Sociodemographic inequalities and excess non-COVID-19 mortality during the COVID-19 pandemic: A data-driven analysis of 1,069,174 death certificates in Mexico

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ABSTRACT (287 WORDS)

BACKGROUND: In 2020, Mexico experienced one of the highest rates of excess mortality globally. However, the extent to which non-COVID deaths contributed to excess mortality, its regional characterization, and the association between municipal- and individual-level sociodemographic inequality has not been characterized.

METHODS: We conducted a retrospective municipal and individual-level study using data from 1,069,174 death certificates to analyze mortality related to COVID-19 and to non-COVID-19 causes using ICD-10 codes. Excess mortality was estimated as the increase in cause-specific mortality in 2020 compared to the average of 2015-2019, disaggregated by primary cause of death, death setting (in-hospital and out-of-hospital) and geographical location. Correlates of individual and municipal non-COVID-19 mortality were assessed using mixed effects logistic regression and negative binomial regression models, respectively.

RESULTS: We identified a 51% higher mortality rate (276.11 deaths per 100,000 inhabitants) compared to the 2015-2019 average period, largely attributable to COVID-19 (76.1% of cases). Non-COVID-19 causes comprised one-fifth of excess deaths, with acute myocardial infarction (46.7 deaths per 100,000 inhabitants) and type 2 diabetes (34.84 deaths per 100,000 inhabitants) as the two leading non-COVID-19 causes of excess mortality. COVID-19 deaths occurred primarily in-hospital, while excess non-COVID-19 deaths decreased in this setting (-48.10%) and increased out-of-hospital (+80.96%) compared to the 2015-2019 average period. Municipal-level predictors of non-COVID-19 excess mortality included levels of social security coverage, higher rates of COVID-19 hospitalization, and social marginalization. At the individual level, lower educational attainment, blue collar employment, and lack of medical care assistance prior to death were associated with non-COVID-19 mortality during 2020.

CONCLUSION: Non-COVID-19 causes of death, largely chronic cardiometabolic conditions, comprised up to one-fifth of excess deaths in Mexico during 2020. Non-COVID-19 excess

deaths occurred disproportionately out-of-hospital and were associated with both individual- and municipal-level sociodemographic inequalities.

Keywords: Excess mortality; inequalities; social lag; COVID-19; Mexico

KEY MESSAGES

- Mexico experienced one of the highest rates of excess mortality in Latin America following onset of the COVID-19 pandemic, but the extent to which non-COVID-19 deaths contributed to excess mortality has not yet been characterized.

- We conducted a retrospective, municipal and individual-level study using data from 1,069,174 death certificates to estimate mortality related to COVID-19 and to non-COVID-19 causes using ICD-10 codes in 2020 compared to 2015-2019.

- There was a 51% higher mortality rate in 2020 compared to the 2015-2019 average, largely attributable to COVID-19 deaths (76.1% of cases), which occurred primarily in-hospital; conversely, one-fifth of excess deaths in Mexico in 2020 were attributable to non-COVID-19 causes, largely attributable to cardiometabolic conditions, which occurred primarily out-of-hospital.

- Southern regions and marginalized communities in Mexico carried a disproportionate burden of excess mortality; municipal-level correlates of these excess deaths included lower healthcare coverage, whereas individual-level factors correlated to non-COVID-19 mortality included lower educational attainment, blue collar employment, and lack of medical care assistance prior to death.

- Excess mortality in Mexico in 2020 was attributed to both COVID-19 and non-COVID-19 causes, likely reflecting a complex interplay between a fragmented and under-resourced health system, strained hospital capacity, and sociodemographic inequalities further unmasked by the pandemic.

INTRODUCTION

Over 6 million deaths attributable to COVID-19 have been reported globally since the onset of the pandemic in early 2020 [1]. Beyond this devastating death toll, there is increasing recognition of the widespread disruption of the pandemic on healthcare services, with a far-reaching impact on the care of non-COVID-19 conditions [2]. Excess mortality has been proposed as a key indicator that captures both deaths caused by COVID-19 and indirect deaths attributed to the pandemic more broadly, due to interruption in routine care of chronic conditions [3,4]. Notably, many low-and-middle-income countries (LMICs), particularly in Latin America, were vulnerable to the direct and indirect effects of the COVID-19 pandemic due to chronic underinvestment in public healthcare [5]. Though several reports have estimated that rates of excess mortality were disproportionately higher in LMICs following the onset of the COVID-19 pandemic, there is limited insight regarding non-COVID-19 deaths and their contribution to the reported rates of excess mortality in Latin America [6].

Mexico is of particular interest given that it ranks as one of the countries with the highest rates of excess mortality in the Latin American region following onset of the COVID-19 pandemic. [7]. A confluence of health and sociodemographic inequalities that predated the COVID-19 pandemic, a high burden of chronic cardiometabolic conditions, and a fragmented healthcare system all contributed to a high and disproportionate burden of excess mortality among marginalized communities [5,8]. A descriptive assessment performed in Mexico showed that chronic cardiometabolic conditions, which are highly prevalent among communities of low socioeconomic status, were the main causes of death independently of registered COVID-19 deaths in Mexico during 2020 [9]. However, whether hospital saturation had ripple effects on out-of-hospital excess mortality, particularly for highly prevalent chronic health conditions across different vulnerable regions, has not yet been characterized. Hence, there is a need to comprehensively assess the extent to which individual and municipal-wide level

sociodemographic inequalities impacted excess mortality to further guide health policies to strengthen existing systems and mitigate ongoing health disparities.

In this study, we sought to: 1) estimate the age-adjusted rates of cause-specific excess mortality due to COVID-19 and non-COVID-19 deaths in 2020 compared to the 2015-2019 period, stratified by in-hospital and out-of-hospital setting; 2) evaluate the geographical distribution of cause-specific excess mortality in Mexico in 2020; and 3) characterize the association between municipal- and individual-level sociodemographic inequality measures and non-COVID-19- related excess mortality.

METHODS

Study design and data sources

Based on the work by Lima et al, we conducted a retrospective municipal and individual-level study using national mortality records from 2015-2019 compared to 2020 [10]. Death certificate records of individuals living in Mexico were collected by the National Institute of Statistics and Geography (INEGI). Briefly, INEGI generates annual mortality statistics from death certificates and vital sociodemographic characteristics issued by the Ministry of Health, which includes the primary cause of death in accordance with the 10th version of the International Statistical Classification of Diseases and Related Health Problems (ICD-10, [11]). Complete methodology of the death certification process, validation, and collected variables are available in **Supplementary Material**.

Variables and definitions

Outcome variables

Cause-specific excess mortality was centered on two primary outcomes: deaths due to COVID-19 and deaths related to non-COVID-19 causes. Overall excess mortality was the sum of excess mortality due to non-COVID-19 causes and all registered COVID-19 deaths.

I. COVID-19 deaths

Deaths attributable to COVID-19 were defined based on the following ICD-10 codes: U071 (identified SARS-CoV-2), U072 (suspected SARS-CoV-2), and deaths after April-2020 classified as J00-J99 (respiratory deaths). This aggregation of COVID-19 deaths considers inadequate registration of COVID-19 cases across 2020, as there is an unknown number of deaths which could have been classified with unspecified respiratory diseases in the early stages of the pandemic due to limited SARS-CoV-2 testing capacity in Mexico [12].

II. Non-COVID-19 cause-specific mortality

All other causes of death were classified as non-COVID-19 related deaths and were coded using the 2020 Mexican list of mortality, which includes 436 specific causes of death [13]. To simplify result presentation, we only display the first 10 cause-specific deaths in the main results, with the full list provided in **Supplementary material**.

Excess Mortality Estimation

According to the approach proposed by Karlinsky and Kobak, we estimated excess mortality as the difference between average deaths during the 2015-2019 period compared to deaths registered during 2020 [14]. We used average deaths for two reasons: 1) the use of average deaths is a simple approach shown to be a reliable assessment based on sensitivity analyses estimations, and 2) given that we are estimating 436 specific causes of death, predictive methods based on generalized linear models may overestimate the standard error for low-frequency causes [9]. Excess deaths were standardized to age-adjusted rates per 100,000 population with age structures by state, municipalities, and regions per 5-year increments using population projections provided by the National Population Council (CONAPO). Percent increase in 2020 compared to 2015-2019 was also used as a proxy of excess mortality.

Stratification by setting of death

We hypothesized that the COVID-19 pandemic posed a significant burden on in-hospital care, which may have influenced increases in excess mortality, particularly for non-COVID-19 related deaths. To evaluate this hypothesis, we stratified excess mortality according to

whether the death occurred out-of-hospital or in-hospital, as registered in death certificates. Out-of-hospital deaths were defined accordingly if the death was not registered in a hospital setting or if they were coded as occurring at the deceased person's home or elsewhere (i.e., in the streets in some instances). Deaths with an unspecified setting were excluded across all the analysis.

Marginalization Index

To quantify the impact of municipal sociodemographic inequalities on excess mortality, we used the 2020 municipal social lag index (SLI) estimated by the National Council for Evaluation of Social Development Policy (CONEVAL, [15]). Since we intended to evaluate social inequalities independently from urbanization and centralized health services, we used residuals of linearly regressed mean urban population density (MUPD) and hospital beds per 100,000 inhabitants using data extracted from CONEVAL to fit an adjusted municipal SLI (aSLI). We then categorized municipalities into four aSLI categories (Low-aSLI, Moderate-aSLI, High-aSLI, and Very-High aSLI) based on the Dalenius & Hodges method (**Supplementary Material**).

Municipal-level correlates of excess mortality

We included the percentage of the population without healthcare coverage and the hospital occupancy due to COVID-19 inpatients as municipal-level factors related to excess mortality. Healthcare coverage was obtained from 2020 CONEVAL estimations. To estimate a surrogate of hospital occupancy, we used the number of hospitalizations with confirmed COVID-19 from the SINAVE dataset collected by the General Directorate of Epidemiology (*DGE*) of the Mexican Ministry of Health, which includes reports of daily updated suspected COVID-19 cases [16]. Complete methodology, the protocol of testing, and the variables included are available in **Supplementary Material**.

Statistical analysis

To visualize differences in deaths over time in 2020 compared with the 2015-2019 period, we first plotted excess mortality per 100,000 inhabitants by month of occurrence, stratified by COVID-19 and non-COVID-19 causes. We then disaggregated excess mortality rates due to COVID-19 or non-COVID-19 causes by state and municipality. Next, to visualize whether the proportion of age-adjusted excess mortality in each municipality increased due to COVID-19 or non-COVID-19 causes we used choropleth maps classified using the quantile method with the *biscale* R package. We further visualized the relationship between excess mortality and aSLI using the same method. The median value for the estimated age-adjusted excess mortality and the aSLI were considered as the cut-off threshold.

Municipal-level factors associated with excess mortality

Next, we evaluated the impact of municipal characteristics on increased risk of age-adjusted excess mortality, using negative binomial regression models to obtain incidence rate ratios (IRRs) **(Supplementary Material)**. Models were adjusted for municipal male-to-female death ratio, education percentage, access to medical assistance, and urbanization (to adjust for residual covariance). We also calculated the ratio of out-of-hospital to in-hospital deaths, which was also adjusted for the above outlined covariates [17]. IRRs were plotted using the *jtools* R Package.

Individual-level factors related with non-COVID-19 mortality

To identify individual-level factors associated with the probability of death attributable to non-COVID-19 causes as compared to COVID-19, we fitted hierarchical random-effects logistic regression models, which included individual and municipal-level variables **(Supplementary Material)**. Individual-level variables included sex, education, self-reported indigenous identity, work occupation, access to medical assistance prior to death, and social security coverage. We perform a municipal-level adjustment that included living in municipalities with low-hospital bed occupancy (<1 bed per 100,000 inhabitants), and municipal aSLI categories. For this model, we used the municipality of death occurrence as a random intercept to account for

intermunicipal variability in death registration in the model and to establish a hierarchical relationship between individual and municipal-level variables. All analyses were performed using R software (Version 4.1.2).

RESULTS

Overall and cause-specific excess mortality in Mexico during 2020

We identified 1,069,174 deaths in Mexico during 2020, compared to 686,567 average deaths in 2015-2019. We estimated an age-adjusted mortality rate of 833.5 deaths per 100,000 inhabitants for 2020, with an estimated age-adjusted excess mortality of 282.41 deaths per 100,000 inhabitants; this represents a 51% increase in mortality compared with the average age-adjusted mortality rates in 2015-2019 (551.09 per 100,000 inhabitants). Peak excess mortality during 2020 was observed during the May to June period. Approximately 76.1% of excess deaths were attributable to confirmed or suspected COVID-19, while 23.9% were attributable to non-COVID-19 causes. The main contributors of excess mortality were suspected or confirmed COVID-19 deaths (199.26 per 100,000 inhabitants). The five leading causes of non-COVID-19 excess mortality were acute myocardial infarction (46.7 deaths per 100,000 inhabitants), type 2 diabetes (34.84 deaths per 100,000 inhabitants), violent assaults (3.45 deaths per 100,000 inhabitants), hypertensive heart disease (3.13 deaths per 100,000 inhabitants), and essential arterial hypertension (2.9 deaths per 100,000 inhabitants). All excess deaths were recorded after April 2020, with a steep increase after this period for COVID-19, acute myocardial infarction, and type 2 diabetes related deaths (**Figure 1**).

Excess mortality according to in-hospital vs. out-of-hospital death

When stratified by the setting of death, we estimated an in-hospital excess mortality rate of 112.47 deaths per 100,000 inhabitants and an out-of-hospital excess mortality rate of 162.54 deaths per 100,000 inhabitants; this represents an increase of 45.4% and 55.5% of in-hospital and out-of-hospital deaths, respectively, compared to the average of 2015-2019. When stratified by the specific cause of death, we observed that excess in-hospital mortality rates

were primarily attributable to COVID-19 deaths, while there was a decrease for in-hospital non-COVID-19 related deaths after March 2020. An estimated 93.2% of all out-of-hospital excess mortality was attributable to non-COVID-19 causes, while only 6.79% were attributable to COVID-19 deaths. Excess deaths attributable to COVID-19 occurred predominantly in the in-hospital setting (83.6%), while most non-COVID-19 deaths occurred largely out-of-hospital (66.9%). Among the 10 leading causes of excess mortality, acute myocardial infarction and type 2 diabetes decreased in-hospital but increased in out-of-hospital after April-2020 (**Figure 2**).

Regional state and municipal-level heterogeneity in COVID-19 and non-COVID-19 excess mortality

When COVID-19 and non-COVID-19 excess mortality was stratified at the state level, Mexico City, Baja California, and Chihuahua displayed the highest COVID-19 age-adjusted excess mortality rate, whereas Chihuahua, Mexico City, and Chiapas had the highest non-COVID-19 excess mortality rates. There was an unequal distribution of non-COVID-19 age-adjusted excess mortality at the state level, with the southern states of Chiapas, Oaxaca, and Michoacan having the highest rates of non-COVID-19 related excess mortality (**Supplementary Figure 1**). Further stratification revealed a geographical aggregation of non-COVID-19 deaths caused by acute myocardial infarction, type 2 diabetes, essential arterial hypertension, and unspecified strokes clustered in the southern states of Mexico (**Supplementary Figure 2**). We also evaluated age-adjusted excess mortality at the municipal level to obtain a more detailed overview of these geographical differences. Excess mortality had a heterogenous geographical distribution and correlated with the social lag index in municipalities in Mexico with higher excess mortality due to both COVID-19 and non-COVID-19 causes (**Supplementary Figure 5**). At the state level, the highest decrease in non-COVID-19 in-hospital deaths was seen in Oaxaca, Yucatán, and Veracruz, whereas the highest

proportion of non-COVID-19 out-of-hospital deaths were observed in Tlaxcala, Yucatan, and Colima (**Supplementary Figure 4**).

Municipal level impact of sociodemographic inequalities in excess mortality

We observed marked geographic variability in age-adjusted excess mortality across municipalities with higher aSLI (**Figure 3A**). After excluding COVID-19 related deaths, only the southern municipalities displayed the highest combination of excess mortality and aSLI (**Supplementary Figure 5**). Stratifying by aSLI categories, age-adjusted mortality rates and excess mortality showed a stepwise increase with each higher marginalization level (**Figure 3B**). Municipalities with very high aSLI displayed both the higher age-adjusted mortality (912.36 per 100,000 inhabitants) and excess mortality (318.12 per 100,000 inhabitants) rates in Mexico.

Municipal-level correlates of excess mortality

To evaluate the hypothesis that excess mortality was correlated with social inequalities in healthcare access and hospital occupancy due to COVID-19 at the municipal level, we fitted negative binomial regression models for age-adjusted excess mortality rates. As observed in the geographic distribution of age-adjusted excess mortality (**Supplementary Figure 5**), municipalities at high and very high social lag had the highest risk for non-COVID-19 age-adjusted excess mortality in 2020. Municipalities with a higher percentage of the population without social security coverage (IRR 1.03, 95%CI 1.02-1.04), higher COVID-19 hospital occupancy (IRR 1.03, 95%CI 1.01-1.06) and higher social lag categories were at higher risk for excess mortality, after adjusting for covariates (**Figure 4**). We observed an interaction effect for higher risk for non-COVID-19 age-adjusted excess mortality in municipalities with very high social lag and higher COVID-19 hospital occupancy (IRR 1.08, 95%CI 1.03-1.12, **Supplementary Figure 6**).

Individual-factors correlates of non-COVID 19 deaths

Finally, we explored the role of sociodemographic conditions and healthcare-related inequalities for the risk for non-COVID 19 deaths using random-effects logistic regression models. We observed that women, people who had lower educational attainment, and who worked as craftsmen, farmers, laborers, or were unemployed had an increased odds for death attributable to non-COVID-19 compared to COVID-19 causes. Regarding healthcare-related factors, people without medical assistance before death, people who reported public or unspecified social security coverage, or who lived in municipalities with low availability of hospital beds had an increased odds of death from non-COVID-19 compared to COVID-19 causes. Finally, people living in municipalities with high and very-high social lag had the highest odds of non-COVID-19 compared to COVID-19 death (**Figure 4**).

DISCUSSION

In this study of 1,069,174 deaths recorded in Mexico between 2015-2020, we report that 51% of deaths in 2020 were in excess compared to the average reported between 2015-2019. Although cause-specific excess mortality during 2020 was largely attributable to COVID-19 (76.1% of cases), non-COVID-19 causes comprised up to one-fifth of excess deaths in Mexico during 2020. Moreover, we report a differential impact in excess mortality related to the setting in which the deaths occurred; while COVID-19 deaths occurred primarily in-hospital, non-COVID-19 deaths sharply decreased in this setting and had a concurrent increase in the out-of-hospital setting. These findings contribute to the growing literature on the far-reaching impact of the COVID-19 pandemic on the health system and suggest both an excess in non-COVID-19 mortality as well as a displacement of these deaths to the out-of-hospital setting in Mexico.

We also observed that excess mortality exhibited marked geographical heterogeneity, which was associated with higher social lag; states in the southern region of Mexico had the highest social marginalization and similarly high rates of non-COVID-19 excess mortality. We showed that lower prevalence of population without social security coverage and higher rates of

316 COVID-19 hospitalization, combined with social marginalization, were municipal-level
317 correlates of non-COVID-19 excess mortality. Finally, at the individual level, lower educational
318 attainment, blue collar employment (laborers, craftsmen, and farmers), unemployment, and
319 lack of medical assistance before death were significant correlates of non-COVID-19
320 compared to COVID-19 mortality during 2020. These findings suggest that excess mortality
321 from non-COVID-19 related causes, which occurred disproportionately out-of-hospital and
322 among populations with social disadvantage, may reflect a complex interplay between a
323 fragmented health system, strained hospital capacity, interruptions in chronic disease care,
324 and sociodemographic inequalities further unmasked by the pandemic. [5]. This situation is
325 applicable to Mexico, but also to countries with similar sociodemographic profiles in the region
326 or with high rates of SARS-CoV-2 infections.
327 Previous reports have documented the high burden of excess mortality caused by the COVID-
328 19 pandemic in Mexico, with excess mortality rates being estimated from 26.1 to 36.0 deaths
329 per 100,000 inhabitants [6,14,18–20]; moreover, Karlinsky et al. projected that Mexico's actual
330 toll of deaths could be twice the number of deaths registered during 2020 [21]. These reports
331 positioned Mexico as one of the leading countries in terms of excess mortality in Latin America
332 and worldwide [6,21]. However, there is limited information regarding cause-specific
333 contributors to global excess mortality rates in Mexico. Although our findings contribute to the
334 literature on COVID-19 excess mortality in Mexico, our results expand this literature by
335 showing that excess deaths were also related to cardiometabolic chronic health conditions,
336 including type 2 diabetes, cardiovascular disease, arterial hypertension, and obesity, which
337 had a steep increase in the out-of-hospital setting [9,22]. Excess non-COVID-19 deaths could
338 be attributable to hospital reconversion policies and healthcare restructuration designed to
339 improve care for COVID-19 cases, which may have reduced access to care for people with
340 chronic health conditions who required continuous medical assistance during the COVID-19
341 pandemic. Other high-income countries have documented the association between hospital

342 occupancy and excess mortality during periods of peak COVID-19 infections [23–25].
343 Explanations related to this phenomenon rely on data on restricted access to healthcare
344 services in places that experienced hospital overload due to COVID-19, reduced out-of-
345 hospital attention due to severely restricted healthcare services and personnel availability,
346 lower insurance coverage, and lower number of healthcare personnel per-capita [26–28].
347 Other reported non-related healthcare contributors were social stigma for being treated in
348 hospitals due to potentially acquiring COVID-19 infection and reduced physical activity due to
349 pandemic restrictions on mobility, which could have exacerbated complications due to chronic
350 health conditions [29]. Overall, excess non-COVID-19 mortality could be interpreted as an
351 indirect indicator of the negative effects attributable to healthcare policies which prioritized in-
352 hospital COVID-19 attention over the care of other chronic health conditions.
353 Notably, increased rates of COVID-19 hospitalizations and mortality in Mexico were observed
354 in municipalities with high marginalization independently of urbanization, leading to increased
355 stress in their healthcare systems [30,31]. This phenomenon may explain the disproportionate
356 impact on non-COVID-19 deaths in marginalized municipalities in Mexico. Our results support
357 the hypothesis that populations with sociodemographic disadvantage experienced the highest
358 impact of excess mortality attributable to hospital saturation, with this impact having an
359 unequal distribution within Mexico. In the European region, countries with high excess
360 mortality, such as Bulgaria, Russia, and Serbia were impacted by diverse social barriers with
361 difficulties to fully adhere to social isolation policies [32,33]. Two recent reports in England
362 revealed that communities with high-density of care homes, with a high proportion of residents
363 on income support, overcrowding conditions, and ethnic minorities were at higher risk of
364 excess mortality and years of life lost due to the COVID-19 pandemic [34,35]. In Latin
365 American countries, the impact of socioeconomic disparities was sharp mainly due to
366 countries experiencing diverse social barriers to sustain lockdown mandates driven by low
367 stipend support, a high proportion of their population working in the informal economy, and

lack of access to health care, even among healthcare personnel [3,32,36]. Nevertheless, this evidence and the comparison between countries should be interpreted with caution given the variation in COVID-19 dynamics, within-country gradients of sociodemographic inequalities, and different epidemiological profiles of high-risk comorbidities.

Our results highlight the impact of healthcare-related and individual-level social inequalities in exacerbating overall and cause-specific excess mortality in Mexico. We show that the main contributor to higher non-COVID-19 excess mortality rates at the municipal level was a lower percentage of the population with access to social security health coverage; in Mexico, social security providers condition the type of healthcare access by individuals, which likely also influences received quality of care and healthcare access. Furthermore, the interaction between a lower percentage of the population with access to social security health coverage and social marginalization confirmed the hazardous interplay between social and healthcare inequalities [37]. At the individual level, we showed that certain socially vulnerable occupations experienced unequal risks for non-COVID-19 mortality. The role of individual and sociodemographic determinants in the risk for adverse COVID-19 outcomes has been previously reported [38,39]. Nevertheless, our findings demonstrate that sociodemographic inequalities impacted individuals with preventable chronic conditions, regardless of public healthcare policies aimed at mitigating the impact of the COVID-19 pandemic in healthcare infrastructure and provision. Overall, our results represent an urgent call to action for local authorities to perform a healthcare restructuration, particularly in marginalized municipalities and with special attention to vulnerable populations to prioritize full coverage of hospital bed capacity, well-trained healthcare personnel, and availability of primary care services that cover the management of chronic health conditions. These policies could prevent associated complications in the context of future COVID-19 waves or other circumstances that increase stress and reduce access to healthcare in Mexico and other LMICs.

Our study has some strengths and limitations. Among the strengths, we highlight the use of 1,069,174 nationwide mortality registries to compare all-cause and cause-specific excess mortality during the COVID-19 pandemic in Mexico in 2020. This approach allowed us to estimate with higher confidence state and municipal-level excess morality rates that helped us to study the regional impact of the COVID-19 pandemic and identify vulnerable zones in Mexico which were especially affected during 2020 compared to previous years. Additionally, the use of sociodemographic variables at different levels gave us insights to evaluate municipal and individual-level correlates of excess non-COVID-19 mortality. Nevertheless, limitations to be acknowledged include the lack of specific clinical information and comorbidity assessment for correlates known to be key determinants of higher risk of death for COVID-19 and non-COVID-19 causes, particularly regarding management of chronic cardio-metabolic conditions. Second, we could not ascertain the number of non-COVID-19 deaths that occurred due to exacerbation of underlying chronic conditions by current or previous SARS-CoV-2 infection, which could increase the risk of long-term complications, including cardiovascular diseases [3]. Third, our COVID-19 death construct included cases which could have been misclassified as atypical pneumonia or severe acute respiratory infections of unknown etiology, registered after the onset of the COVID-19 pandemic; this was done to reduce the risk of underreporting or misclassified COVID-19 deaths, but could have led to overestimation of COVID-19 deaths. Fourth, we used a surveillance dataset to assess COVID-19 hospitalization as a proxy to hospital occupancy; however, identification of COVID-19 related hospitalizations may have varied according to weekly SARS-CoV-2 testing capacity and adequate reporting. Therefore, the use of this proxy could be biased in municipalities with higher marginalization and reduced access to testing. Finally, our municipal-level factors should be interpreted as structural conditions that displayed an association with higher excess mortality rates and therefore, we should avoid an ecological fallacy in determining personal actions in clinical and healthcare management during the COVID-19 pandemic.

In conclusion, we show a high burden of excess mortality in Mexico in 2020, largely attributable to in-hospital COVID-19 and out-of-hospital non-COVID-19 deaths. We observed regional heterogeneity of non-COVID-19 excess mortality, with a disproportionate burden on marginalized municipalities in southern Mexico. High hospital occupancy due to COVID-19 and higher percentage of population without social security coverage were municipal wide-level correlates of excess mortality; whereas individual-level lower educational attainment, vulnerable working occupations, lack of medical assistance before death, and public or underspecified healthcare access were factors related to higher non-COVID-19 mortality likelihood. Our findings underscore the impact of sociodemographic inequalities in excess mortality related to non-COVID-19 causes in Mexico during 2020 compared to the 2015-2019 period. These results should prompt an urgent call to action to improve healthcare coverage and access, particularly in primary care settings and among populations with social disadvantage. Such policies could reduce health disparities in Mexico in circumstances that increase the stress of healthcare systems, including the ongoing COVID-19 pandemic and beyond.

AUTHOR CONTRIBUTIONS

Research idea and study design: NEAV, CAFM, OYBC; data acquisition: NEAV, CAFM; data analysis/interpretation: NEAV, CAFM, JMA, LFC, JPA, AGD, AVV; statistical analysis: NEAV, CAFM, OYBC; manuscript drafting: NEAV, OYBC, CAFM, JMA, LFC, JPA, AGD, AVV, JAS SB, LMGR; supervision or mentorship: NEAV, OYBC. Each author contributed important intellectual content during manuscript drafting or revision and accepted accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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DATA AVAILABILITY: All code, datasets and materials are available for reproducibility of results at https://github.com/oyaxbell/excess_non_covid/

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FIGURE LEGENDS

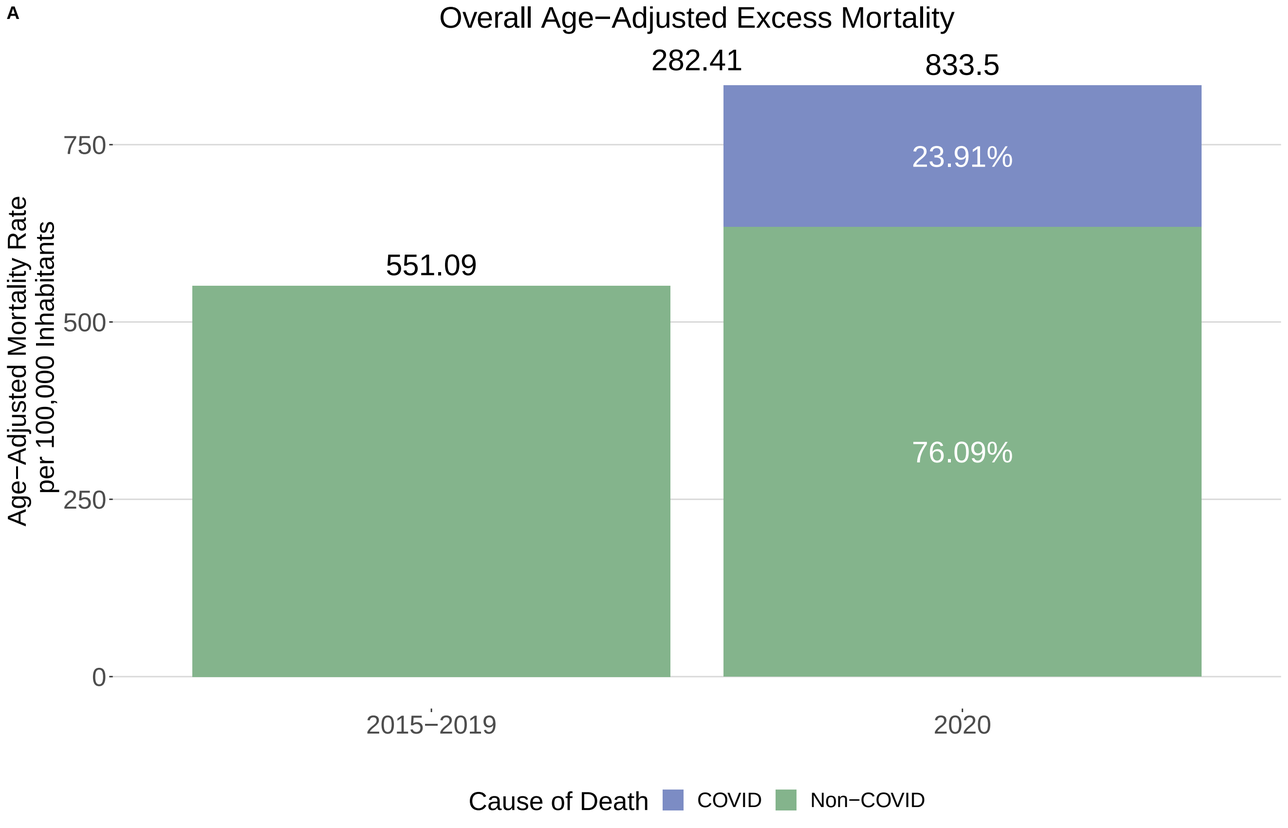
Figure 1: Age-adjusted mortality rates in 2020 compared by the average period of 2015-2019 (A). Distribution of excess mortality in Mexico stratified by deaths associated with COVID-19 and non-COVID-19 for the year 2020 (B). Main 10 causes of age-adjusted excess mortality in México (C) and stratified by month of occurrence (D).

Figure 2: Stratification of in-hospital and out-of-hospital age-adjusted mortality rates in 2020 compared by the average period of 2015-2019 (A). Distribution of excess mortality in Mexico stratified death setting and by deaths associated with COVID-19 and non-COVID-19 for the year 2020 (B). Main 10 causes of age-adjusted excess mortality in México stratified by place of occurrence (C) and by month and place of occurrence of death (D).

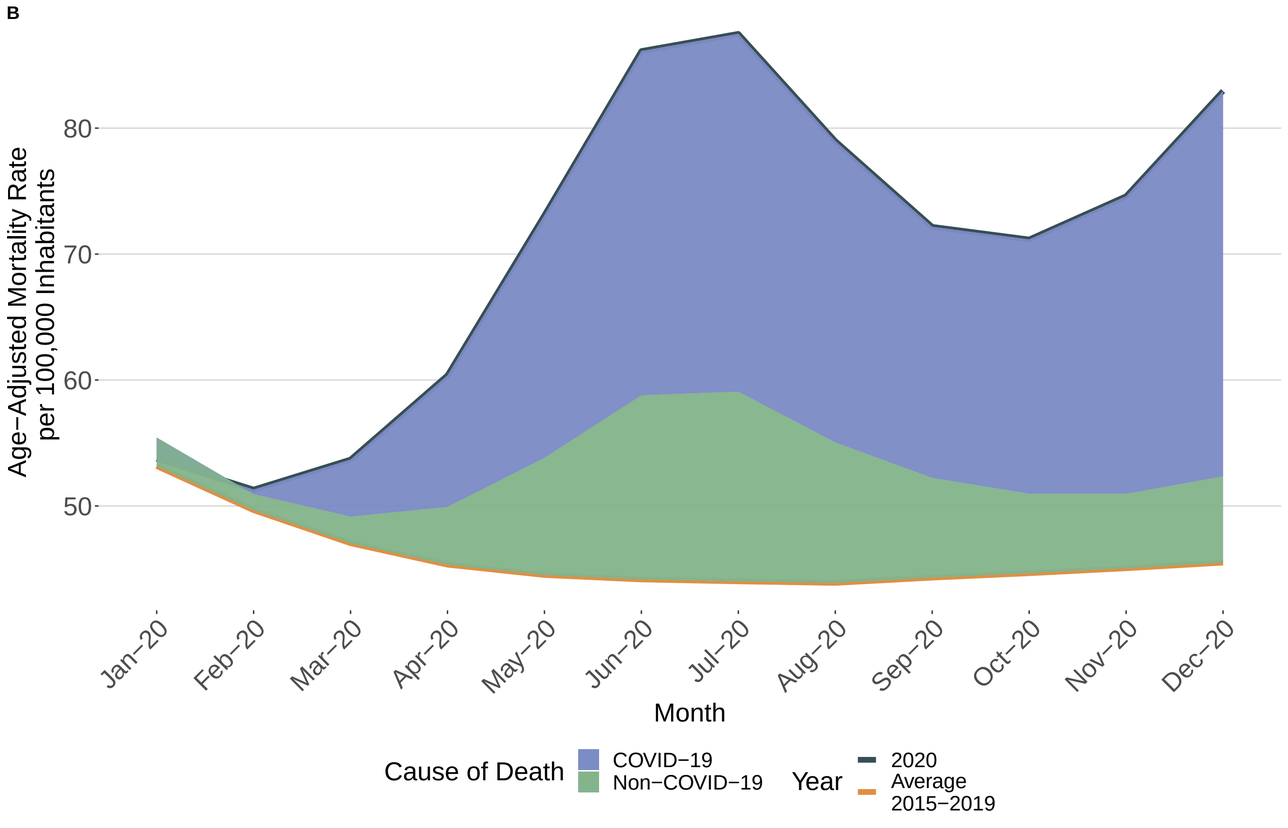
Figure 3: Choropleth map to visualize the geographical distribution of age-adjusted excess mortality and adjusted social lag index by municipality of occurrence in 2020 at Mexico (A). Historical and 2020 age-adjusted mortality rates and excess mortality stratified by adjusted social lag categories (B).

Figure 4: Negative binomial regression model to evaluate municipal-level factors related to excess mortality (A). Logistic regression model to assess individual-related factors linked to the probability of death for non-COVID-19 causes (B).

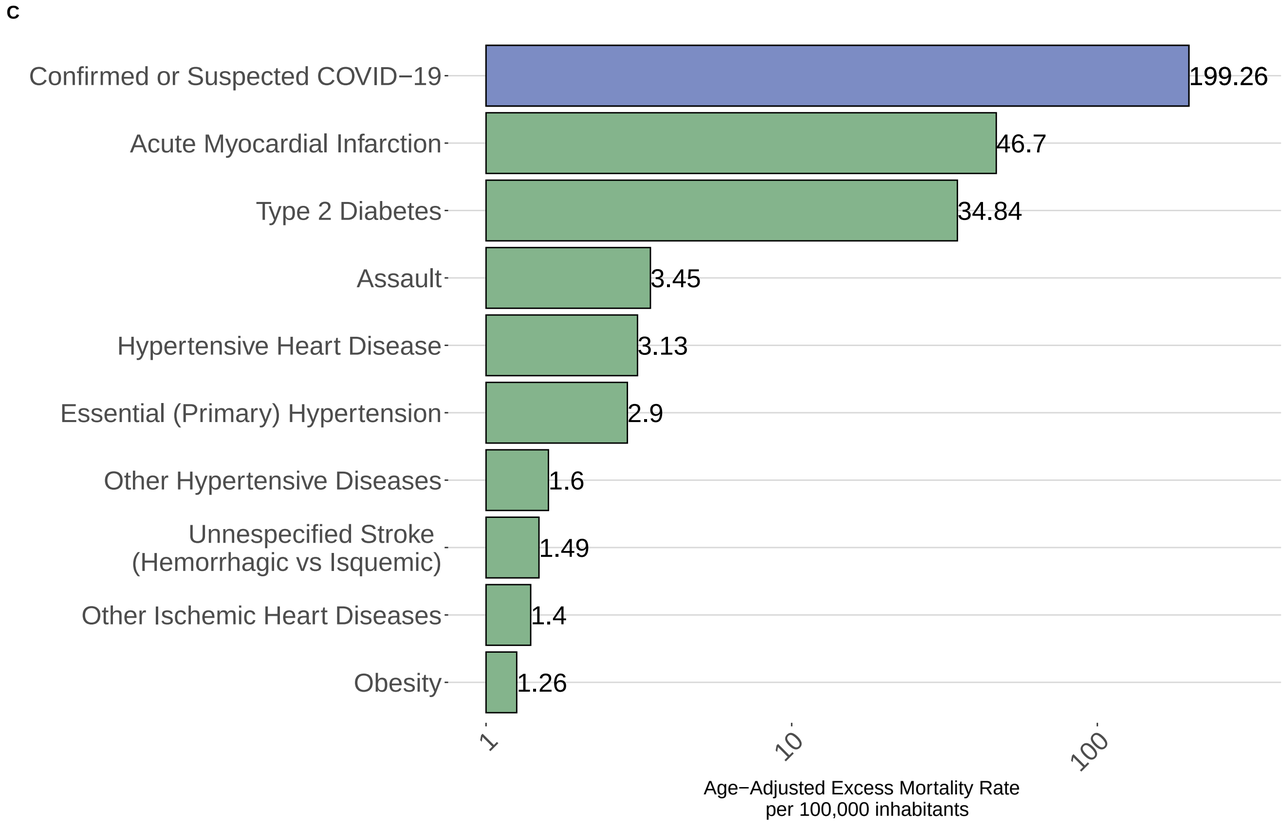
A


Overall Age−Adjusted Excess Mortality
282.41
833.5
23.91%
551.09
76.09%
750
500
250
0
Age−Adjusted Mortality Rate
per 100,000 Inhabitants
2015−2019
2020
Cause of Death
COVID
Non−COVID

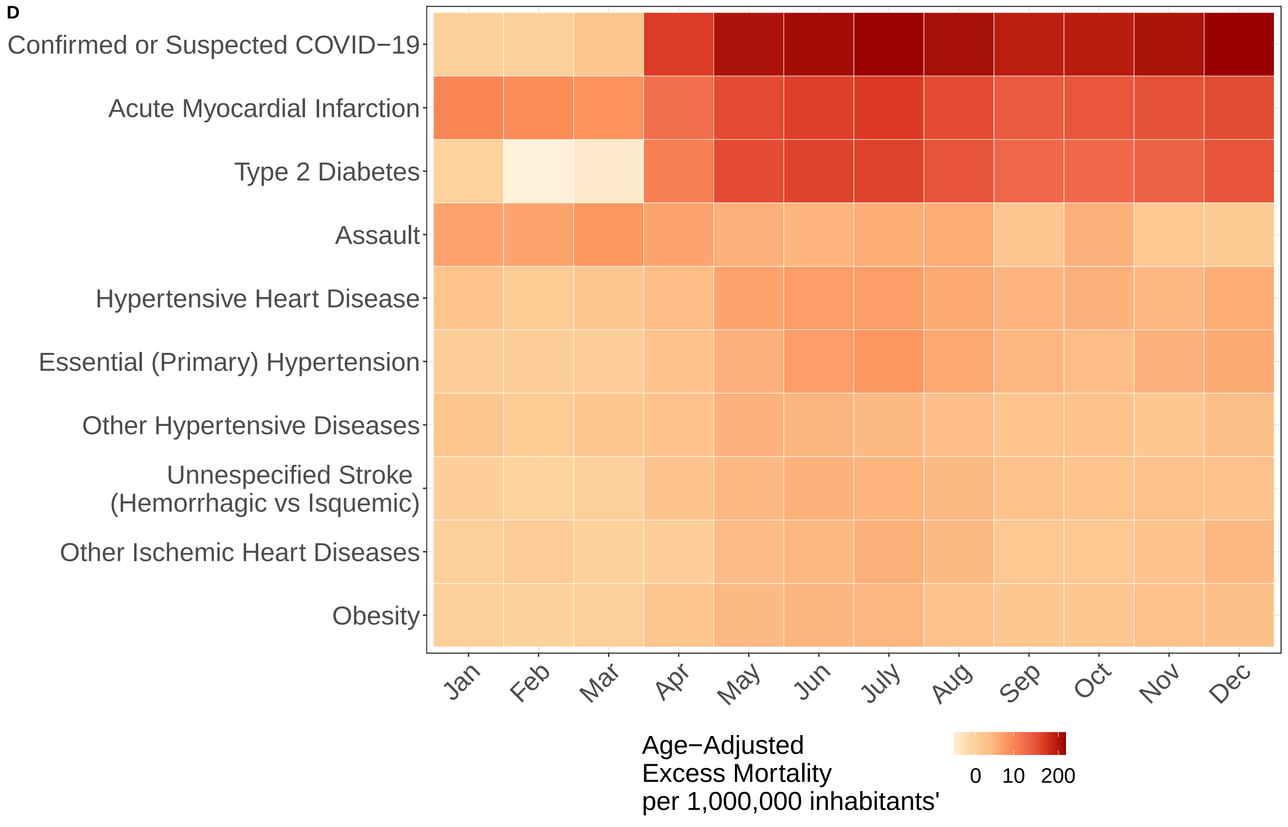
B

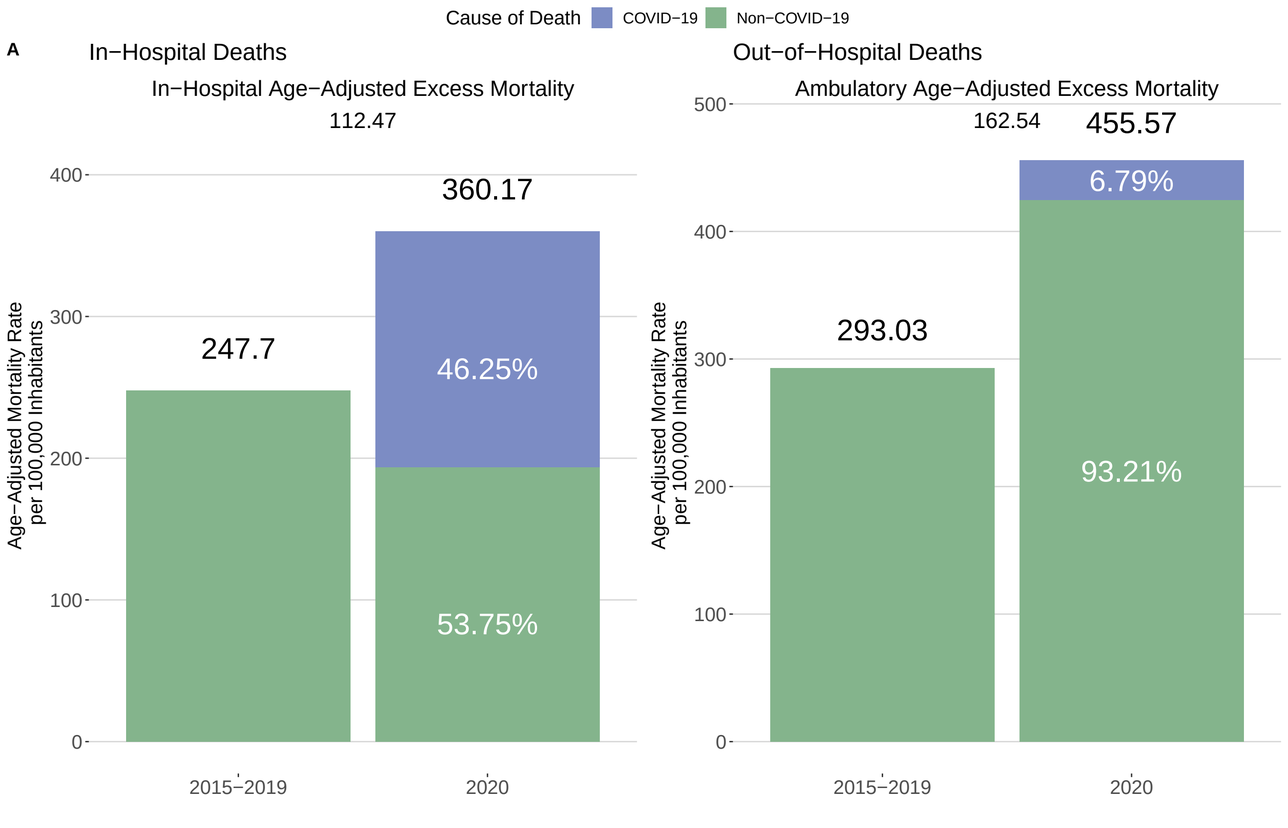

80
70
60
50
Age−Adjusted Mortality Rate
per 100,000 Inhabitants
Jan−20
Feb−20
Mar−20
Apr−20
May−20
Jun−20
Jul−20
Aug−20
Sep−20
Oct−20
Nov−20
Dec−20
Month
Cause of Death
COVID−19
Non−COVID−19
Year
2020
Average
2015−2019

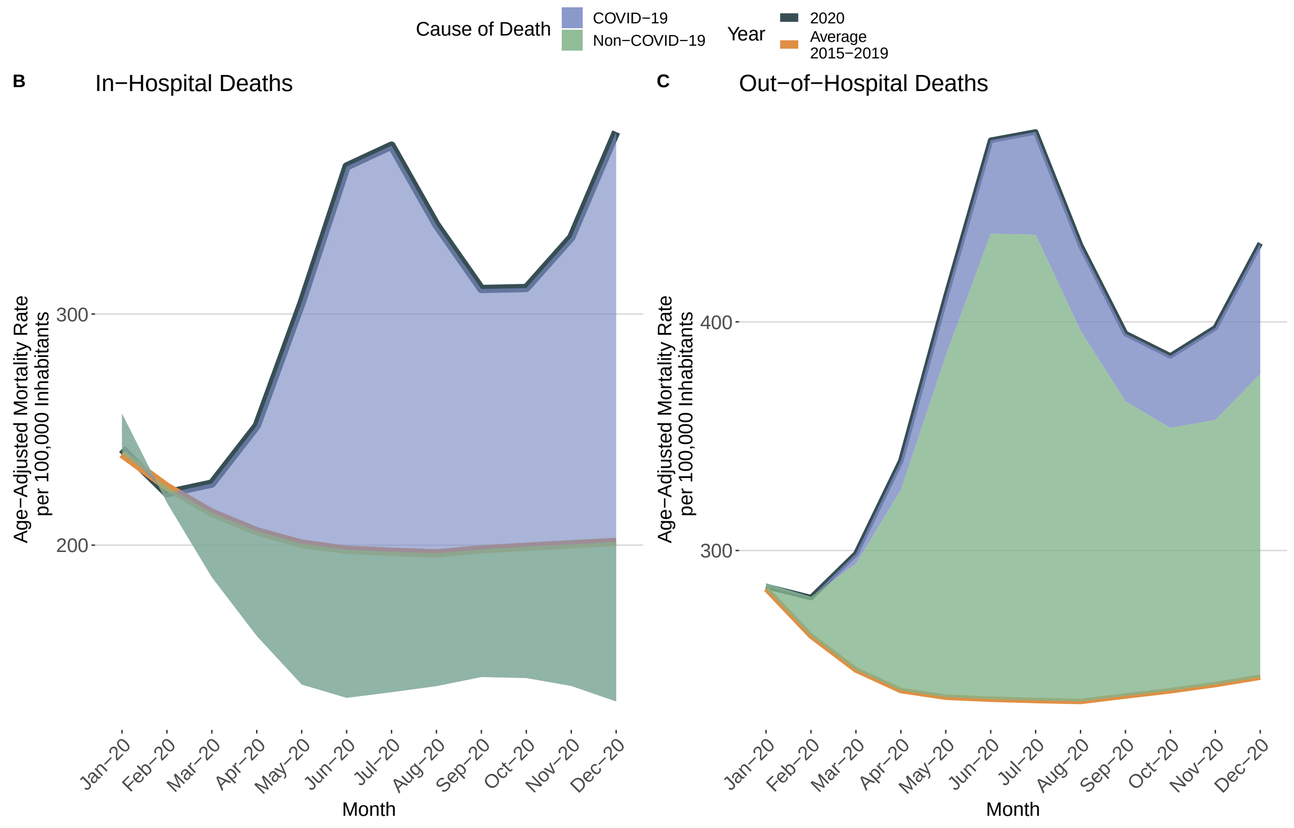
C

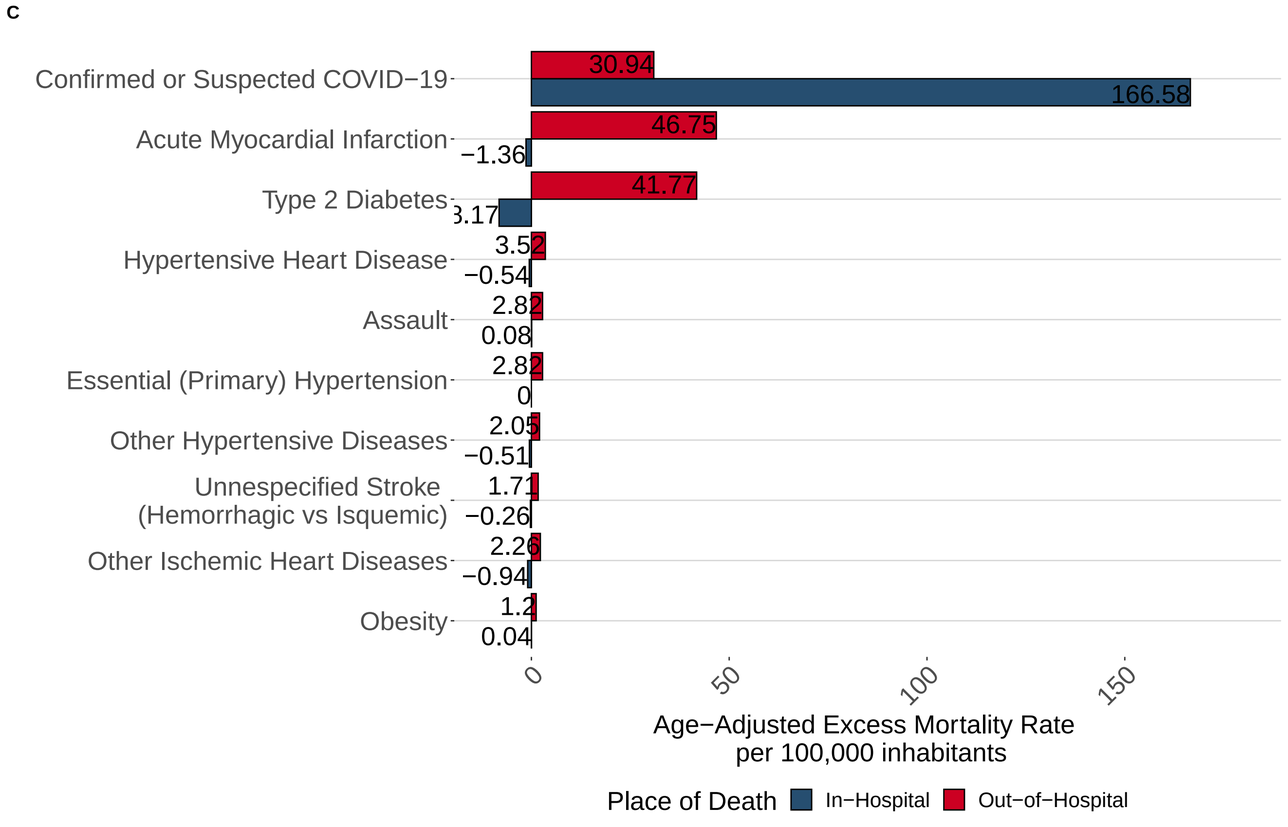

Confirmed or Suspected COVID−19
199.26
Acute Myocardial Infarction
46.7
Type 2 Diabetes
34.84
Assault
3.45
Hypertensive Heart Disease
3.13
Essential (Primary) Hypertension
2.9
Other Hypertensive Diseases
1.6
Unnespecified Stroke
(Hemorrhagic vs Isquemic)
1.49
Other Ischemic Heart Diseases
1.4
Obesity
1.26
1
10
100
Age−Adjusted Excess Mortality Rate
per 100,000 inhabitants

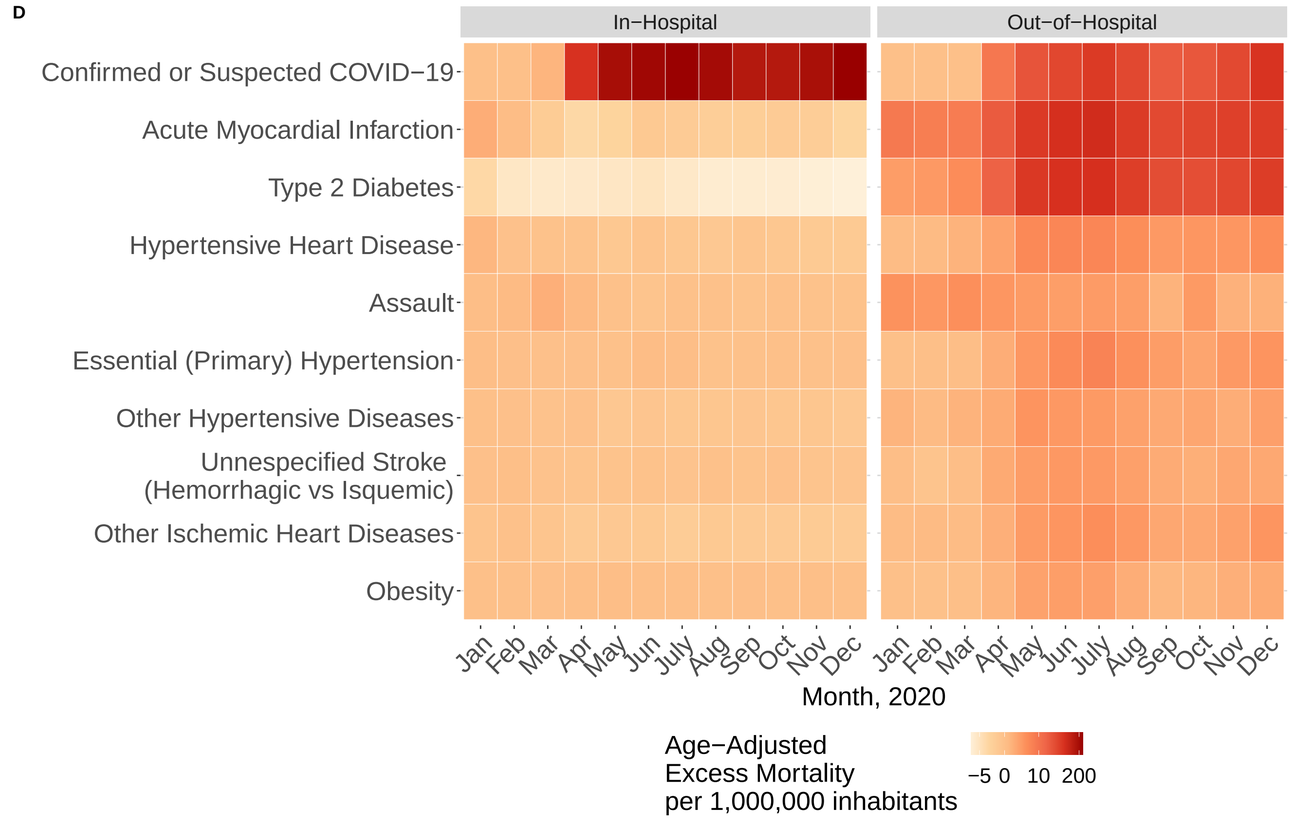
D

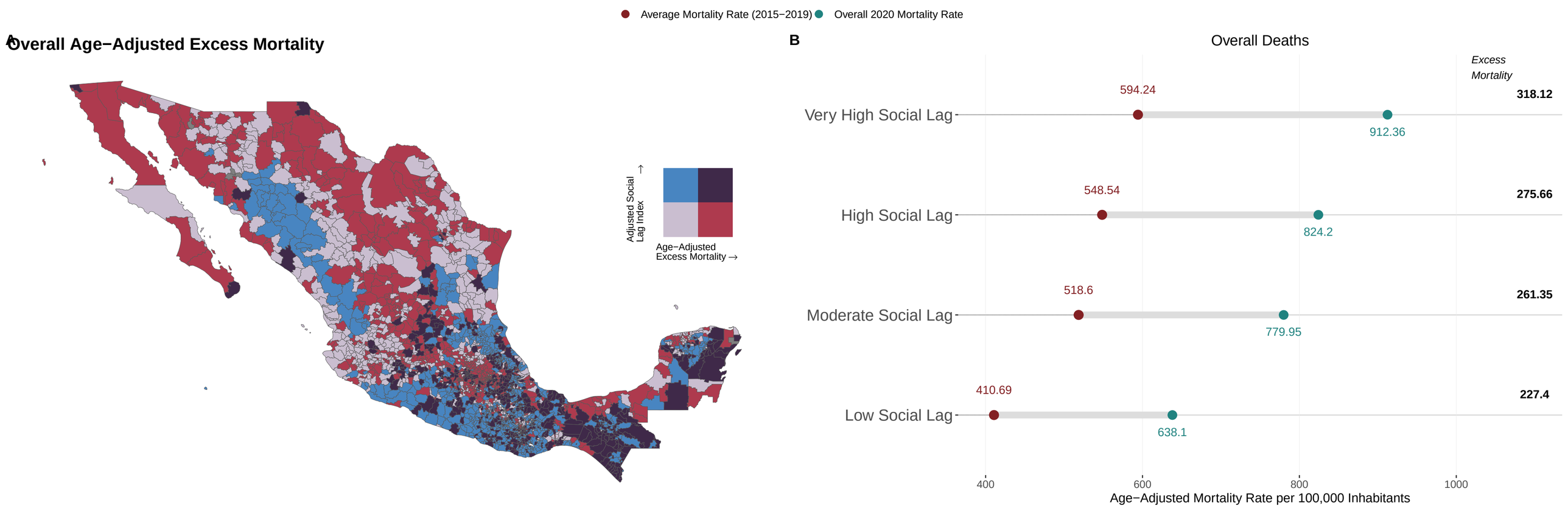

Confirmed or Suspected COVID−19
Acute Myocardial Infarction
Type 2 Diabetes
Assault
Hypertensive Heart Disease
Essential (Primary) Hypertension
Other Hypertensive Diseases
Unnespecified Stroke
(Hemorrhagic vs Isquemic)
Other Ischemic Heart Diseases
Obesity
Jan
Feb
Mar
Apr
May
Jun
July
Aug
Sep
Oct
Nov
Dec
Age−Adjusted
Excess Mortality
per 1,000,000 inhabitants'
0
10
200

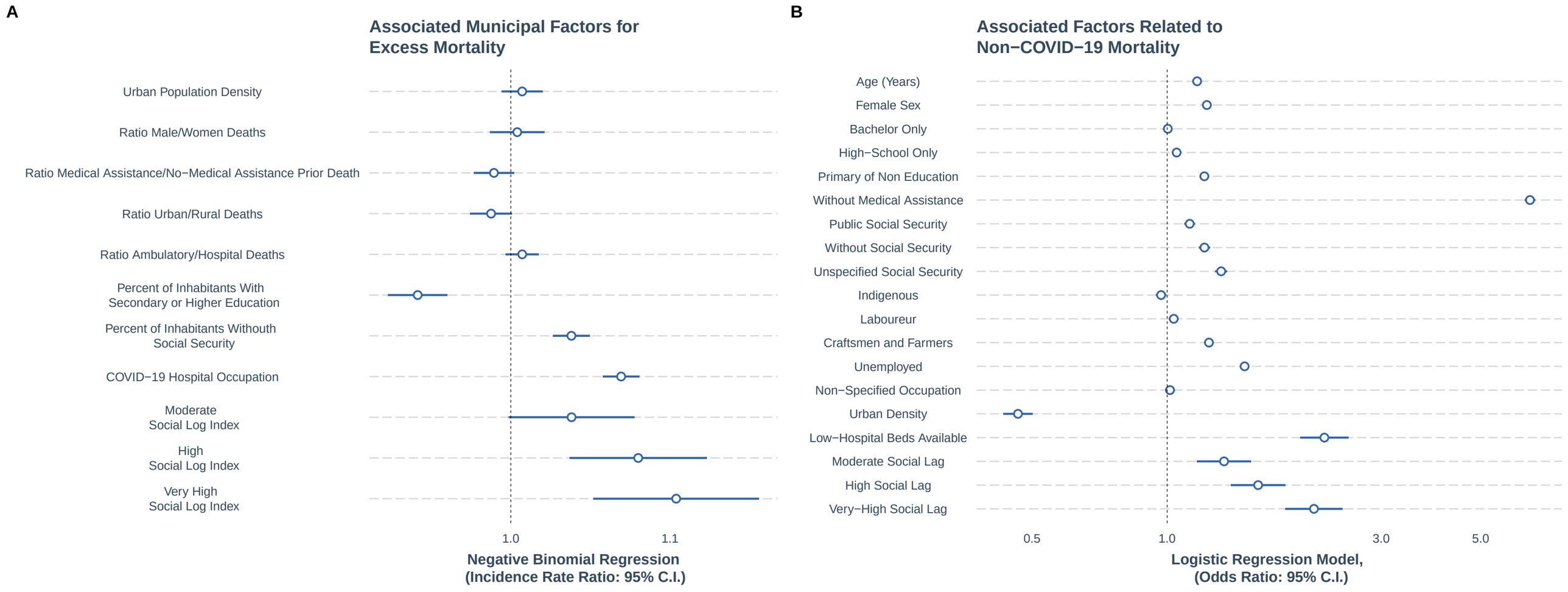

A
Cause of Death
COVID−19
Non−COVID−19
In−Hospital Deaths
In−Hospital Age−Adjusted Excess Mortality
112.47
360.17
247.7
46.25%
53.75%
Age−Adjusted Mortality Rate per 100,000 Inhabitants
2015−2019
2020
Out−of−Hospital Deaths
Ambulatory Age−Adjusted Excess Mortality
162.54
455.57
293.03
6.79%
93.21%


Cause of Death
COVID−19
Non−COVID−19
Year
2020
Average 2015−2019
B
In−Hospital Deaths
Age−Adjusted Mortality Rate per 100,000 Inhabitants
Jan−20
Feb−20
Mar−20
Apr−20
May−20
Jun−20
Jul−20
Aug−20
Sep−20
Oct−20
Nov−20
Dec−20
Month
C
Out−of−Hospital Deaths


C
Confirmed or Suspected COVID−19
30.94
166.58
Acute Myocardial Infarction
46.75
−1.36
Type 2 Diabetes
41.77
3.17
Hypertensive Heart Disease
3.52
−0.54
Assault
2.82
0.08
Essential (Primary) Hypertension
2.82
0
Other Hypertensive Diseases
2.05
−0.51
Unnespecified Stroke (Hemorrhagic vs Isquemic)
1.71
−0.26
Other Ischemic Heart Diseases
2.26
−0.94
Obesity
1.2
0.04
Age−Adjusted Excess Mortality Rate per 100,000 inhabitants
Place of Death
In−Hospital
Out−of−Hospital


D
In−Hospital
Out−of−Hospital
Confirmed or Suspected COVID−19
Acute Myocardial Infarction
Type 2 Diabetes
Hypertensive Heart Disease
Assault
Essential (Primary) Hypertension
Other Hypertensive Diseases
Unnespecified Stroke (Hemorrhagic vs Isquemic)
Other Ischemic Heart Diseases
Obesity
Jan
Feb
Mar
Apr
May
Jun
July
Aug
Sep
Oct
Nov
Dec
Month, 2020
Age−Adjusted Excess Mortality per 1,000,000 inhabitants
−5 0 10 200


Average Mortality Rate (2015−2019)
Overall 2020 Mortality Rate
A
Overall Age−Adjusted Excess Mortality
Adjusted Social Lag Index →
Age−Adjusted Excess Mortality →
B
Overall Deaths
Excess Mortality
Very High Social Lag
594.24
912.36
318.12
High Social Lag
548.54
824.2
275.66
Moderate Social Lag
518.6
779.95
261.35
Low Social Lag
410.69
638.1
227.4
400
600
800
1000
Age−Adjusted Mortality Rate per 100,000 Inhabitants


A
Associated Municipal Factors for Excess Mortality
Urban Population Density
Ratio Male/Women Deaths
Ratio Medical Assistance/No−Medical Assistance Prior Death
Ratio Urban/Rural Deaths
Ratio Ambulatory/Hospital Deaths
Percent of Inhabitants With Secondary or Higher Education
Percent of Inhabitants Withouth Social Security
COVID−19 Hospital Occupation
Moderate Social Log Index
High Social Log Index
Very High Social Log Index
1.0
1.1
Negative Binomial Regression (Incidence Rate Ratio: 95% C.I.)
B
Associated Factors Related to Non−COVID−19 Mortality
Age (Years)
Female Sex
Bachelor Only
High−School Only
Primary of Non Education
Without Medical Assistance
Public Social Security
Without Social Security
Unspecified Social Security
Indigenous
Laboureur
Craftsmen and Farmers
Unemployed
Non−Specified Occupation
Urban Density
Low−Hospital Beds Available
Moderate Social Lag
High Social Lag
Very−High Social Lag
0.5
1.0
3.0
5.0
Logistic Regression Model, (Odds Ratio: 95% C.I.)