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Comprehensive Evaluation of the Impact of Sociodemographic Inequalities on Adverse Outcomes and Excess Mortality During the Coronavirus Disease 2019 (COVID-19) Pandemic in Mexico City

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Background. The impact of the coronavirus disease 2019 (COVID-19) pandemic in Mexico City has been sharp, as several social inequalities at all levels coexist. Here we conducted an in-depth evaluation of the impact of individual and municipal-level social inequalities on the COVID-19 pandemic in Mexico City.

Methods. We analyzed suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases, from the Mexico City Epidemiological Surveillance System from 24 February 2020 to 31 March 2021. COVID-19 outcomes included rates of hospitalization, severe COVID-19, invasive mechanical ventilation, and mortality. We evaluated socioeconomic occupation as an individual risk, and social lag, which captures municipal-level social vulnerability, and urban population density as proxies of structural risk factors. Impact of reductions in vehicular mobility on COVID-19 rates and the influence of risk factors were also assessed. Finally, we assessed discrepancies in COVID-19 and non-COVID-19 excess mortality using death certificates from the general civil registry.

Results. We detected vulnerable groups who belonged to economically unfavored sectors and experienced increased risk of COVID-19 outcomes. Cases living in marginalized municipalities with high population density experienced greater risk for COVID-19 outcomes. Additionally, policies to reduce vehicular mobility had differential impacts modified by social lag and urban population density. Finally, we report an under-registry of COVID-19 deaths along with an excess mortality closely related to marginalized and densely populated communities in an ambulatory setting. This could be attributable to a negative impact of modified hospital admission criteria during the pandemic.

Conclusions. Socioeconomic occupation and municipality-wide factors played a significant role in shaping the course of the COVID-19 pandemic in Mexico City.

Keywords. epidemiology; social inequalities; Mexico City; COVID-19; SARS-CoV-2.

The coronavirus disease 2019 (COVID-19) pandemic brought health inequalities worldwide into sharp relief. Although clinical risk factors for severe outcomes were promptly identified [1, 2], these do not fully explain the disproportionate burden experienced by historically marginalized populations during the COVID-19 pandemic [3–5]. A possible hypothesis according to the "Social Determination of the Health-Disease Process" (SDHDP) approach expresses that the cumulative and yet dynamic interplay between historically, spatially, and socially shaped processes of exposure/imposition, susceptibility and resistance, which dialectically affects health at the singular, particular and general levels, could have been a main contributor [6]. Beyond the better-known "Social Determinants of Health" approach, the SDHDP approach focuses on social processes which underlie the inequitable distribution of risk factors and poor health [6–8]. Similarly, ecosocial epidemiology focuses on the cumulative

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interplay between exposure, susceptibility, and resistance, which leads to health and the notion of *embodiment* [9]. Both approaches regard empirical data on health disparities along socioeconomic, geospatial, racialized, and gendered lines as a starting point to understand processes which shape population health—including the COVID-19 pandemic.

Mexico City is one of the most unequal cities in Latin America, with a large population share working informally and living in poverty, and disparities of >20 years in life expectancy across municipalities in the wider metropolitan region [10]. Furthermore, most of the population do not have proper support networks or social security for in-hospital care [11]. These factors are complicated by the high prevalence of cardiometabolic diseases in Mexicans, which have been shown to worsen COVID-19 outcomes [12, 13]. Despite the high burden of COVID-19 in Mexico, research on COVID-19 and social inequality has been comparatively scarce [14]. Here we performed a comprehensive evaluation of the impact of individual and municipal-level determinants of social inequalities on the course of the COVID-19 pandemic in Mexico City.

METHODS

We analyzed data from individuals living and treated within the 16 municipalities of Mexico City with suspected COVID-19 and recorded in the National Epidemiological Surveillance Study (NESS), an open-source dataset comprising daily-updated cases in Mexico City up to 31 March 2021 [15–17] (Supplementary Materials). Follow-up was calculated from dates of symptom onset, until hospital admission or death. COVID-19 outcomes included status on hospitalization, requirement for invasive mechanical ventilation (IMV), severe COVID-19 using a composite definition including death, requirement for IMV and/or intensive care unit (ICU) admission and/or death attributable to COVID-19 [18].

Definitions of Socioeconomic Occupation Categories

We recodified reported occupation from NESS using definitions by the National Institute of Statistics and Geography (INEGI) as: economically-active, retired, home-care related, healthcare workers (HCWs), nonspecified workers, unemployed subjects, and students (Supplementary Materials). We weighted estimates stratified by socioeconomic occupation using population data of economically active and inactive population >15 years based on trimestral projections from the 2020 National Survey of Occupation and Employment conducted by INEGI [19]. Given the increased occupational risk of HCWs for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, we used this group as reference for all statistical analyses [20].

Urban Population Density-Independent Social Lag Estimation

To quantify the impact of sociodemographic inequalities on the course of the COVID-19 pandemic at a municipal-wide level, we used the 2020 social lag index (SLI), a composite assessment of the degree of healthcare access, economic well-being, and access to basic services in Mexico [21]. Mean urban population density (MUPD) was calculated as proposed by INEGI for all municipalities. Because we intended to evaluate inequalities independent of urbanization, we used residuals of linearly regressed MUPD onto SLI values to approximate a MUPD-independent SLI (DISLI) [22]. Cutoffs for high/low DISLI/MUPD were defined using Jenks optimization method, and stratified as low MUPD/low DISLI, high MUPD/low DISLI, low MUPD/high DISLI, and high MUPD/high DISLI (Supplementary Materials). For population-weighted analyses we used 2020 population projections obtained by the Mexican National Population Council (CONAPO) [23].

Vehicular Mobility Reduction Estimates

To determine the heterogeneous impact of mobility reduction mandates as a mitigation public health policy, we used an open-source dataset of vehicular mobility data collected by Mexico City's government. This data set comprises a relative percentual comparison of vehicular mobility with the same day in 2019 captured by transit records according to the Mobility Department (SEMOVI) by week and municipality [24]. This data set was last updated on 31 December 2020 (Supplementary Materials).

Death Certificates of COVID-19 and Other Non-COVID-19 Causes

Given potential underreports in the number of deaths across Mexico, excess mortality is a more reliable metric of the impact of COVID-19 [25]. We estimated excess deaths of suspected COVID-19 and non-COVID-19 causes using an open-source database of monthly updated death certificates captured by the general civil registry (GCR) of Mexico City [26] (Supplementary Materials).

Statistical Analysis

Epidemiological Rate Estimations

Age-adjusted and standard epidemiological rates of incidence, testing, asymptomatic and mortality were calculated for MUPD/DISLI and socioeconomic occupation categories, respectively. All rates were estimated using population denominators and normalized to rates per 100 000 inhabitants.

Conditions Related to SARS-CoV-2 Outcomes in Mexico City

To assess if socioeconomic occupation and municipal-wide factors were associated with COVID-19 outcomes, we fitted multilevel mixed-effects Cox proportional hazard regression and logistic regression models for IMV requirement, including facility of treatment as a random intercept to model variability in case distribution and care. Models were adjusted by age, sex, cumulative number of comorbidities, and symptoms, along

with treatment modality and were evaluated using the Bayesian information criterion (BIC).

Mobility Trends and their Impact in COVID-19 Rates Across Mexico City

To evaluate whether mobility reduction policies had any effect on incidence, mortality, severe COVID-19, and hospitalization rates according to MUPD/DISLI, we fitted multilevel mixed-effects Poisson models adjusted by age, public-policy epidemiologic period, and number of comorbidities, with population offset stratified by sex. Relative mobility was adjusted using restricted cubic splines with three knots including interaction terms with MUPD/DISLI categories. Granger causality tests were used to assess temporal causality of mobility reduction on COVID-19 rates. Autoregressive-distributed lag (ARDL) models were also fitted for incidence and mortality rates, dividing data by MUPD/DISLI categories and socioeconomic occupation. Best ARDL fit according to lag was selected with BIC. Bounds tests were used to evaluate short and long-term cointegration.

Estimation of Excess Mortality of Non-COVID-19 Deaths

Age-adjusted excess mortality was estimated as the difference between mortality rates by death certificate during 2020–2021 and average mortality rates for the 2017–2019 monthly period adjusted by MUPD/DISLI population as denominators. Impact of MUPD/DISLI categories on underreport and excess mortality was explored using negative binomial regression models, using population denominators as offsets to estimate incidence rate ratios (IRR). Models were further adjusted for dependency and masculinity indexes, which are demographic indicators used to account for population structure [27]. A P-value < .05 was considered as the statistical significance threshold. All analyses were performed using R version 4.0.3.

RESULTS

The COVID-19 Pandemic in Mexico City

Until 31 March 2021, the NESS recorded 2 455 219 suspected COVID-19 cases in 688 medical units, of which 1 993 629 had valid SARS-CoV-2 test and were treated in Mexico City (Supplementary Materials). We observed that 511 655 (25.7%) cases had confirmed SARS-CoV-2. A total of 80 299 (4.0%) cases required hospitalization, 11 755 required IMV (0.6%), and 36 329 (1.8%) had a severe COVID-19. Over this period, 25 266 (1.3%) confirmed COVID-19 deaths were recorded. Testing rates steadily increased from April 2020, with a corresponding increase in the rates of incident SARS-CoV-2 infection. Peaks in mortality rates were observed in May 2020 and December 2020/January 2021, despite implementation of national lockdown mandates (Supplementary Materials).

Socioeconomic Occupation as a Determinant of COVID-19 Risk

Most COVID-19 cases were identified in economically active (50.8%), followed by home-related (15%), other nonspecified workers (11.8%), students (11.2%), HCWs (5.1%), unemployed (3.5%), and retired adults (2.6%). Retired, home-related workers and unemployed adults were older and had increased prevalence of comorbidities. HCWs had the highest testing and incidence rates followed by nonspecified workers. Nevertheless, unemployed, nonspecified workers and retired adults had the highest COVID-19 mortality rates. When analyzing only lethal cases, home-related workers, retired, and unemployed adults were older and had higher burden of comorbidities (Supplementary Materials).

Sociodemographic Inequalities and Their Impact Over the COVID-19 Pandemic

Most tested subjects lived in high MUPD/high DISLI municipalities (62.8%), followed by low MUPD/high DISLI (13.4%), high MUPD/low DISLI (13.6%), and low MUPD/low DISLI (10.1%). Subjects living in low MUPD/low DISLI municipalities were older with higher rates of comorbidities in general and lethal cases (Supplementary Materials). Higher age-adjusted testing rates were observed in low MUPD/high DISLI municipalities; therefore, age-adjusted incidence rates followed a similar pattern. We observed a DISLI-dependent mortality pattern, in which high MUPD/high DISLI and low MUPD/high DISLI municipalities had the highest age-adjusted mortality rates (Figure 1).

Independent Role of Individual- and Municipal-Level Factors on COVID-19 Outcomes

In multivariate analyses, unemployed, nonspecified workers, home-related workers, and retired adults had increased adjusted risk for COVID-19 outcomes compared with HCWs. Economically active workers only displayed higher adjusted risk for IMV, severe COVID-19, and mortality. Cases treated in public healthcare settings, had decreased likelihood for hospitalization and IMV requirement but increased adjusted mortality risk compared with cases treated in private health-care institutions. Municipalities classified as high-MUPD/high DISLI displayed the highest adjusted risk for IMV, severe COVID-19, and mortality compared with low MUPD/low DISLI municipalities (Figure 2).

Influence of Ambulatory Setting on Adverse Outcomes

Given the prioritization of care for patients with severe COVID-19 in Mexico, we evaluated whether outpatient management aggravated the previously identified occupational risk. Retired adults (hazard ratio [HR] 3.30, 95% confidence interval [CI] 2.58–4.21), unemployed subjects (HR 2.28, 95% CI: 1.76–2.95), and other nonspecified workers (HR 1.39, 95% CI: 1.08–1.76) treated in ambulatory settings had increased adjusted mortality risk (Supplementary Materials). We also observed higher

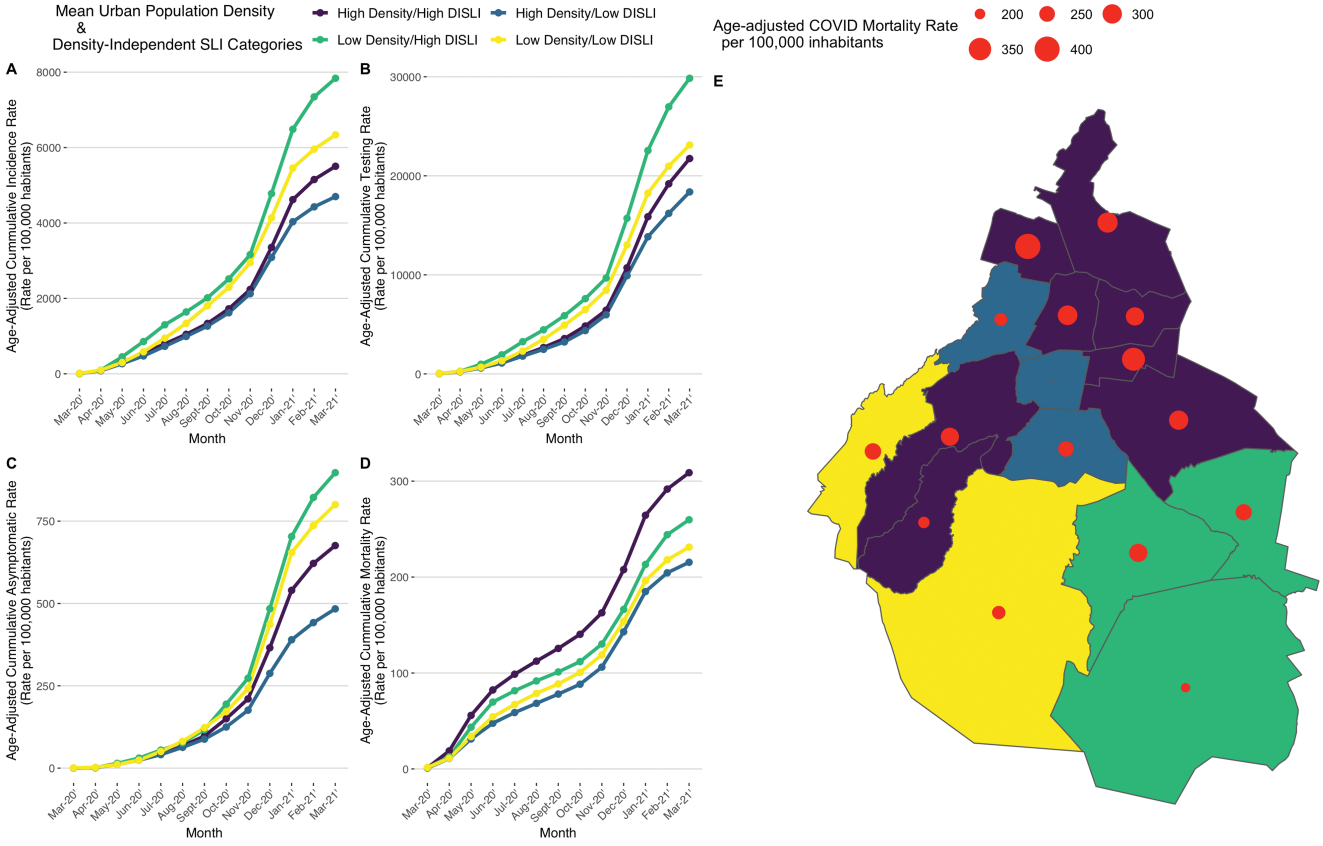

Figure 1. Population age-adjusted analyses of incidence (*A*), testing (*B*), asymptomatic (*C*), and mortality (*D*) rates per 100 000 inhabitants according with their MUPD and DISLI categories in Mexico City. Geographical distribution of age-adjusted COVID-19 mortality rate according to each individual municipality in Mexico City (*E*). Abbreviations: COVID-19, coronavirus disease 2019; DISLI, density-independent social lag index; MUPD, mean urban population density.

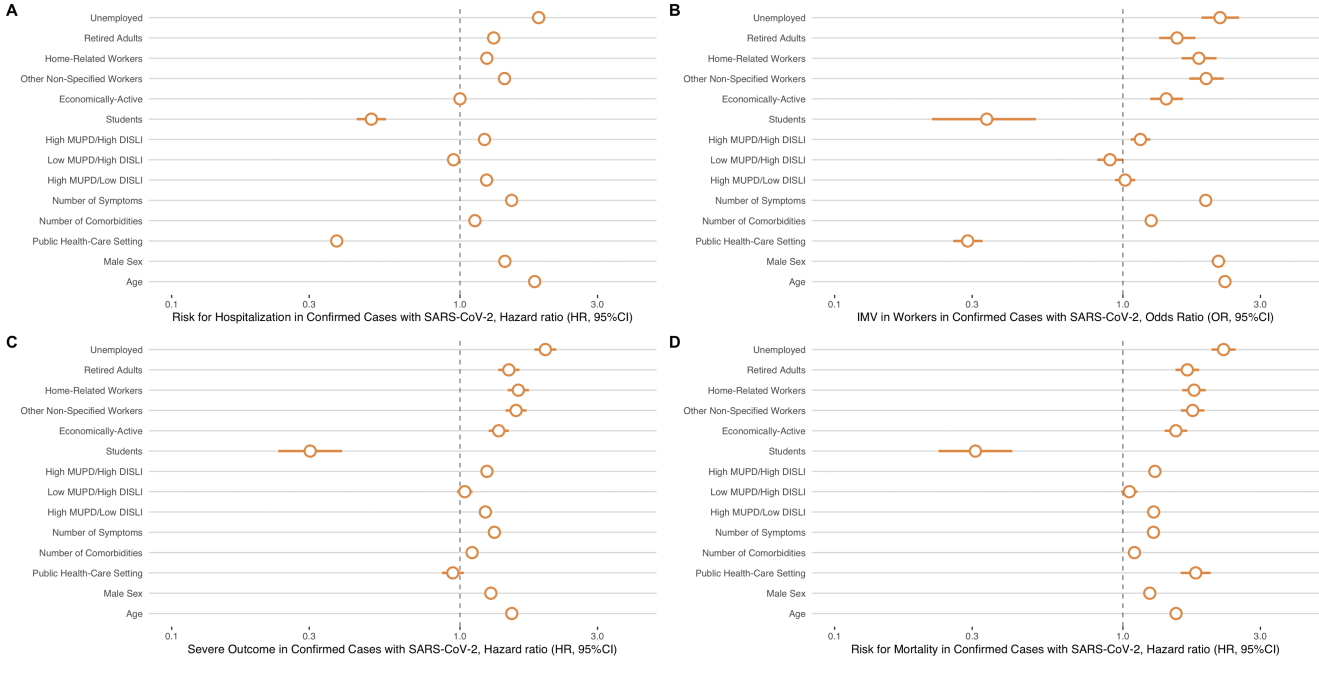

Figure 2. Individual and structural factors associated with hospitalization (*A*), IMV (*C*), severe COVID-19 (*B*), and death (*D*) in patients with suspected SARS-CoV-2 infection in Mexico City. Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; DISLI, density independent social lag index; HR, hazard ratio; IMV, invasive mechanical ventilation; MUPD, mean urban population density; RT-PCR, reverse transcription polymerase chain reaction, SARS-CoV-2,severe acute respiratory syndrome coronavirus 2.

adjusted mortality risk in domestic workers <65 years treated in ambulatory settings (HR 1.32, 95% CI: 1.06–1.63).

Vehicular Mobility had a Heterogeneous Effect on COVID-19 Rates

In high MUPD/low DISLI municipalities a decrease >27.29% in vehicular mobility was associated with decreased rates of severe COVID-19 (IRR 0.72, 95% CI: 0.53–0.99) and greater risk with mobility decreases only <16.39% (IRR 3.01, 95% CI: 1.29–7.02). In contrast, this protective effect was observed in low MUPD/high DISLI municipalities when vehicular mobility was decreased >71.21% (IRR 0.99, 95% CI: .98–1.00). Overall, to be effective, larger mobility reduction decreases were required in marginalized municipalities (Supplementary Materials). Both mobility and mortality rates displayed a bidirectional relationship using Granger causality tests. For instance, Granger causality tests supported that increased COVID-19 incidence had a causal effect on vehicular mobility reductions but not in the opposite direction. In ARDL models for incidence rates, only low MUPD/low DISLI showed significant short and long-term cointegration with mobility reduction, and for mortality rates only low Density/high DISLI showed long-term cointegration (Figure 3).

Discrepancies in Suspected COVID-19 Deaths in Mexico City

Mexico City went through a major hospital reconversion to prioritize COVID-19 care. We hypothesized that a) this systematic hospital reconversion impacted access to care for life-threatening non-COVID-19 diseases; b) that this, coupled with the wide-ranging disruption caused by the pandemic, produced excess mortality; and c) that this effect was influenced by sociodemographic inequalities and unequally distributed within Mexico City. GCR recorded 49 953 deaths with suspected COVID-19, of which 81.2% were registered in hospital, 17.5% in ambulatory settings, and 1.25% were unspecified; conversely, NESS reported 32 482 deaths with confirmed or suspected COVID-19 (91.5% in hospital and 8.5% in ambulatory settings). We report a 65.0% discrepancy between the GCR and the NESS, indicating underreported COVID-19 deaths. Furthermore, when grouping by MUPD/DISLI categories, low MUPD/high DISLI municipalities displayed an increased age-adjusted rate of unregistered suspected COVID-19 deaths. Overall, higher unregistered suspected COVID-19 deaths were associated with increased DISLI (IRR 2.42, 95% CI: 1.03–5.72) (Figure 4).

Unequal Distribution of Excess Mortality During the COVID-19 Pandemic in Mexico City

Age-adjusted mortality rates of non-COVID-19 deaths increased during 2020–2021 (10 805 per 100 000 inhabitants) compared to 2017–2019 (5259 per 100 000 inhabitants). Most non-COVID-19 deaths during 2020–2021 (63.6%) occurred in ambulatory settings, compared with hospital (31.4%) or unspecified settings (5.0%). The ratio of ambulatory to hospital non-COVID-19 deaths increased until reaching a 2:1 ratio (IQR: 1.61–2.59), with no significant differences across MUPD/DISLI categories during the studied period. Age-adjusted excess mortality (5546 per 100 000 inhabitants) had its highest peak in December 2020/February 2021 and was consistently higher in marginalized municipalities, regardless of MUPD. Overall, we observed a nonlinear association for DISLI to predict higher excess non-COVID-19 mortality (Supplementary Materials). High-MUPD/high DISLI (IRR 3.95, 95% CI: 3.47–4.48), low-MUPD/high DISLI (IRR 1.32, 95% CI: 1.15–1.50), and high MUPD/low DISLI (IRR 1.24, 95% CI: 1.08–1.41) municipalities had increased excess non-COVID-19 mortality compared to low-MUPD/low DISLI municipalities (Figure 4).

DISCUSSION

In this work, we evaluated the impact of sociodemographic and structural factors at an individual and municipal level over the course of the COVID-19 pandemic in Mexico City. We observed that socioeconomic occupation and the mix of high MUPD and marginalization, as measured by DISLI, leads to higher risk of COVID-19 outcomes. Social-distancing policies

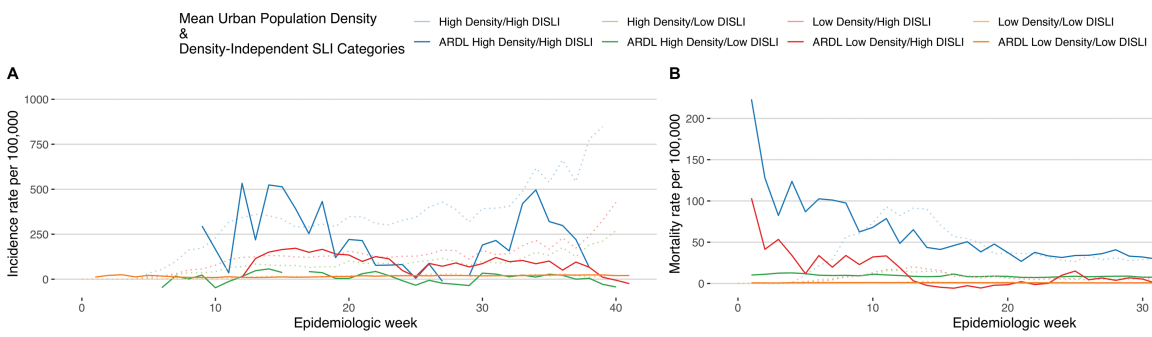

Figure 3. ARDL models assessing the effect of vehicular mobility restriction policies and its influence on COVID-19 incidence and mortality across MUPD and DISLI categories in Mexico City. Abbreviations: ARDL, autoregressive distributed lag; COVID-19, coronavirus disease 2019; DISLI, density independent social lag index; MUPD, mean urban population density.

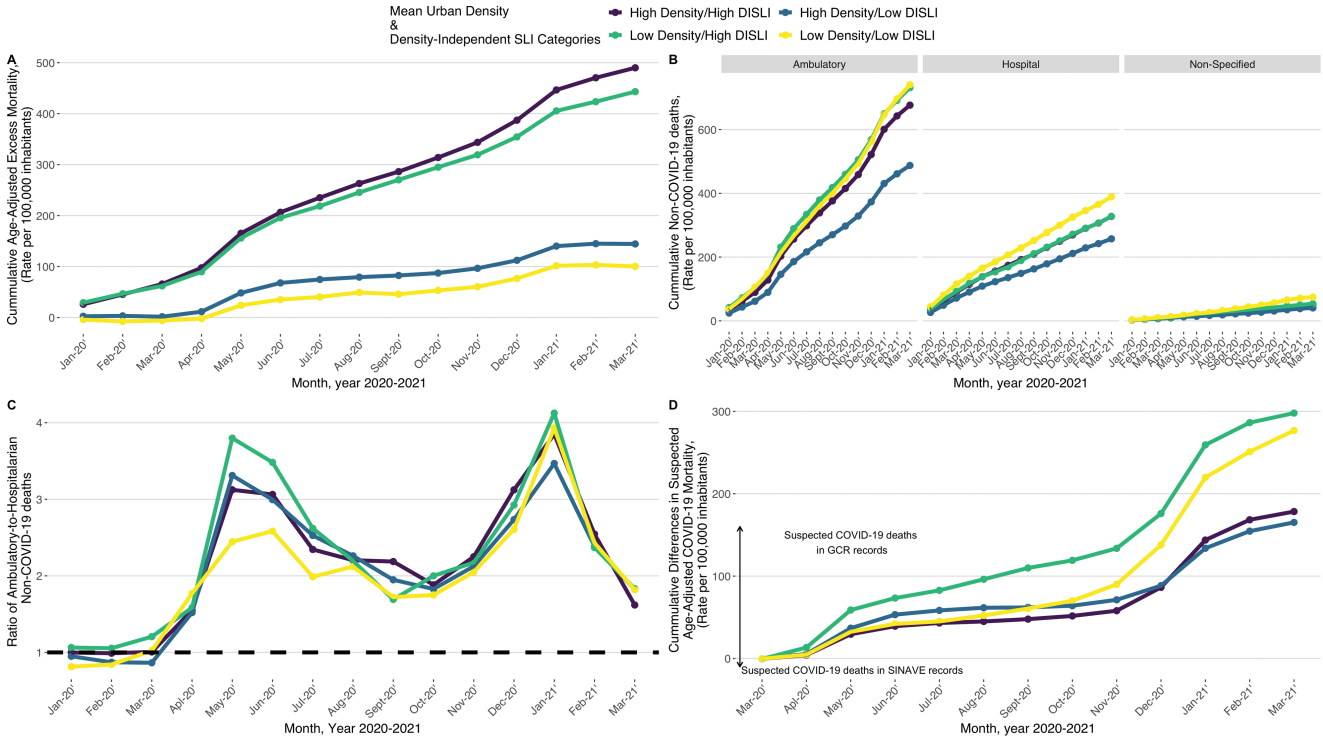

Figure 4. Age-adjusted excess mortality rates compared with year 2019 (*A*), cumulative non-COVID-19 deaths stratified by place of death (*B*), rate of ambulatory-to-hospitalization ratio of non-COVID-19 deaths (*C*) and differences in age-adjusted mortality rates of suspected COVID-19 deaths between the NESS and GCR (*D*) across mean urban population density (MUPD) and density-independent SLI (DISLI) categories in Mexico City. Abbreviations: COVID-19, coronavirus disease 2019; DISLI, density independent social lag index; MUPD, mean urban population density.

as proxied by reduced vehicular mobility [28] also had differential impacts on COVID-19 rates across municipalities depending on MUPD/DISLI. Finally, we observed an excess of COVID-19 and non-COVID-19 deaths, largely influenced by MUPD/DISLI, as seen in other countries [5, 29–31]. Our results support that densely populated and marginalized communities have increased risk of sustained community transmission of infectious diseases, including SARS-CoV-2 [32–34]; this was reflected by increased testing and incidence rates in municipalities with both high DISLI/MUPD. The precise "pathways of embodiment" and the "processes of social determination" through which MUPD/DISLI lead to higher rates of COVID-19 outcomes require further quantitative and qualitative research. Broadly, they can be conceptualized as structural factors and aspects related to healthcare provision, access to care restrictions, limited critical care capacity, and worse outcomes in public sectors, which are translated into health inequalities in Mexico. COVID-19 mortality and excess mortality patterns follow a similar distribution to lower life expectancy, perhaps suggesting that structural factors which increased risk for transmission and adverse outcomes play a larger role than those related to healthcare provision, but this requires further confirmation. This is relevant, as life expectancy is generally thought to be more closely related to standards of living than to healthcare provision [10].

Disparities in Mexico City have translated into social and structural deficiencies which have impacted healthcare access and quality of care even before the COVID-19 pandemic [35]. Although government actions have probably attenuated the impact of COVID-19 on vulnerable communities, our results show that their impact has been unequally distributed. As shown by our results, untargeted strategies to reduce urban mobility may not be equally effective for all areas of Mexico City. Informal workers or unemployed subjects may live in conditions that prevent them guaranteed access to healthcare services and may not adhere to social distancing mandates due to an inability to suspend work to maintain economical sustenance during the pandemic [36, 37]. This additional risk offsets the possible benefit of reduced comorbidity burden of subjects living in high DISLI/MUPD compared to low DISLI/MUPD municipalities and indicate the relevance of socioeconomic factors in determining the course of the pandemic. To be effective in halting the impact of the COVID-19 pandemic, government measures need adaptation to the urban sociodemographic characteristics of Mexico City to guarantee equitable access to health services, prompt detection of SARS-CoV2 infection, and sufficient stipends to facilitate self-isolation.

Excess mortality was predicted as an unwanted and most critical effect of the COVID-19 pandemic [38, 39]. In Mexico City, excess mortality may stem from intrinsic deficiencies

in healthcare provision, along with a fragmented hospital framework which complicates interoperability and an insufficient number of HCWs heavily burdened by the pandemic, which created a triple overload for the Mexican healthcare system [11, 20, 39, 40]. Given the urgent need to mitigate increased pressure of the pandemic on the public healthcare system, government authorities sought to create a strategy based on hospitals' reconversion and modified patient admission criteria to prioritize cases with severe COVID-19. This systematic hospital reconversion likely led to undesired negative externalities, where a vulnerable sector of the population had to restrict attention for non-COVID-19 related ailments and were less likely to seek urgent medical attention in emergency settings. This excess mortality could also be accounted for by unregistered COVID-19 deaths, indirect economic effects or increased mobilization of medical emergencies from neighboring states seeking attention given potential unavailability of medical services. Further work is required to elucidate underlying causes of excess deaths to truly assess negative externalities of hospital reconversion during the COVID-19 pandemic in Mexico.

Our study brings novel insights of the COVID-19 pandemic in Mexico City. The integration of several population-based datasets provides a unique opportunity to assess the role of individual and municipality-wide structural and social determinants which interplayed and ultimately modified the course of the pandemic. Nevertheless, some limitations should be acknowledged. All estimations made in population analyses were based on projections of economic population of the first quarter of 2020 and may not capture dynamics around employment occupation and population structure during the study period. Furthermore, age adjustment for incidence and mortality rates for working groups could not be performed due to unavailability of population structure data disaggregated by working group. Second, categorization by MUPD/DISLI categories was based solely on Mexico City data, which may not represent Mexico's wider socioeconomic disparities or heterogeneity within smaller communities or individual socioeconomic levels within Mexico City. Third, NESS may not fully capture patients with mild and asymptomatic SARS-CoV-2 infection, which represents a bias toward cases with moderate-to-severe COVID-19. Finally, excess mortality data do not report disaggregated etiology of non-COVID-19 deaths, which prevents further assessment of areas that may have required attention during the pandemic to prevent excess deaths.

In summary, individual- and municipal-level socioeconomic and structural factors played a significant role in shaping the course of the COVID-19 pandemic in Mexico City. Notably, despite higher incidence of SARS-CoV-2 infection in economically active workers, a higher burden of adverse COVID-19 outcomes was observed in retired, home-related, unspecified, and unemployed workers. DISLI was a risk factor for COVID-19 outcomes and its effect was modified by MUPD; furthermore, both DISLI/MUPD also modified the protective effect of vehicular mobility reduction policies in Mexico City. Finally, underreport of COVID-19 deaths is related to DISLI, although excess mortality was dependent on both DISLI/MUPD. Inequalities highlighted by the COVID-19 pandemic call for urgent actions to reduce socioeconomic disparities, increase healthcare access, and promote healthier lifestyles in Mexico City and beyond.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Authors' Contributions. Research idea and study design: N. E. A.-V., L. F.-C., J. P.-A., O. Y. B.-C.; data acquisition: N. E. A.-V., L. F.-C., J. P.-A., A. G.-D., O. Y. B.-C.; data analysis/interpretation: N. E. A.-V., L. F.-C., J. P.-A., J. M.-G., A. K.-G., A. V.-V., A. G.-D., C. A. F.-M., A. M.-S., E. C.-G., J. P. B.-L., M. V.-R., J. M.-S., M. E. J.-M., L. M. G.-R., O. Y. B.-C.; statistical analysis: N. E. A.-V., L. F.-C., J. P.-A., O. Y. B.-C.; manuscript drafting: N. E. A.-V., L. F.-C., J. P.-A., J. M.-G., L. M. G.-R., O. Y. B.-C.; supervision or mentorship: L. M. G.-R., O. Y. B.-C. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions about the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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