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# Association between educational level and total and cause-specific mortality: a pooled analysis of over 694 000 individuals in the Asia Cohort Consortium

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## ABSTRACT

**Objective** To study the association of educational level and risk of death from all causes, cardiovascular disease (CVD) and cancer among Asian populations.

**Design** A pooled analysis of 15 population-based cohort studies.

**Setting and participants** 694 434 Asian individuals from 15 prospective cohorts within the Asia Cohort Consortium.

**Interventions** None.

**Main outcome measures** HRs and 95% CIs for all-cause mortality, as well as for CVD-specific mortality and cancer-specific mortality.

**Results** A total of 694 434 participants (mean age at baseline=53.2 years) were included in the analysis. During a mean follow-up period of 12.5 years, 103 023 deaths were observed, among which 33 939 were due to cancer and 34 645 were due to CVD. Higher educational levels were significantly associated with lower risk of death from all causes compared with a low educational level (≤primary education); HRs and 95% CIs for secondary education, trade/technical education and ≥university education were 0.88 (0.85 to 0.92), 0.81 (0.73 to 0.90) and 0.71 (0.63 to 0.80), respectively ($p_{trend}$=0.002). Similarly, HRs (95% CIs) were 0.93 (0.89 to 0.97), 0.86 (0.78 to 0.94) and 0.81 (0.73 to 0.89) for cancer death, and 0.88 (0.83 to 0.93), 0.77 (0.66 to 0.91) and 0.67 (0.58 to 0.77) for CVD death with increasing levels of education (both $p_{trend}$ <0.01). The pattern of the association among East Asians and South Asians was similar compared with ≤primary education; HR (95% CI) for all-cause mortality associated with ≥university education was 0.72 (0.63 to 0.81) among 539 724 East Asians (Chinese, Japanese and Korean) and 0.61 (0.54 to 0.69) among 154 710 South Asians (Indians and Bangladeshis).

**Conclusion** Higher educational level was associated with substantially lower risk of death among Asian populations.

## Strengths and limitations of this study

- ► This is the first and largest (n=694 434) pooled analysis of Asians to evaluate the impact of educational level on mortality in Asia.
- ► Our study is a pooling project of 15 prospective cohort studies from multiple countries with long-term follow-up in the Asia Cohort Consortium (ACC).
- ► This analysis is based on high-quality individual data collected from participating cohorts and harmonised using a standardised process at ACC coordinating centre.
- ► Our study revealed an inverse association of educational levels and risk of death in Asian populations; in Asia, further studies examining the determinants of educational inequalities in mortality are warranted.

## INTRODUCTION

Research has demonstrated that socioeconomic status (SES) has a significant impact on individual health status in terms of mortality, morbidity and disability.[1 2] Educational attainment is closely related to income, occupation, access to medical care and lifestyle habits. As a major determinant of SES, education has been inversely associated with mortality, an overall measure of health.[3 4]

Several cohort analyses have examined the relationship between education and mortality in the Western countries. For example, an analysis of two large American Cancer Society cohorts followed from 1959 to 1996 showed that low educational level was associated with higher all-cause death rates.[5] The follow-up of the US National Longitudinal Mortality Study

(2002–2011) found that both all-cause and cause-specific mortalities were higher among the least-educated than among the most-educated groups, and educational disparities in mortality were more apparent in those aged 50–64 years than those aged 66–79 years.[6] In the Europe, the inverse association between education with total and cause-specific mortality was also supported by a study of eight western European populations (1990–1997).[7] Leinsalu *et al*[8] examined the educational inequalities in mortality in four Eastern European countries (1990–2000); they found mortality rates decreased in similar patterns in all educational groups in Poland and Hungary, whereas in Estonia and Lithuania, mortality rates decreased among the highly educated group but increased among those with low education. Generally, over the past two decades, mortality has declined substantially in lower socioeconomic groups in most European countries; however, relative mortality inequalities widened because the declines were less marked in lower socioeconomic populations.[9]

In Asia, however, relatively few studies have assessed the education/mortality relationship among populations in this area. Further, such investigations were previously conducted only among one single country or area, such as South Korea,[10] the city of Wuhan in China,[11] Japan[12 13] and India.[14] Based on the information from the UNESCO Institute for Statistics (http://data.uis.unesco.org), compared with European countries and the USA, mean years of schooling and higher education rates are relatively lower whereas disease and death burdens are relatively higher in Asian countries.[15–17] Therefore, in this current study, we seek to examine the association of education and mortality in combined Asian populations by using pooled data from 15 prospective cohort studies in the Asia Cohort Consortium (ACC). The large sample size of this pooled analysis provided a strong statistical power to quantify the impact of educational levels on all-cause and major cause-specific mortalities in Asia.

## METHODS

### Study population

Our study is a pooling project of prospective cohort studies in the ACC, a collaborative effort committed to studying the aetiology of diseases in Asian populations.

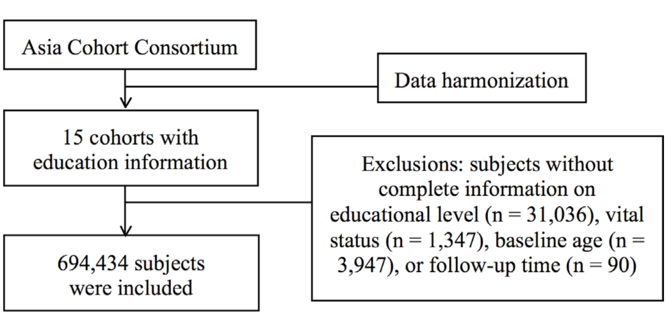


**Figure 1** Flowchart of Asian individuals eligible for inclusion in the study.

The ACC includes more than 20 cohorts representing Japan, China, South Korea, India, Taiwan, Bangladesh and Singapore. Cohorts were identified through a systematic search of the literature in early 2008, followed by a survey sent to each cohort to assess data availability. Details of the ACC and each participating cohorts have been presented elsewhere.[18 19] A total of 15 cohorts had collected information about educational attainment and therefore have been included in this pooled analysis. Individual data from participating cohorts was collected and harmonised for the statistical analysis. This study was approved by the ethics committees of each individual cohort study and by the institutional review board of the ACC coordinating centre (Fred Hutchinson Cancer Research Center, Seattle, USA; National Cancer Center, Tokyo, Japan).

### Patient and public involvement

Patients or public were not involved in this study.

### Data harmonisation

Relevant data from each of the participating cohorts were transferred and harmonised at the ACC coordinating centre. Harmonisation involved several rounds of discussions to ensure that variables were correctly interpreted and extracted. Data were checked for illogical or missing values, and queries were sent back for clarification. The distributions of individual variables were explored to identify false or implausible values. All personal identifiers were removed, but study-specific ID numbers were retained to facilitate referral of all queries to the individual cohort.

### Education level and outcome measurements

We excluded from our analysis participants without complete information on educational level (n=31 036), vital status (n=1347), baseline age (n=3947) or follow-up time (n=90). After these exclusions, 694 434 subjects from the 15 participating cohorts were included, among whom 539 724 were East Asians (Chinese (including cohorts from mainland China, Taiwan, Singapore), Japanese and Koreans) and 154 710 were South Asians (Indians and Bangladeshis). Among all included subjects, 344 702 were men and 349 732 were women (figure 1).

Information about completed education was collected by each cohort through questionnaire and harmonised into the following groups: ≤primary education (ie, no formal education or completed only primary education), secondary education (ie, high school education), technical/trade education (ie, associate degree) and ≥university education (ie, undergraduate or graduate education). Data on all-cause and cause-specific mortality were ascertained through linkage to death certificate data or active follow-up. The diagnosis of cause-specific mortality was made according to the International Classification of Diseases, 9th or 10th Revision (ICD-9 or ICD-10): all cancer (ICD-9 codes: 140–208; ICD-10 codes: C00-C97), cardiovascular diseases (CVDs) (ICD-9 codes: 390–459; ICD-10 codes: I00-I99).

### Statistical analysis

Cox proportional hazards regression models were utilised to estimate HRs and 95% CIs for the association between educational level and the risk of death, with '≤primary education' as the reference group for the estimation. The ages of the subjects when they entered and exited the cohort were used to define the time scale in the Cox models. The entry time was defined as age at the baseline interview, and the exit time was defined as age at death or last follow-up, whichever occurred earlier.

We built up two models: the crude model, adjusted only for baseline age and gender; and the multivariable-adjusted model, which was further adjusted for other potential confounders, including residential location (urban, rural), marital status (single, married, widowed/separated/divorced), body mass index (BMI) (underweight, normal, overweight, obese), smoking status (never, ever), alcohol drinking status (never, ever) and physical activity (<1 hour/week, 1–2 hours/week, 3–4 hours/week, ≥5 hours/week). Cox models were performed for each cohort, and random-effects meta-analyses were conducted to summarise results across cohorts. In all models, the impact of educational level on the risk of death was assumed to be cohort-specific.[20] We assumed that the log-HRs associated with education level had a fixed-effect component that was common to all cohorts within each country and a random effect that was cohort-specific. The random effects for log-HRs were assumed to be normally distributed, with mean zero; namely, we assumed that $\hat{\beta} ij$, the estimated log-HR for the $j$th educational level in an $i$th cohort, follows the distribution $\hat{\beta} ij \sim N(\beta j, \hat{\sigma}^2 ij + \hat{\tau}^2 j)$, where $\hat{\sigma}^2 ij$ is the within-study variance of $\hat{\beta} ij$ and $\hat{\tau}^2 j$ is the between-cohort variance of $\hat{\beta} ij$, as estimated from the Cox regression model.[21 22]

We also conducted stratified analyses by the covariates described above and assessed statistical significance of interaction using the Wald test for cross-product terms of covariates and education in the Cox models adjusted for other confounding factors. Cox model estimation for each cohort was performed using the PHREG procedure in SAS, V.9.4 (SAS Institute). The meta-analysis estimation was performed using STATA, V.14.0 (StataCorp LP). All tests were two-sided, and p<0.05 was considered statistically significant.

## RESULTS

After exclusions, a total of 694434 participants were included in the 15 participating cohorts; half (49.6%) were women. Nearly half (50.2%) of study participants received no formal education or completed only primary education. Approximately 9% of study participants had received university or higher degrees at baseline. Our analysis included 103023 deaths during a mean follow-up period of 12.5 years, among which 33939 (33.0%) were from cancer, 34645 (33.6%) were from CVD and the remaining 34439 (33.4%) were from other causes. Selected characteristics of cohorts included in the present study are listed in table 1.

We found inverse associations of education levels with all-cause mortality among our total population as well as populations from different countries or regions (table 2). When adjusted for age, sex, residential location, marital status, BMI, smoking, alcohol drinking status and physical activity, HRs for mortality were slightly attenuated compared with crude models (age- and sex-adjusted only), but remained statistically significant. No substantial difference was observed between the two models in terms of the pattern of the association. Among all combined cohorts, higher education level was significantly associated with lower risk of death from all causes; compared with ≤primary education, multivariable-adjusted HRs and 95% CIs for secondary education, trade/technical education and ≥university education were 0.88 (0.85 to 0.92), 0.81 (0.73 to 0.90) and 0.71 (0.63 to 0.80), respectively ($p_{trend}$=0.002). The pattern of association among East Asians and South Asians appeared similar; regarding all-cause mortality compared with ≤primary education, multivariable-adjusted HRs and 95% CIs for ≥university education was 0.72 (0.63 to 0.81) among 539724 East Asians (Chinese, Japanese and Korean) and 0.61 (0.54 to 0.69) among 154710 South Asians (Indians and Bangladeshis).

A similar pattern of association was observed for cause-specific mortality due to CVD and cancer, while the strength of the inverse association was weaker for deaths due to cancer than those due to CVD and all causes (table 3). Compared with low educational level (ie, ≤primary education), higher educational level was significantly associated with lower cancer-specific mortality (multivariable-adjusted HR (95% CI) for secondary education=0.93 (0.89 to 0.97), for trade/technical education=0.86 (0.78 to 0.94) and for ≥university degree=0.81 (0.73 to 0.89), $p_{trend}$=0.006), as well as lower CVD-specific mortality (multivariable-adjusted HR (95% CI) for secondary education=0.88 (0.83 to 0.93), for trade/technical education=0.77 (0.66 to 0.91) and for ≥university degree=0.67 (0.58 to 0.77), $p_{trend}$=0.002). As shown in table 3, the significant gradient of the inverse association between education and cancer/CVD-specific mortality also appeared in the East Asian population-only analysis (p<0.05). In South Asians, compared with the reference group (ie, ≤primary education), individuals with ≥university education had significantly lower risk of death from CVD (p<0.05). The association between education and cancer-specific mortality was not statistically significant among South Asians probably due to the small numbers of deaths across different educational groups among South Asians.

We further examined the association between educational levels and risk of death due to all causes stratified by covariates (online supplementary table 1). We observed statistically significant effect modifications by age, gender, residential location, marital status, physical activity, smoking and alcohol consumption status on the association between education and all-cause mortality (p for interactions <0.01). However, for all covariates except

**Table 1** Selected characteristics of participating cohorts

| Cohort | No of subjects | Dates of enrolment | Mean follow-up years | Women (%) | Mean age (SD) at entry | Median (range) of age at entry | Education level ≤ Primary (N (%)) | Secondary (N (%)) | Trade/ technical (N (%)) | ≥University (N (%)) | All causes # death (mortality%) | Cause of death (%) CVD (N (%)) | Cancer (N (%)) | Other (N (%)) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mainland China | | | | | | | | | | | | | | |
| SMHS | 60611 | 2002–2006 | 9.4 | 0 | 55.3 (9.7) | 53 (40–75) | 4084 (6.7) | 20334 (33.6) | 21858 (36.1) | 14335 (23.7) | 5364 (8.9) | 1772 (33.0) | 2328 (43.4) | 1264 (23.6) |
| SWHS | 74925 | 1996–2000 | 14.9 | 100 | 52.6 (9.1) | 50 (40–71) | 16181 (21.6) | 27682 (37.0) | 20890 (27.9) | 10172 (13.6) | 7651 (10.2) | 2490 (32.5) | 3219 (42.1) | 1942 (25.4) |
| SCS | 18100 | 1986–1989 | 16.3 | 0 | 55.3 (5.7) | 56 (35–76) | 5156 (28.5) | 8472 (46.8) | 1067 (5.9) | 3405 (18.8) | 4983 (27.5) | 1686 (33.8) | 1974 (39.6) | 1323 (26.6) |
| Taiwan | | | | | | | | | | | | | | |
| CBCSP | 23810 | 1991–1992 | 15.2 | 49.7 | 47.3 (10.0) | 48(29–66) | 14998 (63.0) | 3279 (13.8) | 3560 (15.0) | 1973 (8.3) | 2767 (11.6) | 558 (20.2) | 1013 (36.6) | 1196 (43.2) |
| CVDFACTS | 5142 | 1990–1993 | 14.9 | 55.9 | 47.5 (15.6) | 48 (18–92) | 2366 (46.0) | 2031 (39.5) | – | 745 (14.5) | 825 (16.0) | 220 (26.7) | 218 (26.4) | 387 (46.9) |
| Singapore | | | | | | | | | | | | | | |
| SCHS | 63247 | 1993–1999 | 11.5 | 55.8 | 56.5 (8.0) | 56 (43–83) | 45379 (71.8) | 14621 (23.1) | 2223 (3.5) | 1024 (1.6) | 10682 (16.9) | 3708 (34.7) | 3887 (36.4) | 3087 (28.9) |
| Japan | | | | | | | | | | | | | | |
| JACC | 69951 | 1988–1990 | 12.5 | 58.6 | 57.4 (10.0) | 58 (40–79) | 41978 (60.0) | 18724 (26.8) | 6918 (9.9) | 2331 (3.3) | 9717 (13.9) | 3011 (31.0) | 3610 (37.2) | 3096 (31.9) |
| JPHC | 40692 | 1990–1992 | 21 | 52.1 | 49.5 (5.9) | 50 (40–59) | 21248 (52.2) | 14761 (36.3) | 2752 (6.8) | 1931 (4.7) | 6608 (16.2) | 1738 (26.3) | 2744 (41.5) | 2126 (32.2) |
| Miyagi | 43525 | 1990 | 16.2 | 52.1 | 52.0 (7.6) | 52 (40–64) | 26101 (60.0) | 11651 (26.8) | 4147 (9.5) | 1626 (3.7) | 5086 (11.7) | 1376 (27.1) | 2359 (46.4) | 1351 (26.6) |
| Ohsaki | 46990 | 1995 | 10.8 | 51.6 | 60.1 (10.3) | 61 (40–80) | 28387 (60.4) | 15060 (32.1) | 2601 (5.5) | 942 (2.0) | 7517 (16.0) | 2422 (32.2) | 2654 (35.3) | 2441 (32.5) |
| Takayama | 31106 | 1992 | 13.6 | 54.2 | 55.9 (12.8) | 55 (35–101) | 19730 (63.4) | 9013 (29.0) | – | 2363 (7.6) | 6076 (19.5) | 2026 (33.3) | 1771 (29.2) | 2279 (37.5) |
| LSS | 47928 | 1963–1993 | 22 | 59.9 | 52.1 (13.6) | 51 (19–99) | 21889 (45.7) | 20605 (43.0) | – | 5434 (11.3) | 24818 (51.8) | 9109 (36.7) | 6734 (27.1) | 8975 (36.2) |
| Republic of Korea | | | | | | | | | | | | | | |
| SeoulM | 13697 | 1992–1993 | 15.6 | 0 | 49.2 (5.2) | 49 (25–82) | 133 (1.0) | 6227 (45.5) | – | 7337 (53.6) | 894 (6.5) | 154 (17.2) | 493 (55.2) | 247 (27.6) |
| India | | | | | | | | | | | | | | |
| Mumbai | 142973 | 1991–1997 | 5.2 | 40.9 | 50.5 (11.1) | 49 (35–98) | 92639 (64.8) | 43908 (30.7) | – | 6426 (4.5) | 9147 (6.4) | 4008 (43.8) | 797 (8.7) | 4342 (47.5) |
| Bangladesh | | | | | | | | | | | | | | |
| HEALS | 11737 | 2000–2002 | 12.3 | 57.1 | 37.1 (10.1) | 36 (17–75) | 8705 (74.2) | 2915 (24.8) | 117 (1.0) | – | 888 (7.6) | 367 (41.3) | 138 (15.5) | 383 (43.1) |
| Total | 694434 | 1963–2006 | 12.5 | 49.6 | 53.2 (10.7) | 52 (17–101) | 348974 (50.2) | 219283 (31.6) | 66133 (9.5) | 60044 (8.7) | 103023 (14.8) | 34645 (33.6) | 33939 (33.0) | 34439 (33.4) |

Participants without complete information on educational level, vital status, baseline age or follow-up time were excluded; among all participants, 12 people aged 17 years and 2 people aged 101 years.
Participants who died from unknown causes were excluded from analysis.
CBCSP, Community-based Cancer Screening Project; CVDFACTS, CardioVascular Disease risk FACtor Two-township Study; HEALS, Health Effects for Arsenic Longitudinal Study Bangladesh; JACC, Japan Collaborative Cohort Study; JPHC, Japan Public Health Center-based prospective Study; LSS, Life Span Study Cohort; Miyagi, Miyagi Cohort; Mumbai, Mumbai Cohort Study; Ohsaki, Ohsaki National Health Insurance Cohort Study; SCHS, Singapore Chinese Health Study; SCS, Shanghai Cohort Study; SMHS, Shanghai Men's Health Study; SWHS, Shanghai Women's Health Study; SeoulM, Seoul Male Cancer Cohort; Takayama, Takayama Study.

**Table 2** Association of educational level with risk of death from all causes in selected study populations in Asia

| | Number | | Model 1 | Model 2 |
|---|---|---|---|---|
| **Population** | **Participants** | **Deaths** | **HR (95% CI)** | **HR (95% CI)** |
| All cohorts combined | | | | |
| ≤Primary education | 348 974 | 64 948 | 1 | 1 |
| Secondary education | 219 283 | 26 652 | 0.86 (0.82 to 0.90) | 0.88 (0.85 to 0.92) |
| Trade/technical education | 66 133 | 5195 | 0.76 (0.68 to 0.86) | 0.81 (0.73 to 0.90) |
| ≥University education | 60 044 | 6228 | 0.66 (0.57 to 0.77) | 0.71 (0.63 to 0.80) |
| P for trend | | | 0.002 | 0.002 |
| Mainland China | | | | |
| ≤Primary education | 25 421 | 7227 | 1 | 1 |
| Secondary education | 56 488 | 5882 | 0.79 (0.76 to 0.83) | 0.82 (0.79 to 0.85) |
| Trade/technical education | 43 815 | 2702 | 0.64 (0.60 to 0.69) | 0.69 (0.66 to 0.73) |
| ≥University education | 27 912 | 2187 | 0.50 (0.48 to 0.54) | 0.56 (0.53 to 0.59) |
| P for trend | | | <0.001 | <0.001 |
| Taiwan | | | | |
| ≤Primary education | 17 364 | 2777 | 1 | 1 |
| Secondary education | 5310 | 478 | 0.83 (0.75 to 0.92) | 0.85 (0.70 to 1.02) |
| Trade/technical education | 3560 | 202 | 0.75 (0.64 to 0.87) | 0.82 (0.70 to 0.95) |
| ≥University education | 2718 | 135 | 0.50 (0.42 to 0.60) | 0.57 (0.48 to 0.68) |
| P for trend | | | 0.03 | 0.08 |
| Singapore | | | | |
| ≤Primary education | 45 379 | 8810 | 1 | 1 |
| Secondary education | 14 621 | 1596 | 0.76 (0.72 to 0.81) | 0.81 (0.77 to 0.86) |
| Trade/technical education | 2223 | 205 | 0.67 (0.58 to 0.76) | 0.75 (0.65 to 0.86) |
| ≥University education | 1024 | 71 | 0.52 (0.41 to 0.66) | 0.63 (0.50 to 0.80) |
| P for trend | | | 0.002 | 0.03 |
| Japan | | | | |
| ≤Primary education | 159 333 | 38 765 | 1 | 1 |
| Secondary education | 89 814 | 15 833 | 0.92 (0.87 to 0.98) | 0.94 (0.88 to 0.99) |
| Trade/technical education | 16 418 | 2075 | 0.90 (0.81 to 1.00) | 0.92 (0.82 to 1.02) |
| ≥University education | 14 627 | 3149 | 0.89 (0.80 to 0.99) | 0.89 (0.80 to 0.99) |
| P for trend | | | 0.47 | 0.36 |
| Republic of Korea | | | | |
| ≤Primary education | 133 | 17 | 1 | 1 |
| Secondary education | 6227 | 480 | 0.75 (0.46 to 1.22) | 0.77 (0.47 to 1.26) |
| Trade/technical education | – | – | – | – |
| ≥University education | 7337 | 397 | 0.48 (0.30 to 0.78) | 0.52 (0.32 to 0.86) |
| P for trend | | | <0.001 | <0.001 |
| India | | | | |
| ≤Primary education | 92 639 | 6663 | 1 | 1 |
| Secondary education | 43 908 | 2195 | 0.83 (0.79 to 0.87) | 0.89 (0.85 to 0.94) |
| Trade/technical education | – | – | – | – |
| ≥University education | 6426 | 289 | 0.55 (0.48 to 0.61) | 0.61 (0.54 to 0.69) |
| P for trend | | | <0.001 | <0.001 |
| Bangladesh | | | | |
| ≤Primary education | 8705 | 689 | 1 | 1 |

Continued

Table 2 Continued

| Population | Number | | Model 1 | Model 2 |
|---|---|---|---|---|
| | Participants | Deaths | HR (95% CI) | HR (95% CI) |
| Secondary education | 2915 | 188 | 0.83 (0.70 to 0.98) | 0.92 (0.77 to 1.08) |
| Trade/technical education | 117 | 11 | 0.92 (0.51 to 1.68) | 1.15 (0.63 to 2.10) |
| ≥University education | – | – | – | – |
| P for trend | | | 0.73 | 0.47 |
| East Asians | | | | |
| ≤Primary education | 247 630 | 57 596 | 1 | 1 |
| Secondary education | 172 460 | 24 269 | 0.86 (0.82 to 0.91) | 0.88 (0.84 to 0.93) |
| Trade/technical education | 66 016 | 5184 | 0.76 (0.67 to 0.86) | 0.80 (0.72 to 0.89) |
| ≥University education | 53 618 | 5939 | 0.70 (0.57 to 0.79) | 0.72 (0.63 to 0.81) |
| P for trend | | | 0.008 | 0.006 |
| South Asians | | | | |
| ≤Primary education | 101 344 | 7352 | 1 | 1 |
| Secondary education | 46 823 | 2383 | 0.83 (0.79 to 0.87) | 0.89 (0.85 to 0.94) |
| Trade/technical education | 117 | 11 | 0.92 (0.51 to 1.68) | 1.15 (0.63 to 2.10) |
| ≥University education | 6426 | 289 | 0.55 (0.48 to 0.61) | 0.61 (0.54 to 0.69) |
| P for trend | | | 0.02 | 0.03 |

Model 1: adjust for baseline age and sex.
Model 2: adjust for baseline age, sex, urban/rural residence, marital status, body mass index, smoking status, alcohol consumption status and physical activity.
East Asians include participants from mainland China, Taiwan, Singapore, Republic of Korea and Japan; South Asians include participants from India and Bangladesh.

residential location and marital status, we did not find material differences among stratified groups in terms of the risk estimates of education on total mortality, although p value for interaction was statistically significant.

## DISCUSSION

In this large (694 434) pooled analysis of Asian populations, we found that higher educational level was associated with a substantially reduced risk of death from all causes, CVD and cancer. This inverse association presented a dose–response pattern. The mortality disparity did not appear to be explained solely by lifestyle factors such as the level of physical activity, smoking and alcohol consumption. Our study provides convincing evidence for the link between education and risk of death in Asian populations.

Our findings in Asian populations are generally similar to the results in studies carried out in Western countries. Kitagawa and Hauser, using 1960 US death records and census data, first examined the SES/mortality relationship. They found not only that both men and women with higher education have lower mortality rates and live longer than those with lower education but also that there is a significant gradient across the seven ordered categories of completed schooling.[23] An additional 4years of education lowered 5-year mortality by 1.8%, according to the US National Bureau of Economic Research.[24] A low level of education was also found to be associated with increased all-cause mortality compared with high levels of education in cohorts with type II diabetes[25–27] and acute coronary syndrome.[28] Recently, Mackenbach *et al* studied the trends in health inequalities in 27 European countries (1980–2014); they found that, in Western Europe, all-cause mortality has declined steadily in both low-educated and highly educated men and women; the trend in mortality was generally stable in both education groups.[29] In Western Europe, absolute inequalities have usually decreased due to the larger absolute declines among the low-educated groups, but relative inequalities have generally increased because relative mortality declines were larger in the highly educated.[29] However, since the 1990s, relative and absolute inequalities in mortality have both increased in Eastern Europe.[8 9] The recent work by Mackenbach *et al* found that mortality has also begun to decline among the low-educated population in Eastern European countries; absolute inequalities in mortality have started to decrease as well.[29]

The inverse association between education and mortality was also found among older people in low-income and middle-income countries by a population-based cohort study of 12 373 people aged ≥65 years from Latin America, China and India.[15] In 2014, Vathesatogkit *et al* performed and published the first meta-analysis of studies from Asia on the association between SES and mortality.[30] Consistent with our findings, they found overall that those with the lowest level of education experienced a 1.4-fold higher risk

**Table 3** Association of educational level with risk of death from cardiovascular diseases and cancers in selected study populations in Asia

| Population | CVD | | | Cancer | | |
|---|---|---|---|---|---|---|
| | Number of deaths | Model 1 HR (95% CI) | Model 2 HR (95% CI) | Number of deaths | Model 1 HR (95% CI) | Model 2 HR (95% CI) |
| **All cohorts combined** | | | | | | |
| ≤Primary education | 22723 | 1 | 1 | 19465 | 1 | 1 |
| Secondary education | 8559 | 0.86 (0.81 to 0.91) | 0.88 (0.83 to 0.93) | 9626 | 0.90 (0.86 to 0.95) | 0.93 (0.89 to 0.97) |
| Trade/technical education | 1478 | 0.73 (0.61 to 0.88) | 0.77 (0.66 to 0.91) | 2322 | 0.81 (0.72 to 0.91) | 0.86 (0.78 to 0.94) |
| ≥University education | 1885 | 0.63 (0.53 to 0.75) | 0.67 (0.58 to 0.77) | 2526 | 0.75 (0.64 to 0.86) | 0.81 (0.73 to 0.89) |
| P for trend | | 0.003 | 0.002 | | 0.01 | 0.006 |
| **Mainland China** | | | | | | |
| ≤Primary education | 2700 | 1 | 1 | 2548 | 1 | 1 |
| Secondary education | 1858 | 0.80 (0.75 to 0.85) | 0.83 (0.78 to 0.89) | 2612 | 0.84 (0.74 to 0.95) | 0.88 (0.79 to 0.97) |
| Trade/technical education | 729 | 0.56 (0.48 to 0.66) | 0.61 (0.51 to 0.73) | 1334 | 0.72 (0.57 to 0.92) | 0.79 (0.65 to 0.96) |
| ≥University education | 661 | 0.47 (0.42 to 0.51) | 0.52 (0.45 to 0.60) | 1027 | 0.58 (0.45 to 0.75) | 0.66 (0.57 to 0.78) |
| P for trend | | <0.001 | 0.001 | | 0.03 | 0.03 |
| **Taiwan** | | | | | | |
| ≤Primary education | 619 | 1 | 1 | 931 | 1 | 1 |
| Secondary education | 97 | 0.76 (0.55 to 1.06) | 0.78 (0.53 to 1.15) | 169 | 0.88 (0.73 to 1.06) | 0.91 (0.77 to 1.09) |
| Trade/technical education | 33 | 0.71 (0.50 to 1.03) | 0.77 (0.53 to 1.11) | 81 | 0.78 (0.62 to 1.00) | 0.84 (0.65 to 1.07) |
| ≥University education | 29 | 0.52 (0.36 to 0.77) | 0.61 (0.42 to 0.90) | 50 | 0.54 (0.40 to 0.73) | 0.63 (0.47 to 0.84) |
| P for trend | | 0.20 | 0.39 | | 0.08 | 0.13 |
| **Singapore** | | | | | | |
| ≤Primary education | 3079 | 1 | 1 | 3150 | 1 | 1 |
| Secondary education | 536 | 0.77 (0.70 to 0.84) | 0.81 (0.74 to 0.90) | 627 | 0.78 (0.71 to 0.85) | 0.84 (0.77 to 0.92) |
| Trade/technical education | 80 | 0.79 (0.63 to 0.99) | 0.87 (0.69 to 1.08) | 75 | 0.62 (0.49 to 0.78) | 0.71 (0.57 to 0.90) |
| ≥University education | 13 | 0.30 (0.17 to 0.51) | 0.35 (0.20 to 0.60) | 35 | 0.64 (0.45 to 0.89) | 0.80 (0.57 to 1.12) |
| P for trend | | <0.001 | 0.002 | | 0.24 | 0.77 |
| **Japan** | | | | | | |
| ≤Primary education | 13187 | 1 | 1 | 12159 | 1 | 1 |
| Secondary education | 4910 | 0.89 (0.81 to 0.97) | 0.91 (0.83 to 0.99) | 5736 | 0.95 (0.92 to 0.99) | 0.96 (0.93 to 1.00) |
| Trade/technical education | 632 | 0.90 (0.78 to 1.04) | 0.92 (0.80 to 1.06) | 830 | 0.93 (0.84 to 1.02) | 0.94 (0.85 to 1.04) |
| ≥University education | 953 | 0.84 (0.72 to 0.96) | 0.83 (0.73 to 0.95) | 1147 | 0.89 (0.84 to 0.95) | 0.89 (0.84 to 0.95) |
| P for trend | | 0.49 | 0.38 | | 0.10 | 0.09 |
| **Republic of Korea** | | | | | | |
| ≤Primary education | 4 | 1 | 1 | 7 | 1 | 1 |
| Secondary education | 74 | 0.51 (0.19 to 1.40) | 0.58 (0.21 to 1.60) | 252 | 0.97 (0.46 to 2.06) | 0.99 (0.46 to 2.11) |
| Trade/technical education | – | – | – | – | – | – |
| ≥University education | 76 | 0.40 (0.15 to 1.10) | 0.51 (0.18 to 1.41) | 234 | 0.69 (0.33 to 1.47) | 0.74 (0.35 to 1.59) |
| P for trend | | 0.14 | 0.43 | | <0.001 | 0.002 |
| **India** | | | | | | |
| ≤Primary education | 2868 | 1 | 1 | 564 | 1 | 1 |
| Secondary education | 987 | 0.89 (0.83 to 0.97) | 0.90 (0.84 to 0.98) | 200 | 0.88 (0.74 to 1.04) | 0.99 (0.84 to 1.18) |

Continued

**Table 3** Continued

| Population | CVD Number of deaths | CVD Model 1 HR (95% CI) | CVD Model 2 HR (95% CI) | Cancer Number of deaths | Cancer Model 1 HR (95% CI) | Cancer Model 2 HR (95% CI) |
|---|---|---|---|---|---|---|
| Trade/technical education | – | – | – | – | – | – |
| ≥University education | 153 | 0.67 (0.57 to 0.79) | 0.68 (0.58 to 0.80) | 33 | 0.77 (0.54 to 1.10) | 0.92 (0.65 to 1.32) |
| P for trend | | <0.001 | <0.001 | | 0.48 | 0.70 |
| Bangladesh | | | | | | |
| ≤Primary education | 266 | 1 | 1 | 106 | 1 | 1 |
| Secondary education | 97 | 1.11 (0.88 to 1.41) | 1.08 (0.84 to 1.38) | 30 | 0.84 (0.56 to 1.26) | 0.97 (0.63 to 1.47) |
| Trade/technical education | 4 | 0.88 (0.33 to 2.38) | 0.88 (0.32 to 2.38) | 2 | 1.04 (0.26 to 4.24) | 1.38 (0.33 to 5.69) |
| ≥University education | – | – | – | – | – | – |
| P for trend | | 0.65 | 0.68 | | 0.76 | 0.63 |
| East Asians | | | | | | |
| ≤Primary education | 19589 | 1 | 1 | 18795 | 1 | 1 |
| Secondary education | 7475 | 0.84 (0.79 to 0.90) | 0.87 (0.82 to 0.92) | 9396 | 0.90 (0.86 to 0.95) | 0.93 (0.89 to 0.97) |
| Trade/technical education | 1474 | 0.73 (0.61 to 0.87) | 0.77 (0.66 to 0.91) | 2320 | 0.81 (0.72 to 0.91) | 0.86 (0.78 to 0.94) |
| ≥University education | 1732 | 0.62 (0.51 to 0.75) | 0.67 (0.57 to 0.78) | 2493 | 0.74 (0.64 to 0.87) | 0.80 (0.72 to 0.89) |
| P for trend | | 0.01 | 0.01 | | 0.02 | 0.01 |
| South Asians | | | | | | |
| ≤Primary education | 3134 | 1 | 1 | 670 | 1 | 1 |
| Secondary education | 1084 | 0.97 (0.79 to 1.19) | 0.95 (0.81 to 1.11) | 230 | 0.87 (0.75 to 1.02) | 0.99 (0.84 to 1.16) |
| Trade/technical education | 4 | 0.88 (0.33 to 2.38) | 0.88 (0.32 to 2.38) | 2 | 1.04 (0.26 to 4.24) | 1.38 (0.33 to 5.69) |
| ≥University education | 153 | 0.67 (0.57 to 0.79) | 0.68 (0.58 to 0.80) | 33 | 0.77 (0.54 to 1.10) | 0.92 (0.65 to 1.32) |
| P for trend | | 0.17 | 0.14 | | 0.61 | 0.80 |

Model 1: adjust for baseline age and sex.
Model 2: adjust for baseline age, sex, urban/rural residence, marital status, body mass index, smoking status, alcohol consumption status and physical activity.
East Asians include participants from mainland China, Taiwan, Singapore, Republic of Korea and Japan; South Asians include participants from India and Bangladesh.
CVD, cardiovascular disease.

of mortality than the highest level of education (all cause: RR=1.41, 95% CI=1.29 to 1.52; CVD: RR=1.66, 95% CI=1.23 to 2.25; cancer: RR=1.16, 95% CI=1.07 to 1.27). However, we note that—unlike our pooled analysis—due to the nature of a meta-analysis based only on reported estimates from previous publications, the detailed educational levels in the comparison groups were not specified in the study by Vathesatogkit *et al*.[30]

Educational attainment may not have a strong causal relationship with adult mortality. One nationwide quasi-experiment was conducted to examine the causal effect of education on mortality among 1.2 million Swedes;[31] the exposure was a 1-year increase in compulsory schooling as an educational reform implemented in Sweden from 1949 to 1962. No significant difference in all-cause mortality between the experimental and control groups was found during the entire follow-up (HR=0.98, 95% CI=0.95 to 1.01) or among those aged ≤40 years (HR=1.03, 95% CI=0.98 to 1.07). Risk of death from all causes in the experimental group aged >40 years was lower than that in the control group with marginally significant association (HR=0.96, 95% CI=0.93 to 0.99).[31] Interestingly, utilising a longitudinal dataset of Danish twins, Behrman *et al* found only weak evidence of an association between educational level and adult mortality among identical twin pairs who shared both the same genetic background and similar childhood social environments; but stronger evidence of the education/mortality relationship was found among fraternal twin pairs and unrelated individuals.[32]

Understanding the mechanisms by which educational attainment influences death risk is highly important for public policy making. There are several possible explanations. On one hand, education may affect health outcomes via people's SES (eg, occupation, income, wealth), social resources (eg, access to health information and healthcare services), health-related behaviours (eg, smoking, alcohol consumption, dietary habits, physical activity) and cognitive skills (eg, communication with physicians and nurses). On the other hand, a person's educational attainment can also act as a surrogate measurement for early-life factors such as parental SES, physical and mental health, childhood environment and social context[4 33]; in other words, education could lie on the pathway between those early-life factors and health outcomes (eg, mortality). Education seems to have an important latent effect on mortality into late life, suggesting that the adverse effect of low educational attainment and socioeconomic sequelae may accumulate across the life course.[34]

A study of 17 European countries (1970–2010) indicated that behavioural factors, including smoking and excessive alcohol consumption, were important contributors to the between-country variations in the magnitude of socioeconomic inequalities in mortality.[35] By comparing estimates (ie, HRs) obtained from the crude model (age- and sex-adjusted only) and the model further adjusted for each modifiable covariate individually, we found that smoking explained the most of the education–mortality association in our pooled data. Tobacco smoking is associated with a substantially increased risk of death among Asian adults, accounting for approximately 2 million deaths in adults aged over 45 years throughout Asia in 2004.[18] Research has shown that smoking rates were higher among lower-educated people in many countries and the educational differences in smoking were more apparent in younger population than older generations.[36–38] In our current study, the inverse associations between education and risk of death are significant in both never-smokers and ever-smokers; the magnitude of the association is slightly larger among those who never smoked (online supplementary table 1). In a study of 14 European countries, Gregoraci *et al* found that smoking-attributable mortality was inversely associated with socioeconomic levels defined by education and occupation in 2000–2004.[39] Though the contribution of smoking to socioeconomic inequalities in mortality has been reduced since 1990–2004, smoking remains one of the most important intervention targets for reducing health equalities in Europe.[39] In Asian populations, further studies examining the determinants of socioeconomic inequalities in mortality are warranted.

Our study has several strengths. First, this pooling project is the first and largest study evaluating the education/mortality relationship using combined Asian populations. Second, in contrast with a meta-analysis based on data from previous publications, our pooled analysis provides more accurate and reliable estimates by directly utilising individual data with standardised exposure measurement. Besides, the detailed covariate information collected in these cohorts enables a careful control for potential confounding and evaluation of effect modifications. We also acknowledge some limitations. First, because educational attainment data are self-reported at baseline in each cohort, we cannot rule out the possibility of misclassification. Additionally, there may be heterogeneity in education level across cohorts. However, we used a standardised harmonisation process on a range of environmental variables, including education level across 15 participating cohorts. Results presented in tables 2 and 3 show the consistency of the association between educational level and risk of death on a per-study level, and the pooled risk estimate is similar to that found in prior studies.[5 27] Thus, bias due to self-report and heterogeneity in educational level is likely to be minimal. Second, we also cannot completely rule out the possibility that some participants might have had further education during follow-up after baseline enrolment (mean age at baseline=53.2 years). However, in Asian countries, pursuit of further education among older adults is not as popular as in Western countries. Thus, such missing information seems less likely to affect our findings.

## CONCLUSION

Despite the limitations mentioned above, our study provides the best estimate of the impact of education on all-cause as well as major cause-specific mortality in Asian populations to date. Our findings may contribute to better public policy decisions, especially regarding increasing educational opportunities for Asian populations as a powerful intervention to reduce both morbidity and mortality.

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