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Letters to the Editor

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COVID-19 and the worsening of health inequities in Santiago, Chile

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The COVID-19 pandemic is already responsible for >1 million deaths worldwide.[1] Latin America is one of the most affected regions worldwide, with >300 000 deaths confirmed by September 2020.[1] Latin America is also one of the most urbanized and unequal regions in the world, with wide inequities in longevity in its cities.[2] Wide inequities in COVID-19 outcomes have been reported in other settings.[3] However, policymakers in some Latin American countries have expressed scepticism about the existence of health inequities in COVID-19 mortality.[4] We used mortality, population and census data to show a worsening of pre-existing inequities in mortality in the municipalities that make up the metropolitan region of Santiago (Chile) during the COVID-19 pandemic.

We obtained data for the 36 *comunas* (municipalities) that make up Greater Santiago, the metropolitan area of the capital of Chile, on: (i) mortality by age for the 2016–2020 period from the Department of Statistics and Health Information (DEIS); (ii) population projections by age for the 2016–2020 period from the National Institute of Statistics (INE); and (iii) average years of schooling among adults aged ≥25 years, and the proportion of households living in overcrowding (>2.5 people/bedroom) from the 2017 Chilean census. We selected these two indicators since they represent either good measures of area-level socio-economic status (SES) or are directly linked to COVID-19 transmission. We computed age-adjusted mortality rates, using the 2000 World Health Organization reference population, from January to August for the pre-pandemic (years 2016–2019) and pandemic (2020) periods. We estimated the association between log(-mortality) and average years of schooling or proportion overcrowded households using a linear model for each period separately. Data and code for replication are available here: https://github.com/usamabilal/COVID_Chile_Inequities.

Figure 1 shows the main results. We found a strong association between SES and mortality in both periods, although this association was stronger in 2020. Specifically, we found a 9.0% lower mortality per 1-year increase in the average schooling years in the pre-pandemic period [relative risk (RR) = 0.91, 95% confidence interval (CI) 0.87 to 0.93] compared with a 13.8% lower mortality in the 2020 period (RR = 0.86, 95% CI 0.83 to 0.89). We also found that a 5% increase in the proportion of overcrowded households was associated with a 22% and 32% higher mortality in the pre-pandemic and pandemic periods, respectively (RR = 1.22, 95% CI 1.16 to 1.28; RR = 1.32, 95% CI 1.23 to 1.42).

In summary, we found a worsening of pre-existing inequities in mortality in the metropolitan area of Santiago de Chile during the COVID-19 pandemic. The association of years of schooling and overcrowding with mortality in the pre-pandemic period (2016–2019) is consistent with previous research in Santiago, showing wide gaps in life expectancy[2] and infant mortality.[5] Our finding that mortality inequities in 2020 were greater than in previous periods contradicts statements made in September 2020 by the Minister of Health of Chile, which indicated that there is no relationship between mortality due to COVID-19 and poverty, as this would imply discriminatory healthcare due to the place of origin of the patients.[4] This assertion ignores existing structural inequalities in Chile, including inequities in healthcare access and utilization by type of insurance both before[6] and during the pandemic,[7] along with social determinants of health beyond the health system. These include factors driving not only incidence and increased exposure to the virus,[3] such as more precarious employment conditions, loss of income and the need to work outside the home, but also an increased prevalence of conditions that aggravate the consequences of the disease, which show a strong social patterning in Chile.[8] Mitigating health inequities was an explicit objective of the Chilean National Health Strategy[9] and the aggravation of these inequities amidst the COVID-19 pandemic represents a step in the wrong direction. Our analysis is limited by the lack of individual-level mortality data and a validated SES index. However, we are using whole-

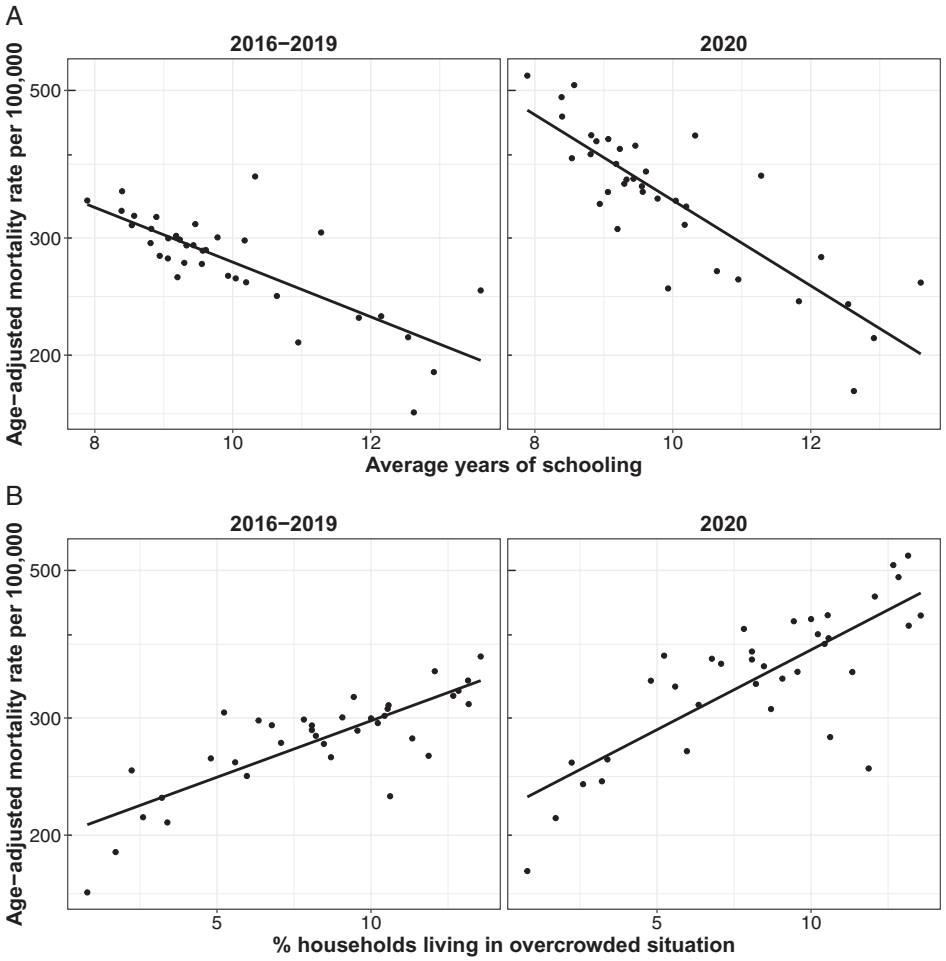

Figure 1 Area-level socio-economic status and age-adjusted mortality in 2016–2019 and 2020 in the municipalities of Santiago, Chile (A) Average years of schooling for adults >25 years of age; (B) percentage of households living in overcrowded situations. The solid line represents a linear fit.

population vital-registration data in a country with a good vital-registration system,[10] which lends strength to our findings.

Interventions to reduce these inequities are greatly needed to avoid the continued widening of these gaps, including but not exclusively focused on healthcare, in addition to addressing the other health and economic consequences of the pandemic, which will likely also affect these vulnerable groups more frequently, intensely and for more prolonged periods of time.

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The data underlying this article are available at https://github.com/usamabilal/COVID_Chile_Inequities/. All analyses were conducted with publicly available de-identified surveillance data.

Conflict of interest

None declared.

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BMI is unlikely to be a plausible intervention target for reducing the incidence of dementia

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Ma and colleagues investigated the relationship between body mass index (BMI) in midlife ($n = 6582$; average age, 62.5 years) and risk of dementia using data from the English Longitudinal Study of Ageing. They report that those who were obese had a 34% [95% confidence interval (CI), 7–61%] increased risk of being diagnosed with dementia over a 15-year follow-up of the study compared with those who were non-obese at baseline.[1] Associations were adjusted for a range of baseline covariates including age, sex, apolipoprotein E-ϵ4 allele status, education, marital status, current smoking, physical activities, hypertension and diabetes. The positive relationship reported by Ma and colleagues is surprising in light of previous observational studies, including one of 2 million participants suggesting the opposite direction of association.[2]

Given these results, is it likely that obesity is a plausible modifiable risk factor for dementia? There have been many studies showing that obesity in midlife is associated with risk of dementia. However, as we know, correlation does not equal causation. The authors correctly note that the incidence of obesity has increased in recent years and, if their estimates did indeed reflect the true causal effect of obesity on risk of dementia, then rates of dementia could be expected to increase in the future. However, some of the best available evidence to date suggests that the age-specific incidence of Alzheimer's disease has declined over time in the UK.[3]

To definitively prove that obesity increases the risk of dementia, we would ideally need to conduct a large randomized–controlled trial of an intervention that modifies BMI (e.g. bariatric surgery). The intervention would have to occur long before the expected onset of dementia,[4] as most types of dementia have a long prodromal period. We would then need to follow up those participants over time to see whether those who received the surgery did indeed have a lower risk of dementia. However, this hypothetical trial would be expensive, time-consuming and potentially unethical to conduct.

An analogous approach is to exploit naturally occurring random variation in BMI as a proxy. For example, genetic variation is known to be robustly associated with, and explains ~6% of the variation in BMI including variants near the FTO gene on chromosome 16.[5] If BMI affects risks of dementia, then we would expect individuals with genetic variants that predispose them to higher levels of BMI across the life course to also have a higher risk of dementia and the most common type of dementia, Alzheimer's disease. This approach, known as Mendelian randomization (MR), is less likely to suffer from bias due to confounding and cannot be affected by reverse causation, because genetic variants are randomly allocated at conception and cannot be modified by subsequent disease. MR estimates suggest that increases in BMI are unlikely to have any clinically meaningful effect on Alzheimer's disease (odds ratio per unit increase in BMI: 0.98; 95% CI, 0.89–1.08 in Korologou-Linden and colleagues; and odds ratio: 1.05; 95% CI, 0.91–1.21 in Larsson and colleagues).[6,7] However, there is evidence that genetic liability to Alzheimer's disease has a causal effect on BMI and the magnitude of this effect increases with age, suggesting that the associations of BMI and Alzheimer's disease reported by observational studies are likely a result of reverse causation or survival bias.

As with all research methods, MR has limitations and can suffer from selection or collider bias, or survival effects. MR assumes a linear effect of the risk factor and may not be able to detect U-shaped