



## Research article

# Impact and evolution of risk factors associated with hospitalization and mortality due to COVID-19 during the six epidemic waves in Mexico

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## ABSTRACT

**Objectives:** This study aims to analyze and compare the main risk factors for hospitalization and deaths due to COVID-19 during the six epidemic waves from February 2020 to June 2023 in Mexico.

**Methods:** First, a descriptive analysis of the risk factors that led to hospitalization and mortality due to COVID-19 was performed. Next, the degree of relationship of each risk factor with hospitalization and death was determined using Cramer's V coefficient. Finally, logistic regression models were applied to estimate the odds ratios of the most statistically significant risk factors for hospitalization and mortality.

**Results:** A direct relationship between age and the possibility of hospitalization and death due to COVID-19 was found. Moreover, the comorbidities most likely to lead to hospitalization and death were pneumonia, hypertension, diabetes, obesity and CKD. It is also remarkable that the second factor of death is endotracheal intubation.

**Conclusion:** The COVID-19 pandemic in Mexico revealed the reality of an epidemiological scenario where infectious diseases and chronic degenerative diseases coexist and interrelate.

## 1. Introduction

Wuhan City in China has been the focus of global attention since December 2019, when the first cases of acute respiratory syndrome caused by a new coronavirus (SARS-CoV-2) were reported [1]. On January 30, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a Public Health Emergency of International Concern and, on March 11, issued a pandemic declaration [2]. Until August 30, 2023, there have been 770,085,713 confirmed cases and 6,956,173 deaths worldwide from this disease [3]. Based on information from the current epidemic in China, it was warned that preexisting noncommunicable diseases (NCDs) and modifiable habits, such as smoking and obesity, increase the vulnerability of COVID-19 patients to becoming seriously ill, which increases the risk of hospitalization and death [4]. A meta-analysis of confirmed COVID-19 cases from China ranked hypertension, diabetes, cardiovascular disease, and respiratory system diseases as the most prevalent NCDs in such cases [5]. Recent studies in European Community

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countries, the United States, and Latin American countries also show that the presence of one or more comorbidities in COVID-19 confirmed cases increases the possibility of hospitalization and death [6–8]. In Mexico, the first case of COVID-19 was confirmed on February 27, 2020. On March 23 of the same year, the health authorities declared this disease a health emergency, calling for social distancing and isolation measures [9]. From February 2, 2020 to June 30, 2023, there are 7,638,518 confirmed cases of COVID-19 and 334,415 deaths due to this disease. COVID-19 vaccination began nationwide in Mexico on December 24, 2020; before this date, the percentage of deaths due to this virus was 12.47% (first epidemic wave) and after vaccination the percentage dropped to 8.55% (second wave), percentages that went down to 0.7% in the last epidemic wave. Previous studies of risk factors for confirmed cases of COVID-19 in Mexico revealed that men were 1.5 times more susceptible to hospitalization than women; people over 50 years old were more prone to hospitalization than younger people. Also, people with hypertension, obesity, and diabetes were more likely to be hospitalized for COVID-19 than people without these comorbidities [10,11]. Regarding mortality from COVID-19, other studies showed that the fatality rate is higher in males than in females and increases with age. Diabetes, hypertension, obesity, immunosuppression, and renal failure also increased the risk of mortality, both in hospitalized and ambulatory patients [12–15]. This study aims to analyze and compare the main risk factors for hospitalization and death due to COVID-19 and their evolution over time. In the period covered by this analysis, from February 27, 2020, to June 30, 2023, six epidemic waves have been identified for confirmed cases since the beginning of the pandemic in Mexico. We expect that this study can assist the nation's health authorities in monitoring and controlling the spread of the epidemic, thereby enabling more efficient health services.

## 2. Methodology

### 2.1. Database

In this study, we used public data from the Dirección General de Epidemiología, an agency of the Secretaría de Salud of the Federal Government of Mexico [16]. The database contains demographic variables such as age, sex, province of residence, etc. It includes the dates on which the patient presented the first symptoms of COVID-19, hospital admission, and death. NCDs such as diabetes, hypertension, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), pneumonia, and other diseases reported by the patient are considered. Habits such as smoking, obesity, and pregnancy are recorded. PCR test results are also recorded. The information indicates whether the patient required hospitalization or was an ambulatory case. In case of hospitalization, whether the patient requires admission to the intensive care unit (ICU) or endotracheal intubation is noted. We analyzed 7,638,518 COVID-19-positive case records from February 27, 2020, to June 30, 2023. This period was divided into the six epidemic waves that have occurred in Mexico. The dates covered by the waves as well as their respective  $n$  numbers of confirmed cases are as follows.

- 1st wave: February 27, 2020–September 23, 2020,  $n = 800,016$ .
- 2nd wave: September 24, 2020–May 1, 2021,  $n = 1,588,514$ .
- 3rd wave: May 2, 2021–November 28, 2021,  $n = 1,552,322$ .
- 4th wave: November 29, 2021–April 16, 2022,  $n = 1,829,235$ .
- 5th wave: April 17, 2022–October 23, 2022,  $n = 1,360,968$ .
- 6th wave: October 24, 2022–June 30, 2023,  $n = 507,463$ .

### 2.2. Statistical analysis

In this paper, the response variables are hospitalization and death, both due to COVID-19, and the explanatory variables are the risk factors, that is, comorbidities such as pneumonia, diabetes, hypertension, CKD, among others, as well as smoking habits or obesity; age and sex of the confirmed cases, and pregnancy in women. As a first step, a detailed descriptive analysis was carried out to obtain the percentages of risk factors for hospitalization and death for each epidemic wave for comparative purposes to know the evolution of the impact of these factors on COVID-19 in México. As a second step, the degree of correlation between the hospitalization and death response variables and the risk factors was determined by applying Cramer's  $V$  coefficient, which is based on the chi-square test for categorical variables. This statistic is calculated by means of the expression:

$$V = \sqrt{\frac{\chi^2}{n(k-1)}} \quad (1)$$

where  $n$  and  $k$  are the numbers of data and variables, respectively. For equation (1), it is stated that.

- $V \in [0, 0.2)$ : minimal relationship between the variables.
- $V \in [0.2, 0.6)$ : moderate relationship.
- $V \in [0.6, 1]$ : strong relationship between the variables.

As a third step we used the multivariate logistic regression model applied to the data of each wave:

$$P(Y) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \dots + \beta_n X_n)}} \quad (2)$$

where  $P(Y)$  is the probability of hospitalization (or death); each  $X_i$  represents a risk factor and  $\beta_i$  is the  $i$ -th regression coefficient. The computing of the coefficients for equation (2), the odds ratios (OR) of the risk factors, and their respective confidence intervals at 95% were obtained using RStudio software, measuring the goodness of fit of the models obtained with their corresponding ROC curves. The logistic regression models for hospitalization had an average area under the ROC curve of 0.822, while for the death variable, the average area under the ROC curve was 0.906.

### 3. Results

#### 3.1. Analysis of risk factors for hospitalization

Table 1 shows the percentages of persons confirmed with COVID-19 hospitalized during the six epidemic waves. The first column on the left lists the risk factors for hospitalization. The ages were divided into groups of 12 years from birth to persons over 60 years old. In the first three waves, there is a direct relationship between age and the percentage of hospitalization. In waves four to six, it is noticeable that the percentages of the first age group are higher than those of the second group; the direct relationship between age and percentage of hospitalization is then given with the last age groups of these waves. Regarding the sex of the person, it can be seen that in the first wave, the percentage of men confirmed with COVID-19 who were hospitalized (15.45%) is higher than the percentage of women hospitalized (9.96%). However, over the waves, the percentages.

become more nearly balanced. Calculating the ratios of hospitalized males to hospitalized females yields the following values for each of the respective waves: {1.6, 1.4, 1.3, 1.2, 0.9, 1}. That is, over the course of the waves, the sex of the individual is not a relevant factor for COVID-19 hospitalization. Concerning comorbidities in hospitalized patients, it is noticeable that as the waves go from the first to the fifth, there is a decrease in the percentages. Then, there is a slight increase in these values as the fifth to the sixth wave passes, but it should be considered that the last wave has the lowest number of confirmed cases. The NCDs that represent the most frequent risk factors for hospitalization are pneumonia, hypertension, diabetes, obesity and CKD (See Fig. 1). On the other hand, patients with COPD represent in the first wave about 1% of those hospitalized, and as the waves progress, these percentages decrease. Immunosuppression and asthma are the last ones in terms of hospitalization percentages. Smokers represented 1.93% of hospitalized patients in the first wave, decreasing to 1.18% in the second wave, and in the rest of the waves, the percentages were less than 1%. Pregnant women comprised, at most, 0.17% (third wave) of hospitalized patients.

#### 3.2. Analysis of risk factors for death

Table 2 shows the percentages of COVID-19 confirmed cases that died during the six epidemic waves. In general, it can be observed that over the course of the waves, the percentages of the risk factors for death decrease from the first to the fifth wave, and then there is a slight increase from the fifth to the sixth wave. However, it can be noted that the percentages of the sixth wave are lower or equal to the percentages of the fourth wave, and it is considered that the last wave has the lowest number of confirmed cases. Similar to the risk factors for hospitalization, we considered groups of 12 years from birth to persons over 60 years old. The age groups most prone to death by COVID-19 are adults aged 48–60 years and over 60 years since they present the highest percentages. From the fourth to the sixth wave, the percentage of death in the first age group is practically double that of the second group. Otherwise, the direct

**Table 1**

Percentages (%) of risk factors that caused hospitalization of patients confirmed by COVID-19, during the six waves.

Risk factor	1st wave	2nd wave	3rd wave	4th wave	5th wave	6th wave
Age (0,12] years	0.27	0.16	0.22	0.22	0.27	0.49
Age (12, 24] years	0.43	0.26	0.39	0.18	0.16	0.21
Age (24,36] years	2.16	1.08	1.25	0.36	0.24	0.39
Age (36,48] years	4.62	2.37	1.89	0.40	0.22	0.35
Age (48,60] years	7.09	4.26	2.19	0.65	0.26	0.52
Age > 60 years	10.84	8.16	3.88	1.85	0.92	2.15
Female sex	9.96	6.75	4.35	1.70	1.05	2.03
Male sex	15.45	9.55	5.49	1.97	1	2.09
Pneumonia	16.71	10.66	6.04	1.75	0.65	1.61
Hypertension	9.29	6.38	3.23	1.35	0.61	1.37
Diabetes	8.17	5.24	2.83	1.1	0.51	1.05
Obesity	5.75	3.18	1.82	0.43	0.16	0.34
CKD	1.28	0.85	0.5	0.33	0.16	0.34
CVD	1.06	0.66	0.35	0.21	0.13	0.33
COPD	0.91	0.54	0.29	0.16	0.1	0.25
Immunosuppression	0.57	0.3	0.18	0.12	0.09	0.19
Asthma	0.56	0.29	0.19	0.07	0.04	0.09
Smoking	1.93	1.18	0.64	0.24	0.12	0.25
Pregnancy	0.16	0.09	0.17	0.1	0.09	0.1

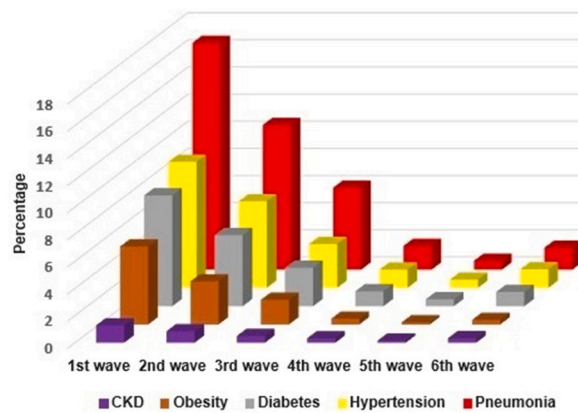


Fig. 1. Percentages of hospitalization due to the main comorbidities during the six waves.

**Table 2**

Percentages (%) of risk factors that caused death in patients confirmed by COVID-19, during the six waves.

Risk factor	1st wave	2nd wave	3rd wave	4th wave	5th wave	6th wave
Age (0,12] years	0.05	0.03	0.02	0.02	0.01	0.02
Age (12, 24] years	0.06	0.04	0.05	0.01	0.005	0.007
Age (24,36] years	0.41	0.24	0.29	0.04	0.01	0.02
Age (36,48] years	1.49	0.84	0.66	0.08	0.02	0.03
Age (48,60] years	3.29	2.04	0.99	0.23	0.04	0.08
Age > 60 years	7.16	5.37	2.26	0.94	0.26	0.53
Female sex	4.46	3.30	1.76	0.53	0.14	0.28
Male sex	8	5.24	2.51	0.79	0.21	0.42
Pneumonia	9.23	6.12	3.02	0.84	0.21	0.53
Hypertension	5.49	3.86	1.75	0.63	0.16	0.32
Diabetes	4.72	3.11	1.5	0.51	0.13	0.26
Obesity	2.93	1.70	0.88	0.18	0.03	0.07
CKD	0.86	0.56	0.29	0.16	0.04	0.09
CVD	0.65	0.40	0.19	0.09	0.03	0.07
COPD	0.59	0.34	0.16	0.08	0.03	0.07
Immunosuppression	0.30	0.17	0.09	0.05	0.02	0.04
Asthma	0.24	0.13	0.08	0.02	0.005	0.01
Smoking	0.97	0.63	0.28	0.1	0.03	0.06
Pregnancy	0.01	0.005	0.01	0.0008	0.0003	0.0002
Admission to ICU	1.31	0.73	0.43	0.11	0.03	0.06
Intubation	3.89	1.37	0.88	0.21	0.05	0.11

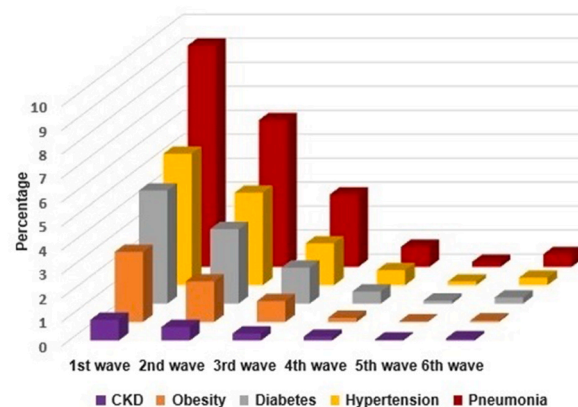


Fig. 2. Percentages of death due to the main comorbidities during the six epidemic waves.

relationship between age and percentage of death is maintained in the rest of the groups in the last three waves. Regarding the sex of the patients, it is observed in the six waves that the percentages of death in men are higher than those in women, although the difference in percentages decreases over the course of the waves. When calculating the ratio of percent male death to percent female death, the values for the six waves are respectively: {1.8, 1.6, 1.4, 1.5, 1.5, 1.5}. That is to say, in the first wave, the number of deaths of men is almost double that of women; the proportions decrease, and then the value of the ratio in the fourth wave (1.5) remains constant until the sixth wave. Concerning comorbidities in confirmed cases who died from COVID-19, the NCDs that represent the most frequent risk factors for death are pneumonia, hypertension, diabetes, obesity and CKD (See Fig. 2). On the other hand, cases with COPD show a percentage of 0.59 % in the first wave, and in the following waves, these percentages are decreasing. Immunosuppression and asthma occupied the last places as diseases that are risk factors for death due to COVID-19. The smoking habit registered a percentage of 0.97 in the first wave, and then the values decreased to 0.03 and 0.06 in the last waves. Pregnancy also presented in all the waves percentages much lower than the 1 %. With respect to patients who were admitted to the intensive care unit (ICU) or required endotracheal intubation, it was observed that the latter presented a

higher percentage of death than the former. When calculating the proportions of the percentages of death of intubated patients among the percentages of death in the ICU, the following ratios are obtained respectively: {3, 1.9, 2, 1.9, 1.7, 1.8}. That is, during the first wave, three people died intubated for each person who died in the ICU; then, from the second to the fourth wave, the number of people who died intubated was almost double the number who died in the ICU. In the fifth and sixth waves, the ratios of intubated to ICU deaths were 1.7 and 1.8, respectively.

### 3.3. Cramer's V statistic

Table 3 shows the Cramer's V coefficients of the hospitalization variable due to COVID-19 about the risk factors considered in the table for the six waves. According to this statistic, pneumonia had a strong relationship with hospitalization during the first three waves and a moderate relationship in the last waves; diabetes and hypertension had a moderate relationship in the first three waves and a minimal relationship in the remaining waves. The other risk factors had little association with hospitalization. Table 4 shows the Cramer's V coefficients of the variable death due to COVID-19 concerning the risk factors. According to this criterion, pneumonia and intubation had a moderate relationship with COVID-19 death during all waves; ICU admission, hypertension, and diabetes had a moderate relationship in the first three waves and a minimal relationship in the remaining waves. The other risk factors had little association with COVID-19 death.

### 3.4. Odds ratios (OR) estimation of hospitalization and death

Fig. 3a) shows the OR of hospitalization for COVID-19 due to the main NCDs during the six waves: CKD, COPD, diabetes, and hypertension. It can be seen that the OR for the comorbidities considered are values greater than 1, indicating that if a person confirmed.

with COVID-19 has any of these NCDs, their chances of being hospitalized is the proportion indicated by their respective OR, relative to the absence of the disease. The range of hospitalization OR values for these diseases is [1.8, 8.6]. Fig. 3b) indicates the OR of death by COVID-19 due to the following risk factors: CKD, COPD, hypertension, and diabetes, as well as ICU admission. These four comorbidities collectively have the range of OR values at [1.83, 3.5]. The last risk factor for death is admission to the ICU. It is notable that in the first three waves, their odds ratios are less than 1, indicating that in those waves, access to the ICU led to a decrease in the chance of death from COVID-19, and although in waves four and five, the odds ratio slightly exceeds the value of 1, in the sixth wave it again decreases in value (OR = 0.93).

## 4. Discussion

The aim of this study was to determine the degree of relationship between hospitalization and death, both due to COVID-19, and the risk factors present in patients confirmed with this virus in Mexico. To the best of our knowledge, we can assure that the present investigation on the risk factors for hospitalization and death by COVID-19 in Mexico constitutes the study that covers the most extended period so far considered: from February 27, 2020, to June 30, 2023, as well as the most significant amount of data used and analyzed: 7,638,518 records of positive cases of COVID-19. As mentioned earlier, dividing the period into six epidemic waves made it possible to show the evolution of the relationship between risk factors and hospitalization and death due to COVID-19, as shown in Tables 1 and 2. Fortunately, the percentages of hospitalized patients and deaths decreased from the first to the fifth wave. Although in

**Table 3**

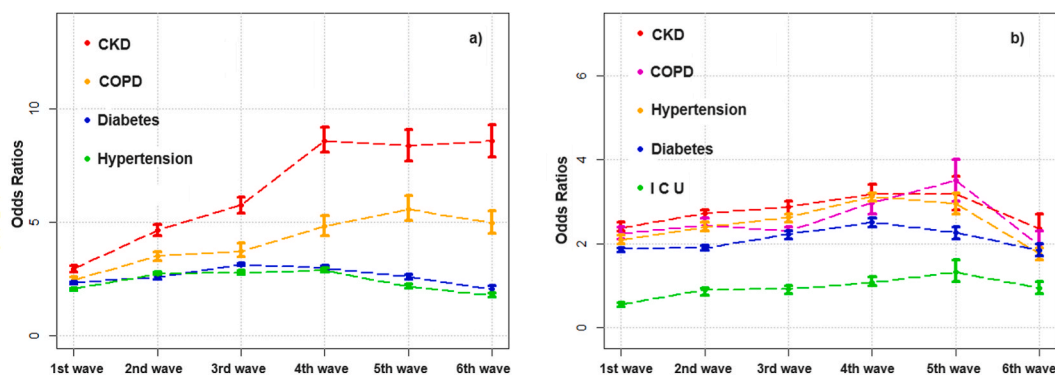
Cramer's V values that measure the correlation between hospitalization and risk factors during the six epidemic waves.

Risk factor	1st wave	2nd wave	3rd wave	4th wave	5th wave	6th wave
Pneumonia	0.683	0.722	0.706	0.564	0.404	0.533
Diabetes	0.269	0.271	0.262	0.198	0.116	0.129
Hypertension	0.254	0.277	0.253	0.193	0.108	0.129
CKD	0.135	0.155	0.16	0.198	0.154	0.173
COPD	0.103	0.11	0.109	0.117	0.102	0.132

**Table 4**

Cramer's V values that measure the correlation between death and risk factors during the six epidemic waves.

Risk factor	1st wave	2nd wave	3rd wave	4th wave	5th wave	6th wave
Pneumonia	0.521	0.557	0.529	0.453	0.317	0.431
Intubation	0.477	0.352	0.403	0.349	0.31	0.302
ICU admission	0.207	0.206	0.228	0.199	0.156	0.173
Hypertension	0.235	0.242	0.219	0.16	0.077	0.085
Diabetes	0.234	0.227	0.217	0.159	0.076	0.086

**Fig. 3.** Odds ratios (OR) and 95 % confidence intervals of the main risk factors a) for hospitalization b) for death.

the sixth wave, there was a slight increase in the values of the percentages concerning the fifth wave, it should be taken into account that the lowest number of confirmed cases of COVID-19 formed the last epidemic wave. The aforementioned suggests that this epidemic disease has been decreasing its lethality, mainly due to the application of vaccines against COVID-19, which took place in Mexico on December 24, 2020. In fact, since the start of COVID-19 vaccination and through March 2022, just over 97 million people have been vaccinated with at least one dose: medical personnel, the elderly, pregnant women, children, youth and teachers. This represents 76.7% of the Mexican population [17]. However, we must be aware that this disease has not become extinct but rather endemic. Regarding the analysis by age groups, this study shows that as a person gets older and is infected by COVID-19, there is a greater chance of being hospitalized or dying from the disease. The most prone age groups considered here are those between 48 and 60 years old and those over 60 years old since they are the ones that registered the highest percentages. Studies from other countries also showed that older people were more prone to be hospitalized or die from COVID-19 [4,7,18]. Thus, it is essential to have adequate health programs for this age range population to address NCDs and infectious diseases such as COVID-19. Concerning the sex of the confirmed cases, it was found that in the first and second waves, the male gender was notably more prone to hospitalization and death from COVID-19. However, during the following waves, it was observed that the proportions between the percentages of hospitalized men and women approached 1. In contrast, the ratios between the percentages of men and women who died remained at 1.5 from the third to the sixth wave. Similar results were obtained in previous studies in countries like the United States, Brazil, and India [7,8,19]. About the comorbidities already present in the confirmed COVID-19 cases, the diseases that caused the most significant possibility of hospitalization and death during the six epidemic waves were pneumonia, hypertension, diabetes, obesity and CKD. Studies from different countries also showed that the comorbidities mentioned above increase the risk of COVID-19 infection with consequent hospitalization and death [4,6,20,21]. On the other hand, immunosuppression and asthma were the comorbidities with the lowest percentages as factors of hospitalization and death in Mexico. As a factor in hospitalization by COVID-19, smoking had a percentage of 1.93% in the first wave (Table 1), and this percentage decreased to values below 1%. As a death factor, its highest percentage was 0.97 % in the first wave (Table 2), and the values decreased in the following waves. The maximum Cramer's V value obtained between smoking and hospitalization is 0.022, while the maximum value between smoking and death is 0.013. Therefore, the above-mentioned suggests that smoking has a shallow relationship with hospitalization or death due to COVID-19 in Mexico. Pregnancy cases in patients confirmed with COVID-19 showed percentages below 1% during the six epidemic waves both as a factor for hospitalization (highest value: 0.17%, in the third wave, Table 1) and for death (highest value: 0.01%, first and third waves, Table 2); this is coherent with the correlation tests since its maximum Cramer's V value for hospitalization is 0.045, while the maximum value for death is 0.028, so it can be assumed that pregnancy is not a relevant risk factor for hospitalization or death due to COVID-19 in Mexico.

The present study takes into consideration the following limitations: The database used consists only of confirmed cases that went to a health center to verify that they had COVID-19. It is likely that there were people infected with this virus but who, being asymptomatic, did not require medical attention and therefore were not reported in the database. On the other hand, it is important to mention that the records of existing comorbidities in the confirmed cases were reported by the patients themselves or their relatives, according to their own clinical experience. Finally, although the descriptive analyses show that the percentages of risk factors for hospitalization and death decrease over the course of the epidemic waves, there is no data or information about the medical recommendations followed by the confirmed cases for the treatment and mitigation of their chronic degenerative diseases.



## 5. Conclusions

This study revealed the relationship between NCDs and a greater possibility of being infected by COVID-19, thus leading to hospitalization and death. Regarding age, the data showed a direct relationship between this variable and being hospitalized or dying. The diseases that caused the most hospitalization and deaths throughout the six waves were pneumonia, hypertension, diabetes, obesity and CKD. Once the patients confirmed for COVID-19 were hospitalized, the data showed that intubation led to more deaths than admission to the ICU. The COVID-19 pandemic in Mexico revealed the existing reality of an epidemiological scenario where infectious and chronic degenerative diseases coexist and are interrelated. Therefore, it is essential to design new strategies to prevent and control NCDs in Mexico and prepare and adapt health services in a pandemic scenario of infectious diseases and NCDs.

## Data availability statement

The raw data required to reproduce the above findings are available to download from [<https://www.gob.mx/salud/documentos/datos-abiertos-152127>]. The processed data required to reproduce the above findings are available to download from [[github.com/FerClark/six-waves-Covid-19-Mexico](https://github.com/FerClark/six-waves-Covid-19-Mexico)].

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## Additional information

No additional information is available for this paper.

## CRediT authorship contribution statement

**Fernando Saldaña-Jiménez:** Writing – review & editing, Writing – original draft, Software, Investigation, Formal analysis, Data curation. **Francisco Javier Almaguer-Martínez:** Validation, Supervision, Project administration, Conceptualization. **Francisco Hernández-Cabrera:** Validation, Supervision, Project administration, Conceptualization. **José Abraham Morales-Vidales:** Software, Investigation, Formal analysis, Data curation. **M. Valentina I. Soto-Rocha:** Writing – review & editing, Supervision, Software. **Otoniel Walle-García:** Writing – review & editing, Supervision, Software.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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