

# Educational and social inequalities and cause-specific mortality in Mexico City: a prospective study

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## Summary

**Background** Social inequalities in adult mortality have been reported across diverse populations, but there is no large-scale prospective evidence from Mexico. We aimed to quantify social, including educational, inequalities in mortality among adults in Mexico City.

**Methods** The Mexico City Prospective Study recruited 150 000 adults aged 35 years and older from two districts of Mexico City between 1998 and 2004. Participants were followed up until Jan 1, 2021 for cause-specific mortality. Cox regression analysis yielded rate ratios (RRs) for death at ages 35–74 years associated with education and examined, in exploratory analyses, the mediating effects of lifestyle and related risk factors.

**Findings** Among 143 478 participants aged 35–74 years, there was a strong inverse association of education with premature death. Compared with participants with tertiary education, after adjustment for age and sex, those with no education had about twice the mortality rate (RR 1·84; 95% CI 1·71–1·98), equivalent to approximately 6 years lower life expectancy, with an RR of 1·78 (1·67–1·90) among participants with incomplete primary, 1·62 (1·53–1·72) with complete primary, and 1·34 (1·25–1·42) with secondary education. Education was most strongly associated with death from renal disease and acute diabetic crises (RR 3·65; 95% CI 3·05–4·38 for no education vs tertiary education) and from infectious diseases (2·67; 2·00–3·56), but there was an apparent higher rate of death from all specific causes studied with lower education, with the exception of cancer for which there was little association. Lifestyle factors (ie, smoking, alcohol drinking, and leisure time physical activity) and related physiological correlates (ie, adiposity, diabetes, and blood pressure) accounted for about four-fifths of the association of education with premature mortality.

**Interpretation** In this Mexican population there were marked educational inequalities in premature adult mortality, which appeared to largely be accounted for by lifestyle and related risk factors. Effective interventions to reduce these risk factors could reduce inequalities and have a major impact on premature mortality.

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## Introduction

Social inequalities in health have been observed in many populations, although their nature and extent differ.<sup>1,2</sup> Studies in Europe and North America have repeatedly shown higher mortality among more socially disadvantaged groups.<sup>1,3,4</sup> Qualitatively similar social gradients in mortality have been reported in Latin American populations,<sup>5–9</sup> and one of the few large-scale prospective studies from this region showed an almost doubling of premature mortality rates among Cuban adults who had not completed primary education when compared with those with university education.<sup>7</sup> However, detailed understanding of the size and nature of social inequalities in mortality in other Latin American populations is lacking, reflecting limitations of study designs (eg, ecological studies<sup>8</sup> and small study populations<sup>6</sup>) and data

(eg, a reliance on routine data)<sup>5,6</sup> used to investigate them. Reported prospective associations of education, or other socioeconomic indicators, with mortality among the Mexican population are limited to small-scale studies, generating mixed findings.<sup>10–12</sup> Large-scale evidence is restricted to that from studies reliant on routine data, precluding detailed understanding of the nature of inequalities or factors contributing to them.<sup>13</sup> Given the complexity of social patterning of health and disease, and influences—including context-dependent influences—on this, the generalisability of findings between regions and countries is unclear. Robust large-scale prospective evidence is needed to understand and mitigate social inequalities in health in the Mexican population.

We aimed to report the associations of education, and other socioeconomic indicators, with cause-specific

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## Research in context

### Evidence before this study

We undertook a literature search in PubMed to identify articles published in English from database inception to before June 23, 2023, that reported on prospective studies examining the association of education, or other indicators of socioeconomic position, with mortality in a Mexican or Latin American population, using the terms ("socioeconomic" OR "socio-economic" OR "education") AND ("mortality" OR "death") AND ("Mexico" OR "Mexican" OR "Latin America" OR "Latin American"). Reference lists of relevant articles were also reviewed. There were few prospective studies examining social inequalities in mortality among adults in Mexico. The largest involved fewer than 14 000 participants and investigated only overall mortality. None investigated factors mediating the association of education with mortality. One large prospective Latin American population-based study was identified, including approximately 150 000 adults in Cuba. This study found a strong inverse association between education and death, a third of which was explained by lifestyle factors in men and a fifth in women. However, generalisability of these findings to other countries in the region with very different social and economic contexts is unclear.

### Added value of this study

The present study, including approximately 150 000 men and women from Mexico City, showed strong social, including educational, inequalities in premature adult mortality. There was

an inverse association of education with overall adult mortality; given age and sex, the death rate ratio (RR) at ages 35–74 years for participants with no education, when compared with participants with tertiary education, was 1.84. Deaths from renal disease and acute diabetic crises (RR 3.65) and from infectious disease (2.67) were most strongly associated with education, but higher education was associated with lower risk of death from most, if not all, specific causes. Income among men and an area-based measure of social development—the Social Development Index—were also inversely associated with overall and cause-specific mortality. Lifestyle factors (ie, smoking, alcohol consumption, and leisure time physical activity) and their physiological correlates (ie, adiposity, diabetes, and blood pressure) appeared to account for a large proportion (approximately 80%) of the association of education with death. Applying our RRs for overall mortality to 2020 Mexican national death rates, men and women with no formal education were estimated to have approximately 6 years lower life expectancy from age 35 years than those with tertiary education.

### Implications of all the available evidence

There are marked social inequalities in mortality among adults in Mexico City. Addressing major behavioural disease risk factors and their associated physiological correlates would be expected to contribute to reducing these disparities in health and, in turn, to reducing premature adult mortality in this population.

mortality in a prospective cohort of 150 000 adults from Mexico City who have been followed up for nearly two decades.

## Methods

### Study design and participants

The Mexico City Prospective Study design, methods, and population have been described previously.<sup>14</sup> Briefly, between 1998 and 2004, households in two districts of Mexico City (Coyoacán and Iztapalapa) were visited and household members aged 35 years and older were invited to participate in the study. Of 112 333 households with eligible inhabitants, one or more individuals from 106 059 (94%) households consented to participate.<sup>14</sup> Ethics approval was obtained from the Mexican Ministry of Health, the Mexican National Council for Science and Technology, and the University of Oxford, UK. All participants provided written informed consent.

### Data collection

During household visits, trained nurses administered electronic questionnaires collecting information on sociodemographic and lifestyle factors (including smoking, alcohol consumption, and physical activity), and measured height, weight, hip circumference, waist circumference, and sitting blood pressure using

calibrated instruments and standard protocols. A non-fasting venous blood sample was collected into an EDTA (edetic acid) vacutainer and separated into two plasma and one buffy coat aliquots for long-term storage at  $-150^{\circ}\text{C}$ . Glycated haemoglobin ( $\text{HbA}_{1c}$ ) concentrations were measured in buffy coat samples using a validated high-performance liquid chromatography method<sup>15</sup> on HA-8180 analysers with calibrators traceable to International Federation of Clinical Chemistry standards.<sup>16</sup> A repeat survey performed between 2015 and 2019 and including approximately 10 000 surviving participants collected the same information as at the baseline survey.

### Assessment of socioeconomic position

Self-reported indicators of socioeconomic position included highest education level and personal (ie, individual) monthly income. An area-based measure of social development—the Social Development Index (ie, the Índice de Desarrollo Social, 2010)<sup>17</sup>—was obtained for each participant based on their block of residence (determined from Global Positioning System coordinates recorded at the baseline household visit). The Social Development Index is a composite score calculated from block or manzana-level (each including just one or a small group of houses or buildings)

measures of six domains: quality and space of housing (33·8% weighting), access to health and social security (29·1%), education (24·4%), ownership of household goods (6·0%), adequate access to water supply and drainage (3·8%), and energy (2·9%).<sup>17</sup>

### Follow-up for mortality

Participants are followed up for cause-specific mortality through probabilistic linkage (based on name, including phonetic coding of names, age, and sex [information on place of birth was not available]) to the Mexican System for Epidemiologic Death Statistics (Sistema Epidemiológico y Estadístico de Defunciones or SEED) electronic death registry in Mexico City, administered by the Ministry of Health. Field validation of more than 7000 matched deaths confirmed the reliability of the matching algorithm in more than 95% of deaths. Death registration in Mexico City is reliable and complete, with almost all deaths certified medically.<sup>18</sup> Diseases recorded on death certificates are coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, with subsequent review by study clinicians (who are unaware of baseline information) to recode, when necessary, the underlying cause of death.<sup>15</sup> Participant deaths were tracked until Jan 1, 2021.

### Statistical analysis

Analyses excluded participants aged 85 years or older, with missing education data, missing or extreme covariate or mediator data, or who had an uncertain cause of death. Education was categorised to reflect Mexico's main phases of schooling: none, incomplete primary, complete primary, secondary, and tertiary education. Monthly income was grouped into five categories: no income reported, less than 1500 pesos, 1500 to less than 3000 pesos, 3000 to less than 4500 pesos, 4500 or more pesos. At the time of recruitment, 1500 pesos was equal to approximately 150 US dollars. The Social Development Index was subdivided into five groups by the quintiles of its distribution; high scores represent high social development, indicative of low relative deprivation of an area.

Cox proportional hazards regression models, with time since entry into the study as the underlying timescale, were used to assess the relevance of education, income (among men only since 64% of women reported no income), and the Social Development Index for all-cause and cause-specific mortality (appendix pp 2–3). The log hazard ratio from a Cox model provides a useful summary statistic for the average log mortality rate ratio (RR) across the different time periods of follow-up. These mortality RRs were stratified by age-at-risk (5-year groups) and, for analyses of men and women combined, by sex. This allows for a different baseline hazard in each stratum, so the proportional hazards assumption was made only within strata of age-at-risk (and, when

relevant, sex). Group-specific variances were estimated (reflecting the amount of data in each exposure category), such that the RR for each category, including the reference category, is associated with a group-specific 95% CI, enabling comparisons between any two categories and not only with the reference group.<sup>19</sup> Participants who did not die from the cause of interest were censored at the earliest of death from any other cause, the end of the age-at-risk period of interest, or Dec 31, 2020. The main analyses examined premature mortality (ie, deaths before 75 years of age),<sup>15</sup> but the relevance of education for mortality at 75–84 years of age was also examined.

Prospective cohort studies of non-representative cohorts of individuals—as in the current case of Mexican adults from just two Mexico City districts—can generate reliable evidence about the associations of risk factors with health outcomes that are generalisable to a wider underlying population.<sup>20–22</sup> With this assumption, and also assuming causality and generalisability of the distributions of education and the causes of death in our study to the rest of Mexico, we estimated what the hypothetical effect might be of differing levels of education on survival from age 35 years to 70 years at 2020 Mexican mortality rates. For example, if the national death rate for Mexican men in 2020<sup>23</sup> for a given 5-year age range was A, we calculated the death rates for each of the five education groups (ie, none, incomplete primary, complete primary, secondary, and tertiary) that would ensure that their prevalence-weighted average equalled A and the relative differences between them matched the RRs in our study.

The extent to which the association of education with mortality was accounted for by lifestyle (ie, smoking status, alcohol consumption, and leisure time physical activity) and related factors (ie, adiposity [weight, height, waist circumference, and hip circumference], diabetes status, and systolic blood pressure) was assessed in exploratory analyses in two ways. First, by estimating the proportional reduction in the  $\chi^2$  statistic associated with the five-level education variable before versus after including the potential mediators in the model, and second, by estimating the proportional reduction in the log RR for those with no education versus tertiary education before versus after including the potential mediators in the model. In these models, smoking status was categorised into five groups (ie, never, former, occasional, fewer than ten cigarettes per day, or ten or more cigarettes per day), as was alcohol consumption (ie, never, former, less than weekly, up to two days per week, or more than two days per week), physical activity into three groups (ie, none, up to twice weekly, or at least three times weekly), diabetes status into five groups (ie, no diabetes, undiagnosed diabetes [no previous diabetes diagnosis and HbA<sub>1c</sub> of 6·5% [48 mmol/mol] or more], previously diagnosed diabetes with HbA<sub>1c</sub> less than 9% [75 mmol/mol], previously

See Online for appendix

	Men (n=46 674)				Women (n=96 804)					
	None (n=3390)	Incomplete primary (n=7529)	Complete primary (n=11403)	Secondary (n=12633)	Tertiary (n=11719)	None (n=12 358)	Incomplete primary (n=20083)	Complete primary (n=28 257)	Secondary (n=24313)	Tertiary (n=11 793)
Age, years*	60.7 (10.4)	57.8 (10.4)	53.1 (10.3)	47.5 (9.8)	46.9 (9.3)	58.8 (10.4)	54.8 (10.4)	50.1 (9.7)	45.5 (9.0)	44.6 (8.2)
Income, pesos per month	1306 (2065)	1723 (1663)	2358 (2900)	3195 (3712)	6679 (8747)	288 (673)	366 (911)	545 (1272)	1075 (2039)	3166 (4842)
Social Development Index†	0.72 (0.08)	0.73 (0.09)	0.74 (0.10)	0.76 (0.10)	0.81 (0.11)	0.72 (0.09)	0.73 (0.10)	0.75 (0.10)	0.77 (0.11)	0.82 (0.11)
Smoking status										
Current smoker	1488 (44%)	3631 (48%)	5939 (52%)	7172 (57%)	5564 (47%)	1503 (12%)	3378 (17%)	6693 (24%)	7701 (32%)	3811 (32%)
Ex-smoker	1195 (35%)	2619 (35%)	3341 (29%)	3162 (25%)	3160 (27%)	1565 (13%)	2613 (13%)	3886 (14%)	3679 (15%)	2186 (19%)
Never smoked	707 (21%)	1279 (17%)	2123 (19%)	2299 (18%)	2995 (26%)	9290 (75%)	14092 (70%)	17 678 (63%)	12 933 (53%)	5796 (49%)
Drinking behaviour										
Current drinker	2162 (64%)	5366 (71%)	8698 (76%)	10129 (80%)	9862 (84%)	5930 (48%)	11 571 (58%)	18 051 (64%)	16755 (69%)	8595 (73%)
Former drinker	931 (27%)	1750 (23%)	2070 (18%)	1844 (15%)	1112 (9%)	2033 (16%)	2786 (14%)	3190 (11%)	2277 (9%)	867 (7%)
Never drinker	297 (9%)	413 (5%)	635 (6%)	660 (5%)	745 (6%)	4395 (36%)	5726 (29%)	7016 (25%)	5281 (22%)	2331 (20%)
Leisure-time physical activity										
None	2895 (85%)	6043 (80%)	8353 (73%)	8416 (67%)	6826 (58%)	11 148 (90%)	17 459 (87%)	23 319 (83%)	18 685 (77%)	7980 (68%)
Up to 2 times per week	175 (5%)	618 (8%)	1405 (12%)	2136 (17%)	2046 (17%)	473 (4%)	872 (4%)	1284 (5%)	1423 (6%)	992 (8%)
≥3 times per week	320 (9%)	868 (12%)	1645 (14%)	2081 (16%)	2847 (24%)	737 (6%)	1752 (9%)	3654 (13%)	4205 (17%)	2821 (24%)
Anthropometry, blood pressure, and HbA <sub>1c</sub>										
BMI, kg/m <sup>2</sup>	27.7 (4.3)	28.2 (4.2)	28.2 (4.2)	28.1 (4.2)	27.8 (4.1)	30.2 (5.3)	30.4 (5.2)	30.0 (5.1)	29.1 (5.0)	28.0 (4.9)
Waist circumference, cm	97 (10)	97 (10)	96 (10)	96 (10)	96 (10)	97 (12)	96 (12)	94 (12)	91 (12)	89 (12)
Hip circumference, cm	100 (8)	101 (8)	101 (8)	101 (8)	102 (8)	107 (12)	107 (11)	107 (11)	106 (11)	104 (11)
Systolic blood pressure, mm Hg	133 (17)	132 (17)	129 (16)	126 (14)	126 (14)	134 (19)	130 (17)	126 (16)	122 (15)	120 (14)
Diastolic blood pressure, mm Hg	85 (10)	85 (10)	85 (10)	84 (10)	84 (9)	85 (11)	84 (10)	83 (10)	81 (10)	80 (9)
HbA <sub>1c</sub> , %‡	5.8 (1.1)	5.8 (1.1)	5.7 (1.0)	5.6 (1.0)	5.5 (0.8)	5.9 (1.2)	5.8 (1.1)	5.7 (1.0)	5.5 (0.8)	5.4 (0.7)
Previous diseases§										
Diabetes	643 (19%)	1414 (19%)	1807 (16%)	1285 (10%)	940 (8%)	2827 (23%)	3814 (19%)	3611 (13%)	1637 (7%)	528 (4%)
Cardiovascular disease	116 (3%)	288 (4%)	353 (3%)	257 (2%)	248 (2%)	354 (3%)	487 (2%)	554 (2%)	335 (1%)	152 (1%)
Cancer	14 (<1%)	38 (1%)	72 (1%)	54 (<1%)	67 (1%)	179 (1%)	302 (2%)	407 (1%)	348 (1%)	188 (2%)
Other¶	182 (5%)	450 (6%)	613 (5%)	536 (4%)	547 (5%)	1160 (9%)	2090 (10%)	2948 (10%)	2153 (9%)	1074 (9%)

Data are n (%) or mean (SD). HbA<sub>1c</sub>=glycated haemoglobin. \*Median 50.5 years (IQR 41.5–59.5) for men and 48.5 years (41.5–58.5) for women. †Higher scores represent higher area-based social development. ‡HbA<sub>1c</sub> among participants without previously diagnosed diabetes. §Self-reported diseases. ¶Other diseases include emphysema, chronic kidney disease, peptic ulcer, cirrhosis, and peripheral arterial disease.

Table: Baseline characteristics of men and women aged 35–74 years by education at recruitment

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diagnosed diabetes with HbA<sub>1c</sub> greater than or equal to 9% and less than 11% [97 mmol/mol], or previously diagnosed diabetes with HbA<sub>1c</sub> 11% or more), and weight, height, waist circumference, hip circumference, and systolic blood pressure were included as continuous variables.

Analyses were conducted using SAS (version 9.4) and R (version 3.6.2).

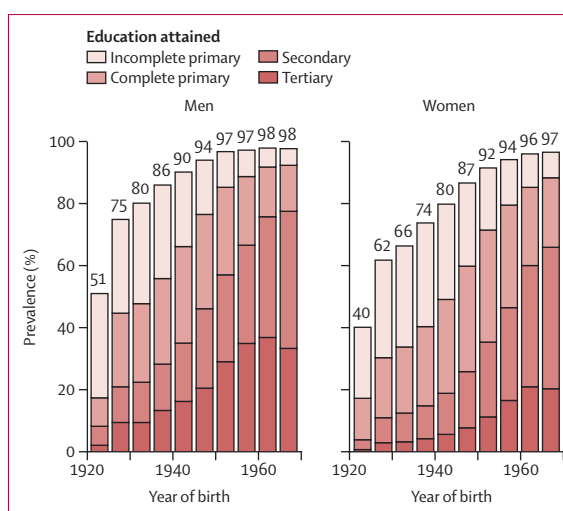
### Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

## Results

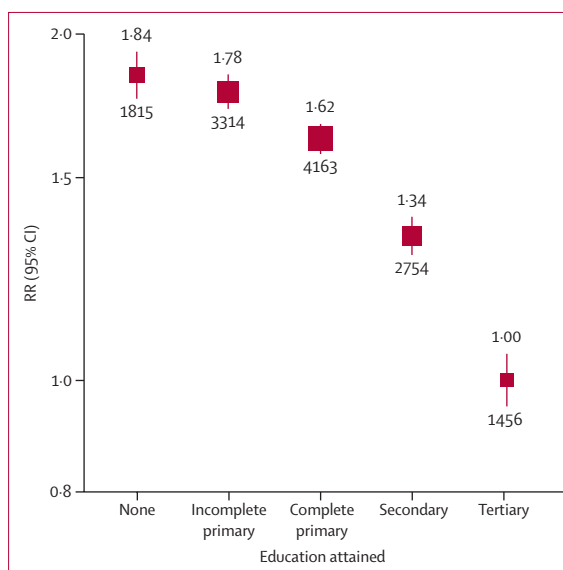
Of 159 755 participants recruited, 7456 (5%) were excluded from the present analyses. These comprised 2466 (2%) aged 85 years or older at recruitment, a further 2802 (2%) with missing education data or missing or extreme data on covariates or mediators, a further 1960 (1%) with uncertain mortality linkage, and a further 228 who were recruited twice (data from the first visit at which a blood sample was collected were used for these participants). Of the remaining 152 299 participants, 143 478 (94%) were aged 35–74 years and 8821 (6%) were aged 75–84 years at recruitment.

Among participants aged 35–74 years at recruitment (table), 46 674 (33%) were men and the mean age was 50.7 years (SD 10.8). Men were, on average, more highly educated than were women. Among men, 3390 (7%) reported no education, 7529 (16%) incomplete primary education, 11 403 (24%) complete primary education, 12 633 (27%) secondary education, and 11 719 (25%) tertiary education. Corresponding figures among women were 12 358 (13%), 20 083 (21%), 28 257 (29%), 24 313 (25%), and 11 793 (12%), respectively. At recruitment, more highly educated participants tended to be younger, consistent with patterns of education by birth cohort (figure 1). Higher levels of education were associated with higher monthly income, more frequent leisure time physical activity, and higher prevalence of current alcohol drinking. More highly educated women were more likely to be current or former smokers and to have lower adiposity levels. There was no clear trend in smoking status or adiposity according to education among men. Men and women with less education had higher blood pressure, more frequently reported a previous diagnosis of diabetes and, among those without a previous diagnosis of diabetes, tended to have higher HbA<sub>1c</sub> levels. The prevalence of other previously diagnosed chronic diseases differed little by education. Baseline characteristics of participants aged 35–74 years, separately for the two study districts, are provided in the appendix (p 4). When 9941 participants were resurveyed, on average, 16 years after the baseline survey, self-reported education was unchanged among 7185 (72%; kappa=0.64 for agreement between baseline and resurvey; appendix p 5).



**Figure 1: Education by year of birth**

Analyses among 143 478 participants aged 35–74 years at recruitment. Numbers above the bars are the percentage of participants in that birth cohort with any formal education.

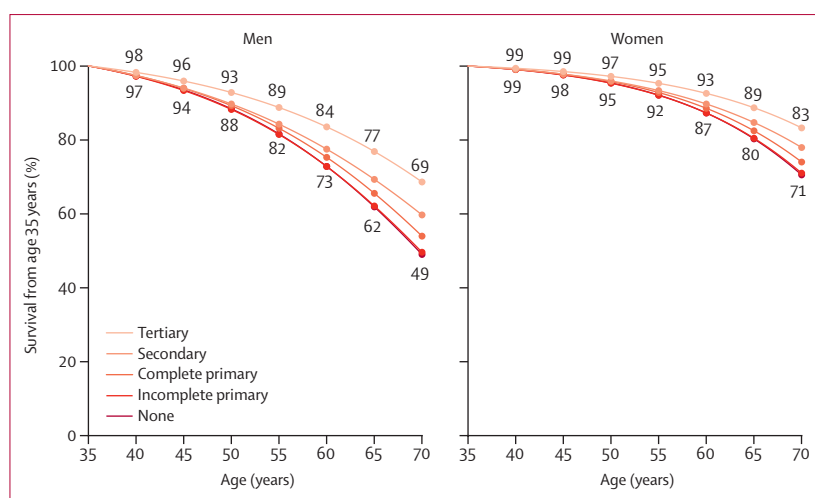


**Figure 2: Relevance of education to mortality from any cause at ages 35–74 years**

RRs are stratified by age-at-risk and sex. The numbers above the squares are the RRs and the numbers below the squares are the number of deaths in that group. The area of each square is proportional to the amount of statistical information. The error bars represent 95% CIs. RR=rate ratio.

During an average of 18.4 (IQR 17.6–19.7) years of follow-up, 13 502 participants died at ages 35–74 years, including 3679 deaths from vascular disease (including 2585 cardiac and 800 stroke deaths), 1140 from hepatobiliary disease, 2710 from renal disease and acute diabetic crises, 2246 from cancer, 1779 from respiratory disease, and 857 from infectious disease (appendix pp 2–3). Among 152 299 participants aged 35–84 years at recruitment, 7908 died at ages 75–84 years.





**Figure 3: Hypothetical effect of mortality RRs associated with education on survival from age 35–70 years, at 2020 mortality rates in Mexico**

Absolute death rates at ages 35–70 years among people with different levels of education were estimated by combining age and sex-specific 2020 national death rates in the eight component 5-year age groups<sup>23</sup> with study RRs for all-cause mortality at ages 35–59 years and 60–69 years, assuming 7% of men had no education, 16% incomplete primary education, 24% complete primary education, 27% secondary education, and 25% tertiary education, with corresponding proportions among women of 13%, 21%, 29%, 25%, and 12%, respectively. For example, for each 5-year age group, the average annual mortality rate among men with tertiary education was estimated as A, and among men with other levels of education was estimated as the mortality RR for that level of education versus tertiary education multiplied by A, with A chosen such that  $(0.07 \times \text{RR}_{\text{no education}} \times A) + (0.16 \times \text{RR}_{\text{incomplete primary education}} \times A) + (0.24 \times \text{RR}_{\text{complete primary education}} \times A) + (0.27 \times \text{RR}_{\text{secondary education}} \times A) + (0.25 \times A)$  equalled the 2020 Mexican mortality rate for that 5-year age group in men. RR=rate ratio.

Education was strongly inversely associated with premature mortality; after adjustment for age and sex, participants with no education had almost twice the death rate of those with tertiary education (RR 1.84; 95% CI 1.71–1.98; figure 2). The association appeared stronger in women (RR 2.03; 95% CI 1.87–2.21) than in men (1.62; 1.45–1.81; appendix p 9). Moreover, among women the inverse association was apparent at all levels of education (incomplete primary education RR 1.93 [95% CI 1.79–2.09]; complete primary education 1.68 [1.56–1.81]; and secondary education 1.39 [1.28–1.51]), while among men, death RRs were similar for those with no education (1.62; 1.45–1.81), incomplete primary (1.67; 1.53–1.82), and complete primary (1.62; 1.50–1.75) education. Sensitivity analyses showed no notable change in mortality RRs associated with education during the follow-up period (appendix p 6).

Applying our RRs for death from any cause to the 2020 Mexican national death rates, figure 3 shows estimated survival trajectories for men and women aged 35–70 years by education. Among men, the 35-year probability of survival would be 69% in those with tertiary education compared with 49% in those with no formal education. Equivalent probabilities in women would be 83% in those with tertiary education and 71% in those with no formal education. These correspond to approximately 6 years lower life expectancy from age 35 years among men and women with no formal education when compared with those with tertiary education.

There was an inverse association of education with premature death from most, if not all, specific causes studied (figure 4). RRs for death comparing those with no education versus those with tertiary education were highest for the composite of death from renal disease or an acute diabetic crisis (RR 3.65 [95% CI 3.05–4.38]), death from infectious disease (2.67 [2.00–3.56]) and, to a lesser extent, death from hepatobiliary diseases (2.31 [1.83–2.92]) and stroke (2.28 [1.67–3.12]). Death RRs for respiratory disease were lower only among participants with tertiary education, with no gradient in mortality rates at lower education levels (RRs between 1.47 [95% CI 1.23–1.75] and 1.54 [1.26–1.88], compared with tertiary education). There appeared to be only a weak inverse association with cancer mortality among participants who reported some education (RR 1.13 [95% CI 0.98–1.31] for incomplete primary vs tertiary education). The associations of education with death from specific causes were slightly stronger in women (appendix p 10) than in men (appendix p 11) with the exception of death from hepatobiliary disease, for which there was no apparent difference between sexes. Education was less strongly associated with mortality at ages 75–84 years than at 35–74 years (appendix pp 12–13).

In exploratory mediation analyses, 84% of the model  $\chi^2$  relating education to mortality at ages 35–74 years appeared to be attributable to lifestyle factors (ie, smoking, alcohol consumption, leisure time physical activity), adiposity, diabetes status, and systolic blood pressure (appendix p 7). These same factors accounted for a similar proportion of the  $\chi^2$  for death from renal diseases (79%) and from infectious diseases (79%), moderately less—approximately 70%—of the  $\chi^2$  for death from vascular diseases (69%) and hepatobiliary diseases (74%), and a smaller proportion (51%) of the  $\chi^2$  for death from respiratory diseases.

Among men, the associations of income with other baseline characteristics were broadly similar to those of education (appendix p 8), and premature mortality rates were higher at lower income levels (appendix p 14). Men reporting no monthly income had more than twice the mortality rate of those reporting an income of 4500 or more pesos per month (RR 2.32 [95% CI 2.12–2.55]; appendix p 14). Income was most strongly related to death from stroke (RR 2.89 [95% CI 1.96–4.26] for men with no reported income vs  $\geq 4500$  pesos per month), hepatobiliary disease (3.53 [2.63–4.73]), and renal disease and acute diabetic crises (4.13 [3.30–5.17]; appendix p 15). Analyses examining the relevance of income for mortality among women are not presented since 64% reported no personal monthly income. Participants living in areas with a lower Social Development Index (indicating higher relative area-based deprivation) had higher death rates (appendix p 16). The death RR comparing those living in areas in the bottom quintile of the Social Development Index with those living in areas in the top quintile was 1.58

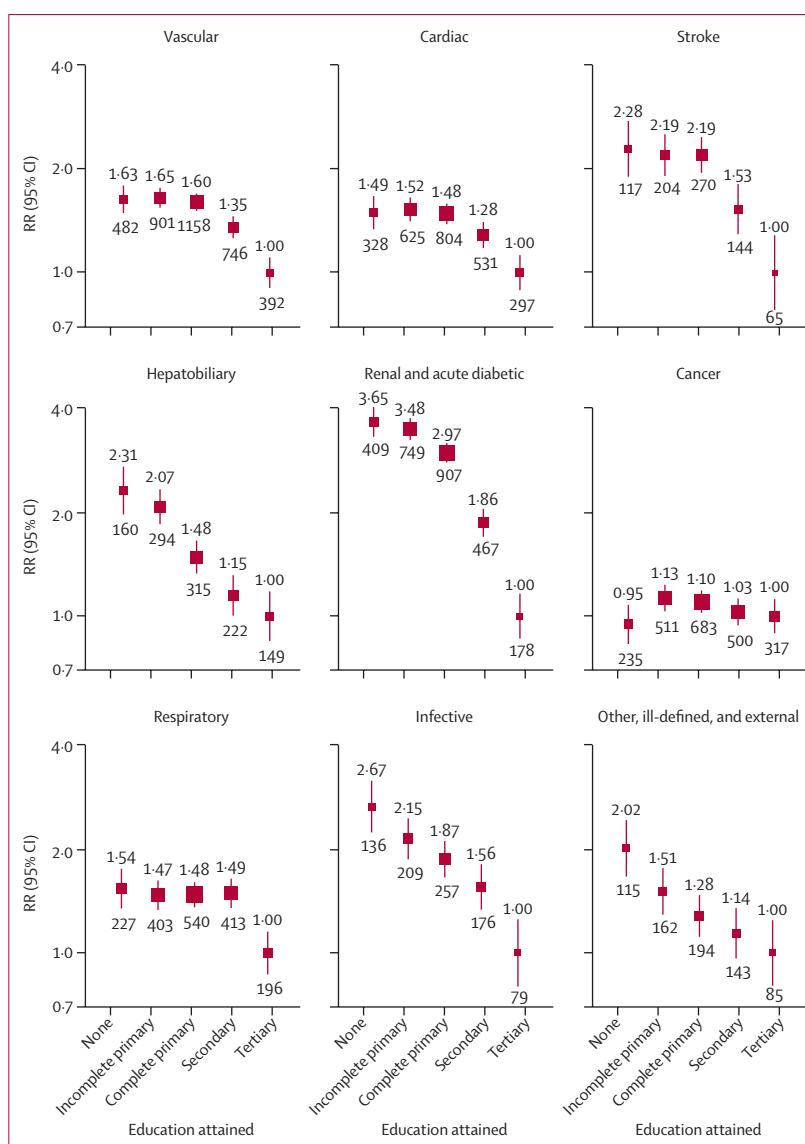
(95% CI 1.49–1.67). The association was modestly weaker in men than in women (appendix p 17). Inverse associations were also observed with death from most specific causes studied, with the exception of death from cancer for which there was no clear relationship (appendix p 18).

## Discussion

In this study of adults from two districts of Mexico City, we found marked social inequalities in mortality. Participants without formal education had premature death rates almost twice those of participants with tertiary education. Moreover, directionally consistent mortality gradients were observed with other socioeconomic exposures, including income (among men) and a population-specific social development index. Lifestyle and related physiological risk factors accounted for a large proportion of the observed educational inequalities in mortality.

Previous prospective evidence on the relevance of education for mortality in Mexico is limited to that from much smaller studies among older populations.<sup>10–12</sup> The largest of these, based on data for approximately 14000 participants in the Mexican Health and Aging Study, showed 30% lower risk of mortality from any cause among participants with tertiary education when compared with those with no formal education after adjusting for age and sex.<sup>11</sup> This result is not inconsistent with our findings after accounting for the older age (>50 years) of the Mexican Health and Aging Study population.<sup>11</sup> However, reliance on this and other previously-published prospective evidence,<sup>10–12</sup> all based on data from older populations than the Mexico City Prospective Study population, could underestimate the extent of educational inequalities in premature mortality. By contrast, we observed an approximately two-fold higher premature mortality rate among adults with no formal education, when compared with those with tertiary education, which is qualitatively and broadly quantitatively consistent with relationships reported in other populations.<sup>2,7,24</sup>

There were stronger inverse associations of education with death from acute renal and diabetic causes (which accounted for one in five premature deaths) and from infectious diseases than with deaths from other specific causes in the present study. Higher diabetes prevalence among participants with lower education, coupled with notably high diabetes-associated mortality from renal diseases and infectious diseases<sup>15</sup> in this population, likely contributed to these strong associations. Moreover, this finding appears consistent with previous evidence from Mexico, showing higher diabetes-related excess mortality in states with greater social disadvantage.<sup>25</sup> Lower mortality with higher education was evident across all education levels for most causes of death. However, only adults with tertiary education had lower respiratory mortality, and education was only weakly inversely



**Figure 4: Relevance of education to cause-specific mortality at ages 35–74 years**

RRs are stratified by age-at-risk and sex. The numbers above the squares are the RRs and the numbers below the squares are the number of deaths in that group. The area of each square is proportional to the amount of statistical information. The error bars represent 95% CIs. RR=rate ratio.

associated with cancer death. These findings contrast with those from previous studies, which have consistently reported inverse associations of education with respiratory<sup>3,7</sup> and cancer<sup>3,7,24</sup> mortality across all levels of education, possibly reflecting populations' differing smoking patterns. There was no clear association of education with smoking among men in the Mexico City population, whereas more highly educated women were more likely to have smoked. This finding contrasts with a higher prevalence of smoking in lower socioeconomic groups observed in many high-income, middle-income, and low-income settings,<sup>26,27</sup> but is consistent with nationwide representative surveys in Mexico,<sup>11,28</sup> and could

reflect the relatively early stage of the tobacco epidemic in Mexico at the time of recruitment into the current study.<sup>28</sup>

We observed differences according to education level in the frequency of adverse lifestyle factors (with the exception of smoking among men) and in the levels of physiological correlates (including adiposity among women and blood pressure and diabetes in both sexes). The strong educational gradient in diabetes prevalence in the absence of similarly strong gradients in adiposity measures likely reflects the influence of poor glycaemic control on weight loss among participants with diabetes. Adjustment for these modifiable risk factors—for which associations with mortality have been described previously<sup>15,29–31</sup>—in exploratory mediation analyses suggested that more than 80% of the association of education with premature mortality could be attributed to them. Many of these same factors have been found to partially account for the associations of socioeconomic position with mortality in other diverse populations,<sup>7,32</sup> although direct comparisons between studies are complicated by differences in mediators explored and methods used. In the present study, the mediators studied appeared to account for a greater proportion of the association of education with deaths from renal diseases and from infectious diseases than deaths from other causes, reflecting the greater relevance of diabetes to these causes in this population. Addressing social patterning of the lifestyle factors and physiological correlates studied (eg, through fiscal interventions shown to reduce social inequalities in health outcomes)<sup>33</sup> could contribute significantly to reducing the observed inequalities and premature adult mortality more generally in this population. However, identification and effective mitigation of additional causes of inequalities will be important, perhaps particularly for deaths from, for example, respiratory and vascular diseases, for which these risk factors explained less of the association. Additional causes likely include the influence of education on knowledge-related assets, employment, and, as shown in the present study, income and living conditions throughout the life course, as well as social inequalities in access to effective health care.<sup>34</sup> Some of these same factors have been proposed to underlie sex-differences in the association of education with mortality<sup>4</sup> and could explain those observed in this population. However, determinants of social inequalities in health are complex. Although important, addressing mediating risk factors such as those studied herein is unlikely to be sufficient to eliminate health inequalities without accompanying efforts to address their social determinants.<sup>35</sup>

Investigation of the association of education and other measures of social position with mortality in a large single study with prolonged follow-up are major strengths of the presented analyses, enabling reliable estimates of educational and social inequalities in mortality. The focus on education reflects its relative

ease of accurate measurement, its stability throughout adulthood (shown by the consistency of self-reported education at baseline and resurvey in the present study), and its lesser susceptibility than other socioeconomic indicators to reverse causality within the context of mortality in middle-age. However, through additionally investigating income and the Social Development Index, we were able to show the consistent presence of social inequalities in mortality. The study also has limitations. Data were collected on individual income, which precluded assessment of the relevance of shared economic resources at the household level. As a consequence, we were unable to explore the association of income with mortality among women since almost two-thirds reported none, which could reflect high or low socioeconomic position. This finding is consistent with the relatively high proportion of female participants who reported working in the household (approximately 70% at recruitment) and with described income patterns in Mexico.<sup>36</sup> Inclusion of a health-related domain in the Social Development Index could lead to endogeneity bias in its association with mortality.<sup>37</sup> However, qualitatively similar mortality gradients across quantiles of the Index's six individual domains suggest that any such bias was absent or negligible. Furthermore, we investigated the three socioeconomic indicators individually, but there might be value in studying them jointly to understand the complexity of pathways underlying inequalities in mortality. We were unable to assess all potential mediating factors and were reliant on single baseline assessments of a few likely key mediators, which might have underestimated their contribution.<sup>32</sup> Given these limitations, the presented mediation analyses should be considered largely exploratory. Moreover, we could not account for unmeasured confounders influencing these associations. This might be expected to be particularly relevant for some specific causes of death studied (eg, deaths from external causes). Misclassification of education level would tend to lead to some underestimation of the strength of the relationship between education and mortality. Since information on access to social security was available for only a subset of participants (collection of these data commenced part way through recruitment), it was not possible to reliably explore the relevance of social security for the observed social inequalities in mortality. The study population, from two districts of Mexico City, is not representative of the Mexican population. Although studies aiming to estimate absolute risks require a representative population sample,<sup>20,21</sup> the same is not generally true of studies attempting to characterise the relative risks of disease associated with exposures.<sup>20,21</sup> Collider bias can affect studies of non-representative population samples in which the exposure and outcome, or other risk factors for the outcome, are associated with the probability of recruitment into the study.<sup>20</sup> However, this would not be



expected to explain the magnitude of associations observed in the present study,<sup>20</sup> and large prospective studies of non-representative populations with heterogeneity of exposure status have been shown to provide reliable and generalisable evidence about the associations of risk factors with disease.<sup>20–22</sup> By combining the generalisable education-associated mortality RRs from the Mexico City Prospective Study with national mortality data we derived estimates of absolute mortality risks from age 35 years associated with lower educational attainment in the Mexican population. This illustrates the potential public health relevance of the observed educational inequalities in mortality at a national level. However, these estimates do not consider potential differences in causes of death between the study population and those of the whole of Mexico (eg, those resulting from between-state differences in rates of homicide and femicide among adults in early middle-age).<sup>38</sup> Finally, the relatively small number of deaths from cancer—reflecting Mexico's low cancer mortality rates<sup>39</sup>—precluded exploration of the association of education with cancer subtypes, of particular interest given the weak association observed when compared with other studies.<sup>3,7,24</sup>

In conclusion, in this large prospective study of adults from two districts of Mexico City, there were substantial social inequalities in mortality. When assessed through education, these accounted for an estimated 6-year gap in life expectancy between the most and least educated men and women. Known lifestyle and related physiological risk factors appeared to account for a large proportion of the observed mortality gradients, and effective population-level interventions to reduce these risk factors could lessen social inequalities in health and substantially reduce premature deaths among adults in Mexico City and in Mexico more generally.

#### Contributors

PK-M, RC, RP, JA-D, and RT-C established the cohort. PK-M, RC, RP, JRE, JA-D, and RT-C obtained funding. All authors contributed to data acquisition, analysis, or interpretation of data. FB drafted the first version of the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors have seen and approved the final version and agreed to its publication. JRE and JA-D had full access to all the data in the study, verified the underlying data, and take responsibility for the integrity of the data and the accuracy of the analysis.

#### Declaration of interests

We declare no competing interests.

#### Data sharing

Data from the Mexico City Prospective Study are available to bona fide researchers. The study's Data and Sample Sharing policy can be downloaded (in English or Spanish). Available study data can be examined in detail through the study's Data Showcase.

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For the **Data and Sample Sharing policy** see <https://www.ctsu.ox.ac.uk/research/mcps>

For the **Data Showcase** see <https://datashare.ndph.ox.ac.uk/mexico/>

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