Educational inequalities in mortality and their mediators among generations across four decades: nationwide, population based, prospective cohort study based on the ChinaHEART project

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2023;382:e073749
http://dx.doi.org/10.1136/bmj-2022-073749

Accepted: 01 June 2023

ABSTRACT

OBJECTIVES
To assess the different educational inequalities in mortality among generations born between 1940 and 1979 in China, and to investigate the role of socioeconomic, behavioural, and metabolic factors as potential contributors to the reduction of educational inequalities.

DESIGN
Nationwide, population based, prospective cohort study.

SETTING
The ChinaHEART (China Health Evaluation And risk Reduction through nationwide Teamwork) project in all 31 provinces in the mainland of China.

PARTICIPANTS
1 283 774 residents aged 35-75 years, divided into four separate cohorts born in 1940s, 1950s, 1960s, and 1970s.

MAIN OUTCOME MEASURES
Relative index of inequality and all cause mortality.

RESULTS
During a median follow-up of 3.5 years (interquartile range 2.1-4.7), 22 552 deaths were recorded. Among the four generations, lower education levels were found to be associated with a higher risk of all cause death: Compared with participants with college level education or above, the hazard ratio for people with primary school education and below was 1.4 (95% confidence interval 1.2 to 1.7) in the 1940s cohort, 1.8 (1.5 to 2.1) in the 1950s cohort, 2.0 (1.7 to 2.4) in the 1960s cohort, and 1.8 (1.4 to 2.4) in the 1970s cohort. Educational relative index of inequality in mortality increased from 2.1 (95% confidence interval 1.9 to 2.3) in the 1940s cohort to 2.6 (2.1 to 3.3) in the 1970s cohort. Overall, the mediation proportions were 37.5% (95% confidence interval 32.6% to 42.8%) for socioeconomic factors, 13.9% (12.0% to 16.0%) for behavioural factors, and 4.7% (3.7% to 5.8%) for metabolic factors. Except for socioeconomic measurements, the mediating effects by behavioural and metabolic factors decreased in younger generations.

CONCLUSION
Educational inequalities in mortality increased over generations in China. Improving healthy lifestyles and metabolic risk control for less educated people, especially for younger generations, is essential to reduce health inequalities.

WHAT IS ALREADY KNOWN ON THIS TOPIC
Based on census data, inequalities in mortality related to education levels have increased substantially due to the social, economic, and political transformation in some high income countries.

Previous studies found that the effect of education on mortality was partially mediated by behavioural and metabolic factors.

WHAT THIS STUDY ADDS
Educational inequalities in mortality have widened from 1940s cohort to 1970s cohort, with substantial heterogeneity between rural and urban.

The socioeconomic, behavioural, and metabolic factors mediated almost half of the association between education levels and mortality across generations.

The mediation proportions of modifiable behavioural and metabolic factors shrank in younger generations, in which sufficient leisure time physical activity had the leading effects.

Introduction
Education attainment, as one of the socioeconomic characteristics that is an antecedent to others (eg, occupation and income), plays an important part in following healthy lifestyles and accessing health care. Level of education attainment is known to be inversely associated with the risk of death among Chinese and other populations,[1-3] also known as educational inequalities in mortality. In the twentieth century, the literacy rate of the world population had increased dramatically from 21% to 82%,[4] but educational inequalities in mortality have increased recently in some high income countries, due to the social, economic, and political transformation.[5-9]

Understanding the evolution and intermediate factors of educational inequalities in mortality is essential for targeted efforts to promote health equity; however, relevant evidence is scarce. Few studies have investigated education related health inequalities in a long term, such as among people from different generations, particularly in low and middle income countries that have had an unprecedented development in education. Although previous studies have implied that the effect of education on mortality was partially mediated by behavioural and metabolic factors,[10 11] the contributions of specific factors and the heterogeneities across subgroups of population (eg, different generations) have not been well evaluated.

We divided data from about 1.28 million adults from the China Health Evaluation And risk Reduction through nationwide Teamwork (ChinaHEART) project into four cohorts according to their decade of birth, to assess the differences of educational inequalities in mortality among people from different generations. We also aimed to investigate the roles of socioeconomic, behavioural, and metabolic factors as potential mediators.

Methods

Study design and population

The ChinaHEART project is a government funded public health programme designed for screening of cardiovascular disease risk and for intervention in community based populations throughout China. The design of ChinaHEART project has been described previously.[12] Briefly, from 20 November 2014 through 31 December 2021, 351 county level regions in all 31 provinces in the mainland of China were selected as study sites to provide diversity in geographical distribution, population structure, and exposure to risk factors and disease patterns (supplementary method). Study site selection also considered population size, population stability, and local capacity to support the project. A total of 12 323 531 residents aged 35-75 years, who had lived in the community for at least six months in the previous 12 months, were invited in this project, and about 4.5 million residents were recruited.

In baseline interviews of the 4.5 million ChinaHEART participants, people with the serial project ID number ending with 1, 3, 5, or 7, were selected as a representative sample to provide more detailed information of behavioural risk factors and morbidities at the baseline. Among them, 1 295 871 participants born between 1940s and 1970s were considered eligible for this study. After exclusion of 12 097 (0.93%) participants with incomplete data for education status data (n=11 886) or date of death (n=211), 1 283 774 remained for analysis. Missing data were noted in 8.8% of participants and were mainly related to lifestyle. We used a widely accepted random forest method to conduct the imputation for categorical and the continuous variables[13 14] (missForest package in R; supplementary method).

Data collection and variable definition

For each participant, a standardised interview was conducted in person by trained personnel to collect information on education and other socioeconomic status (ie, annual household income, health insurance, marital status, and occupation), lifestyle (ie, tobacco smoking, alcohol drinking, diet patterns, and leisure time physical activity; supplementary method), and medical history at baseline. Education was categorised according to the International Standard Classification of Education scale: primary school or below was equivalent to level 0 and 1; middle school was equivalent to level 2; high school was equivalent to level 3 and 4; and college or above education was equivalent to level 5 to 8.[15]

For behavioural factors, tobacco smoking status was categorised into never, formerly, or currently smoking. Alcohol drinking frequency was categorised into never, once or less per month, two to four times per month, two to three times per week, or more than four times per week. The amount of alcohol consumption during a typical drinking day was also estimated. Leisure time physical activity was quantified by typical types of activity at different intensity (swimming, running, or aerobic exercise were vigorous intensity activities; ball games, walking, gymnastics, folk dancing, Tai-Chi, qigong, or other exercise were moderate intensity activities), frequency, and exercise duration per week. A qualitative food frequency questionnaire was used to collect habitual dietary intake by asking frequency of eating 12 food components over the previous year (supplementary method). For each food component, five frequency categories were provided to choose (ie, daily, four to six days per week, one to three days per week, one to three days per month, and never or almost never).

More specifically, a participant with healthy behaviours was defined as: never smoking or formerly smoking who stopped for reasons other than illness[16]; never drinkers, or drinkers who drank no more than 25 g (three units) for men or 15 g (two units) for women per day on average; individuals having sufficient leisure time physical activity (ie, at least 150 min moderate intensity aerobic activities or 75 min vigorous intensity aerobic activities per week); and individuals with a healthy diet score of 4 or higher based on weekly food intake of six components (ie, daily intake of fresh fruit, fresh vegetables, and whole grains; eating fish and other seafood at least one day per week, bean and bean food at least four days per week, and red meat fewer than seven days per week).

As metabolic factors, blood pressure, blood glucose, lipids, weight, height, and waist circumference at baseline were measured using the standardised protocols and unified devices (supplementary method). Hypertension was defined as systolic blood pressure of 140 mmHg or more, diastolic blood pressure was 90 mmHg or higher, or a self-reported disease history of hypertension, or the use of anti-hypertensive medications, according to the US and Chinese definitions.[17-19] Diabetes was defined as blood glucose greater than 7 mmol/L after at least 8 h after last meal or random blood glucose greater than 11.1 mmol/L according to the Chinese Guidelines for prevention and treatment of type 2 diabetes, or a self-reported disease history of diabetes, or usage of hypoglycaemic agents. Dyslipidaemia was defined as an elevated total cholesterol (≥6.2 mmol/L) or low density lipoprotein (≥4.1 mmol/L) according to guidelines for dyslipidaemia in Chinese adults,[20] or self-reported lipid lowering drugs usage. Body mass index was defined as weight in kilograms divided by the square of height in metres. History of cardiovascular disease was defined as self-reported medical histories or received the treatments, including myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention, and stroke.

Ascertainment of outcomes

Participants' vital status and cause of death were collected through a passive follow-up process in which a linkage of data was established between the cohort

Table 1 | Characteristics of study participants by education level. Data are mean (standard deviation) or median (interquartile range) for continuous variables and number (%) for categorical variables

Characteristics	Aggregate (n=1 283 774)	College or above (n=89 996)	High school (n=182 854)	Middle school (n=419 126)	Primary school or below (n=591 798)	P for trend
Percentage of total study participants, %		7.0	14.2	32.6	46.1	—
Mortality	22 552 (1.8)	587 (0.7)	2091 (1.1)	5798 (1.4)	14 076 (2.4)	<0.001
Cardiovascular disease mortality	9107 (0.7)	219 (0.2)	814 (0.4)	2255 (0.5)	5819 (1.0)	<0.001
Median follow-up duration, years (interquartile range)	3.5 (2.1-4.7)	3.6 (2.2-4.8)	3.6 (2.6-4.7)	3.6 (2.2-4.7)	3.5 (2.0-4.7)	<0.001
Basic characteristics						
Age, years	56.9 (9.4)	51.0 (9.2)	55.1 (8.7)	55.2 (8.9)	59.6 (9.0)	<0.001
Sex:						
Male	516 191 (40.2)	45 774 (50.9)	84 045 (46.0)	187653 (44.8)	198 719 (33.6)	<0.001
Female	767 583 (59.8)	44 222 (49.1)	98 809 (54.0)	231473 (55.2)	393 079 (66.4)	
Urbanity:						
Urban	504 882 (39.3)	55 236 (61.4)	111 184 (60.8)	181946 (43.4)	156 516 (26.4)	<0.001
Rural	778 892 (60.7)	34 760 (38.6)	71 670 (39.2)	237 180 (56.6)	435 282 (73.6)	
Medical history						
Hypertension	629 733 (49.1)	33 887 (37.7)	82 337 (45.0)	196 297 (46.8)	317 212 (53.6)	<0.001
Type 2 diabetes	239 796 (18.7)	14 693 (16.3)	34 581 (18.9)	75 574 (18.0)	114 948 (19.4)	<0.001
Cardiovascular diseases	47 698 (3.7)	2835 (3.2)	7084 (3.9)	14 968 (3.6)	22 811 (3.9)	<0.001
Dyslipidaemia	143 943 (11.2)	10 010 (11.1)	22 829 (12.5)	44 806 (10.7)	66 298 (11.2)	<0.001
Healthy lifestyle behaviours						
No smoking	1 016 992 (79.2)	71 379 (79.3)	143 033 (78.2)	321 273 (76.7)	481 307 (81.3)	<0.001
None or moderate alcohol use	1 244 578 (96.9)	87 305 (97.0)	177 427 (97.0)	405 301 (96.7)	574 545 (97.1)	0.002
Sufficient leisure-time physical activity	364 443 (28.4)	40 845 (45.4)	74 693 (40.8)	128 061 (30.6)	120 844 (20.4)	<0.001*
Healthy diet	150 000 (11.7)	16 837 (18.7)	31 733 (17.4)	54 092 (12.9)	47 338 (8.0)	<0.001*
Metabolic factors						
Systolic blood pressure, mmHg	136.6 (20.1)	129.7 (18.6)	133.7 (19.1)	135.4 (19.4)	139.4 (20.6)	<0.001
Diastolic blood pressure, mmHg	81.4 (11.2)	80.7 (11.6)	81.1 (11.1)	81.7 (11.1)	81.5 (11.3)	<0.001
Total cholesterol, mmol/L	4.6 (1.1)	4.5 (1.1)	4.6 (1.1)	4.6 (1.1)	4.6 (1.1)	<0.001
Blood glucose, mmol/L	6.2 (1.7)	6.0 (1.5)	6.2 (1.6)	6.2 (1.7)	6.2 (1.8)	<0.001
Waist circumference, cm	84.1 (9.7)	83.8 (9.7)	84.4 (9.6)	84.4 (9.6)	83.8 (9.8)	<0.001
Body mass index	24.8 (3.4)	24.6 (3.2)	24.8 (3.3)	24.9 (3.4)	24.7 (3.5)	<0.001
Socioeconomic factors						
In marriage	1 204 202 (93.8)	86 900 (96.6)	174 308 (95.3)	400 385 (95.5)	542 609 (91.7)	<0.001*
Household income >50 000 RMB Yuan	238 516 (18.6)	49 887 (55.4)	57 843 (31.6)	78 267 (18.7)	52 519 (8.9)	<0.001*
Having health insurance	1 264 437 (98.5)	88 670 (98.5)	179 367 (98.1)	412 654 (98.5)	583 746 (98.6)	<0.001
Farmer	644 409 (50.2)	1247 (1.4)	27 328 (14.9)	185 339 (44.2)	430 495 (72.7)	<0.001

*A decreasing trend was identified.

and the National Mortality Surveillance System and Vital Registration of China Center for Disease Control and Prevention that covers urban and rural areas in all the 31 provinces of the mainland of China. The death records in this system were reported by health care institutions almost in real time then checked against local residential records and health insurance records annually.

In this National Mortality Surveillance System and Vital Registration, the main cause of death was coded using the 10th edition of the International Classification of Diseases (ICD-10). We considered that cardiovascular disease is the leading cause of death in China, and behavioural and metabolic factors are the leading risk factors for cardiovascular disease incidence and prognosis. Cardiovascular disease mortality (ICD-10 codes I00-I99) was also included as a study outcome in our analyses.

Statistical analyses

We described participant characteristics by education levels using percentages for categorical variables and mean (standard deviation) or median (interquartile range) as appropriate for continuous variables. To compare the trends of characteristics from higher to lower education levels, analysis of variance tests for continuous variables and Mantel-Haenszel χ^2 test for categorical variables were conducted.

To evaluate the cumulative influences of socioeconomic, behavioural, and metabolic factors on the educational inequalities, a series of stepwise Cox proportional hazard models were used to calculate hazard ratios and 95% confidence interval for the education level with all cause mortality in different generations and in overall cohort. Socioeconomic, behavioural, and metabolic factors were adjusted in sequence. In model 1, we adjusted for age, sex, urbanity, and geographical region. In model 2, socioeconomic factors (ie, marriage status, household income, medical insurance, and whether work as a farmer) were additionally adjusted for. In model 3, healthy lifestyle behaviours (ie, never smoking or stopped smoking for reasons other than illness, drinking no alcohol or no more than 25 g (for women) or 15 g (for

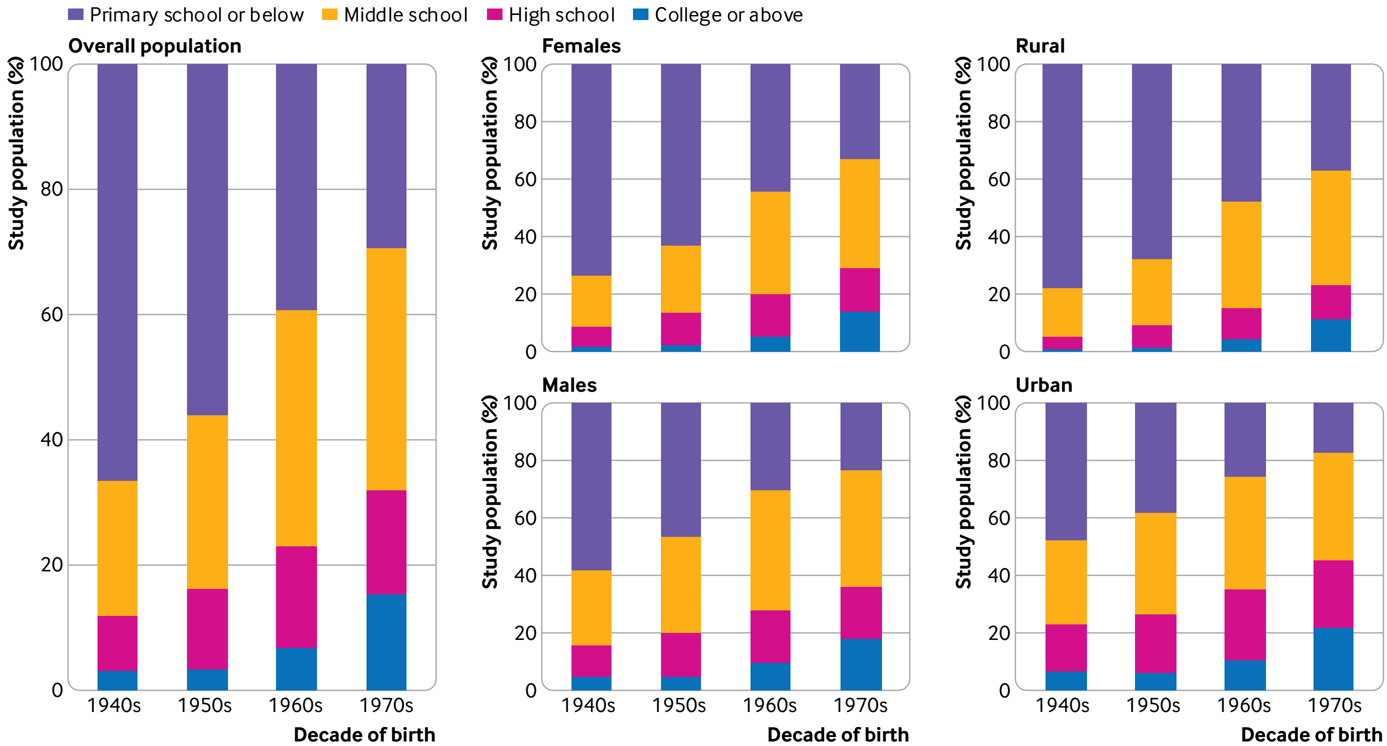

Fig 1 | Educational composition of study participants in overall population, and by sex, and urbanity

men) per day on average, having sufficient leisure time physical activity, and having a healthy diet score ≥4) were added too. In model 4, metabolic factors (ie, total cholesterol, blood glucose, systolic blood pressure, diastolic blood pressure, body mass index, and waist circumference) were further included. To evaluate the separate influence of socioeconomic, behavioural, and metabolic factors on the educational inequalities, Cox proportional hazard models were fitted in adjustment to socioeconomic, behavioural, and metabolic factors separately. We tested the proportion hazard and linear assumption of the Cox models (supplementary method). Considering that the relation between these metabolic factors and outcomes were not linear, we divided each of them into 20 groups and then included them as dummy variables into the model. As the mortality data were available up to 31 December 2021, we censored follow-up at this date or the date of death, whichever occurred first in all models.

The Kunst-Machkenbach's relative index of inequality was calculated by a structure regression framework to estimate the extent of educational inequality in mortality and how this inequality varied among people from different generations.[21] Relative index of inequality can be interpreted as the ratio of the mortality rate predicted for the hypothetical lowest end of the education continuum to the rate predicted for the hypothetical highest end. To evaluate the effects of three categories of potential contributing factors (ie, behavioural, metabolic factors, and socioeconomic factors) on the educational inequalities in mortality, relative index of inequalities were estimated by fitting Cox regression models adjusted for each category, in addition to age and sex. According to the causal structure of the association between education and mortality (supplementary method), mediation analyses were conducted using the public %MEDIATE SAS macro (https://ysph.yale.edu/cmips/research/software/mediate) to estimate the mediating effects of those factors on the relation between education levels and all cause mortality among people from different generations. Mediators' effects were reported, if existed, as the proportion of the relationship mediated through them.

We conducted several sensitivity analyses. Firstly, we repeated all analyses in participants without missing value in behaviours or socioeconomic factors (n=1 186 327). Secondly, we conducted causal mediation analysis using the mediation R package to compare the results from the traditional mediation analysis. Thirdly, as a result of the significantly different distributions of education levels across sex and urbanity, we conducted all analyses stratified by sex (female and male) and urbanity (rural and urban). Fourthly, to further assess the health effect of education inequality on cardiovascular diseases, we repeated all analyses with cardiovascular disease mortality as the outcome. Lastly, we used polytomous variables of health lifestyle behaviours in Cox regression models to test the influence of binary variables.

A two side P value of <0.05 was considered statistically significant. All analyses were conducted with SAS 9.4 (SAS Institute Inc, Cary, NC, USA) and R 4.1.1.

Table 2 | Mediation proportion (95% confidence interval) of modifiable risk factors on educational associated all cause mortality

Risk factors	Overall	1940s	1950s	1960s	1970s
Socioeconomic factors	37.5 (32.6 to 42.8)*	40.9 (31.6 to 50.8)*	34.3 (27.1 to 42.2)*	33.7 (24.7 to 44.0)*	49.9 (27.9 to 72.0)*
In marriage	1.3 (1.0 to 1.6)*	1.7 (1.1 to 2.7)*	1.2 (0.8 to 1.7)*	0.4 (0.2 to 0.8)*	1.4 (0.7 to 2.6)*
Annual household income >50 000 RMB Yuan	10.3 (8.4 to 12.6)*	9.1 (6.0 to 13.6)*	9.0 (6.4 to 12.6)*	11.4 (7.7 to 16.6)*	20.4 (11.8 to 32.9)*
Having health insurance	−0.01 (−0.5 to 0.0)	−0.03 (−0.4 to 0.0)	0.04 (0.0 to 0.4)	0.0 (0.0 to 100.0)	−0.2 (−0.6 to −0.04)
Occupation of farmer	31.5 (27.2 to 36.2)*	34.9 (27.0 to 43.8)*	29.4 (23.1 to 36.7)*	27.1 (19.2 to 36.7)*	37.2 (19.8 to 58.7)*
Healthy lifestyle behaviours	13.9 (12.0 to 16.0)*	16.2 (12.6 to 20.7)*	14.6 (11.6 to 18.3)*	8.7 (5.7 to 13.2)*	4.9 (1.3 to 16.2)
No smoking	2.0 (1.5 to 2.6)*	3.1 (2.0 to 4.6)*	1.7 (1.1 to 2.6)*	1.0 (0.5 to 2.0)*	0.8 (0.2 to 3.9)
None or moderate alcohol use	−0.1 (−1.0 to −0.01)	−0.8 (−1.5 to −0.4)	−0.02 (−0.5 to 0.4)	0.1 (0.02 to 0.5)	0.1 (0.01 to 1.1)
Sufficient LTPA	11.0 (9.4 to 12.8)*	12.7 (9.7 to 16.3)*	11.4 (9.0 to 14.5)*	7.4 (4.6 to 11.6)*	4.3 (1.1 to 15.2)
Healthy diet patterns	1.8 (1.2 to 2.5)*	2.2 (1.2 to 3.9)*	2.3 (1.4 to 3.6)*	0.5 (0.1 to 4.6)	−0.1 (−2.0 to 3.0)
Metabolic factors	4.7 (3.7 to 5.8)*	7.0 (5.0 to 9.8)*	5.5 (3.9 to 7.6)*	5.1 (3.3 to 7.6)*	0.3 (0.0 to 99.0)
Total cholesterol	0.1 (0.0 to 1.9)	−0.9 (−1.8 to −0.4)	−0.2 (−1.5 to −0.03)	0.9 (0.4 to 1.8)*	−0.8 (−5.6 to −0.1)
Blood glucose	−0.9 (−1.5 to −0.5)	−0.7 (−2.8 to −0.2)	−1.1 (−2.1 to −0.6)	−1.4 (−2.6 to −0.8)	0.4 (0.02 to 6.9)
Systolic blood pressure	1.8 (1.3 to 2.3)*	2.0 (1.3 to 3.2)*	2.4 (1.7 to 3.4)*	2.4 (1.6 to 3.6)*	−0.6 (−14.3 to −0.02)
Diastolic blood pressure	1.1 (0.7 to 1.5)*	2.5 (1.7 to 3.6)*	1.3 (0.8 to 2.1)*	−0.3 (−3.0 to −0.02)	−1.8 (−3.7 to −0.9)
Body mass index	3.7 (3.2 to 4.4)*	4.9 (3.6 to 6.4)*	4.5 (3.6 to 5.7)*	3.2 (2.4 to 4.3)*	2.0 (1.0 to 4.0)*
Waist circumference	1.9 (1.6 to 2.4)*	3.1 (2.2 to 4.4)*	2.7 (2.0 to 3.8)*	1.2 (0.7 to 2.1)*	0.7 (0.2 to 2.7)

Mediators' effects are reported as the proportion of the relationship mediated through them. LTPA=leisure time physical activity.
*P<0.05.

Patient and public involvement

No participants were involved in setting the research question or the outcome measures, nor were they involved in developing plans for the design or implementation of the study. No participants were asked to advise on interpretation or writing up of the results. We know that the public involvement has great value in improving the quality of research; however, we did not have the necessary funding to invite participants for their advice. We intend to engage participants and the public in the dissemination of the results of our study.

Results

Participant characteristics

Among 1 283 774 included participants, the mean age was 56.9 years (standard deviation 9.4), 767 583 (59.8%) were female, and 778 892 (60.7%) were living in rural areas (table 1). Of all participants, 46.1% had an education level of primary school or below, 32.6% had middle school level, 14.2% had high school level, and 7.0% had college or above level (table 1). Participants with a lower education level had higher proportions of morbidities, but lower adherence to sufficient leisure time physical activity and healthy diet than those with higher education levels (P for trend <0.001). Additionally, significant decreasing trends in systolic blood pressure, total cholesterol, blood glucose, waist circumference, and body mass index were observed with the increase of education levels.

In the study population, 162 949 (12.7%) of participants were born in the 1940s, 422 076 (32.9%) were born in the 1950s, 427 651 (33.3%) were born in the 1960s, and 271 098 (21.1%) were born in the 1970s. For the 1940s, 1950s, 1960s, and 1970s cohorts, female participants accounted for 54.3%, 57.8%, 62.7%, and 61.6% in these four generations, respectively, and participants living in rural areas accounted for 61.7%, 59.9%, 61.6%, and 59.8%. Overall, 5248 (3.2%) of participants from the 1940s cohort had a college education or above, compared with 13 922 (3.3%) from the 1950s cohort, 29 146 (6.8%) from the 1960s cohort, and 41 680 (15.4%) from the 1970s cohort. This trend was consistent in subgroups by sex and urbanity (fig 1, supplementary table 1, table 2, and supplementary fig 1).

The differences in socioeconomic and behavioural factors among participants with varied education levels were similar across the four generations. With regard to metabolic factors, systolic blood pressure and diastolic blood pressure were negatively associated with education levels in all four generations; blood glucose, body mass index, and waist circumference were positively associated with education levels in older generations, but negatively in younger generations; and total cholesterol was negatively associated with education levels in older generations but positively in younger generations. Detailed characteristics of study participants stratified by generation were showed in supplementary table 2.

Education with mortality and educational inequalities in mortality

During a total of 4.3 million person years of follow-up (median duration 3.5 years (interquartile range 2.1-4.7)), 22 552 (1.8%) deaths occurred. Among them, 9107 (40.4%) were due to cardiovascular disease, with the proportion decreasing from 44.3% in 1940s to 34.0% in 1970s. The mortality rates declined with the increase of education levels in the overall population, and across all four generations (table 1). With the adjustment for socioeconomic, behavioural, and metabolic factors, the hazard ratios of education level for all cause mortality reduced but remained statistically significant in overall population and across generations (fig 2 and supplementary figure 2). Compared with participants with college level education or above, the hazard ratio for people with primary school education and below was 1.4 (95% confidence interval 1.2 to 1.7) in the 1940s cohort, 1.8 (1.5 to 2.1) in the 1950s cohort, 2.0 (1.7 to 2.4) in the 1960s cohort, and 1.8 (1.4 to 2.4) in the 1970s cohort.

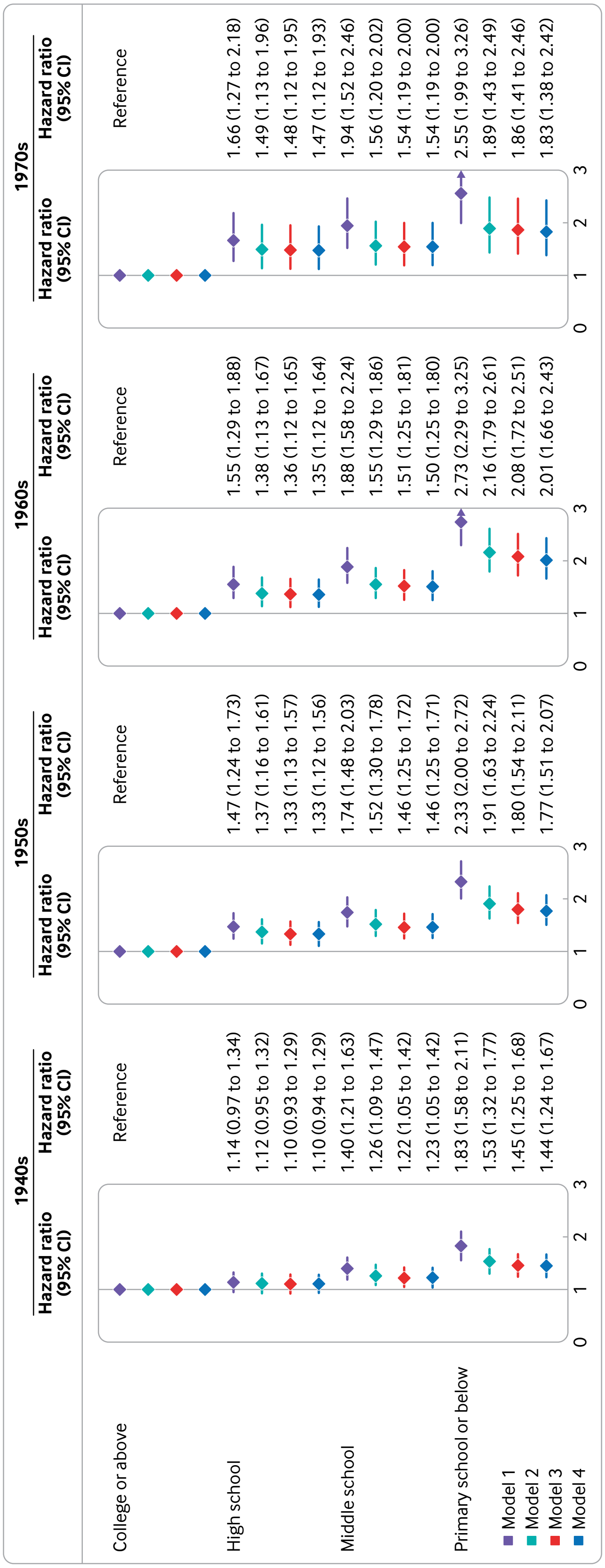

Fig 2 | Hazard ratios of all-cause mortality between different education groups by generation. Model 1 adjusted for age, sex, urbanity, and geographical region. Model 2 additionally adjusted for socioeconomic factors based on model 1. Model 3 additionally adjusted for healthy lifestyle behaviours based on model 2. Model 4 additionally adjusted for metabolic factors based on model 3. HR=hazard ratio

Similar results were also found in men and women, rural and urban population, for cardiovascular disease mortality, and when polytomous behavioural variables used in Cox models (supplementary table 3 and 4).

In the overall population, educational relative index of inequality in mortality increased from 2.1 (95% confidence interval 1.9 to 2.3) in the 1940s cohort to 2.6 (2.1 to 3.3) in the 1970s cohort after adjusting for age, sex, urbanity, and geographical region (fig 3, model 1). The educational disparities in mortality were significantly different among generations. In rural areas, the adjusted relative index of inequality increased from 1.8 (1.6 to 2.0) in the 1940s cohort to 3.2 (2.4 to 4.2) in the 1970s, while in urban areas the result decreased from 2.4 (2.1 to 2.8) in the 1940s cohort to 1.6 (1.0 to 2.3) in the 1970s (supplementary table 5). In the stepwise adjustment for the three categories of factors (ie, behavioural, metabolic factors, and socioeconomic factors), the relative index of inequalities declined gradually but remained statistically significant within every cohort. Among all four generations, adjustment for socioeconomic factors led to larger reductions in relative index of inequalities, in comparison with other two categories of factors. Furthermore, adjusting for healthy lifestyle behavioural factors led to larger reductions in relative index of inequalities than metabolic factors in the two older generations, but smaller reductions in the two younger generations. The influence of related factors on the relative index of inequality reduction was similar in men and women and in a rural or urban population (supplementary table 5). Similar results were reported in complete case analysis (supplementary figure 3).

Effects of potential mediators on educational inequalities in mortality

In the overall population, the cumulative mediation proportion by socioeconomic, behavioural, and metabolic factors was 43.5% (95% confidence interval 37.9% to 49.2%). The cumulative mediation proportion was 48.5% (37.8% to 59.4%) for the 1940s cohort, 41.6% (33.2% to 50.5%) for the 1950s cohort, 40.7% (30.3% to 52.0%) for the 1960s cohort, and 51.5% (28.7% to 73.7%) for the 1970s cohort. Similar cumulative mediation proportions for all cause mortality were observed in men (43.1% (36.4% to 50.0%)) and women (45.5% (35.5% to 55.9%)). A much lower cumulative mediation proportion was observed in the rural population (37.6% (31.2% to 44.5%)) than in the urban (50.6% (41.0% to 60.2%)) (supplementary table 6).

The mediation proportion by socioeconomic factors was 37.5% (95% confidence interval 32.6% to 42.8%), by behavioural factors was 13.9% (12.0% to 16.0%), and by metabolic factors was 4.7% (3.7% to 5.8%) (table 2). Except a surge for socioeconomic factors in the 1970s (for income and occupation in particular), trends decreased with generations in mediating proportions. The mediation proportion by healthy lifestyle behaviours decreased from 16.2% (12.6% to 20.7%) in the 1940s cohort to 4.9% (1.3% to 16.2%)

doi: 10.1136/bmj-2022-073749 | *BMJ* 2023;382:e073749 | the bmj

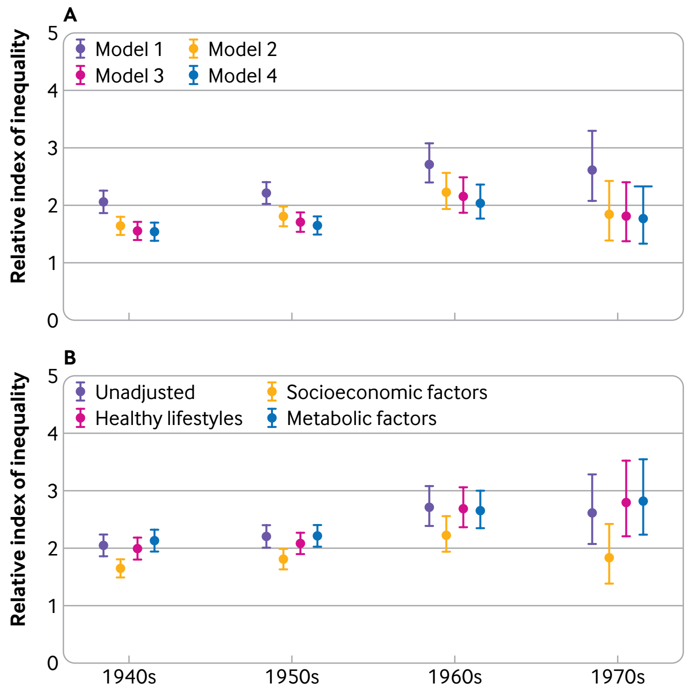

Fig 3 | Relative index of inequality on all cause mortality across different generations. (A) Model 1 adjusted for age, sex, urbanity, and geographical region. Model 2 additionally adjusted for socioeconomic factors based on model 1. Model 3 additionally adjusted for healthy lifestyle behaviours based on model 2. Model 4 additionally adjusted for metabolic factors based on model 3. (B) Adjusted for each category of factors separately

in the 1970s cohort, as did the mediation proportion by metabolic factors from 7.0% (5.0% to 9.8%) in the 1940s cohort to 0.3% (0.0% to 99.0%) in the 1970s cohort. Furthermore, among each of the modifiable behavioural or metabolic risk factors, sufficient leisure time physical activity had the greatest mediating effect, followed by body mass index, healthy diet, systolic blood pressure, and waist circumference (table 2, supplementary table 7 and 8). Similar results were reported in complete case analysis (supplementary table 9).

Discussion

Principal findings

This study is the first to evaluate the differences of educational inequalities in mortality across generations in China, we found that educational inequalities in mortality have widened from the 1940s cohort to the 1970s cohort, with substantial heterogeneity between rural and urban populations. The socioeconomic, behavioural, and metabolic factors mediated almost half of the association between education levels and mortality across all generations. The mediation proportions of modifiable behavioural and metabolic factors shrank in younger generations, in which sufficient leisure time physical activity had the leading effects.

Comparison with other studies

On educational disparity in health, our study has deepened understanding in several aspects. The enlarging educational inequalities in mortality also existed across generations, as was similarly shown in a shorter duration analysis.[8 9] Several explanations could be possible. On one hand, higher level of education is typically associated with better jobs and higher incomes,[22] and younger generations in China have experienced, at their exploration or establishment stage of career development,[23] an era of rapid development in which science and technology are the number one productive forces. Thus for younger generations, higher education could be more easily translated into richer resources and better environments than for their older generation counterparts. On the other hand, compared with the younger generations, older generations in our analysis and in prior studies had generally higher proportions of healthy lifestyles, such as sufficient leisure time physical activity, resulting in relatively attenuated educational disparities in these factors,[24 25] which could diminish education's association with health outcomes.

Heterogeneity was notable in trends of educational inequality in mortality between rural and urban areas. In China, the issue of unbalanced development between rural and urban areas has been a focus of public policy. However, growing educational inequality in health within rural populations has been unacknowledged and understudied. This lack of attention could be partly explained by the rapidly increasing diversity in rural population and daily lives, which has led to multiple resource channels. For example, the number of township and village enterprises has increased from 1.5 million in 1978 to 27.4 million in 2010, with their number of employees from 28 million (3.5% of rural population) to over 159 million (23.6% of rural population).[26] Thus, except for farmers, younger rural residents have had more varied occupation choices and income streams that are more dependent on their knowledge and skills, but which have probably widened socioeconomic disparities. In this context, the growing education related disparities in living environment and working conditions among rural population are unsurprising. Previous studies indicated that disparity in health literacy across educational levels in younger rural residents were much larger than in their urban counterparts.[27] And more notably, given the poorer healthcare service in rural areas,[28] residents' health literacy could have a more important role in maintaining health through self-management, which jointly worsened the health inequality related to education there.

The mediating effects of behavioural factors were generally stronger than the metabolic ones, indicating potential targets for preventing deaths. Even through prior studies on this topic rarely conducted quantitative comparisons between these two categories of modifiable factors,[11 29 30] comparison seems plausible in two ways. Behavioural factors such as sufficient leisure time physical activity are proved effective in preventing deaths of a wider array of causes, compared with the metabolic ones such as blood pressure that are mainly related to cardiometabolic diseases.[31]

Behavioural factors have closer associations with education and other socioeconomic characteristics: the higher the education of a participant, the healthier their lifestyle. In comparison, associations between education and metabolic factors were much more complex (ie, different trends of blood glucose and obesity *v* total cholesterol with education levels across generations) that blurred the potential mediating effects. Furthermore, consistent with our findings, a prior systematic review reported that the mediating effect of education on mortality by health lifestyles increased with age.[11] The negligible mediating effects of behavioural and metabolic factors in younger generations could be explained by their lower mortality rate and smaller portion of total cardiovascular disease death.

Policy implications

Our study has potential implications for health promotion. China has made achievements in population education, including implementation of a nine year compulsory education and popularity of higher education.[32] Nevertheless, the educational inequalities in mortality has worsened, particularly in rural areas, which calls for more targeted strategies. The Healthy China Initiative (2019-30)[33] is a guideline that promotes healthy lifestyles and improving metabolic factors management that has been implemented as one of key strategies to prevent chronic diseases. However, mitigating educational disparities in health has yet to be included, and should be put on the national agenda. In addition to the structural strategy of improving socioeconomic status of the population that has a lower education level, behavioural factors such as leisure time physical activity and diet were highlighted as potential intervention targets for universal health promotion. Comprehensive actions, rather than only on the basis of perceptions of victim blaming, should be implemented. Policy makers could consider fostering an environment for individuals with little education (or other socioeconomic limitations) to enable people who are less educated to easily understand how physical activities and different types of food affect their health. Additionally, exercising facilities and healthy foods at low cost should be provided in their near neighbourhood. Moreover, although the mediating effects of behavioural and metabolic factors were negligible in younger generations, low adherence to healthy lifestyle behaviours in the younger population, especially for people who had a low education level, and the potential consequent metabolic problems in the future, calls for more attention.

Limitations of study

This study had following limitations. Firstly, the study sample was not collected based on a random sampling design. And only local residents aged 35-75 years were recruited in this study. However, the educational composition in our study cannot represent, but was very close, to the distribution in the whole Chinese population (proportion of people with an educational level of college or above was 3.5% and 13.8% in those born in the 1940s and 1970s, based on 2020 national census data;[34] the corresponding proportion in this study was 3.2% and 15.4% in the 1940s and 1970s cohort in this study, supplementary method). Although the representativeness might not be essential for analytical studies, potential selection or collider biases from non-random sampling can influence the study findings.[35] Secondly, some recall biases and measurement errors were inevitable because behavioural factors and morbidities were self-reported, even if we used the standardised questionnaires, which had been used and validated in other large population studies.[36 37] Thirdly, data for socioeconomic status and behavioural and metabolic factors were collected at baseline. Apart from education level, other covariates could have changed during the follow-up, which might have affected the estimation of their mediating effects. Fourthly, although the National Mortality Surveillance System and Vital Registration of Chinese Center for Disease Control and Prevention covered urban and rural areas in all 31 provinces of the mainland of China, death records could be missing, particularly in remote rural areas, but the proportion would be very small. Fifthly, the follow-up duration of this study is short, which might lead to unstable estimates in the regression models. Lastly, we used binary variables to evaluate mediating effects of healthy lifestyles on educational inequalities in mortality, and such data reduction might affect the precision of the results. In the sensitivity analysis that used a polytomous variable, we found no changes to the main findings. To keep comparable with other studies and highlight the modifiable targets, we kept the results based on binary variables as the main findings.

Conclusions

Although the education level has increased during the past four decades in China, the educational inequalities in mortality increased across generations, which was particularly striking in rural areas. Use of comprehensive actions through fostering a more friendly and accessible healthcare environment to promote healthy lifestyles and improve metabolic factors for people with a lower level of education, especially younger generations, is one of the most effective strategies to reduce the educational inequalities in health.

We appreciate the multiple contributions made by study teams at the National Center for Cardiovascular Diseases and the local sites in the collaborative network in the realms of study design and operations, particularly data collection by Hao Dai, Binbin Jin, and Hui Zhong.

Contributors: JLu and CW contributed equally to the paper as joint first authors. XL (xi.li@nccd.org.cn) and JLi (lijing@fuwai.com) are joint corresponding authors. XL and JLi conceived the ChinaHEART project and take responsibility for its all aspects. JLu and CW conceived this article. JLu and CW wrote the manuscript, with further contributions from XZ, YY, JC, WX, LS, HY, WH, YZ, JLi, and XL. CW, XZ, and JLu completed all the statistical analysis. All authors interpreted data, contributed to critical revisions, and read and approved the final version of the article. The corresponding author (XL) attests that all

listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: This study was supported by the CAMS Innovation Fund for Medical Science (2021-1-I2M-011); the National High Level Hospital Clinical Research Funding (2022-GSP-GG-4, 2023-GSP-RC-20); the Ministry of Finance of China and National Health Commission of China; the 111 Project from the Ministry of Education of China (B16005). The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the decision to submit the manuscript for publication.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: The central ethics committee at the China National Center for Cardiovascular Diseases approved this study (approval no. 2014-574). All enrolled participants provided written informed consent.

Data sharing: The data are not publicly available. The China Health Evaluation And risk Reduction through nationwide Teamwork (ChinaHEART) project only provides conditional data access for qualified researchers with legitimate requests; a formal application and research proposal is required. Please contact cvd-project@nccd.org.cn to seek approval for data access.

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Dissemination to participants and related patient and public communities: Results of this study will be disseminated to study participants and the general public via emailed newsletters relevant to the individual cohorts, institutional and cohort specific websites, and social media channels, where available.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Web appendix: Online appendix