

COVID-19 mortality in two waves of the pandemic in Cali, Colombia, before and during vaccination roll-out

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ABSTRACT

Objective. To describe the variation in COVID-19 mortality among residents of Cali, Colombia, in the second wave of the pandemic, before vaccines, and in the fourth wave, with vaccination roll-out in process, taking into account variables of sex, age group, comorbidities, and interval between onset of symptoms and death, and to estimate the number of deaths averted by vaccination.

Methods. A cross-sectional study of second wave and fourth wave deaths and vaccination coverage. The frequencies of attributes of deceased population in the two waves were compared, including comorbidities. Machado's method was used to calculate an estimate of the number of deaths averted in the fourth wave.

Results. There were 1 133 deaths in the second wave and 754 deaths in the fourth wave. It was calculated that approximately 3 763 deaths were averted in the fourth wave in Cali in the context of vaccination roll-out.

Conclusions. The decline in COVID-19-associated mortality observed supports the continuation of the vaccination program. Given the lack of data to explain other possible reasons for this decline, such as on the severity of novel viral variants, the limitations of the study are discussed.

Keywords

COVID-19; COVID-19 vaccines; mortality; Colombia.

The COVID-19 epidemic emerged in China in December 2019 and spread globally, faster than countries could contain it. The first reports from China and Europe showed a significant number of deaths from previously unseen sequelae. Although the initial case fatality rate was between 3% and 5%, the sheer number of infected people considerably increased the possibility of dying, especially in high-risk populations such as people over 60 and those with preexisting comorbidities (1).

In China, the case fatality rate was 14.8% among adults over 80 and 8% among those aged 70–79. In European countries, nearly 95% of COVID-19 fatalities were over 60 (2). In Latin America, studies show that the highest mortality rate during the first year of the outbreak was in Ecuador (19.5 per 100 000 population), followed by Brazil (13.3) and Peru (12.2) (3). In Colombia, 6 092 403 cases and 139 796 fatalities were reported for the year 2021 (4).

In the absence of an effective and early treatment, health authorities, academics, and the pharmaceutical industry began testing vaccines that could induce immunity in the general population. The World Health Organization (WHO) established the Strategic Advisory Group of Experts on Immunization (SAGE) to review vaccines under investigation, support their usage, and set COVID-19 vaccination priorities (5). Subsequently, SAGE authorized mass vaccine deployment as an emergency measure, and WHO outlined and approved a risk-based immunization procedure. The Government of Colombia purchased vaccines for free administration to the entire population, in accordance with the phases and stages outlined in the National COVID-19 Vaccination Plan (NVP) (6).

In Cali, Colombia's third-largest city, the "We Vaccinate for Life" initiative led by the Public Health Secretariat (Secretaría de Salud Pública de Cali—SSP), with the participation of academia, the municipal administration, and the community, reduced morbidity and death in this city (4). SSP has monitored

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vaccination coverage under the PAICOVID platform since the NVP began, focusing on cases and mortality. At the end of the fourth wave, at least 80% of people had received one vaccine dose and the case fatality rate was 0.85%, compared to 3.03% in the first wave, 2.53% in the second, and 1.35% in the third (7, 8). This suggests that the NVP may have reduced risk-factor-related deaths.

An ecological longitudinal study by the Colombian Ministry of Health and Social Protection (MSPS) estimated 22 000 deaths averted by mass vaccination of adults over 60 in the first year of the NVP (9). COVID-19 deaths could be prevented by any effective therapeutic approach, but even more so by vaccine-generated personal immunity preventing infection progression to death—the most significant expected effect of vaccination.

The objective of this study was to describe COVID-19 mortality among residents of Cali in the second wave of infections (13 December 2020 to 3 February 2021) before vaccines and in the fourth wave (28 December 2021 to 31 January 2022) with vaccination roll-out in progress, and to estimate the number of deaths averted.

MATERIALS AND METHODS

SSP records on vaccination coverage and deaths in the second and fourth waves of the COVID-19 pandemic in Cali were examined using a cross-sectional study design. The frequency of attributes of the deceased population were described for the second and fourth waves of infections. The Instituto Nacional de Salud (INS) defines positive and deceased cases (10).

The second wave in Cali lasted 52 days, with 54 862 positive cases and 1 133 deaths. The fourth wave lasted 35 days, with 90 085 positive cases and 754 deaths. These durations were estimated using the method described by Bortman (11), reducing the follow-up period from years to weeks of positive cases when COVID-19 increased in the city. The two-wave sample had 1 887 deaths and 144 947 positive COVID-19 cases; thus, all positive cases and deaths in these two periods were considered.

Inclusion criteria were any resident of Cali vaccinated with one or two doses and booster doses, any resident unvaccinated when the fourth wave was recorded, and any resident reported positive for SARS-CoV-2 infection, vaccinated or unvaccinated. Non-residents of Cali, under-18s, and records with inconsistent vaccination data were excluded. The covariates were sex, age, comorbidities (cancer, diabetes, chronic kidney disease, heart disease, HIV infection, chronic obstructive pulmonary disease [COPD]), nationality, and days between onset of symptoms and death.

The deaths in the second and fourth waves were identified using SSP COVID-19 vaccination databases and RT-PCR or antigen test positive cases. The date of application of any NVP vaccine was used to determine if the individual tested positive 14 days after vaccination with the complete scheme. This study does not contain any individual personal data, and no intervention was performed on any person.

The analysis compares the frequencies of attributes of deceased population in the two waves studied. The chi-squared test for categorical variables and Student's *t*-test for numerical variables were used to estimate differences between groups.

The Z-test proportion comparison test (Equation 1) (12) was used to estimate differences between the case fatality rate in the fourth wave and in the second wave.

$$z = \frac{p_A + p_B}{\sqrt{pq/n_A + pq/n_B}}$$

In Equation 1, p_A is the observed proportion of deaths with positive cases of wave 2 (n_A), p_B is the observed proportion of deaths with positive cases of wave 4 (n_B), and pq is the global proportion.

Deaths averted were calculated with the method described by Machado used in the MSPS Colombia study (9), which is based on the effectiveness of vaccines in preventing negative health outcomes, population coverage, and the change in frequency of these outcomes after applying the vaccination intervention (13). For this calculation, an estimated 81% overall effectiveness (VE_j) of vaccines to prevent death (14) was used in the following equation:

$$D_a = \sum_{ij} \left[D_{oij} \times \frac{FV_{i-2j} \times VE_j}{1 - (FV_{i-2j} \times VE_j)} \right]$$

In Equation 2, D_{oij} is the deaths observed in week i of the fourth wave in age group j , FV_{i-2j} is full vaccine coverage two weeks before week i of the fourth wave for age group j , and VE_j is the effectiveness of vaccination in age group j .

Based on the number of deaths observed, vaccination coverage with a complete scheme after a two-week interval, and vaccine effectiveness measured in Cali, an estimate is made of the deaths that could have occurred if COVID-19 vaccination were not available in Cali during the fourth wave.

R software (version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria) was used for all the above methods (15).

RESULTS

Table 1 shows the attributes of the variables used in the analysis. In the second wave, 1 133 people died, of whom 426 (37.6%) were women and 707 (62.4%) men. In the fourth wave, 754 people died, of whom 317 (42.0%) were women and 437 (58.0%) men. There were no statistically significant differences between women and men between the two waves ($p > 0.05$). Mortality decreased by 270 cases (38.2%) in men and 109 cases (25.5%) in women in the fourth wave. The average age of the deceased was 72.6 years in the second wave and 77.9 years in the fourth wave ($p = 0.2$). In the fourth wave, there was a statistically significant increase in the proportion of deceased over 80 years of age ($p = 1.4e-12$) and a decrease in those aged 60 to 79 years ($p = 3.03e-3$), 50 to 59 years ($p = 8.03e-3$), 40 to 49 years ($p = 0.01$), and 30 to 39 years ($p = 0.01$), with no statistical difference for those aged 18 to 29 years ($p = 0.8$).

The average interval between onset of symptoms and death was 20 days in the second wave and 14 days in the fourth wave. In terms of associated comorbidities, diabetes cases decreased from 228 (20.1%) in the second wave to 76 (10.1%) in the fourth wave ($p < 6.1e-6$), kidney disease decreased from 75 (6.6%) to 21 (2.8%) ($p = 0.0002$), and heart disease decreased from 96 (8.5%) to 36 (4.8%) ($p = 0.002$). Age, sex, nationality, and other comorbidities (cancer, COPD, HIV) did not differ between waves. In general, comorbidity rates and percentage weights decreased, but not all decreases were significant.

TABLE 1. Frequency of attributes of the deceased by COVID-19 wave, Cali

Variable	Category	Wave 2 (n = 1 133)	Wave 4 (n = 754)	P value
Sex	Female	426 (37.6%)	317 (42.0%)	0.05
	Male	707 (62.4%)	437 (58.0%)	0.05
Mean age (SD)		72.6 (13.5)	77.9 (14.3)	0.2
	>80	397 (35.0%)	404 (53.6%)	1.4e-12
	60-79	561 (49.5%)	291 (38.6%)	3.03e-3
Age group	50-59	111 (9.8%)	32 (4.2%)	8.03e-3
	40-49	34 (3.0%)	10 (1.3%)	0.01
	30-39	21 (1.9%)	4 (0.5%)	0.01
	18-29	8 (0.7%)	6 (0.8%)	0.8
	Mean days between onset of symptoms and date of death (SD)		20.2 (19.3)	14.5 (7.57)
Nationality	Colombian	1 128 (99.6%)	749 (99.3%)	0.5
	Foreign	5 (0.4%)	5 (0.7%)	0.5
Cancer	Yes	43 (3.8%)	24 (3.2%)	0.4
	No	1 090 (96.2%)	730 (96.8%)	0.4
Diabetes	Yes	228 (20.1%)	76 (10.1%)	6.1e-6
	No	905 (79.9%)	678 (89.9%)	6.1e-6
Kidney disease	Yes	75 (6.6%)	21 (2.8%)	0.0002
	No	1 058 (93.4%)	733 (97.2%)	0.0002
Heart disease	Yes	96 (8.5%)	36 (4.8%)	0.002
	No	1 037 (91.5%)	718 (95.2%)	0.002
Human immunodeficiency virus (HIV)	Yes	7 (0.6%)	1 (0.1%)	0.1
	No	1 126 (99.4%)	753 (99.9%)	0.1
Chronic obstructive pulmonary disease (COPD)	Yes	98 (8.6%)	52 (6.9%)	0.2
	No	1 035 (91.4%)	702 (93.1%)	0.2

Source: Prepared by the authors based on the study data.

Figure 1 shows that the frequency of daily deaths in the fourth wave is similar to that of the second wave during the first 38 days registered, a trend which from that point onwards is differentiated by the lower number of deaths registered in the fourth wave, measured until day 53, when the second wave ends, 15 days longer than the fourth wave. Given the higher number of infected people in the fourth wave (Table 1), COVID-19 deaths were lower in the fourth wave compared to the second.

Table 2 presents the attributes of the deceased in the fourth wave of COVID-19 according to vaccination status using the same statistical methods as Table 1. The unvaccinated variable represents people who did not have any vaccine dose against SARS-CoV-2, and the vaccinated variable represents people who completed the vaccination schedule. In the fourth wave, 465 unvaccinated people died, 56.8% of whom were men and 43.2% women, while 289 fully vaccinated people died, 59.9% of whom were men and 40.1% women, showing no statistical differences between the two groups. The fourth wave saw 33.4% fewer COVID-19 deaths than the second wave.

The unvaccinated deceased averaged 76.3 years of age, while the vaccinated averaged 80.6 years ($p = 1.41e-12$). When categorized by age, only those over 80 years show statistically significant differences, with 52 fewer deaths among the vaccinated (176) than the unvaccinated (228) ($p = 0.001$). Deaths are concentrated in the 60-79 and 80+ years groups. The unvaccinated died on average 13.8 days after symptom onset, compared to 15.7 days for the vaccinated ($p = 0.0005$).

In the fourth wave, 9.2% of the unvaccinated deceased had diabetes, accounting for 5.7% of the total number of deaths. Of the deceased vaccinated with a complete scheme, 30.1% had any comorbidity, and 11.4% had diabetes, accounting for 4.4% of all fourth-wave deaths. Some 61.6% of fourth-wave deceased were unvaccinated. The second and fourth waves had different case fatality rates, with the fourth wave having a higher proportion of positive cases and a lower death rate. Thus, the Z-test proportion comparison test (Equation 1) estimates statistically significant differences between the case fatality rate of 0.8% in the fourth wave and 2.5% in the second wave (Table 3).

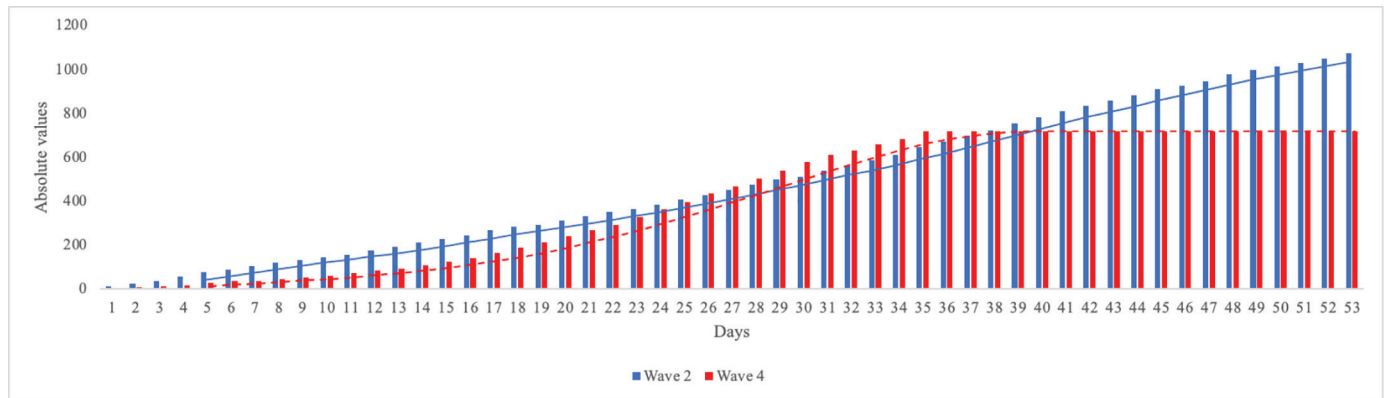
Table 4 shows the possible deaths during the fourth wave if second wave case fatality rates were maintained based on the number of fourth wave COVID-19 cases: 2 004 deaths would be expected in people over 18, concentrated in the 60-79 age group and then in the over 80 group.

Deaths averted were calculated with the method described by Machado used in the MSPS Colombia study (9). Associated with the effect of vaccination, approximately 3 763 deaths were averted in the fourth wave in Cali (Table 5).

DISCUSSION

Based on the deaths when vaccination was unavailable (second wave), this study indicated that an expected 3 763 deaths were prevented in Cali's fourth wave, especially among high-risk age groups (over 80 and 60-79 years). Between December 2020 and November 2021, more than 33 European countries

FIGURE 1. Cumulative COVID-19 deaths, second and fourth waves, Cali



Source: Prepared by the authors based on the study data.

TABLE 2. Frequency of attributes of the deceased in the fourth wave of COVID-19 infections by vaccination status, Cali

Variable	Category	Unvaccinated (n = 465)	Vaccinated (n = 289)	P value
Sex	Female	264 (56.8%)	173 (59.9%)	0.4
	Male	201 (43.2%)	116 (40.1%)	0.4
Mean age (SD)		76.3 (15.8)	80.6 (11.0)	1.41e-12
Mean days between onset of symptoms and date of death (SD)		13.8 (7.34)	15.7 (7.79)	0.0005
Age group	>80	228 (49.0%)	176 (60.9%)	0.001
	60-79	190 (40.9%)	101 (34.9%)	0.1
	50-59	23 (4.9%)	9 (3.1%)	0.2
	40-49	9 (1.9%)	1 (0.3%)	0.06
	30-39	4 (0.9%)	0 (0%)	0.1
	18-29	4 (0.9%)	2 (0.7%)	0.8
Nationality	Colombian	462 (99.4%)	287 (99.3%)	0.9
	Foreign	3 (0.6%)	2 (0.7%)	0.9
Cancer	Yes	13 (2.8%)	11 (3.8%)	0.4
	No	452 (97.2%)	278 (96.2%)	0.4
Diabetes	Yes	43 (9.2%)	33 (11.4%)	0.3
	No	422 (90.8%)	256 (88.6%)	0.3
Kidney disease	Yes	13 (2.8%)	8 (2.8%)	0.9
	No	452 (97.2%)	281 (97.2%)	0.9
Heart disease	Yes	19 (4.1%)	17 (5.9%)	0.2
	No	446 (95.9%)	272 (94.1%)	0.2
Human immunodeficiency virus (HIV)	Yes	0 (0%)	1 (0.3%)	0.2
	No	465 (100%)	288 (99.7%)	0.2
Chronic obstructive pulmonary disease (COPD)	Yes	33 (7.1%)	19 (6.6%)	0.7
	No	432 (92.9%)	270 (93.4%)	0.7

Source: Prepared by the authors based on the study data.

TABLE 3. Comparison of case fatality rate between the second and fourth waves of COVID-19, Cali

Waves	Chi squared	DF	P value	Relative frequency	Case fatality rate
Wave 2	94 991	1	2.2e-16	0.02	2.5%
Wave 4				0.008	0.8%

DF: degrees of freedom.

Source: Prepared by the authors based on the study data.

TABLE 4. Expected deaths in the fourth wave of COVID-19 based on the case fatality rate of the second wave, Cali

Age group	Number of cases (Wave 4)	Case fatality rate (Wave 2)	Expected deaths (Wave 4)
>80	2 826	26.3%	743
60–79	11 888	7.9%	950
50–59	11 923	1.6%	194
40–49	16 074	0.5%	78
30–39	20 884	0.1%	27
18–29	21 255	0.05%	11
Total			2 004

Source: Prepared by the authors based on the study data.

TABLE 5. Number of deaths averted during the fourth wave of COVID-19, population aged 18 years and older, Cali

Age group	Population size	Vaccinated people	Unvaccinated people	Case fatality rate Wave 2	Vaccination coverage Wave 4	Deaths observed Wave 4	Deaths averted Wave 4
>80	62 078	61 916	162	15.0%	100%	404	2 732
60–79	318 565	285 591	32 974	2.4%	90%	291	865
50–59	268 541	252 854	15 687	0.3%	95%	32	135
40–49	281 172	220 374	60 798	0.08%	80%	10	20
30–39	325 186	204 976	120 210	0.04%	65%	4	5
18–29	363 557	202 986	160 571	0.02%	58%	6	5
Total	1 619 099	1 228 697	390 402	1.1%	81%	747	3 763

Source: Prepared by the authors based on the study data.

averted 469 186 deaths among over-60s. Israel, Malta, and the United Kingdom had lower anticipated mortality, notably in persons over 80 (16). In Colombia, MSPS conducted an ecological analysis that predicted 22 000 deaths averted in people over 60, or 32.4% of expected deaths in 2021 (9).

Whereas 2 004 people could have been expected to die in the fourth wave, the fourth wave had fewer fatalities than the second, possibly due to vaccination. Public health and epidemiological strategies like vaccination, confinement, and early case detection reduced deaths during outbreaks in Colombia (17). In the fourth wave, the Omicron variant was predominant, which WHO characterized as highly transmissible but with a lower rate of severe disease and deaths (18).

This study found that 60% of the deceased during the fourth wave were unvaccinated, and a higher proportion were among people at higher risk due to older age and comorbidities. This result is consistent with a review of data from China, Italy, and the United States of America, in which Ejaz et al. (19) state that “underlying diseases, such as hypertension, CVD [cardiovascular disease], diabetes, malignancy, COPD, and asthma, have been reported as risk factors for severe disease and also increased the mortality rate.” In China, 23% of hypertensive cases with COVID-19 were reported with a 6% case fatality rate, and in diabetic patients a COVID-19 fatality rate of 8% was reported (19).

In addition, mean age of the deceased differed between waves, at 72.6 years in the second wave and 77.9 in the fourth, which may be directly linked to the effect of different viral genomic variants on mortality in older patients, especially in the unvaccinated population. Other studies estimate a higher risk of disease progression associated with advanced age (2).

The mean interval between onset of symptoms and death was 20.2 days in the second wave and 14.5 days in the fourth. However, the available literature does not specify a cause for

the change in the interval between onset of symptoms and death as outcome between waves. Hypotheses include differences in the viral variants, age groups, late presentation at health services for timely care, and comorbidities that are linked to age (20).

This study has limitations. The study is observational, and proving causation requires different methodology. It did not include immunological and antibody response data to determine if vaccination and transmissibility of circulating viral variants explain the age group differences in mortality between the two waves (21). In addition, availability of testing data was limited due to the prioritization of sampling in the INS guidelines and the depletion of resources to conduct testing (10). The number of people with comorbidities who could have died before the fourth wave is a limitation in the analysis of the decrease in mortality.

The strengths of the study include that it has the advantage of a large sample size, and it describes and analyzes information from the two waves and the number of deaths possibly averted by vaccination coverage, as used in exploratory COVID-19 studies (22–23).

The findings of this study support prioritizing vaccination of risk groups to prevent fatalities. To better understand this pandemic and future ones, epidemiological surveillance and communication with MSPS and international agencies must be strengthened. Continued observation and analysis of COVID-19 variables and widespread vaccine use are essential.

In conclusion, this study allowed us to estimate the deaths that were possibly averted, based on the prevalence of COVID-19 positive cases, the case fatality rates for each of the two waves, and estimating a reduction in mortality in the fourth wave compared to the second. These possible deaths averted were in the context of vaccination coverage for older age groups in the city of Cali.

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Mortalidad por COVID-19 en dos olas de la pandemia en Cali, Colombia, antes y durante el despliegue de las vacunas

RESUMEN

Objetivo. Describir la variación en la mortalidad por COVID-19 en los residentes de Cali, Colombia, en la segunda ola de la pandemia (antes de las vacunas) y en la cuarta ola (durante el despliegue de las vacunas). Se tomaron en cuenta las variables referidas al sexo, grupo de edad, comorbilidades e intervalo entre el inicio de los síntomas y la muerte y se estimó el número de muertes evitadas por la vacunación.

Métodos. Estudio transversal sobre las muertes en la segunda y cuarta olas de la pandemia de COVID-19 y la cobertura de vacunación. Se compararon las frecuencias de los atributos correspondientes a la población fallecida durante las dos olas, incluidas las comorbilidades. Se utilizó el método de Machado para estimar el número de muertes evitadas en la cuarta ola.

Resultados. Se registraron 1 133 muertes en la segunda ola y 754 en la cuarta. Se calculó que, en el contexto del despliegue de las vacunas, en la cuarta ola se evitaron aproximadamente 3 763 muertes en Cali.

Conclusiones. La disminución observada en la mortalidad asociada a la COVID-19 respalda la continuación del programa de vacunación. Dada la falta de datos para explicar otras posibles causas de esta disminución, como puede ser la gravedad causada por las nuevas variantes virales, se analizan las limitaciones del estudio.

Palabras clave

COVID-19; vacunas contra la COVID-19; mortalidad; Colombia.

Mortalidade por COVID-19 em duas ondas da pandemia em Cali, Colômbia, antes e durante a disponibilização das vacinas

RESUMO

Objetivo. Descrever a variação da mortalidade por COVID-19 entre residentes de Cali, Colômbia, na segunda onda da pandemia (antes das vacinas) e na quarta onda (com a implantação da vacinação já em andamento), considerando as variáveis sexo, faixa etária, comorbidades e intervalo entre início dos sintomas e óbito, bem como estimar o número de óbitos evitados pela vacinação.

Métodos. Estudo transversal de mortes e cobertura vacinal na segunda e quarta ondas da pandemia. Foram comparadas as frequências dos atributos da população que foi a óbito durante as duas ondas, incluindo comorbidades. Foi utilizado o método de Machado para estimar o número de mortes evitadas na quarta onda.

Resultados. Houve 1.133 mortes na segunda onda e 754 mortes na quarta onda. Calcula-se que cerca de 3.763 mortes foram evitadas na quarta onda em Cali, no contexto da disponibilização das vacinas.

Conclusões. A queda observada na mortalidade associada à COVID-19 apoia a continuidade do programa de vacinação. Considerando a falta de dados para explicar outros possíveis motivos para esta queda, como a gravidade das novas variantes do vírus, discutem-se as limitações do estudo.

Palavras-chave

COVID-19; vacinas contra COVID-19; mortalidade; Colômbia.
