was 11.5%; risk of hospitalization, 2.7%; and risk of death due to COVID-19, 1.2%. Moreover, these risks were even lower in the subset that received a

booster: 7.8% for COVID-19 infection; 2.7% for hospitalization; and 0.7% for death due to COVID-19. The listed differences between groups were statistically significant ($P < 0.01$). Table 3 lists the outcomes' occurrence and their time-to-event in detail, according to the exposure group.

In relation to the survival analysis, a lower survival was found in those unvaccinated compared with fully vaccinated individuals. Furthermore, the difference in the survival time when comparing unvaccinated subjects to those who received a booster was not as large as that found when the comparison was made between the unvaccinated and the fully vaccinated groups; and this trend persisted over time. The unadjusted survival analysis curves are depicted in Figure 2.

On the other hand, the overall effectiveness of the complete vaccination schedule was 73.3% (95% CI, 68.9%-77.0%) to prevent COVID-19 infection; 83.7% (95% CI, 78.7%-87.5%) to prevent hospitalization; and 92.1% (95% CI, 88.8%-94.4%) to prevent death due to COVID-19. Table 4 shows the effectiveness estimates of being fully vaccinated according to age groups.

Likewise, the effectiveness of the vaccine booster to prevent the study outcomes was higher for death due to COVID-19 (94.5%; 95% CI, 89.8%-97.1%), followed by hospitalization (86.9%; 95% CI, 79.4%-91.6%) and COVID-19 infection (76.7%; 95% CI, 70.6%-81.5%). Similar results were obtained in both age groups (16–59 y and 60 y and older), with only a minimum difference between age groups by outcome. The complete estimates of the vaccine booster effectiveness according to age groups are presented in Table 5.

Finally, the effectiveness of all the complete vaccination and booster schedules are presented in Tables S1 and S2 (SDC, <http://links.lww.com/TP/C615>). A high effectiveness of the analyzed vaccines was observed with all the homologous and heterologous combinations analyzed. However, some estimates were very imprecise with wide confidence intervals given the small sample size for some of the studied groups. Finally, it is important to highlight that in all cases the effectiveness in preventing hospitalization and death due to COVID-19 was greater than in preventing the occurrence of confirmed infection.

DISCUSSION

This research found a high effectiveness of the complete vaccination schedule and the vaccination with booster in

TABLE 3.
Study outcomes in unvaccinated and fully vaccinated solid-organ transplant recipients in Colombia, ESPERANZA cohort

Outcome	Unvaccinated (n = 1038) n (%)	Fully vaccinated ^a (n = 5925) n (%)	Vaccine booster (n = 2072) n (%)	Total (n = 6963) n (%)
Confirmed COVID-19 infection	272 (26.4)	679 (11.5)	153 (7.8)	951 (13.7)
COVID-19 hospitalization	99 (9.6)	160 (2.7)	33 (1.7)	259 (3.7)
Death due to COVID-19	77 (7.5)	70 (1.2)	14 (0.7)	147 (2.1)
Time-to-outcome (d) ^b				
Time-to-infection; median (IQR)	411 (255–411)	292 (222–309)	103 (62–147)	294 (223–316)
Time-to-hospitalization; median (IQR)	411 (411–411)	298 (264–313)	111 (71–153)	300 (268–338)
Time-to-death; median (IQR)	411 (411–411)	298 (267–315)	112 (72–153)	301 (272–344)

^aThis group includes people with full schedule, which is made up of 2 subgroups: 1) those who completed the schedule and did not receive any booster during the entire study period and 2) those who completed the schedule and had a booster but were included analytically in the period before receiving the booster (censored booster doses).

^bThe follow-up time of unvaccinated individuals was longer for all the assessed outcomes. Given that this group was made up of individuals who remained unvaccinated throughout the whole study period, they contributed a larger time-to-event than vaccinated people, whose time-to-event only counted after receiving the vaccine.
COVID-19, coronavirus disease 2019; IQR, interquartile range.

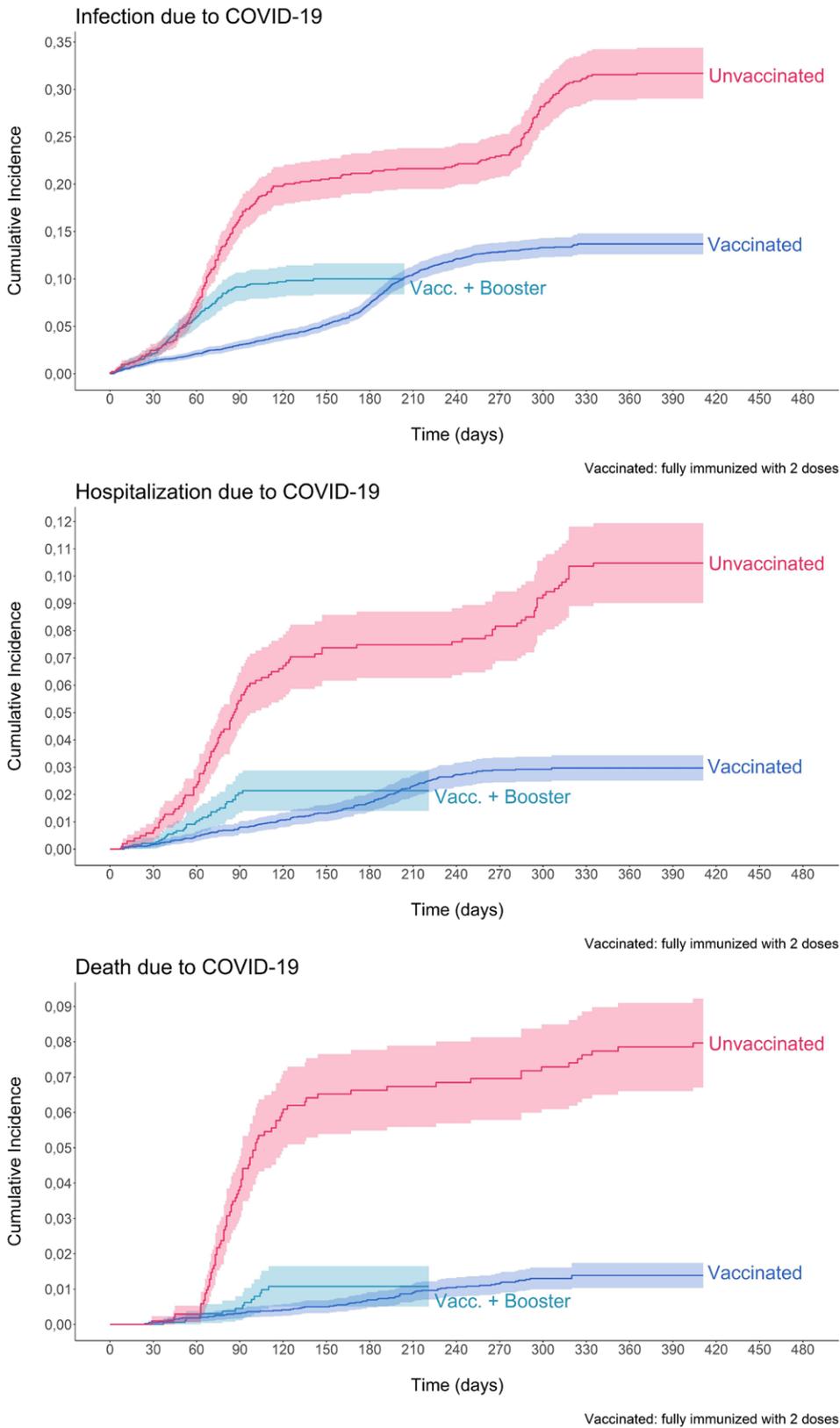


FIGURE 2. Kaplan-Meier survival curves for COVID-19 infection, hospitalization, and death, according to vaccination status in solid-organ transplant recipients in Colombia. ESPERANZA cohort. COVID-19, coronavirus disease 2019.

SOTRs, which represents a significant impact of vaccination in immunized SOTRs when compared with unvaccinated individuals. It is important to highlight that our findings are a measure of the infection and complications risk reduction

within the SOTR population; hence, they cannot be directly extrapolated to other populations, nor are they comparable to effectiveness estimates from immunocompetent people, who are known to have a better response to vaccines.²³ To

TABLE 4.**COVID-19 complete schedule effectiveness for infection, hospitalization, and death in solid-organ transplant recipients in Colombia, by age group, ESPERANZA cohort**

Age group	COVID-19 complete schedule effectiveness					
	Infection		Hospitalization		Death	
	% (95% CI)	<i>P</i>	% (95% CI)	<i>P</i>	% (95% CI)	<i>P</i>
All age groups	73.3 (68.9-77.0)	<0.001	83.7 (78.7-87.5)	<0.001	92.1 (88.8-94.4)	<0.001
16–59	73.1 (67.8-77.5)	<0.001	83.3 (76.6-88.1)	<0.001	93.6 (89.5-96.1)	<0.001
60 and older	72.6 (63.6-79.3)	<0.001	82.5 (72.8-88.8)	<0.001	91.0 (84.8-94.7)	<0.001

Estimates adjusted for sex, affiliation regime, municipality of residence, presence of comorbidities (CKD, cancer, DM, HBP, and HIV infection), and prevalent variant at the time of infection. Unvaccinated individuals were the reference group in all models.

CI, confidence interval; CKD, chronic kidney disease; DM, diabetes mellitus; HBP, high blood pressure.

TABLE 5.**COVID-19 booster effectiveness for infection, hospitalization, and death in solid-organ transplant recipients in Colombia, by age group, ESPERANZA cohort**

Age group	COVID-19 booster effectiveness					
	Infection		Hospitalization		Death	
	% (95% CI)	<i>P</i>	% (95% CI)	<i>P</i>	% (95% CI)	<i>P</i>
All age groups	76.7 (70.6-81.5)	<0.001	86.9 (79.4-91.6)	<0.001	94.5 (89.8-97.1)	<0.001
16–59	75.9 (67.1-82.3)	<0.001	84.2 (69.6-91.8)	<0.001	95.8 (86.2-98.8)	<0.001
60 and older	70.2 (56.5-79.6)	<0.001	86.4 (74.2-92.8)	<0.001	91.1 (80.9-95.9)	<0.001

Estimates adjusted for sex, affiliation regime, municipality of residence, presence of comorbidities (CKD, cancer, DM, HBP, and HIV infection), and prevalent variant at the time of infection. Unvaccinated individuals were the reference group in all models.

CI, confidence interval; CKD, chronic kidney disease; DM, diabetes mellitus; HBP, high blood pressure.

make comparisons against other groups, impact measures (absolute estimates) would be required, which is beyond the scope of the present investigation.

The obtained results also suggest the protection granted by immunization in SOTRs begins with a complete vaccination schedule, initially defined by the manufacturers, and that a booster could strengthen such protection in time. On the other hand, this research included one of the biggest SOTR samples evaluated to this day, which not only was assessed in real-life conditions but also allowed the estimation of the vaccination effectiveness by using national epidemiologic data, whereas most of the published research in the SOTR population regarding this topic are immunogenicity studies.^{8,14,15,24-26} Furthermore, this investigation also estimated the effectiveness of several heterologous schedules, including combinations of inactivated, adenovirus vector-based and mRNA-based vaccines and adjusted for prevalent SARS-CoV-2 variants in Colombia, evidencing a high effectiveness of the COVID-19 vaccines in the SOTR population.

The need to vaccinate immunosuppressed individuals was also underlined because our findings showed immunization significantly reduced mortality and morbidity relative to not receiving any vaccine in this group. This strengthens the public policy of vaccination aimed at preventing disease and the risk prioritization as a main component of public health, primary healthcare systems, and national vaccination programs. Accordingly, our findings also suggest the prioritization of SOTRs in Colombia might have significantly impacted the reduction of the morbimortality of this population subset.

Our work also allows recognition of vaccination as a potential cost-effective strategy in terms of the burden of disease caused by COVID-19 and years of potential life lost because of mortality or disability in a young population that has several comorbidities.²⁷⁻²⁹ There are also implications for clinical practice because receiving immunosuppressive drugs is a direct risk factor for COVID-19 death,³⁰ although vaccination could be a preventive intervention for it. It also has to be considered that both the ability to prevent infection by activating the immune system and the risk of COVID-19 infection are related to the person's immunosuppression status and to its competence to mount an immune response; therefore, the greater the immunodeficiency, the higher chance of an inadequate response to the biologic or the vaccine-induced immunization. Risk factors for an insufficient immune response comprise several individual aspects, such as age and receiving immunosuppressive therapy, which, in the case of SOTRs, needs to be considered along the underlying disease that caused the organ transplant in the first place (eg, kidney or liver failure). Thus, an adequate immune response cannot be assumed in all cases despite vaccination confers benefits to immunosuppressed individuals; therefore, the relevance of booster doses.³¹⁻³⁴ Unfortunately, this study could not collect information about the transplanted organ or the therapy the participants were using, which impeded the analysis of their role in the effectiveness of vaccines.

Previous investigations have also found vaccination to be a good strategy in SOTRs to prevent COVID-19. For example, a research found a reduction in the incidence of symptomatic COVID-19 in vaccinated SOTRs (0.065 per 1000 person-days; 95% CI, 0.024-0.17) compared with unvaccinated subjects

(0.34 per 1000 person-days; 95% CI, 0.26-0.44), which evidences a high effectiveness in this risk group.³⁵ Other examples include an investigation carried out in Israel, where a cohort was immunized with mRNA-based vaccines and the effectiveness for symptomatic COVID-19 infection was found to be 71% (95% CI, 37%-87%) in immunosuppressed patients, whereas it was 94% (95% CI, 88%-97%) in general population³⁶; and retrospective studies that have suggested a lower vaccination effectiveness to prevent COVID-19-related hospitalization in immunocompromised patients, as shown in a population with an immunosuppression prevalence of 44%.³⁷

With regard to the booster dose, a study also found that only two-thirds of the included SOTRs generated anti-SARS-CoV-2 antibodies.³⁸ This correlates to our findings, in which the survival time between the unvaccinated and vaccinated with boosted individuals was lower than when the comparison was made between the unvaccinated and the fully vaccinated subjects. Additionally, previous publications have also reported a poor response to COVID-19 vaccines in SOTRs, as indicated in a meta-analysis that estimated seroconversion was 16 times less likely to occur after vaccination in SOTRs.³⁹

Results on this subject are heterogeneous and show that differences in control groups influence the conclusions. It is important to clarify that information related to the effectiveness of booster vaccines in SOTR was not found because most published studies assessed the vaccine-induced immune response, with a focus on the humoral response, but did not estimate its impact on the protection against SARS-CoV-2, which does not allow a direct comparison with our results.^{8,11,40}

The limitations of this work comprise of high effectiveness estimates of the COVID-19 vaccines because the comparison was made against unvaccinated SOTRs instead of nontransplanted individuals. Moreover, these estimates might be affected by the lack of inclusion of certain covariates that could act as potential confounders, such as other diseases, the type of the administered immunosuppressive drugs, the educational level or the transplanted organ (although kidney transplants are the most frequent in Colombia). Lastly, vaccination effectiveness throughout time was not estimated, which is one of the main questions to be answered, considering the insufficient immune response seen in SOTRs. New studies are required that aim to not only respond this query but also address the impact of the hybrid immunity and compare the vaccines, effectiveness over time against other immunocompromised individuals and the general population.

In conclusion, our research evidences the relevant and coherent measures taken by the Colombian government when implementing the COVID-19 vaccination, which focused on prioritizing the most vulnerable groups, intervening the possible virus-related mortality causes, and decreasing the health inequities potentially caused by the COVID-19 syndemic. This study also serves as input to keep the recommendation to prioritize SOTR vaccination worldwide and to guarantee the timely access to booster doses.

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