

Educational inequalities and premature mortality: the Cuba Prospective Study



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Summary

Background Although socioeconomic status is a major determinant of premature mortality in many populations, the impact of social inequalities on premature mortality in Cuba, a country with universal education and health care, remains unclear. We aimed to assess the association between educational level and premature adult mortality in Cuba.

Methods The Cuba Prospective Study (a cohort study) enrolled 146 556 adults aged 30 years and older from the general population in five provinces from Jan 1, 1996, to Nov 24, 2002. Participants were followed up until Jan 1, 2017, for cause-specific mortality. Deaths were identified through linkage to the Cuban Public Health Ministry's national mortality records. Cox regression models yielded rate ratios (RRs) for the effect of educational level (a commonly used measure for social status) on mortality at ages 35–74 years, with assessment for the mediating effects of smoking, alcohol consumption, and BMI.

Findings A total of 127 273 participants aged 35–74 years were included in the analyses. There was a strong inverse association between educational level and premature mortality. Compared with a university education, men who did not complete primary education had an approximately 60% higher risk of premature mortality (RR 1.55, 95% CI 1.40–1.72), while the risk was approximately doubled in women (1.96, 1.81–2.13). Overall, 28% of premature deaths could be attributed to lower education levels. Excess mortality in women was primarily due to vascular disease, while vascular disease and cancer were equally important in men. 31% of the association with education in men and 18% in women could be explained by common modifiable risk factors, with smoking having the largest effect.

Interpretation This study highlights the value of understanding the determinants of health inequalities in different populations. Although many major determinants lie outside the health system in Cuba, this study has identified the diseases and risk factors that require targeted public health interventions, particularly smoking.

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Introduction

Socioeconomic status is a major determinant of premature mortality worldwide.^{1–6} Educational level is a well established proxy measure for socioeconomic status because it is established early in life, it shapes income and employment, and it impacts health-related and health-seeking behaviours.^{7,8} Understanding the relationship between education and premature death can be used to inform policies that address health inequalities and population health. To date, only a few studies (all with fairly small sample sizes), have explored the effect of educational level on mortality in Latin America.^{9–14}

Cuba represents a unique opportunity to explore the effect of educational level on premature mortality in Latin America. Following the 1959 revolution, major structural and governmental changes were made in Cuba. These changes led to economic centralisation and a nationalisation of the educational and health systems.

Cuba offers all children and young adults equal access to education from primary school to university, which is managed and financed by the government. Yet, there might be other determinants that influence educational attainment, such as family structure, childhood health, and cognition.^{15–17} In addition, Cuba currently has a universal health-care system that focuses on preventive medicine and primary health care, which is delivered primarily through community-based family clinics.¹⁸ However, premature adult mortality in Cuba remains high,¹⁹ and the effects of any social inequalities, as defined by educational level, on premature mortality in Cuba remain unclear.

The main objective of this analysis is to assess the association between educational level and premature adult mortality using the Cuba Prospective Study of nearly 150 000 adults. The analysis investigates the underlying mechanisms by: describing the associations

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Research in context

Evidence before this study

We did a literature search to identify prospective studies done in Cuba or in Latin America that reported on the effect of social inequalities on mortality. We searched PubMed for articles published from database inception up until March 23, 2022, in any language, using the search string "(Cuba* OR Latin America*) AND (inequalit* OR socioeconomic OR socio-economic OR education*) AND "mortality" AND ("prospective" OR "cohort" OR "longitudinal)". We also searched the reference lists of retrieved articles to identify further relevant publications. We identified one large study (>10 000 participants) and three smaller studies (<8000) that assessed the effect of social inequality on mortality outcomes in Latin America; only one study (with a small sample, n=2813) was conducted in Cuba. None of the included studies quantified the population-attributable fraction of ill health resulting from social inequalities.

Added value of this study

To our knowledge, this is the largest prospective study to assess the impact of social inequalities on premature mortality in Cuba

or in Latin America. In this study of nearly 150 000 Cuban adults, we observed a strong inverse association between educational level and premature adult mortality, despite equitable access to education and health care. 28% of premature deaths could be accounted for by social inequalities, as defined by educational level. Excess mortality in women was primarily due to vascular disease, while vascular disease and cancer were equally important in men. Approximately one-third of the association between educational level and premature mortality in men and one-fifth in women could be explained by common modifiable risk factors, with smoking accounting for the largest proportion.

Implications of all the available evidence

This large prospective study has demonstrated the presence of a strong educational gradient of premature mortality in Cuba. It has also shown that about 30% of premature deaths could be accounted for by social inequalities, and smoking was the behavioural risk factor with the strongest mediating effect on the association between educational level and all-cause mortality.

with both all-cause and cause-specific mortality; exploring the mediating role of major modifiable risk factors on the relationship between educational level and premature mortality; and calculating the number of excess deaths associated with lower educational levels.

Methods

Study design and participants

Details on the Cuba Prospective Study (a cohort study) have been previously published.²⁰ In brief, 146 556 adults aged 30 years and older were recruited from the general population in five of the 14 provinces in Cuba (Havana city and four regional provinces: Pinar del Río, La Habana, Matanzas, and Camagüey) between Jan 1, 1996, and Nov 24, 2002.²⁰ Family medical practices were randomly selected within each province and clinical staff sought to recruit all adults living in the catchment area of the clinics (215 medical clinics were approached and none refused to participate). Among the eligible adults who were residing in the corresponding clinic catchment areas, 74% agreed to participate. During household visits, clinical staff recorded information on age, sex, highest level of education, occupation, alcohol consumption, smoking habits, medical history, and current medication use. Measurements on height, weight, and blood pressure were subsequently taken at the local medical practice (see appendix pp 2–3 for the Spanish questionnaire and English translation). To assess the temporal variation in these factors during the follow-up period, 22 365 participants were resurveyed in 2006–08 using the same procedures as at recruitment. Ethical approval was by the National Institute of Cardiology Ethics Committee,

Havana (reference 0404134). Participants provided written informed consent.

Mortality follow-up

Follow-up was censored at Jan 1, 2017, loss to follow-up, or death. Deaths were identified through linkage to the Cuban Public Health Ministry's national mortality records using the study participants' national identification number (which incorporates birth date).²⁰ In Cuba, deaths are certified by a doctor and the underlying and contributing causes of death are coded according to standard WHO recommendations. The causes of death in the present study were coded using the International Classification of Diseases ninth and tenth editions (ICD-9 and ICD-10); ICD-9 codes were used for deaths between 1996 and 2000, and ICD-10 codes for deaths from 2001 onwards (appendix p 4).

Statistical analysis

Analyses excluded participants outside the age range of interest (35–74 years at baseline), and those with missing data on educational level or other key covariates (appendix p 5). These age cutoffs were chosen because there were no deaths among those younger than 35 years, and age younger than 75 years is a commonly used cutoff for premature mortality.^{21,22} Educational level was categorised based on the level of education completed: less than primary (primary school not completed), primary school, secondary school, high school (combines formal technician and skilled worker training, which is an alternative to high school and is normally completed at about the same age), and university. In Cuba, primary

See Online for appendix

	Less than primary	Primary school	Secondary school	High school	University	All
Men						
Number of participants	2552	12 807	15 619	19 859	5915	56 752
Age, years	60 (11)	59 (11)	51 (11)	49 (10)	47 (9)	52 (11)
White	1983 (78%)	10 143 (79%)	12 027 (77%)	15 053 (76%)	4661 (79%)	43 926 (77%)
Black	365 (14%)	1729 (14%)	2312 (15%)	3058 (15%)	799 (14%)	8286 (15%)
Mixed or other	204 (8%)	935 (7%)	1265 (8%)	1748 (9%)	455 (8%)	4540 (8%)
Professional*	38 (2%)	64 (1%)	141 (1%)	616 (3%)	2987 (51%)	4200 (7%)
Current cigarette smokers†	1225 (48%)	6468 (51%)	7731 (50%)	8976 (45%)	2058 (35%)	26 163 (46%)
Consume alcohol at least weekly	697 (27%)	3906 (31%)	4967 (32%)	6335 (32%)	1396 (24%)	17 082 (30%)
Systolic blood pressure, mm Hg	124 (16)	125 (15)	125 (14)	126 (13)	126 (13)	125 (14)
BMI, kg/m ²	23.7 (3.4)	23.9 (3.4)	24.1 (3.4)	24.1 (3.3)	24.4 (3.4)	24.1 (3.4)
History of diabetes	87 (3%)	435 (3%)	547 (4%)	894 (5%)	331 (6%)	2213 (4%)
Women						
Number of participants	4432	20 053	20 146	19 400	6490	70 521
Age, years	60 (10)	58 (10)	50 (10)	47 (9)	45 (9)	52 (11)
White	3413 (77%)	15 782 (79%)	15 472 (77%)	14 531 (75%)	4809 (74%)	54 019 (77%)
Black	603 (14%)	2567 (13%)	2881 (14%)	2968 (15%)	1064 (16%)	10 085 (14%)
Mixed or other	412 (9%)	1725 (9%)	1793 (9%)	1901 (10%)	623 (10%)	6347 (9%)
Professional*	62 (1%)	80 (0.4%)	222 (1%)	834 (4%)	3595 (55%)	5360 (8%)
Current cigarette smokers†	1387 (31%)	5916 (30%)	5701 (28%)	5063 (26%)	1460 (23%)	19 182 (27%)
Consume alcohol at least weekly	191 (4%)	862 (4%)	947 (5%)	1125 (6%)	253 (4%)	3244 (5%)
Systolic blood pressure, mm Hg	124 (18)	124 (17)	124 (16)	123 (15)	122 (14)	124 (16)
BMI, kg/m ²	24.4 (4.3)	24.4 (4.2)	24.5 (4.1)	24.3 (3.9)	24.4 (3.8)	24.5 (4.1)
History of diabetes	319 (7%)	1404 (7%)	1309 (7%)	1416 (7%)	467 (7%)	4866 (7%)

Data are n, n (%), or mean (SD). Participants with no follow-up at ages 35–74 years, those with missing information on education or covariates, and those with extreme values for systolic blood pressure or BMI were excluded. Primary school education is usually completed at 11–12 years, secondary school at 14–15 years, high school (which includes technicians and skilled workers) at 17–18 years, and university at 23–24 years. In the baseline questionnaire, skin colour was categorised into White, Black, mixed, or other (see appendix pp 2–3). *Professional status was defined as occupations requiring a degree or equivalent. †2572 (5%) men and 380 (1%) women smoked only cigars (but not cigarettes) and are not included here. With the exception of age, all estimates have been adjusted to the mean age in the population at baseline.

Table 1: Baseline characteristics of the 127 273 participants included in the main analyses, by sex and educational level, adjusted for age

school education is usually completed at 11–12 years, secondary school at 14–15 years, high school at 17–18 years, and university at 23–24 years.

The main analyses were of sex-specific premature adult mortality by educational level. Cox regression models were used to calculate mortality rate ratios (RRs), with university education as the reference category. Models were adjusted for age-at-risk (in 5-year age groups), and stratified by province (five provinces), and where appropriate, sex. Confidence intervals (CIs) were calculated using the variance of the log risk, which appropriately attributes variance to all groups (including the reference with RR of 1.0), and as such, allows CIs to be used to compare risks between any two groups.²³ The absolute excess risk at different educational levels was estimated by multiplying RRs by a common factor so that the inverse variance-weighted average of the RRs matched the annual mortality rate at 35–74 years in Cuba for 2017.²⁴

The extent to which major lifestyle risk factors (smoking, alcohol consumption, and BMI) mediated the

association between educational level and premature mortality was assessed by calculating the change in log-likelihood χ^2 statistic on the addition of the educational variable into models with and without a particular mediator. The likelihood ratio statistic comparing the inclusion of each mediator into these adjusted models quantifies the proportion of the association of educational level with premature mortality that can be attributed to measured (or reported values) of the mediator. All mediator analyses were based on the same sample size.²⁵ In these analyses, smoking was categorised into six groups (never; ex-smoker; current smoker in groups of <20, 20, and >20 cigarettes per day; and other smoker [mostly cigar-only smokers]); alcohol consumption into five groups (non-drinker; less than weekly; at least weekly drinker in groups of less than one, one to less than three, and three or more 35 cL bottles of rum [or equivalent alcohol] per week); and BMI into six groups (<20, 20 to <22.5, 22.5 to <25, 25 to <27.5, 27.5 to <30, and ≥ 30 kg/m²).²⁶

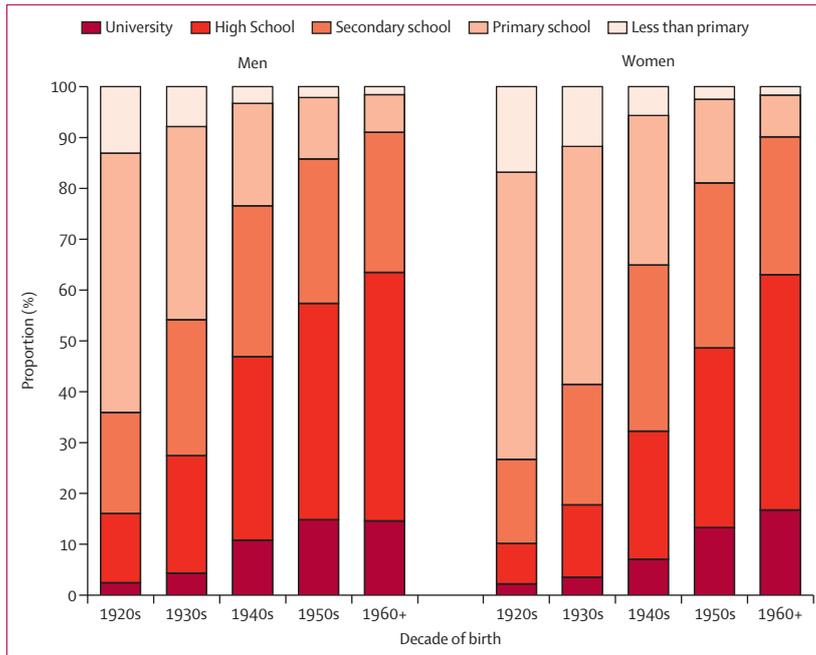


Figure 1: Distribution of men and women by highest educational level in each decade of birth
Analyses among 127 273 participants. Exclusions and conventions as in table 1.

Sensitivity analyses of the main prospective associations were conducted by: further adjusting for other potential confounders, including marital status (two groups: single or widowed, married);²⁷ performing subgroup analyses by birth cohort (born before 1940 or 1940 onwards to reflect those who completed their education before the Cuban revolution in 1959); and assessing differences in treatment among those with chronic disease at baseline by educational level. Additional analyses were conducted to assess the effect of occupation on all-cause mortality.

Sex-specific population-attributable fractions were calculated using the formula $P_e(RR-1)/RR$, where P_e is the proportion of deaths that occurred in a given educational group and RR is the adjusted cause-specific RR compared with those who completed university.^{28,29} Estimates of the number of excess deaths among lower educational level groups in Cuba were made by applying the population-attributable fractions to the total deaths in Cuba in 2017 using mortality data from WHO.³⁰ SAS (version 9.4) was used for statistical analyses and graphs were plotted with R (version 4.1.2).

Role of the funding source

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

Results

Of the 146 556 participants included in the study, 19 283 were excluded from the main analyses: 14 754 because they were aged 75 years or older at

baseline, 5166 because of missing or unreliable information on educational level or other covariates, and 232 due to baseline–mortality linkage uncertainty, which left 127 273 (56 752 men and 70 521 women) in the main analyses (exclusion criteria are not mutually exclusive; appendix p 5).

The mean age at baseline was 52 years (SD 11), 97 945 (77%) participants were White, and 70 521 (55%) were women (table 1 and appendix p 6). Overall, mean systolic blood pressure was 124 mm Hg (SD 15) and mean BMI was 24.3 kg/m² (SD 3.8), and these means were similar in men and women. 26 163 (46%) men and 19 182 (27%) women were smokers, and 17 082 (30%) men and 3244 (5%) women consumed alcohol at least weekly. The prevalence of diabetes was slightly higher in women than men (4866 [7%] vs 2213 [4%]).

Among women, education was inversely related to current smoking (1387 [31%] among less than primary education vs 1460 [23%] among university educated) but was not related to the frequency of alcohol consumption, mean BMI, mean systolic blood pressure, or the prevalence of diabetes. For men, the prevalence of both smoking and drinking was highest among those with moderate levels of education (primary or secondary), and there were slight positive associations with mean BMI, mean systolic blood pressure, and the prevalence of diabetes (appendix p 7).

Figure 1 illustrates the substantial increases in educational level by birth cohort. Among those born in the 1920s, 2189 (35%) men and 1891 (25%) women completed secondary school (ie, for about two-thirds of adults, the highest level of education was primary school or less), and 301 (5%) attended university. However, among those born after 1960, 16 206 (90%) men and women completed secondary school, and 2899 (15%) attended university. Among the subset of participants who were resurveyed after about 8.6 years of follow-up, the same questions about educational level elicited the same responses as they did at the baseline survey (with the exception of those who reported less than primary education at baseline, among whom 109 [7%] of 1526 reported a primary school education at resurvey). However, there was more variability between occupation reported at baseline and at resurvey, with 2018 (9%) of 22 365 participants changing occupation category (appendix p 8).

In the main analyses, there were 2.19 million person-years of follow-up at ages 35–74 years (mean 17.2 years per person, SD 3.9), during which 12 313 deaths occurred: 4664 due to vascular causes (2408 ischaemic heart disease and 2256 stroke or other vascular cause), 4013 due to cancer (1048 lung and 2965 other type of cancer), 1114 due to respiratory causes (499 chronic obstructive pulmonary disease and 615 other respiratory cause), 1832 due to other medical causes, and 647 due to external causes (table 2, appendix p 4).

Overall, higher educational levels were inversely associated with all-cause mortality (figure 2, table 2).

	Deaths	Less than primary		Primary school		Secondary school		High school		University	
		Deaths	RR (95% CI)	Deaths	RR (95% CI)	Deaths	RR (95% CI)	Deaths	RR (95% CI)	Deaths	RR (95% CI)
Vascular	4664	378	1.87 (1.69–2.07)	1646	1.70 (1.61–1.78)	1281	1.40 (1.33–1.48)	1104	1.24 (1.16–1.32)	255	1.00 (0.88–1.13)
Ischaemic heart disease	2408	189	1.74 (1.51–2.01)	807	1.53 (1.43–1.65)	678	1.35 (1.25–1.46)	592	1.19 (1.10–1.29)	142	1.00 (0.85–1.18)
Stroke	925	88	2.42 (1.96–2.99)	334	1.93 (1.72–2.17)	248	1.56 (1.38–1.77)	211	1.38 (1.20–1.59)	44	1.00 (0.74–1.35)
Other	1331	101	1.77 (1.45–2.16)	505	1.87 (1.70–2.05)	355	1.41 (1.28–1.57)	301	1.25 (1.11–1.40)	69	1.00 (0.79–1.27)
Cancer	4013	249	1.39 (1.23–1.58)	1219	1.39 (1.31–1.48)	1199	1.31 (1.24–1.39)	1072	1.16 (1.09–1.24)	274	1.00 (0.89–1.13)
Lung	1048	76	2.19 (1.75–2.75)	344	1.99 (1.78–2.23)	295	1.60 (1.43–1.79)	276	1.43 (1.26–1.61)	57	1.00 (0.77–1.30)
Female reproductive	664	42	0.89 (0.66–1.21)	194	0.87 (0.75–1.01)	204	0.89 (0.78–1.02)	159	0.78 (0.67–0.92)	65	1.00 (0.78–1.28)
Breast	333	22	0.80 (0.53–1.23)	96	0.74 (0.60–0.91)	102	0.80 (0.66–0.97)	78	0.71 (0.56–0.89)	35	1.00 (0.71–1.40)
Other reproductive	331	20	1.00 (0.64–1.55)	98	1.03 (0.83–1.27)	102	1.00 (0.83–1.21)	81	0.87 (0.69–1.09)	30	1.00 (0.69–1.44)
Other	2301	131	1.33 (1.11–1.58)	681	1.40 (1.29–1.52)	700	1.38 (1.28–1.49)	637	1.22 (1.13–1.33)	152	1.00 (0.85–1.17)
Respiratory	1114	124	2.72 (2.27–3.25)	431	1.97 (1.78–2.17)	303	1.48 (1.32–1.65)	200	1.03 (0.89–1.19)	56	1.00 (0.77–1.30)
COPD	499	61	3.45 (2.67–4.45)	194	2.21 (1.91–2.56)	131	1.53 (1.29–1.82)	89	1.08 (0.87–1.33)	24	1.00 (0.67–1.50)
Other	615	63	2.23 (1.73–2.86)	237	1.78 (1.56–2.04)	172	1.43 (1.23–1.66)	111	0.99 (0.82–1.20)	32	1.00 (0.70–1.42)
Other medical	1832	125	1.76 (1.47–2.10)	599	1.71 (1.57–1.86)	531	1.42 (1.30–1.54)	461	1.20 (1.09–1.31)	116	1.00 (0.83–1.20)
External	647	40	2.44 (1.78–3.34)	201	2.39 (2.06–2.77)	186	1.74 (1.51–2.00)	181	1.43 (1.23–1.67)	39	1.00 (0.73–1.37)
All*	12 313	918	1.79 (1.68–1.91)	4111	1.65 (1.59–1.70)	3513	1.40 (1.35–1.44)	3029	1.20 (1.16–1.24)	742	1.00 (0.93–1.08)

RR at ages 35–74 years by highest completed level of education, adjusted for age, sex, and province. Some of the sex-specific RRs might be unreliable due to too few events and should be interpreted with caution. Exclusions and conventions as in table 1. COPD=chronic obstructive pulmonary disease. RR=rate ratio. *Includes 43 ill-defined deaths.

Table 2: Cause-specific mortality versus educational level in Cuba

Among women, there was a dose–response relationship throughout the educational range. Women who did not complete primary education had about twice the all-cause mortality rate (RR 1.96, 95% CI 1.81–2.13) of those with a university education. The association was similar in men, except there was little evidence that men with less than primary school education had higher all-cause mortality than those who completed only primary school. Men who completed only primary education had about 60% higher all-cause mortality than those educated at university level (1.64, 1.56–1.71), as did those with less than primary school education (1.55, 1.40–1.72; appendix p 9). Predicted survival trajectories for Cuban adults aged 35 years and older were generated to estimate the probability of premature all-cause mortality by sex and educational level (appendix p 10).

In analysis of both sexes combined, there were strong inverse associations of educational level with each major cause of premature death, including vascular disease, cancer, respiratory disease, and external causes (table 2). However, the strength of these associations varied within disease categories. For instance, there was a somewhat stronger association for stroke than for ischaemic heart disease, for lung cancer than for female reproductive cancer, and for chronic obstructive pulmonary disease than for other respiratory causes. After stratifying by sex, there was notably stronger association for vascular mortality in women and for cancer mortality in men (appendix p 9).

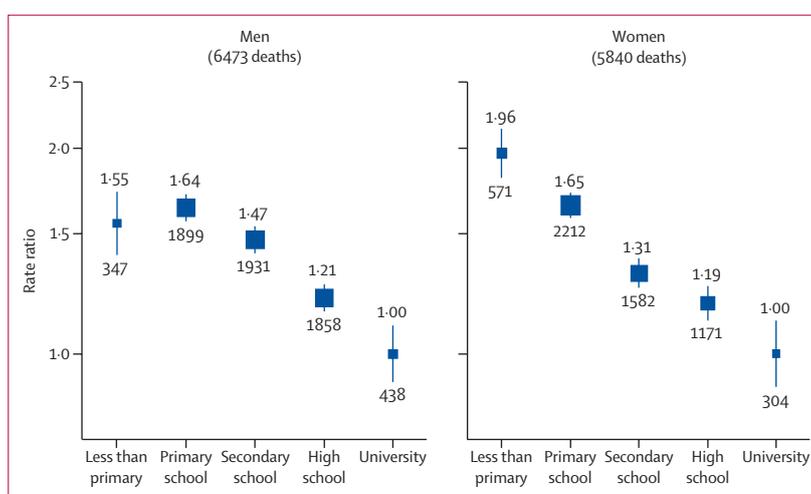


Figure 2: All-cause mortality versus educational level in Cuba, by sex

Rate ratios at ages 35–74 years by highest completed level of education, adjusted for age, sex, and province. Exclusions and conventions as in table 1. Error bars show 95% CIs. The number above each plot is the rate ratio and the number below is the number of deaths. The area of the square is proportional to the amount of information within each education category (ie, inversely proportional to the variance of the log-risk), which also determines the confidence interval.

Figure 3 shows the estimated absolute risks by educational level, using national mortality rates for 2017 in Cuba. Although the RR for all-cause mortality in the lowest versus highest educational category was greater in women than in men (appendix p 9), the higher absolute risk of all-cause mortality in men meant that there were similar differences in absolute risk in both

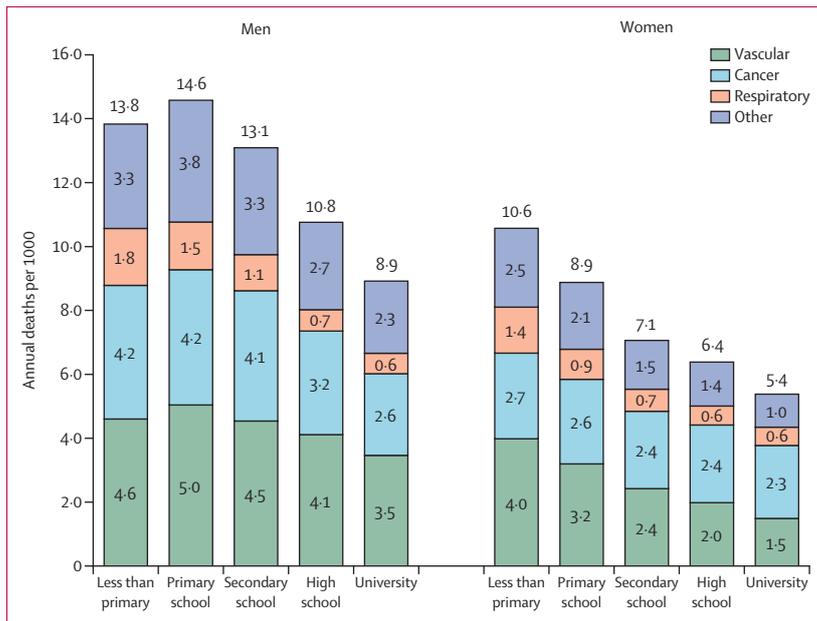


Figure 3: Mortality rates at ages 35–74 years in Cuba in 2017, overall and for main disease categories, versus educational level

Rate ratios at ages 35–74 years, adjusted for age, sex, and province, were multiplied by a common factor (ie, floated) to make the weighted average match the age-standardised mortality rates in Cuba at ages 35–74 years in 2017. Conventions and exclusions as in table 1.

sexes. For instance, the difference in absolute risk of premature death for the lowest versus highest educational groups was 4.9 deaths per 1000 in men and 5.2 deaths per 1000 in women. Among women, much of the excess absolute risk of death among the lower educational groups was from vascular disease (lowest vs highest education groups: 2.5 deaths per 1000) and, to a much lesser extent, cancer (0.4 per 1000), respiratory (0.8 per 1000), and other causes (1.5 per 1000); however, in men, there were less marked differences between the major disease categories: vascular (1.1 per 1000), cancer (1.6 per 1000), respiratory (1.2 per 1000), and other deaths (1.0 per 1000).

If all participants had the same mortality rate as those with a university education, then there would have been about 30% fewer deaths (28% [95% CI 24–31] in men, 29% [26–33] in women; figure 4). This would be equivalent to 13 141 excess premature deaths in Cuba in 2017 (men: 7762 deaths, women: 5379 deaths). Of the potential excess deaths among men, 2139 (28%) were vascular, 2501 (32%) were cancer, and 940 (12%) were respiratory. Among women, 2715 (50%) of the excess deaths were vascular, 534 (10%) were cancer, and 536 (10%) were respiratory.

Baseline measures of smoking, alcohol consumption, and BMI accounted for 31% of the association with educational level on all-cause mortality among men and 18% in women (appendix p 11). In men, these three risk factors accounted for 26% of the effect of education on vascular mortality, 47% of the effect on cancer mortality,

and 24% of the effect on respiratory mortality. In women, these factors accounted for 15%, 31%, and 21% of the association with vascular, cancer, and respiratory mortality, respectively. Smoking had the strongest independent effect among the three modifiable risk factors, accounting for 24% of the effect of education on all-cause mortality in men and 12% in women. After excluding those with previous disease, the results of the mediation analysis did not materially change (data not shown).

In sensitivity analyses, associations of all-cause mortality with educational level were not materially changed following further adjustment for marital status, and prospective analyses of occupation were less predictive of all-cause mortality than educational level (appendix p 12). Furthermore, there were no major differences by educational level in treatment among those with chronic disease at baseline (appendix p 13). There was also little evidence that the associations differed by birth cohort (before 1940 vs 1940 or later; appendix p 14).

Discussion

In this large prospective cohort study of 127 273 Cuban adults, lower levels of education were strongly associated with higher risks of premature mortality. Excess mortality in women was primarily due to vascular disease, while vascular disease and cancer were equally important in men. About a third of the effect of educational level on all-cause mortality in men and a fifth in women was explained by three common behavioural risk factors—smoking, alcohol, and BMI—with smoking having the strongest effect. If all participants had the mortality rate of those with a university education, then there could have been 28% fewer deaths in this cohort.

To our knowledge, this is the largest prospective study to quantify the inverse social gradient of premature mortality, and to explore its underlying mechanisms, in Latin America. Educational level is a well established measure of socioeconomic status, and previous international studies have also described a strong inverse association with educational level and premature mortality.^{1–6} For instance, the PURE study (a cohort of 154 169 adults in 20 countries) reported an adjusted hazard ratio for all-cause mortality among those with a lower level (no or primary school education only) versus higher level (completion of trade school, college, or university) of education of 1.50 (95% CI 1.14–1.98) in high-income countries, 1.80 (1.58–2.06) in middle-income countries, and 2.76 (2.29–3.31) in low-income countries.² In Latin America, an analysis of 10 147 adults aged 40 years and older from the Chilean Social Protection Survey showed that, compared with those with little formal education (0–4 years), those with a secondary (9–12 years) or tertiary (13+ years) education had a 34% and 41% reduced mortality risk, respectively.¹³

Education had a stronger effect on vascular mortality in women, while the associations were stronger for cancer

mortality in men. Previous studies have also demonstrated different health inequalities among men and women for cardiovascular and cancer mortality.^{4,31,32} The higher burden of premature mortality in men and women might be due to the socially patterned distribution of behavioural risk factors, such as unhealthy diet, smoking, and alcohol consumption.^{33–35} However, unlike some previous studies,^{36,37} we did not observe an association between educational level and female reproductive cancers or breast cancer mortality, which might be due to the implementation of a nationwide cancer screening programme in Cuba.³⁸

Three common risk factors partially accounted for the observed effect of educational level on all-cause and cause-specific mortality, which is broadly consistent with previous studies.^{39,40} We reported that smoking was the strongest independent mediator on the relationship between education and premature mortality, especially for cancer mortality (explaining 39% in men and 26% in women) and for all-cause mortality among men and women. This aligns with previous analyses of the Cuba Prospective Study, which showed that smoking was a significant contributor to premature mortality in both sexes in Cuba.⁴¹ These findings indicate that addressing smoking, through population-based and individual-based public health strategies such as increased taxation and wider access to smoking cessation, might reduce both health inequalities and premature adult mortality.

The present study also highlights that addressing major lifestyle risk factors alone is unlikely to fully address health inequalities. This suggests that further investigation is required to understand the other major determinants of health and how their interplay might account for the remaining effect of education on premature mortality.^{42,43} For instance, educational attainment can affect employment opportunities, with implications for general living and working conditions.^{7,8} Additionally, even within a universal health-care system, education can have a direct effect on an individual's ability to access and navigate the health-care system, as well as impacting health literacy and the ability to adhere to medical advice.^{44,45}

Our results highlight both the importance and the limitations of the 2015 UN Sustainable Development Goals and WHO's triple billion targets for universal health care. It has often been suggested that equitable access should markedly reduce health inequalities, but social inequalities still exist in all countries, even those with universal health care (eg, Scandinavian countries).^{4,5,46} Moreover, the health-care system in Cuba provides equitable access to health-care services and it ensures that care is provided to those who need it most.⁴⁷ Indeed, we did not observe an educational gradient in the frequency of medication use for common conditions among those with chronic diseases at baseline, which is similar to other studies conducted in Cuba.^{35,48} Despite this, there is still a need to improve the monitoring of health inequalities, and better understand the underlying

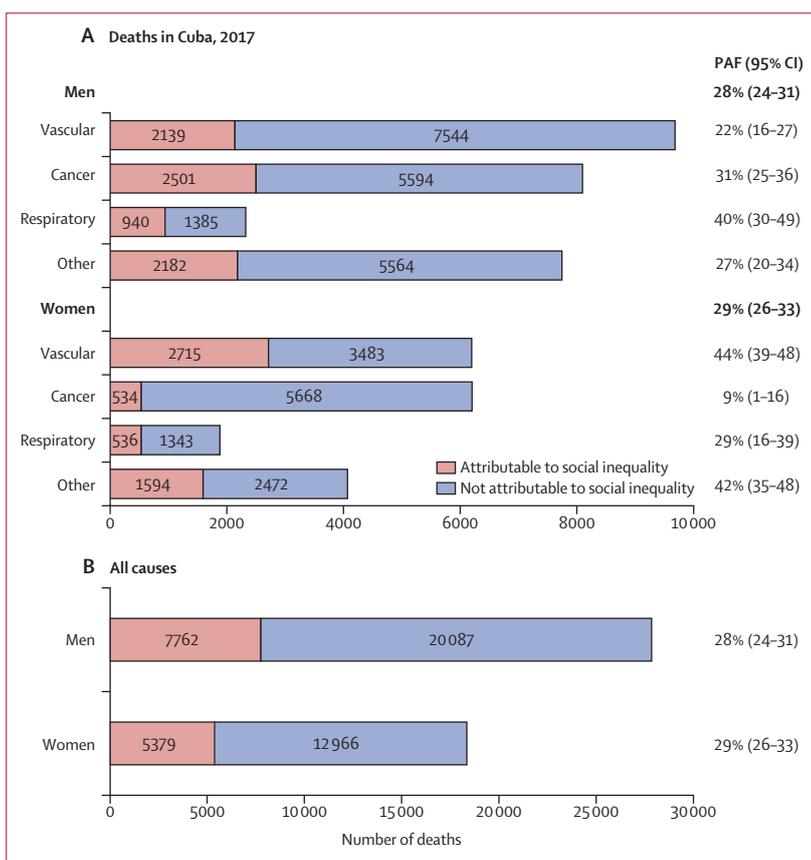


Figure 4: Premature adult mortality attributable to educational level in Cuba, 2017
Excess deaths at ages 35–74 years in 2017 among lower educational groups (compared with expected deaths given mortality rates in the highest educational group), calculated by applying cause-specific PAFs for education in the Cuba Prospective Study to the total deaths in Cuba at ages 35–74 years in 2017 (Source: WHO³⁹). The overall PAF for all-cause mortality was 28% for men, 29% for women, and 28% for both sexes combined. Exclusions and conventions as in table 1. PAF=population-attributable fraction.

mechanism within and outside the health-care system to achieve health equity.

This study has several key strengths. It is the largest study to explore the association between educational level and premature death in Cuba. For instance, a cross-sectional survey in Cuba⁴⁴ reported that educational level was associated with self-reported health but it had a sample size of 4124, while our prospective cohort study consisted of 127 273 participants. Our study collected information on educational level at baseline: education is more stable than many other indicators of socioeconomic status (eg, income or occupation) and it reduces the risk of reverse causality since it is established early in life. The study also benefited from the routine collection of high-quality mortality records, with physician-certified deaths. However, there are some limitations to the study that warrant discussion. First, measurement error in the assessment of lifestyle risk factors means analyses might have underestimated the mediating effects of smoking, alcohol consumption, and BMI. Second, we were unable to explore the mediating effect of other modifiable risk

factors, such as diet or physical activity, which might account for some of the remaining association between educational level and premature mortality. We were also not able to explore the association of education with non-fatal disease, or to assess the associations with other aspects of inequality, such as household income or poor living conditions (ie, inadequate housing, unhealthy environments, and crowded conditions).

In conclusion, this prospective study observed a strong educational gradient in premature mortality in Cuba. About 30% of deaths in this cohort might have been avoided if all groups had the same mortality rate as those with a university education. Smoking accounted for about one-quarter of these excess deaths, but addressing major lifestyle factors alone is unlikely to fully address health inequalities in Cuba. Although Cuba's social protection infrastructure has not completely eliminated the impact of social inequality on premature mortality, its universal health-care system has no doubt helped to reduce some important disparities by ensuring equitable access to health care for all of its citizens.

Contributors

NAR, RP, and SL directed the study. NAR was responsible for field supervision. NAR, PV-P, MCM, EL-V, SBC, JMMR, OJHL, MAMM, IAA, FAE, MDG, NRM, and MCA collected the data. SR, NAR, JS, JAB, PS, SL, and BL had full access to the data and were responsible for data cleaning and data management, data analysis, interpretation, and reporting. SR, NAR, JS, BL, and SL drafted the article, which was revised by all authors. SR, NAR, and JS contributed equally as first authors; BL and SL contributed equally as senior authors. SR, JAB, and SL accessed and verified the data. All authors had final responsibility for the decision to submit for publication. The corresponding author confirms that all authors have seen and approved the final text.

Declaration of interests

JE reports research funding to the University of Oxford from Boehringer Ingelheim outside the submitted work. All other authors declare no competing interests.

Data sharing

The datasets generated and/or analysed are not publicly available, but are available from the corresponding author on reasonable request. Requestors will need to sign a data access agreement.

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