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# Risk of mortality among older adults hospitalized for COVID-19 with and without vaccination in Mexico

## Riesgo de mortalidad en adultos mayores hospitalizados por COVID-19 con y sin vacuna en México

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### Abstract

**Background:** COVID-19 mortality increases exponentially with age, with age being the main predictor of fatal outcomes. In older adults, susceptibility to infections is associated with immunosenescence. The SARS-CoV-2 vaccines approved for emergency use were authorized based on interim analyses of phase III clinical trials, which demonstrated acceptable efficacy and safety in the context of the pandemic. However, the efficacy observed under real-life conditions may differ from theoretical efficacy due to population heterogeneity.
**Objective:** This study aimed to evaluate the risk of COVID-19–related mortality in hospitalized older adults with or without vaccination during the pandemic.
**Material and methods:** A cross-sectional study was designed to evaluate the risk of COVID-19–related mortality in hospitalized older adults with or without vaccination. This study used patient records from a Mexican Social Security Institute (IMSS) hospital in Aguascalientes, Mexico. The study included 1516 adults aged 60 years or older who were hospitalized with COVID-19 between January 2021 and March 2022.
**Results:** The COVID-19 mortality rate in hospitalized older adults was 48.4%. Mortality was 16% higher in men than in women. Multivariate analysis showed that the risk of a vaccinated older adult dying from COVID-19 is 34% lower than that of an unvaccinated older adult (OR = 0.66; 95% CI: 0.52 to 0.85).
**Conclusions:** The study demonstrates the importance of older adults receiving the COVID-19 vaccine to reduce their risk of mortality.

### Resumen

**Introducción:** la mortalidad por COVID-19 se incrementa con la edad, siendo el principal predictor de desenlace fatal. En adultos mayores, la susceptibilidad a infecciones se asocia a la inmunosenescencia. Las vacunas contra SARS-CoV-2 aprobadas para uso de emergencia basaron su autorización en análisis intermedios de ensayos clínicos fase III, que demostraron un perfil de eficacia y seguridad aceptable en pandemia. Sin embargo, la eficacia observada en condiciones reales puede diferir de la teórica.
**Objetivo:** evaluar el riesgo de mortalidad relacionada con COVID-19 en adultos mayores hospitalizados con o sin vacuna durante la pandemia.
**Material y métodos:** estudio transversal comparativo que evaluó el riesgo de mortalidad relacionada por COVID-19 en adultos mayores hospitalizados con o sin vacuna contra la COVID-19. Se utilizaron los expedientes de pacientes de un hospital del IMSS en Aguascalientes, México. El estudio incluyó a 1516 adultos de 60 años o más hospitalizados por COVID-19 entre enero de 2021 y marzo de 2022.
**Resultados:** la tasa de mortalidad por COVID-19 en adultos mayores hospitalizados fue del 48.4%. La mortalidad fue 16% mayor en hombres que en mujeres. El análisis multivariado mostró que el riesgo de que un adulto mayor vacunado muera por COVID-19 es 34 % menor que el de un adulto mayor no vacunado (OR = 0.66; IC95%: 0.52 - 0.85).
**Conclusiones:** el estudio demuestra la importancia de que los adultos mayores reciban la vacuna contra la COVID-19 para reducir el riesgo de mortalidad.

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## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is caused by a highly virulent coronavirus that triggered a pandemic in March 2020 (COVID-19). This disease affects people of all ages worldwide. However, the mortality rate among older adults represents nearly 15% of total fatalities.[1] The risk of COVID-19 mortality in older adults is 6 to 13 times higher than in younger populations.[2] The rapid increase in contagious cases and the high number of COVID-19–related deaths created an urgent need to develop a vaccine to reduce the impact of COVID-19 on the population. Since the World Health Organization (WHO) declared COVID-19 a pandemic, many countries have experienced multiple outbreaks, resulting in sustained transmission and deaths. Several waves of infection have occurred since the onset of the pandemic, each correlating with the emergence and spread of new virus variants. During the first quarter of 2021, the Alpha variant emerged during the second wave, whereas in Mexico the B.1.1.519 variant predominated,[3] followed by the Delta variant in May 2021, which marked the beginning of the third wave.[4] Beginning in November 2021, the Omicron variant became dominant, leading to the fourth wave of the pandemic.[5]

In December 2020, several clinical trials began reporting the safety and efficacy of COVID-19 vaccines.[1,2,6,7,8] By January 2021, COVID-19 had caused approximately 2.5 million deaths worldwide, according to the WHO. In Mexico, by February 2021, the Federal Commission for Protection against Sanitary Risk (COFEPRIS) had granted emergency use authorization for the Pfizer–BioNTech (mRNA), Sinovac (inactivated virus), Oxford–AstraZeneca, Sputnik V, and CanSino (non-replicating viral vector) vaccines. These vaccines were initially administered to high-risk groups, such as healthcare personnel (the first line of defense against COVID-19) and vulnerable populations, including older adults.[9,10] Until the end of 2021, vaccines in Mexico were available only through the Mexican Institute of Social Security (IMSS), the governmental institution that provides social security services to Mexican workers and their families.

Mexico experienced its highest COVID-19 mortality rate during the second wave in 2021, with 1.04 deaths per thousand inhabitants. This rate declined to 0.44 deaths per thousand inhabitants during the third wave in 2022. Among adults aged 60 years and older, the incidence of COVID-19 was 62.8 per thousand inhabitants, and the fatality rate was 21 per 100 adults aged 60 or older who tested positive.[11] Vaccines became available in Mexico following the second wave. Receiving at least one COVID-19 vaccine dose has been associated with a 33% reduction in mortality during hospitalization.[12] Moreover, among adults older than 79 years, vaccine effectiveness against death during the Omicron wave was 15–20% lower than that observed during the Delta wave.[13]

This cross-sectional observational study aimed to evaluate the risk of COVID-19 mortality in older Mexican adults with or without a COVID-19 vaccine.

## Materials and methods

This study is an observational, cross-sectional, retrospective analysis including patients with a positive COVID-19 diagnosis at the General Hospital Zone 1 of the IMSS in Aguascalientes, Mexico. The study population consisted of adults aged 60 years or older with a confirmatory PCR test for COVID-19 who were hospitalized between January 1, 2021, and March 31, 2022, ensuring adequate follow-up. The protocol was reviewed and approved by the Research Ethics Committee (1018) and the Health Research Committee (010), with registration number R-2024-101-102.

## Study Population

Records were obtained for 1,898 patients diagnosed with COVID-19 who had complete information on vaccination status, disease severity, sociodemographic factors, and clinical characteristics. The analysis focused solely on patients who did not undergo endotracheal intubation (indicating similar severity) and who experienced either death or clinical improvement (the dependent variable). This approach minimized potential biases, including selection, survival, and follow-up bias. Intubated patients were excluded because they constituted a very small subgroup ($n$ = 12) with numerous missing data points, which could compromise data integrity, statistical stability, and internal validity. Furthermore, these patients had substantially different clinical characteristics and were less representative of the broader population. Twenty cases were randomly selected and examined to ensure database quality and cleanliness.

An operational manual was created to standardize variables for quality control. Cross-verifications were conducted among variables with related information; for example, if an individual was recorded as vaccinated, the vaccine type was verified to ensure data accuracy. These measures improved data quality and enhanced the validity of comparisons.

The final population with complete and valid information consisted of 1516 patients. The following sociodemographic and clinical variables were analyzed: sex, age, occupation, smoking status, and comorbidities (high blood pressure [HBP], diabetes mellitus [DM], chronic obstructive pulmonary disease [COPD], cardiovascular disease,

obesity, chronic kidney disease [CKD], immunosuppression, asthma, and neurological disease). Variables related to COVID-19 and vaccination were also included, such as the predominant COVID-19 variant, cases recorded per quarter, vaccination status, number of doses administered, and vaccine brand. COVID-19 variants were categorized into Alpha–Beta/Gamma, B.1.1.519, Delta, and Omicron, corresponding to the periods during which each variant predominated in Mexico. Vaccine doses were categorized as none (not vaccinated), one dose (partially vaccinated), or two doses (fully vaccinated).

Sociodemographic, clinical, and laboratory information for participants meeting the inclusion criteria was obtained from the Family Medicine Information System via the IMSS digital medical record. All participant data were anonymized through a dissociation procedure to prevent any association with personal identifiers and ensure confidentiality.

## Statistical Analysis

Descriptive analyses were performed using frequencies and percentages, as all variables were categorical. In the bivariate analysis, associations between variables were evaluated using the Chi-square test, with statistical significance defined as a *p*-value < 0.05. A polychoric correlation analysis with 95% confidence intervals (Rho ± 1.96 × S.E.) was also conducted. This correlation analysis assessed redundancy among study variables, helping to address multicollinearity that could bias regression estimator consistency.

The association between mortality (yes/no) and COVID-19 vaccination (yes/no) was evaluated using a parsimonious multivariate logistic regression model, adjusted for confounding variables identified through univariate, bivariate, and correlational analyses. Adjusted variables included sociodemographic characteristics, comorbidities, and COVID-19–related and vaccine-related factors. Model validity was assessed using the link test for correct specification, the Hosmer-Lemeshow test for calibration of observed versus expected outcomes, goodness-of-fit criteria using Akaike (AIC) and Bayesian (BIC) information criteria, and discrimination measured by the area under the curve (AUC).

All statistical analyses were conducted in Stata version 18 (Stata Corporation, College Station, Texas, USA).

## Results

The study population consisted of 1516 patients who met the inclusion criteria: being 60 years of age or older and having a confirmatory PCR test for COVID-19. The lethality rate among hospitalized COVID-19 patients was 48.4%.

When comparing patients who died with those who survived, mortality was 16% higher in men than in women. Differences in mortality of 2.8% were observed in patients aged 70–79 years and 3.9% in those aged 80 years or older. Mortality was also 3.5% higher among patients with immunosuppression. Among patients with COPD, obesity, and CKD, survivors predominated, with differences of 7.4%, 0.5%, and 3.3%, respectively. Table I presents the characteristics of patients who died and those who survived, along with the statistical significance of comparisons between the two groups.

Comparing the COVID-19-related characteristics of patients who died and those who survived revealed a 12.5% higher mortality rate during the first quarter, dominated by the B.1.1.519 variant. Additionally, an 11% higher mortality rate was observed in patients without vaccine doses. Overall, unvaccinated patients who died represented 33.7% of the total study population. Table II illustrates the statistical significance of comparing these characteristics and mortality.

Polychoric correlational analysis shows that mortality is negative related with female sex (Rho= -0.14; [95%CI, -0.22 to -0.06]), COPD (Rho= -0.21; [95%CI, -0.30 to -0.11]), cardiovascular disease (Rho= -0.17; [IC95%, -0.28 to -0.07]), CKD (Rho= -0.13; [95%CI, -0.24 to -0.02]), COVID-19 vaccination (Rho= -0.15; [95%CI, -0.26 to -0.11]) and others factors like COVID variants, schedule vaccination and quarterly developed. Figure 1 shows all results with a 5% statistical significance level.

The final multivariate logistic regression model included confounding variables that showed statistical significance in the bivariate analysis, excluding those that did not contribute to a good model fit.

The COVID-19 vaccine was found to protect against COVID-19 mortality, with an odds ratio (OR) of 0.66 [95%CI, 0.52 to 0.85]. This result shows that older adults who received the COVID-19 vaccine have a 34% lower risk of dying compared to those who did not receive the vaccine, regardless of the confounding variables age, sex, COPD, immunosuppression, HBP, and quarter. Additionally, a lower risk of mortality was observed in women, with an OR of 0.69 [95%CI, 0.56 to 0.86] compared to men. An increase in age presents a risk factor of 36% for those older than 70 (OR = 1.36, [95% CI, 1.07 to 1.72]) and 63% for those older than 80 (OR = 1.63, [95%CI, 1.23 to 2.16]) compared to individuals younger than 70. Comorbidities, such as immunosuppression, and HBP were identified as risk factors, with odds ratios (ORs) of 4.32 [95%CI, 2.17 to 8.61] and 1.31 [95%CI, 1.05 to 1.64], respectively. Additionally, Hos-

**Table I** Characteristics of older adults hospitalized for COVID-19

| Patient characteristics | Total *n* = 1,516 (100) *n* (%) | Death *n* = 734 (48.4) *n* (%) | Survived *n* = 782 (51.6) *n* (%) | Chi$^2$ *p* value |
|---|---|---|---|---|
| Sex | | | | |
| Men | 810 (53.4) | 426 (58.0) | 384 (49.1) | 0.001 |
| Female | 706 (46.6) | 308 (42.0) | 398 (50.9) | |
| Age | | | | |
| 60 to 69 | 633 (41.8) | 281 (38.3) | 352 (45.0) | 0.015 |
| 70 to 79 | 552 (36.4) | 278 (37.9) | 274 (35.1) | |
| > 80 | 331 (21.8) | 175 (23.8) | 156 (19.9) | |
| Occupation | | | | |
| Unemployed | 47 (3.1) | 22 (3.0) | 25 (3.2) | NS |
| Housework | 398 (26.2) | 176 (23.7) | 224 (28.6) | |
| Retired | 248 (16.4) | 130 (17.3) | 121 (15.5) | |
| Other occupations | 823 (54.3) | 416 (56.0) | 412 (52.7) | |
| Smoking | | | | |
| No | 1241 (81.9) | 606 (82.6) | 635 (81.2) | NS |
| Yes | 275 (18.1) | 128 (17.4) | 147 (18.8) | |
| Comorbidities | | | | |
| HBP | 911 (60.1) | 456 (62.1) | 455 (58.2) | NS |
| DM | 650 (42.9) | 317 (43.2) | 333 (42.6) | NS |
| COPD | 217 (14.3) | 77 (10.5) | 140 (17.9) | < 0.001 |
| Obesity | 171 (11.3) | 81 (11.0) | 90 (11.5) | 0.002 |
| Cardiovascular disease | 156 (10.3) | 57 (7.8) | 99 (12.7) | NS |
| CKD | 133 (8.8) | 52 (7.1) | 81 (10.4) | 0.02 |
| Immunosuppression | 49 (3.2) | 37 (5.0) | 12 (1.5) | < 0.001 |
| Asthma | 27 (1.8) | 12 (1.6) | 15 (1.9) | NS |
| Neurological disease | 12 (0.8) | 8 (1.1) | 4 (0.5) | NS |

Abbreviations: CKD, chronic kidney disease; COPD, Chronic obstructive pulmonary disease; DM, diabetes mellitus; HBP, high blood pressure; NS, non-significant

mer and Lemeshow's test yielded a *p*-value of 0.44, AIC = 2003.63, BIC = 2067.52, and ROC-AUC = 0.66, indicating a good-fitting model. Figure 2 presents the results of the mortality association with the COVID-19 vaccine, along with the confounding variables.

## Discussion

The primary objective of our study was to evaluate the strength of the association between the administration of the anti-COVID vaccine and mortality among older adults. Our main findings revealed that mortality among vaccinated individuals was significantly lower compared to the unvaccinated group; specifically, older adults who received the vaccine were 34% less likely to die than those who did not.

In the descriptive results, the proportion of elderly individuals hospitalized for COVID-19 was similar for men and women; however, a slight predominance of men was observed (52%), aligning with the proportion Cegolon *et al.*[14] reported Seppälä *et al*. also noted a similar outcome for both sexes, but with a slight majority of women, as they reported 53%.[15] These findings contrast those reported by Navarrete Mejía *et al*., who found that twice as many men were affected by COVID-19 compared to women.[16]

In the age group variable, this study observed a higher frequency in the 60 to 69 age group (41.5%). Seppälä, *et al.* report a predominance in the 65 to 79 age group (76%).[15] Weigert *et al*. report 80% in the 60 to 79 age group.[13]

HBP was the most frequently reported comorbidity, at a rate of just over 60%, followed by DM at 40%. Other stu-

**Table II** Characteristics of COVID-19 and the COVID-19 vaccine

| | Total *n* = 1,516 (100) *n* (%) | Death *n* = 734 (48.4) *n* (%) | Survived *n* = 782 (51.6) *n* (%) | *p* value |
|---|---|---|---|---|
| COVID-19 vaccination, yes | 547 (36.1) | 223 (30.4) | 324 (41.4) | 0.001 |
| COVID variants | | | | |
| • B.1.1.519 | 547 (36.1) | 279 (38.0) | 268 (34.3) | NS |
| • Delta | 613 (40.4) | 294 (40.1) | 319 (40.8) | |
| • Omicron | 356 (23.5) | 161 (21.9) | 195 (24.9) | |
| Cases registered by quarter | | | | |
| • 2021 (Q1) | 365 (24.1) | 224 (30.5) | 141 (18.0) | 0.001 |
| • 2021 (Q2) | 182 (12.0) | 55 (7.5) | 127 (16.2) | |
| • 2021 (Q3) | 287 (18.9) | 143 (19.5) | 144 (18.4) | |
| • 2021 (Q4) | 326 (21.5) | 151 (20.6) | 175 (22.4) | |
| • 2022 (Q1) | 356 (23.5) | 161 (21.9) | 195 (24.9) | |
| Vaccination schedule | | | | |
| • Not vaccinated | 969 (63.9) | 511 (69.6) | 458 (58.6) | 0.001 |
| • Partially vaccinated | 113 (7.5) | 43 (5.9) | 70 (9.0) | |
| • Fully vaccinated | 434 (28.6) | 180 (24.5) | 254 (32.4) | |
| Brand of COVID-19 vaccine | | | | |
| • Pfizer- BioNTech | 123 (8.1) | 48 (6.5) | 75 (9.6) | 0.001 |
| • Sinovac | 228 (15.0) | 97 (13.2) | 131 (16.8) | |
| • Astra Zeneca | 75 (4.9) | 29 (4.0) | 46 (5.9) | |
| • Others | 11 (0.7) | 4 (0.5) | 7 (0.9) | |
| • Unknown | 110 (7.3) | 45 (6.1) | 65 (8.3) | |

dies also report a higher frequency of hypertension, but with lower percentages, around 30% and 20% for DM.[14] In the Hippisley-Cox study, a significant percentage of patients with DM was found (73%). These findings are attributed to the global prevalence of both diseases.[16,17]

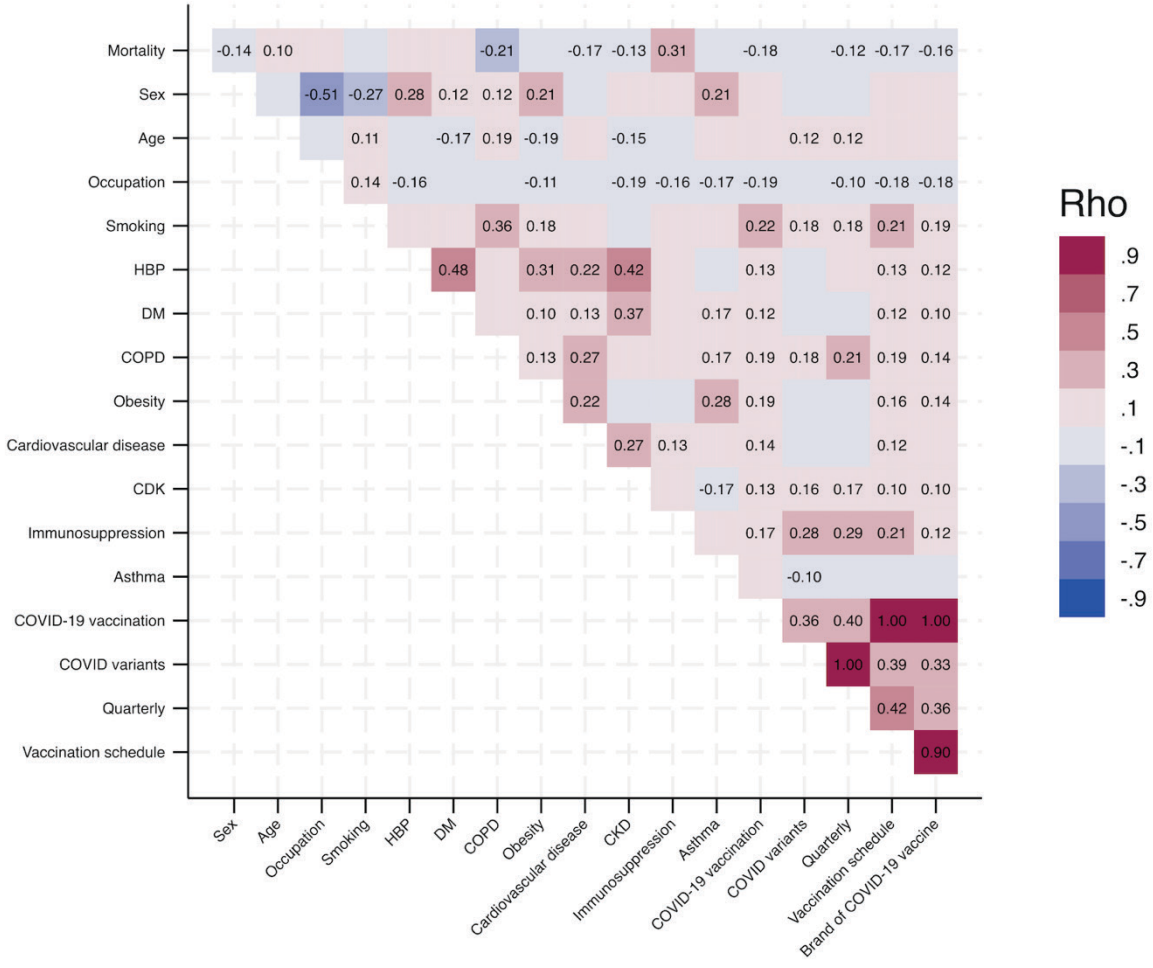
Regarding mortality, this work reported a mortality rate of 33.7% when the vaccine was not applied. These results differ from those reported by López *et al*., who noted only 13.3% mortality among unvaccinated older adults.[18] The data are also significantly different from those reported by Cegolon *et al*., where only 4.3% of individuals who did not receive the vaccine died.[14] This variability in mortality rates can be attributed to the vaccine's effectiveness.[1,2]

Stratification by vaccine dose reveals a decrease in the proportion of mortality. Specifically, those with an incomplete vaccination schedule have a mortality rate of 5.3%, while Cegolon *et al*. report that mortality in this specific case is 0.9%. There is consistency in the observation that the more vaccine doses a patient has, the lower the mortality rate.[14]

In this study population, being vaccinated resulted in a protective effect of 34%. A previous study reported that individuals over the age of 60 who had not received the vaccine were 42 times more likely to die. When considering the number of doses, those with a complete vaccination schedule were 30% less likely to die. The authors indicate that individuals without a complete vaccination schedule are twice as likely to die compared to those who have one. The existing evidence is also widely documented globally.[19] Bajči *et al*. found in another study that those who are not vaccinated are twice as likely to die.[20]

One finding by Johnson *et al*. was that, depending on the subtype of COVID-19, the risk of mortality varied from 2.8 to 8.3 times more likely to die when not vaccinated in adults over 80 years of age.[21] Meanwhile, in another study conducted by Cruz *et al*., they reported a mortality rate of 18.8% in an adult population over 80 years of age who were vaccinated.[22] A study conducted in Brazil reported that patients aged 70 to 79 who had been vaccinated experienced a protective effect of 0.33, which translates to a 77% lower chance of dying. In the 80 to 89 age group, the protective effect was 0.27, while those aged 90 and over had a protective effect of 0.25.[23] A study in Mexico found that unvacci-

**Figure 1** Polychoric matrix correlation of study factors. CKD, chronic kidney disease; COPD, Chronic obstructive pulmonary disease; DM, diabetes mellitus; HBP, high blood pressure



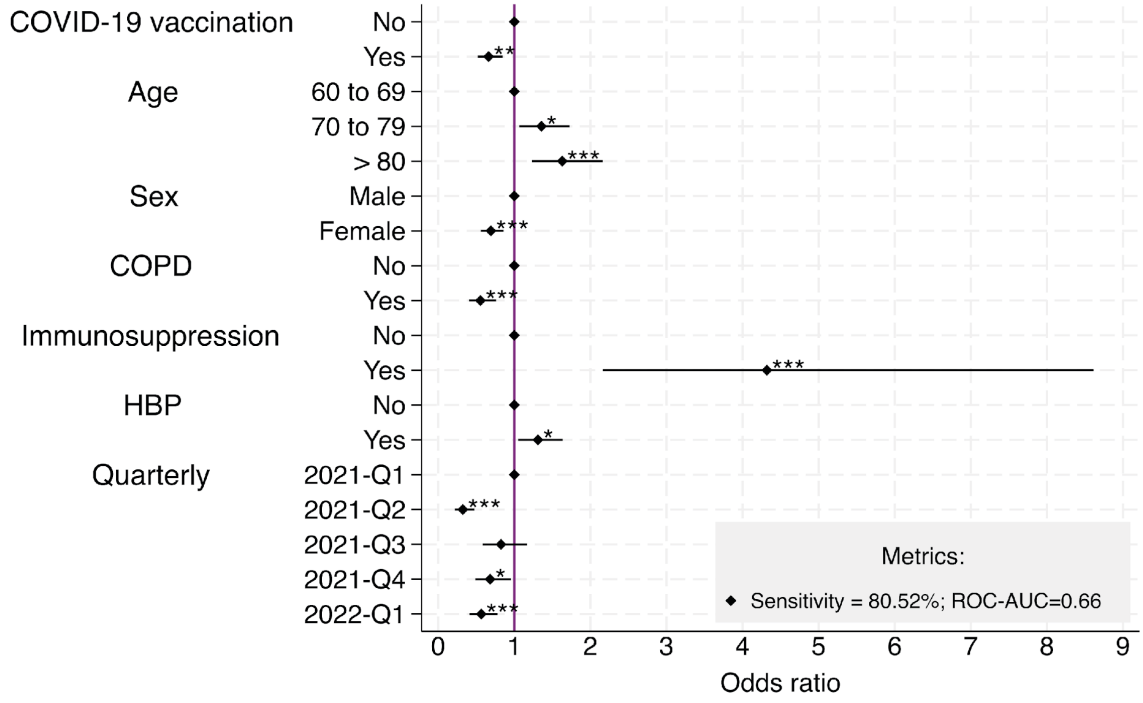

nated patients over 65 were 2.5 times more likely to die.[24] Furthermore, COVID-19 vaccines administered to patients over 65 have been shown to reduce the incidence of pleural complications, particularly pneumothorax. In addition, mortality in older adults who were not vaccinated was 89%.[25]

Our results align with previous studies. Older adults with a history of receiving at least two doses of the anti-COVID vaccine had a 12% lower risk of dying, while those who received three doses had an 18% lower risk compared to those who received no doses.([21]) A study conducted in Israel reported a mortality rate of 13.58% for unvaccinated older adults, whereas the rate for vaccinated individuals was 1.58%, which is significantly lower, further supporting our findings.[26] Even in a study conducted globally in 164 countries, a 10% increase in vaccination was associated with an 18.1% decrease in mortality after 6 months and a 16.8% decrease after 12 months; in addition, a 10% increase in booster vaccination rates was associated with a 33.1% decrease in COVID-19 mortality.[27] Research has also been conducted on mortality rates in Europe. For instance, Agostini *et al*. reported that in 26 countries across the continent, a 10-percentage point increase in the vaccination rate per 100 inhabitants was associated with a 5.08 decrease in deaths from COVID-19 per million inhabitants.[28]

As mentioned, regardless of the variability in the reduction of mortality risk associated with the application of the anti-COVID-19 vaccine, this action is of the utmost importance, especially in older adults.[29,30,31]

This study has both, strengths and limitations. The strengths include the sample size, which allowed for the collection of a representative sample of older adults aged 60 and above. Among the limitations, the use of clinical records for data extraction stands out. Additionally, the study was conducted in a secondary-level hospital in Aguascalientes, which suggests the need for further studies in other cities and/or contexts within Mexico to enhance generalizability.

**Figure 2** Risk of COVID-19 Mortality among Vaccinated Older Adults. COPD, Chronic obstructive pulmonary disease; HBP, high blood pressure




***$p < 0.001$; **$p < 0.01$; *$p < 0.05$

## Conclusions

This study found that the percentage lethality rate due to COVID-19 among hospitalized older adults at the Mexican Institute of Social Security (Mexico's public health system) was 48.4%. The research indicated that receiving the anti-COVID-19 vaccine is a protective factor against mortality, revealing a negative association with an odds ratio of 0.66 (95%CI, 0.52 to 0.85). Our results suggest that older adults who receive the vaccine have a 34% lower risk of dying from COVID-19 compared to those who are unvaccinated, a result obtained after adjusting for age, sex, COPD, cardiovascular diseases, and immunosuppression.

**Conflict of interest disclosure:** The authors have completed and sent the Spanish-translated form of the Declaration for Potential Conflicts of Interest of the International Committee of Medical Journal Editors, and no conflicts of interest were reported related to this article.

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