

Economic Evaluation

Burden of COVID-19 in Córdoba, A Department of Colombia: Results of Disability-Adjusted Life-Years

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Carga de COVID-19 en Córdoba, un Departamento de Colombia: Resultados de los Años de Vida Ajustados por Discapacidad

Ana Lozano, MD, MSc, Fernando Salcedo-Mejía, MSc(c), Josefina Zakzuk, MD, PhD, Nelson Rafael Alvis-Zakzuk, MBA, Lina Moyano-Tamara, PMS, Héctor Serrano-Coll, MD, MSc, PhD, Bertha Gastelbondo, MSc, PhD, Salim Mattar, MSc, PhD, Nelson J. Alvis-Zakzuk, MSc, Nelson Alvis-Guzman, MD, MSc, PhD

RESUMEN

Objetivos: Estimar la carga de COVID-19 aguda en Córdoba, uno de los departamentos (estados) más afectados de Colombia, a través de la estimación de años de vida ajustados por discapacidad (AVISAS).

Métodos: Los AVISAS se estimaron con base en el número de casos de infección por severe acute respiratory syndrome coronavirus 2 reportados por fuentes oficiales colombianas. Se calculó una matriz de probabilidad de transición entre estados de gravedad a partir de los datos obtenidos de una cohorte retrospectiva que incluyó a 1.736 sujetos confirmados con COVID-19 residentes en Córdoba.

Resultados: Córdoba tuvo 120,23 defunciones por cada 100.000 habitantes durante el periodo de estudio (marzo de 2020 a abril de 2021). Los AVISAS totales estimados fueron 49.243 (2.692 AV por 100.000 habitantes), en su mayoría atribuidos a los casos mortales (99,7%). En promedio, se perdieron 25 años de vida debido a las muertes secundarias a esta infección. Una proporción relevante de años de vida perdidos a causa de la COVID-19 (46,6%) fue atribuible a las personas menores de 60 años y fue mayor en los hombres. Las personas \geq 60 años presentaron un mayor riesgo de progresión a estado crítico en comparación con las personas entre 35-60 años (hazard ratio 2,5; intervalo de confianza 95% 2,5-12,5) y menores de 35 años (9,1; intervalo de confianza 95% 4,0-20,6).

Conclusión: En Córdoba, la mortalidad prematura por COVID-19 estuvo sustancialmente representada por las personas menores de 60 años y fue mayor en el sexo masculino. Nuestros datos pueden ser representativos de poblaciones latinoamericanas con gran propagación de infecciones durante el primer año de la pandemia y aportan aspectos metodológicos novedosos para la estimación de parámetros que pueden ser útiles para medir la carga de COVID-19 en otros países de la región.

Palabras clave: años vividos con discapacidad, años de vida ajustados por discapacidad, años de vida perdidos, infecciones por coronavirus, severe acute respiratory syndrome.

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ABSTRACT

Objectives: This study aimed to estimate the burden of acute COVID-19 in Córdoba, one of the most affected departments (states) in Colombia, through the estimation of disability-adjusted life-years (DALYs).

Methods: DALYs were estimated based on the number of cases of severe acute respiratory syndrome coronavirus 2 infection cases reported by official Colombian sources. A transition probability matrix among severity states was calculated using data obtained from a retrospective cohort that included 1736 COVID-19 confirmed subjects living in Córdoba.

Results: Córdoba had 120.23 deaths per 100 000 habitants during the study period (March 2020 to April 2021). Estimated total DALYs were 49 243 (2692 DALYs per 100 000 inhabitants), mostly attributed to fatal cases (99.7%). On average, 25 years of life were lost because of death by this infection. A relevant proportion of years of life lost because of COVID-19 (46.6%) was attributable to people < 60 years old and was greater in men. People \ge 60 years old showed greater risk of progression to critical state than people between the age of 35 and 60 years (hazard ratio 2.5; 95% confidence interval 2.5-12.5) and younger than 35 years (9.1; 95% confidence interval 4.0-20.6).

Conclusion: In Córdoba, premature mortality because of COVID-19 was substantially represented by people < 60 years old and was greater in males. Our data may be representative of Latin American populations with great infection spread during the

first year of the pandemic and contribute to novel methodological aspects and parameter estimations that may be useful to measure COVID-19 burden in other countries of the region.

Keywords: coronavirus infections, disability-adjusted life-year, severe acute respiratory syndrome, years of life lost, years lived with disability.

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Introduction

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The COVID-19 pandemic has had a great impact on most regions of the world,¹ with > 6 million of deaths recorded worldwide until August 2022.² Colombia, as other countries in the Latin American region, has been strongly affected by COVID-19. Despite long lockdowns periods, improvement of health capabilities to manage moderate-severe cases and a coordinated national system for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) detection,³ mortality excess was considerable.⁴ Up to now, the confirmed cases reported in Colombia rose to 6.27 million and 141 000 deaths.⁵ Nevertheless, the effect of COVID-19 has been different among its territories in terms of incidence, mortality, and fatality rates.⁵ The national vaccination program started at February 2021 with a first phase including only 80+-year-old inhabitants. In January 2022, 72.6% of the Colombian population is fully vaccinated and 29 per 100 have been boosted.⁶

Córdoba is a state located to the north of Colombia with approximately 1.9 million people and 30 municipalities,⁷ where 45 661 cases of COVID-19 and 2172 deaths were recorded until April 11, 2021.⁵ Its mortality rate (120.9 per 100 000 habitants) was close to the observed in the whole country for that time (139.9 per 100 000). Its main city, Montería, was strongly affected at the beginning of the pandemic, presenting the highest mortality rate at the cutoff date compared with other Colombian main cities (215 per 100 000).⁵ After the first peak of the epidemics, this viral infection was detected in approximately a half of its inhabitants.⁸

Mortality and fatality rates can provide an insight into the scale of diseases; therefore, they have been frequently reported during the COVID-19 pandemic.^{1,9} Nevertheless, these indicators do not allow us to plainly compare the impact of COVID-19 in a region in relationship with others or other diseases.¹⁰ In that sense, it may be necessary to estimate summary measures that combine morbidity and mortality of the disease, such as disability-adjusted life-years (DALYs).¹¹ This study, we sought to estimate the disease burden of COVID-19 in Córdoba, a department located in the north of Colombia.

Methods

To estimate the COVID-19 DALYs in Córdoba, the methodology proposed by Wyper et al¹⁰ was adapted. The cutoff date for this analysis was April 11, 2021. At this time point, the vaccination rate was < 5%.

Study Location

Córdoba is one of the 32 states of the Republic of Colombia located to the north (latitude, 8°45′00″N; longitude, 75°53′00″ W) in the Caribbean Region. It is divided into 30 municipalities, and 28% of its inhabitants live in the capital city, Montería. For 2020, Córdoba was the seventh most populous state in Colombia with 1 828 947 inhabitants and a population density of 76.27/km^{2.12}

Data Sources

The age and gender distribution of confirmed COVID-19 cases and deaths for Córdoba and its municipalities were extracted from the official national databases held by the National Institutes of Health.⁵ Demographic data were extracted from the 2020 projections of the 2018 Colombian census.¹³ The case definitions of COVID-19 are outlined in the study of De la Hoz-Restrepo et al.¹⁴ The standard life expectancy was extracted from the Global Burden of Disease (GBD) 2019 study.¹⁵ Patient comorbidity information (hypertension, diabetes, and cancer) in patients with COVID-19 was extracted from publicly available databases prepared by the Colombian Ministry of Health.¹⁶

An administrative database of the open cohort of patients with COVID-19 between March 2020 and October 2020 from an insurance company was consulted to estimate transition probabilities among severity states. A retrospective cohort was built with 1736 confirmed cases of COVID-19 from Córdoba with a complete follow-up since symptoms onset until recovery or death. The selection of these patients is summarized in Appendix Figure 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2 023.03.005. Sociodemographic data, COVID-19 symptoms, and location status (ie, home, hospital, and intensive care unit) of patients were extracted.

Model Parameters

The parameters used to calculate the DALYs (which include years of life lost [YLL] and years lived with disability [YLD] estimations) were obtained from the sources referred earlier. The disability weights (DWs) according to 3 COVID-19 health states, proposed by Wyper et al,¹⁰ were implemented. Duration and probability of being in each health state were calculated based on the health insurance administrative database. We filtered the database to select patients with a follow-up that started in the health state level/moderate to evaluate the progression to other health states (severe or critical) and end states, including recovery and death. The risk of progression was estimated using the Cox instantaneous risk and multistate survival models; then, a transition probability matrix by age groups was estimated using the Aalen-Johansen estimator.¹⁷ Finally, mean and standard deviation time duration in each health state were estimated (Appendix Table 1 in Supplemental Materials found at https:// doi.org/10.1016/j.vhri.2023.03.005). Detailed information on source health state names, descriptions, and the equivalent health states determined within the administrative database (data input proxy) are presented in Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2023. 03.005.

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DALY Estimation

The formula used to calculate the YLL was as follows:

$$YLL = \sum_{j=1}^{n} number of deaths_j \times (Remaining life expectancy_j - 2.5)$$

where *j* corresponds to the 5-year age groups and *n* the number of age groups.¹⁰ We used a midpoint correction (2.5) of the remaining life expectancy, to avoid over or underestimation of YLL.

The YLD formula was:

$$YLD = \sum_{h=1}^{n} number of cases \times duration in years_h \times dw_h \times P_h$$

where h represents the health states, n the number of health states, and P the estimated probability of being in each state of health.

DALYs were computed as the sum of the YLL and YLD. We merged the INS and SISPRO databases using each patient's unique identification number and then calculated the DALYs according to the comorbidity reported. We also calculate the YLL, YLD, and DALY per 100 000 people, according to the population of Córdoba and its municipalities.

Statistical Analysis

The model parameters were calculated using R v4.0.3. (R Core Team, R Foundation for Statistical Computing). For survival analysis, we used the packages "survival" version 3.2-13. Given the parameters uncertainty, a Monte Carlo simulation was performed with 1000 iterations where the model parameters were randomized according to assumptions of statistical distribution. The estimation of the DALYs was summarized as the median of their values and the confidence interval (CI) at 95% from the 2.5% and 97.5% percentile of the simulation.

Results

During the observation window, 45 665 confirmed cases of COVID-19 and 2199 deaths were reported in Córdoba. The study population's cumulative incidence rate was 2497 per 100 000 people with a standardized mortality ratio of 121.17 per 100 000 people. Close to 60% of cases occurred in Montería. Mortality and incidence rates were similarly distributed among municipalities (Fig. 1, Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2023.03.005) and were highly correlated (r = 0.81, P = .0001).

About a Half of YLL Were due to People < 60 Years Old

Deaths because of this infection translated to nearly 49 131 YLLs (2686 YLLs per 100 000 capita and 22.34 YLLs per death). YLLs were greater in men than in women in almost all age groups, except for those aged 25 to 34 years (Fig. 2, Appendix Table 4 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2 023.03.005). No deaths were reported for men in the 5- to 9-year and 10- to 14-year age groups. The YLLs per 100 000 people increased with age, decreasing sharply in men aged 75 to 80 years (Fig. 2, Table 1). The highest YLL was found in the 65- to 69-year-old group, whereas the highest YLLs per 100 000 inhabitants was in the 70- to 74-year-old group. A relevant proportion of YLL due to COVID-19 was attributable to people younger than 60

years; 46.6% of the YLL due to premature mortality occurred before this age, with an average of 42.1 YLL.

YLD in Córdoba

People aged 60 years or older showed a greater risk of progression to critical state than people between 35 and 60 years old (hazard ratio 2.54; 95% CI 2.54-12.49) and younger than 35 years (hazard ratio 9.08; 95% CI 4.00-20.62), respectively (Fig. 3, Appendix Table 5 in Supplemental Materials found at https://doi. org/10.1016/j.vhri.2023.03.005). For this reason, to calculate YLDs, 3 transition probability matrixes were used: for people < 35 years, 35 to 60 years, and > 60 years old (Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2023.03. 005).

In the study population, 111.9 YLDs were attributable to COVID-19 during the observation window. Women lost slightly more years of life due to disability than men, with 58.9 versus 53.0 YLD, respectively. The number of YLDs reflects the age distribution of the reported cases for people younger than 60 years (Appendix Fig. 2 in Supplemental Materials found at https://doi.org/10.1 016/j.vhri.2023.03.005). Correspondingly, 57.3% of the YLD for both men and women were attributable to people younger than 60 years, but people aged 60 to 64 years were hit the hardest with 13.41 YLDs (Fig. 4, Appendix Table 4 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2023.03.005).

Regarding the overall population, the number of YLDs rose steadily with age, strikingly rising in those 60 years and older (Fig. 4, Table 1) and reaching the highest YLDs in those aged 80+ years with 24.70 YLDs per 100 000 people. There were 6.1 YLDs per 100 000 people in the study period. For women, this value was 6.4 YLD per 100 000 people, slightly higher than for men, with 5.8 YLD per 100 000 inhabitants.

COVID-19 Disease Burden (DALY)

Altogether, the Córdoba population lost 49 243 DALYs because of COVID-19 during the study period (2692 DALYs per 100 000 people). Most of the DALYs were attributed to the YLL with a share of 99.77%. There were slight differences in the relative contribution of YLD between people < 35 and \ge 35 years old with a mean contribution of 0.6% and 0.2%, respectively, excluding the 10- to 14-year age group, in which no deaths were reported.

According to the Monte Carlo simulation, the DALYs for women were 18 719 (95% CI 18 680-18 999) and men 30 496 (95% CI 30 460-30 748), giving a total of 49 215 (95% CI 49 140-49 747) DALYs for Córdoba.

As shown in Figure 1, Montería had the highest number of DALYs per 100 000 (4923.4), followed by Cereté (3623.1) and Lorica (3408.8). The municipality with the highest relative contribution to DALYs in Córdoba was Montería with 50.5%, followed by Cereté and Lorica, with 8% each (Appendix Table 7 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2 023.03.005).

Comorbidities and Disease Burden

The distribution of the DALYs according to the comorbidities is represented in Figure 5. Approximately 40% of the total DALYs for Córdoba involved people with hypertension, diabetes, or cancer. Hypertension alone accounted for 86.70% of comorbidities.

Discussion

Assessment of the combined impact of morbidity and mortality is necessary to understand and compare the impact of 12



Figure 1. Geographical distribution of COVID-19 at the municipality level. Map of Córdoba. Municipalities are colored according to population size, incidence, death rate, or DALYs (per 100 000 people for all 3 indicators).

DALY indicates disability-adjusted life-year

COVID-19 on health, relative to other disease causes, in both scenarios, within subnational efforts and international comparisons.¹⁸ Estimation of DALYs is a useful summary measure tool that allows more standardized international comparisons of the epidemiological impact of a disease. The COVID-19 pandemic had a great impact on health and economics productivity in the whole world, but burden disease estimations are still an unmet need for most regions.¹⁸ In this study, we analyze the disease burden of acute COVID-19 in a state of Colombia with available data (national statistics and real-world data from a COVID-19 cohort from a health insurance company) that permit more accurate estimations using standardized GBD methods, but also integrating age differences in transition probabilities within severity stages that may improve estimations of disease-secondary disabilities at the population-level. According to our analyses, the Department of Córdoba lost an estimated 49 243 DALYs because of COVID-19 between March 20, 2020, and April 11, 2021. Disease burden mainly was attributed to fatal cases (99.7%, 49 131 YLLs) and 0.1% to YLD (111.9 YLDs) and was higher in males. On average, 25 years of life were lost among COVID-19 deaths, observing a substantial proportion of total YLLs in people younger than 60 years. The main municipality of the state showed the highest COVID-19 disease burden and contributed the most to the total DALYs.

Our work and the published by Hidalgo-Troya et al¹⁹ in the state of Nariño are subnational estimations from Colombia and the only available literature from the Latin American region, and both indicate a higher impact of COVID-19 than in the rest of the world. As found in Nariño (2460 in 100 000), DALYs in Córdoba (2690 in 100 000) were 6 times higher than the global DALYs estimated by Fan et al²⁰ (4274 in 100 000). In Europe, a multinational analysis indicated that the top 3 countries with the highest COVID-19-related DALYs (per 100 000) were Italy (65), Sweden (53), and Czech Republic (52).²¹ In India, reports ranged from 31 in the state of Karnakata²² to 102 per 100 000 habitants in the whole country.²³ Another report from Malta, which covered a larger period, also found a high burden with 1300 DALYs per 100 000



Figure 2. YLL due to premature mortality due to COVID-19 distributed by age and sex.

YLL indicates years of life lost.

inhabitants.²⁴ As observed, burden disease associated with COVID-19 may greatly differ among countries, and several factors may influence results. Given that DALY is mainly driven by mortality, a main influencing factor is the health capability to confront the epidemiological waves, the demographic structure of the population, genetic factors, and other more technical issues related with surveillance systems that register cases and deaths and model adaptations to real-world data for more accurate estimations. Considering all these aspects, we consider that our estimations are highly representative of the Latin American context where COVID-19 strongly affected both middle-aged and older people, generating high mortality excess rates.⁴ In addition, our study also covered a 2021 period (January to March) that was not included in most DALY estimations from other parts of the world, except Malta,²⁴ and that coincided with a strong wave of COVID-19 in Latin America and the highest mortality rate. All

Table 1. Age pattern of YLL, YLD, and DALY per 100 000 people in Córdoba.

Age group	Men			Women			Total		
	YLL	YLD	DALY	YLL	YLD	DALY	YLL	YLD	DALY
00-04	306.85	0.45	307.31	107.55	0.42	107.98	209.71	0.44	210.14
05-09	0.00	0.64	0.64	102.41	0.68	103.08	49.95	0.66	50.61
10-14	0.00	1.09	1.09	0.00	1.20	1.20	0.00	1.14	1.14
15-19	443.67	1.57	445.25	182.52	1.94	184.46	314.93	1.75	316.68
20-24	613.93	2.35	616.28	350.99	3.36	354.35	482.49	2.85	485.34
25-29	530.76	3.70	534.46	1121.46	4.77	1126.23	829.81	4.24	834.06
30-34	814.93	4.40	819.33	1205.47	5.14	1210.60	1015.11	4.78	1019.89
35-39	2559.26	8.15	2567.41	1409.16	8.81	1417.96	1966.20	8.49	1974.69
40-44	3955.84	7.89	3963.73	2021.34	8.37	2029.71	2958.78	8.13	2966.92
45-49	4026.36	6.52	4032.88	2496.90	7.34	2504.25	3241.86	6.94	3248.80
50-54	5577.60	6.98	5584.58	3089.69	7.98	3097.67	4310.08	7.49	4317.56
55-59	8546.46	7.67	8554.14	3851.67	8.56	3860.23	6152.23	8.12	6160.35
60-64	9890.09	17.37	9907.45	6723.52	19.92	6743.44	8270.20	18.67	8288.87
65-69	14 658.03	19.59	14 677.63	7991.07	19.24	8010.31	11 243.64	19.41	11 263.05
70-74	19 492.87	21.76	19 514.63	9476.80	19.20	9496.00	14 366.91	20.45	14 387.36
75-79	16 177.56	21.58	16 199.15	9769.44	19.45	9788.89	12 912.50	20.49	12 933.00
80+	14 959.63	26.39	14 986.02	8801.99	23.02	8825.01	11 856.16	24.69	11 880.85
Total	3348.14	5.83	3353.97	2031.42	6.40	2037.82	2686.30	6.12	2692.41

DALY indicates disability-adjusted life-year; YLD, years lived with disability; YLL, years of life lost.

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Figure 3. Probability of progression to the different severity states of COVID-19 according to age.

these factors may explain why we observed the highest DALYs (per 1000 habitants) reported so far. In the 50- to 69-year-old population, DALYs (per 100 000) caused by COVID-19 in Córdoba were even greater than GBD 2019 estimations for ischemic heart disease and diabetes, the main causes of disease burden in Colombia.¹⁵ Furthermore, the high similarity with DALYs reported from Nariño, Colombia,¹⁹ supports that COVID-19 generated a strong health impact on Colombia.

As in most studies,^{19,23} men had higher YLLs than women, probably due to men having a greater risk of death than women.^{25,26} On the contrary, women are more likely to be infected, maybe due to their occupations, which may explain the higher YLDs observed.²⁷ The male predisposition to more severe COVID-19 has not been fully elucidated, but genetic links with androgenic pathways have been found.²⁸

We found that the highest rate of YLDs per 100 000 people were found in the 60-year and older group. This differs from previous COVID-19 disease burden studies where the highest number of YLDs was found in the productive age groups due to a higher risk of infection.^{23,29,30} Nevertheless, these studies differ from ours given that it assumes that the proportion of severe cases is the same for all ages. In contrast, our study used an age-specific severity distribution. This allowed us to state that although people aged 60 years and older have fewer infections, they are more prone to develop severe forms of the disease, which generate a greater DW. Thus, our proposed methodology for calculating the probability of transition between severity states of COVID-19 could lead to more efficient strategies for estimating disability secondary to the disease. This methodology can be advantageous in regions where there are no follow-up data on patients with COVID-19, their severity states and duration of each state.

According to previous studies, people aged > 60 years have a greater risk of severe COVID-19 and death.^{31,32} This was also reflected in our results, given that we found that these age groups had the highest DALYs per 100 000 people due to higher YLL and YLD. Nevertheless, there is still an important loss of years of life





YLD indicates years lived with disability.

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Figure 5. Distribution of YLL, YLD, and DALY according to the comorbidities diagnosed in people with COVID-19 in Córdoba.



DALY indicates disability-adjusted life-year; YLD, years lived with disability; YLL, vears of life lost

due to COVID-19 in people younger than 60 years. Although the probability of dying at those ages is lower, the people who died lost approximately 42 years of life, meaning that the COVID-19 disease significantly affected younger people. For this Latin American population, the rate is considerably higher than in other studies with similar designs and observation windows. In Germany, for example, < 70-year-old people lost a mean of 25 years of life.³³ This example can be traced to different high-income countries; meanwhile for low- and mid-income countries appears a pattern similar to ours.³⁴ In Córdoba, probably, this is due to the higher mortality in people younger than 29 years, which drive to a higher life of years lost. The mortality rate in these ages was higher than in other Latin American regions.³¹

Montería contributed to 50.5% of the disease burden in Córdoba. Montería has been one of the cities with the most COVID-19 cases in Colombia, with a cumulative incidence of 5339 cases per 100 000 inhabitants during the study period. Although Montería only concentrates 28% of the population of Córdoba, most of the population live in its urban perimeter. These urban areas have been the epicenter of SARS-CoV-2 transmission in many countries, possibly due to the higher population density, connectivity, crowded living conditions, and occupations with a high probability of exposure.³⁶⁻³⁸

The limitations of our study are as follows: (1) it is based on secondary data. The COVID-19 cause of death may have been underreported or misclassified. Nevertheless, WHO classified as "average" the accuracy of the underlying cause of death in Colombia.³⁹ In addition, due to surveillance capacity, the cases analyzed may not represent all actual cases of SARS-CoV-2 infection.^{40,41} (2) Another limitation is related to YLD estimation. The DWs proposed for Wyper et al⁴² have the disadvantage that is not specific to COVID-19 and does not evaluate other symptomatology of the disease, but currently these DWs are the most used $^{43-45}(3)$ Our results were only representative of COVID-19 as an acute disease, underestimating future disability for severe or long COVID-19 cases. Nevertheless, we used the best evidence available to estimate the YLD. It is currently recognized that different clinical manifestations may persist or develop after the resolution of

acute symptoms.⁴⁶⁻⁴⁸ Life guality and loss of productivity are expected to derive from post-COVID,^{49,50} and disease burden estimation must also be calculated in further analyses. Other DALYs estimations, as the article published by Wyper et al⁴² analyzing disease burden in Scotland, indicated that YLD contributed to 2% of DALYs; meanwhile in Malta, this value reached 5%.²⁴ Post-COVID sequel may have a deep impact on disability; nevertheless, given that death rates are high in those severely affected, many potential DLYs end up in YLLs. Finally, our results showed the impact of COVID-19 before vaccination started to exclude the possible impact of COVID-19 vaccines on mortality and disability.⁵¹⁻⁵³ Future results of seroprevalence studies⁸ and clinical research will lead to more accurate parameters for the correct assessment of COVID-19 health disability.

Conclusion

DALYs' estimations led us to appreciate that COVID-19 had a substantial health impact on Córdoba, Colombia. Premature mortality due to COVID-19 was substantially represented by people < 60 years old and was greater in males. Given that our data may be representative of Latin American populations with great infection spread during the first year of the pandemic, it contributes with novel methodological aspects and parameter estimations that may be useful to analyze COVID-19 in other countries of the region.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2023.03.005.

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Author Affiliations: ALZAK Foundation, Cartagena, Colombia (Lozano, Salcedo-Mejía, Zakzuk, N. R. Alvis-Zakzuk, Moyano-Tamara); Grupo de Investigación en Economía de la Salud, Universidad de Cartagena, Cartagena, Colombia (Lozano, Zakzuk, Alvis-Guzman); Instituto de Investigaciones Biológicas del Trópico, Universidad de Córdoba, Montería, Córdoba (Serrano-Coll, Gastelbondo, Mattar); Facultad de Medicina, Universidad CES, Medellín, Colombia (Serrano-Coll); Instituto Colombiano de Medicina Tropical-Universidad CES, Medellín, Colombia (Serrano-Coll); Departamento de Ciencias de la Salud, Universidad de la Costa, Barranguilla, Colombia (N. J. Alvis-Zakzuk, Alvis-Guzman); Programa de posgraduación en Epidemiología, Universidad de São Paulo, São Paulo, Brasil (N. J. Alvis-Zakzuk).

Correspondence: Nelson J. Alvis-Zakzuk, MSc, Departamento de Ciencias de la Salud, Universidad de la Costa, Calle 58 # 55 - 66, Barranguilla, Colombia, Email: nalvis1@cuc.edu.co

Author Contributions: Concept and design: Lozano, N. R. Alvis-Zakzuk, Gastelbondo, Mattar, N. J. Alvis-Zakzuk, Alvis-Guzmán

Acquisition of data: Lozano, Salcedo-Mejía Analysis and interpretation of data: Lozano, Salcedo-Mejía, Zakzuk,

Serrano, Gastelbondo, Mattar, Alvis-Guzmán

Drafting of the article: Lozano, Salcedo-Mejía, Zakzuk, N. R. Alvis-Zakzuk, Moyano-Tamara, Serrano, Gastelbondo, Mattar, N. J. Alvis-Zakzuk, Alvis-Guzmán

Critical Revision of the article for important intellectual content: Lozano, Salcedo-Mejía, Zakzuk, N. R. Alvis-Zakzuk, Moyano-Tamara, Serrano, Gastelbondo, Mattar, Alvis-Guzmán

Statistical analysis: Lozano, Salcedo-Mejía

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