Review

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Effects of education and income on cardiovascular outcomes: A systematic review and meta-analysis

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Abstract

Objective: Previous studies have reported discrepancy effects of education and income on cardiovascular diseases. This systematic review and meta-analysis was therefore conducted which aimed to summarize effects of education and income on cardiovascular diseases.

Methods: Studies were identified from Medline and Scopus until July 2016. Cohorts were eligible if they assessed associations between education/income and cardiovascular diseases, had at least one outcome including coronary artery diseases, cardiovascular events, strokes and cardiovascular deaths. A multivariate meta-analysis was applied to pool risk effects of these social determinants.

Results: Among 72 included cohorts, 39, 19, and 14 were studied in Europe, USA, and Asia. Pooled risk ratios of low and medium versus high education were 1.36 (95% confidence interval: 1.11–1.66) and 1.21 (1.06–1.40) for coronary artery diseases, 1.50 (1.17–1.92) and 1.27 (1.09–1.48) for cardiovascular events, 1.23 (1.06–1.43) and 1.17 (1.01–1.35) for strokes, and 1.39 (1.26–1.54) and 1.21 (1.12–1.30) for cardiovascular deaths. The effects of education on all cardiovascular diseases were still present in US and Europe settings, except in Asia this was present only for cardiovascular deaths. Effects of low and medium income versus high on these corresponding cardiovascular diseases were 1.49 (1.16–1.91) and 1.27 (1.10–1.47) for coronary artery diseases, 1.17 (0.96–1.44) and 1.05 (0.98–1.13) for cardiovascular events, 1.30 (0.99–1.72) and 1.24 (1.00–1.53) for strokes, and 1.76 (1.45–2.14) and 1.34 (1.17–1.54) for cardiovascular deaths.

Conclusion: Social determinants are risk factors of cardiovascular diseases in developed countries, although high heterogeneity in pooling. Data in Asia countries are still needed to update pooling.

Keywords

Cardiovascular diseases, cardiovascular death, education, income, meta-analysis, social determinants of health

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Introduction

Non-communicable diseases (NCD) are responsible for more than two-thirds of global mortality with a total of 52 million deaths projected by 2030.[1] The majority of diseases are cardiovascular diseases (CVD) followed by cancers, respiratory diseases, and diabetes. CVDs are a major public health problem accounting for about 30% of annual global mortality (17.5 million annually) and 10% of the global disease burden.[1]

The Framingham Heart Study,[2] WHO-MONICA project,[3] and INTERHEART[4] study provided evidence for the major risk factors of CVDs. Interventions that modify these risk factors are known to reduce cardiovascular morbidity and mortality. Despite much effort

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invested in primary and secondary prevention, CVD remains a major problem in industrialized and high income countries, and in low- and middle-income developing countries (LMICs).[1]

Many studies have identified additional risk factors for CVDs. Recently, the fifth epidemiological transition proposed that social upheaval,[5] a breakdown in existing social and health structures, leads to increased CVD morbidity and mortality. Since then, many social determinants of health (SDH) have been increasingly considered. Many studies have shown that SDH indirectly influence CVD by impacting on behavioral and metabolic cardiovascular risk factors (CVRFs), psychosocial factors, and environmental living conditions.[6,7] Some landmark[8–10] and numerous other epidemiological studies[11–14] show an inverse relationship between SDH and CVD morbidity and mortality.

Some evidence shows association between education and CVRFs, i.e. those with low education were more likely to develop CVRFs (e.g. hypertension, diabetes, dyslipidemias, overweight, etc.), and have less healthy dietary habits.[15–17] Evidence also showed that lower education is associated with atherosclerosis, ischemic heart disease (IHD), cerebrovascular diseases, CVD mortality and all-cause mortality.[15,18] Similar to education, an inverse relationship of income on IHD, coronary events, pre-hospital coronary death and CVD mortality has also been reported.[19–21] These effects of education and income are more consistent in developed countries, but the results are still inconclusive in LMICs.[22]

Several narrative and systematic reviews[23–28] assessed the relationship between socioeconomic status (SES) and CVDs, including myocardial infarction (MI), stroke, heart failure (HF), and death. Two meta-analyses have reported the effects of education and income on MI[23] and CVD mortality.[27] In both studies, education and income were roughly categorized as low and high and SES classes were not uniformly classified and pooled, resulting in inability to assess SES gradients. Only a few studies included participants from LMICs. We therefore conducted a systematic review and meta-analysis to pool the effects of low to high education and income on various cardiovascular outcomes by including more studies conducted in developing countries.

Methods

The review protocol has been registered with the international prospective register of systematic review (PROSPERO number CRD42016046615).[29]

Search strategy

Relevant studies were identified from Medline and Scopus databases since inception to 31 July 2016. Titles and abstracts were screened, and full articles were retrieved if the decision to include based on title and abstract could not be made. Reference lists were checked for studies overlooked by our searching. The search terms used and search strategies for both databases are described in the online Supplementary Material, Appendix A.

Selection of studies

Retrospective/prospective cohorts published in English were selected if they met following criteria: (a) assessed associations between education/income and cardiovascular outcomes in general adults or specific diseases; (b) measured education or income; (c) had at least one outcome of interest (i.e. coronary artery diseases (CADs), cardiovascular events (CVEs), strokes and cardiovascular deaths); (d) had contingency data between education/income and cardiovascular outcomes, or a beta-coefficient. Studies were excluded if data for education and income were combined; or income was based on ownership of car/house/health insurance/zip-code. For missing data, we made three attempts to contact authors to request additional data.

Study factors

Education and income were our study factors, which were reported differently across studies. To standardize data for pooling across studies, they were re-categorized into three groups as low, medium, and high for education years ≤ 9 (i.e. illiteracy/no education/basic/primary education), 10–12 (i.e. secondary/high school/intermediate/technical/apprenticed/trade/vocation), and >12 years (i.e. university/college/associates/master/professional/doctor of philosophy (PhD)), respectively. Income expressed in other currencies was converted to US currency/year using the reported exchange rates or the online exchange converter at the time of retrieval/identify.[30] Salary income was re-categorized as low, medium, and high for income $\leq$20,000, 20,001 to 40,000, and $>$40,000 US$/year, respectively. If original studies reported income as quartiles, the 1st, 2nd, and 3rd + 4th quartiles were re-classified as low, medium, high incomes, respectively. If the income was reported as quintiles, the 1st + 2nd, 3rd, and 4th + 5th quintiles were classified as low, medium, and high, respectively.

Outcomes

Outcomes of interest were CVDs including CAD (e.g. acute MI, IHD, coronary heart disease (CHD)), CVE (e.g. HF, hospital admission due to cardiac causes, revascularization and composite CVDs (e.g. IHD or stroke)), strokes (ischemic or hemorrhagic strokes), and cardiovascular deaths. These were defined according to original studies.

Data extraction

Two reviewers (WK and SAV) independently extracted general characteristics of studies/patients (e.g. country, age, gender, body mass index (BMI), smoking, alcohol consumption, diabetes, hypertension, etc.). Cross-tabulated data between education/income groups and individual outcomes were extracted for pooling. Summary statistics (e.g. relative risk (RR), or hazard ratio (HR)) along with 95% confidence interval (CI) were extracted instead if frequency data were not reported. Data were computerized and validated, any disagreements were resolved by consensus.

Risk of bias assessment

Quality of studies were independently assessed by two reviewers (WK and SAV) using the Newcastle and Ottawa risk of bias criteria (Supplementary Material, Appendix B). Three domains were evaluated, i.e. selection of study groups, comparability of groups and ascertainment of exposure and outcome. Each domain was graded by giving stars if it was low risk of bias. A total grade of seven or more stars was regarded as indicating higher quality or lower risk of bias.

Statistical analysis

RRs of each outcome between low versus high (RR_1) and medium versus high (RR_2) education/income groups were calculated from frequency data where frequency data were available. These were then combined with reported summary statistics if frequency data were not available. Multivariate random-effect meta-analysis[31] was applied for pooling two RRs simultaneously. Variance-covariance between RR_1 and RR_2 was assumed to be zero for those studies reporting summary RRs. Heterogeneity was assessed using Cochrane's Q test and I^2 statistic. Heterogeneity was present if the p-value of the Q test was <0.1 or $I^2 \geq 25\%$.

Subgroup analyses were performed to explore potential sources of heterogeneity by fitting each of co-variables (i.e. country, country income level,[32] number of co-variables adjustment, age group, BMI, sex, diabetes, obesity, hypertension, high physical activity, smoking, alcohol drinking, dyslipidemia, and chronic kidney disease) in a meta-regression model.

Finally, exploration of publication bias was visualized using a funnel plot and Egger's test.[33] If any of these indicated asymmetry, a contour-enhanced funnel plot[34] was constructed to distinguish whether asymmetry was due to publication bias or heterogeneity.

All analyses were performed using STATA[35] version 14.1. Values of $p < 0.05$ were considered statistically significant, except for the test of heterogeneity where $p < 0.10$ was used.

Results

We identified 354 studies from Medline and 1335 studies from Scopus databases with 11 additional studies identified from reference lists. Of these 1700 studies, 115 were duplicates, leaving 1585 to be screened. After screening titles and abstracts, 1399 studies did not answer our primary question, leaving 72 studies for inclusion. Reasons for exclusion of the studies are presented in Figure 1 following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guideline.[36]

General characteristics of included studies

Characteristics of the 72 included cohorts published between 1982–2016 are described, see Supplementary Material, Table 1. Among them, 14, 39 and 19 studies were conducted in Asia, Europe, and the USA respectively. Most studies were from high-income countries (93.1%); mean age and mean BMI ranged from 38.5–78 years and 23.02–30.33 kg/m^2, respectively. Percentages of males, diabetes, smoking or hypertension varied from 35.9–78%, 1.3–42%, 7.28–72.64%, and 6.25–72.5% respectively. Among 72, 33, 10, and 29 studies assessed association effects of education, income, and both on cardiovascular outcomes, with a sample size ranged from 128–4,157,202.

Risk of bias assessment

Results of "risk of bias" assessment of the included studies are shown in Supplementary Material, Table 2. Total stars ranged from 5–9 with a median of seven. Among the included studies, 45 out of 72 (62%) had a low risk of bias and 27 out of 72 (38%) had a high risk of bias.

Education and cardiovascular outcomes

A total of 62 studies assessed the association between education and cardiovascular death ($n = 35$ and 31 for low and medium vs high), CAD ($n = 21$ and 18 for low and medium vs high), CVE ($n = 13$ and 15 for low and medium vs high) and stroke ($n = 15$ and 13 for low and medium vs high). Among these, only a few studies assessed relative effects of education without adjusting co-variables, or frequency data were available (three in

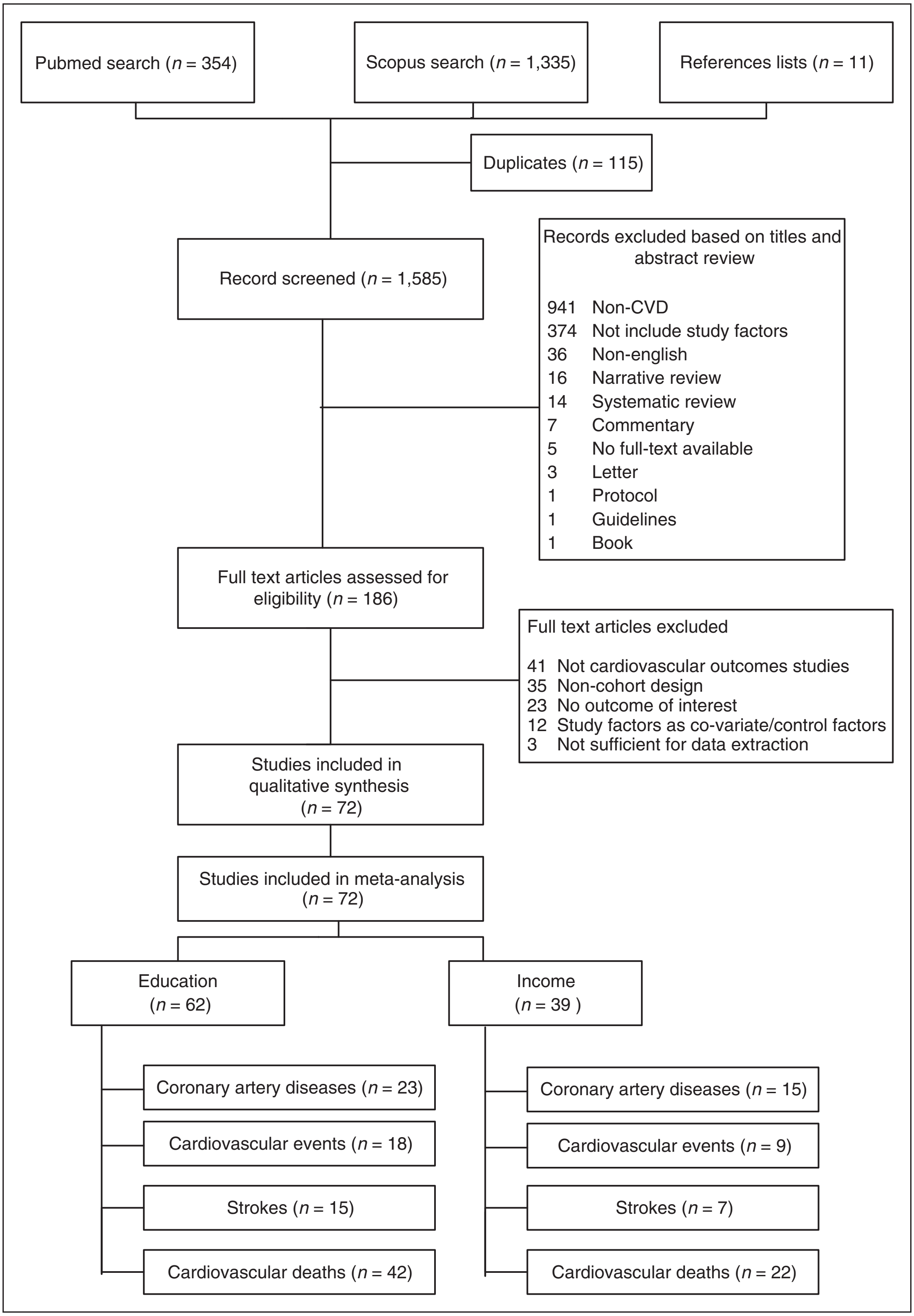

Figure 1. Flow diagram for selection of studies.
CVD: cardiovascular disease.

Table 1. Estimations of pooled effects of education and income on cardiovascular outcomes (co-variate adjusted studies only).

	Coronary artery diseases				Cardiovascular events			
	n	RR (95% CI)	Q *p*-value	I^2 (%)	*n*	RR (95% CI)	Q *p*-value	I^2 (%)
Education								
Medium vs high	15	1.21 (1.06–1.40)	0.005	96	12	1.27 (1.09–1.48)	0.003	83
Low vs high	17	1.36 (1.11–1.66)	0.002	94	13	1.50 (1.17–1.92)	0.001	99
Income								
Medium vs high	10	1.27 (1.10–1.47)	0.001	95	7	1.05 (0.98–1.13)	0.131	99
Low vs high	10	1.49 (1.16–1.91)	0.002	98	6	1.17 (0.96–1.44)	0.117	97
	Strokes				Cardiovascular deaths			
	n	RR (95% CI)	Q *p*-value	I^2 (%)	*n*	RR (95% CI)	Q *p*-value	I^2 (%)
Education								
Medium vs high	12	1.17 (1.01–1.35)	0.034	99	28	1.21 (1.12–1.30)	<0.001	98
Low vs high	13	1.23 (1.06–1.43)	0.005	83	34	1.39 (1.26–1.54)	<0.001	98
Income								
Medium vs high	6	1.24 (1.00–1.53)	0.049	99	12	1.34 (1.17–1.54)	<0.001	96
Low vs high	6	1.30 (0.99–1.72)	0.061	98	21	1.76 (1.45–2.14)	<0.001	99

CI: confidence interval; Q *p*-value: *p*-value for Q test for heterogeneity: RR: relative risk.

cardiovascular deaths[37–39] and CADs,[37,40,41] two in CVEs,[38,39] and two in strokes).[37,40] For consistency, only studies with adjusted relative education effects were pooled. Effects of education on outcomes were heterogeneous across studies with the I^2 ranging from 83–99% (Table 1). Multivariate meta-analysis was applied indicating significant educational effects on all outcomes (Table 1 and Figure 2). The strongest education effect was on CVE, where low and medium education increased risk of CVE by 50% and 27% compared to high education. A similar trend was observed for cardiovascular deaths, in which the risks for low and medium vs high education were 39% and 21%, respectively. Additionally, patients with low education showed 36% higher risk, and patients with medium education showed 21% higher risks for CAD. Furthermore, low and medium education levels were associated with 23% and 17% higher risks, respectively for developing stroke when compared to high education level.

Sources of heterogeneity were next explored by meta-regression or subgroup analyses (Table 2 and Supplementary Material, Tables 3–6). Geographical regions were grouped as Asia, Europe, and USA but few studies in the Asian setting were available for most outcomes. Effects of both low/medium education still remained for all four cardiovascular outcomes after pooling within Europe and USA, but not for Asia, which was likely due to the small numbers of studies (Table 2).

We performed subgroup analyses by co-variables including number of adjusted variables, age ($\leq$60 vs >60 years), BMI (<25 kg/m^2 vs $\geq$25 kg/m^2), percentage of males, diabetes, and smoking (Supplementary Material, Tables 3–6); and none of these was identified as a source of heterogeneity. However, education levels were associated with all four CVD outcomes in the subgroup younger than 60 years (Supplementary Material, Tables 3–6). Risk of cardiovascular death and CAD outcomes was higher in studies comprising a higher percentage of male participants. Likewise, risk of CVD (except CAD) was higher in studies with a higher proportion of diabetic participants. Association between BMI and CVE was detected in the BMI subgroup $\geq$25 kg/m^2 (Supplementary Material, Tables 3–6).

There was no evidence of publication bias using Egger's test except for low versus high education level on CVD outcomes (Egger's test: $\beta = 2.33$, $p = 0.008$), for which funnel plots showed asymmetry (Supplementary Material, Figures 1 and 2). Contour-enhanced funnel plot showed that some studies fell in both non-significant and significant areas, so asymmetry was more likely due to heterogeneity (Supplementary Material, Figures 3 and 4). No individual study significantly changed the overall estimates based on results of the sensitivity analysis.

Income and cardiovascular outcomes

Thirty-nine studies assessed income effects on cardiovascular death ($n = 22$ and 13 for low and medium vs high), CAD ($n = 13$ and 14 for low and medium vs high), CVE (both $n = 8$ for low and medium vs high) and stroke (both $n = 7$ for low and medium vs high).

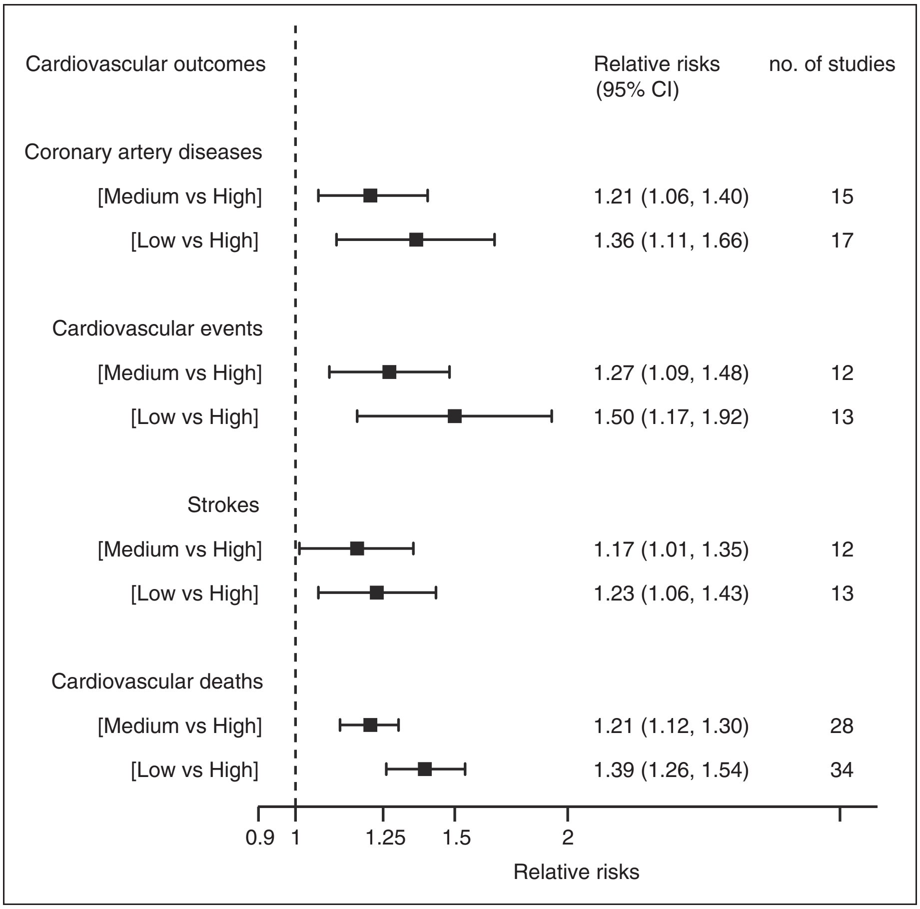

Figure 2. Pooling effects of educations on cardiovascular outcomes (co-variate adjusted studies only).
CI: confidence interval.

Five studies (1, 3, 2, and 1 for cardiovascular deaths,[40] CADs,[40–42] CVEs,[43,44] and strokes)[40] reported unadjusted relative effects of income were excluded. Effects of income on these outcomes were highly heterogeneous across studies, i.e. I^2 95% to 99% (Table 1 and Figure 3). The largest income effect was observed for cardiovascular death, with 76% and 34% higher risk of cardiovascular death for low and medium versus high income, respectively. Comparable effects were seen on CAD, with 49% and 27% higher risks, respectively. Furthermore, low income patients showed 17% higher risk, and medium income patients showed 5% higher risk for CVE. Additionally, low and medium incomes were associated with about 30% and 24% higher risks of developing stroke compared to high income.

Sources of heterogeneity were explored by meta-regression or subgroup analyses (Table 2 and Supplementary Material, Tables 3–6). By geographical region, European studies showed income effects similar to the overall pooled effect (Table 2). Subgroup analyses were performed by age groups indicating low income was associated with higher risk for cardiovascular death, CAD and CVE, in the studies with participants aged $\leq$60 years (Supplementary Material, Tables 3–6).

No publication bias was identified by Egger's test except for medium versus high income level groups with CAD outcome (Egger's test: $\beta = 2.98$, $p = 0.009$), but funnel plots showed asymmetry (Supplementary Material, Figures 5 and 6). Contour-enhanced funnel plots suggested that asymmetry was more likely due to heterogeneity (Supplementary Material, Figures 7 and 8). Overall estimates were similar to the sensitivity analyses.

Discussion

We performed a systematic review and meta-analysis to pool the effects of education and income on CVD outcomes. Our findings indicate that groups with low to medium education and income are at higher risk of CAD, CVE, stroke and cardiovascular death than those with high education and income. The pooled RRs for low and medium versus high education were 1.36 and 1.21 respectively for CAD, 1.50 and 1.27

Table 2. Pooled education and income effects on cardiovascular outcomes by regions.

		Education				Income			
		n	RR (95% CI)	Q *p*-value	I^2	*n*	RR (95% CI)	Q *p*-value	I^2
Cardiovascular deaths									
Asia	Medium vs high	2	1.12 (0.78–1.60)	0.540	5	0	NA	NA	NA
	Low vs high	8	1.34 (1.04–1.72)	0.024	99	4	1.69 (1.07–2.67)	0.024	96
Europe	Medium vs high	15	1.17 (1.06–1.29)	0.001	99	12	1.40 (1.18–1.67)	<0.001	97
	Low vs high	19	1.32 (1.17–1.49)	<0.001	91	14	1.89 (1.47–2.44)	<0.001	99
USA	Medium vs high	14	1.30 (1.14–1.49)	<0.001	72	1	NA	NA	NA
	Low vs high	8	1.69 (1.28–2.22)	<0.001	95	4	NA	NA	NA
CAD									
Asia	Medium vs high	3	1.03 (0.85–1.25)	0.750	28	0	NA	NA	NA
	Low vs high	4	1.03 (0.79–1.33)	0.839	45	0	NA	NA	NA
Europe	Medium vs high	11	1.04 (0.72–1.50)	0.852	99	11	1.39 (1.18–1.63)	<0.001	92
	Low vs high	15	1.24 (0.97–1.60)	0.086	96	12	1.74 (1.31–2.32)	<0.001	98
USA	Medium vs high	4	1.21 (0.97–1.51)	0.085	75	3	NA	NA	NA
	Low vs high	2	1.51 (0.93–2.45)	0.099	47	1	NA	NA	NA
CVE									
Asia	Medium vs high	2	1.47 (0.82–2.63)	0.191	61	2	NA	NA	NA
	Low vs high	4	1.85 (0.93–3.70)	0.081	96	2	NA	NA	NA
Europe	Medium vs high	8	1.26 (1.06–1.49)	0.090	76	5	1.05 (0.95–0.37)	0.368	99
	Low vs high	9	1.36 (1.07–1.72)	0.011	95	5	1.24 (0.98–1.58)	0.080	98
USA	Medium vs high	5	1.07 (0.69–1.66)	0.758	78	1	NA	NA	NA
	Low vs high	0	NA	NA	NA	1	NA	NA	NA
Strokes									
Asia	Medium vs high	4	1.22 (0.91–1.65)	0.192	87	0	NA	NA	NA
	Low vs high	5	1.27 (1.07–1.50)	0.006	34	0	NA	NA	NA
Europe	Medium vs high	6	1.46 (1.23–1.72)	<0.001	87	5	1.37 (1.24–1.52)	<0.001	70
	Low vs high	7	1.61 (1.28–2.02)	<0.001	76	5	1.54 (1.33–1.79)	<0.001	64
USA	Medium vs high	3	0.98 (0.81–1.19)	0.848	89	2	0.89 (0.62–1.27)	0.514	49
	Low vs high	3	0.99 (0.83–1.20)	0.957	53	2	0.91 (0.58–1.41)	0.661	78

CAD: coronary artery disease; CI: confidence interval; CVE: cardiovascular event; NA: not available or insufficient data; Q *p*-value: *p*-value for Q test for heterogeneity: RR: relative risk.

respectively for CVE, 1.23 and 1.17 respectively for stroke, and 1.39 and 1.21 respectively for cardiovascular death. The pooled RRs for low and medium versus high income for these corresponding outcomes were 1.49 and 1.27, 1.17 and 1.05, 1.30 and 1.24, and 1.76 and 1.34, respectively.

Direct or indirect mechanisms linking education and income with CVD have been described showing behavioral risk factors,[45] lifestyle or living environment conditions,[46] health literacy,[47] and psychological factors[48] play important roles. Those with low education or low income had a higher prevalence of risk behaviors (smoking, obesity, physical inactivity, unhealthy diet, etc.), were more likely to have poor polluted environment, poor health literacy (ability to read/understand comprehend medical information, lacking awareness of impact of lifestyle behavior, poor adherence/incorrect medication, ignorance of medical checkups), and had higher prevalence of depression with poorer coping in response to cumulative stress. Consequently, mortality was high, potentially due to delayed access to medical care, poor understanding in disease progress management, and lack of post-disease cardiac rehabilitation.[49]

Moreover, education and income have mutual causal influences on CVD morbidity and mortality and one should not rely on single, potentially biased parameters.[50] Combined effects of education and income had been studied previously,[51] and persons with low income and education had the highest risk of incident CHD, when compared with high education/low income, low education/high income, and high education/high income. However, some researchers have suggested education and income should not be

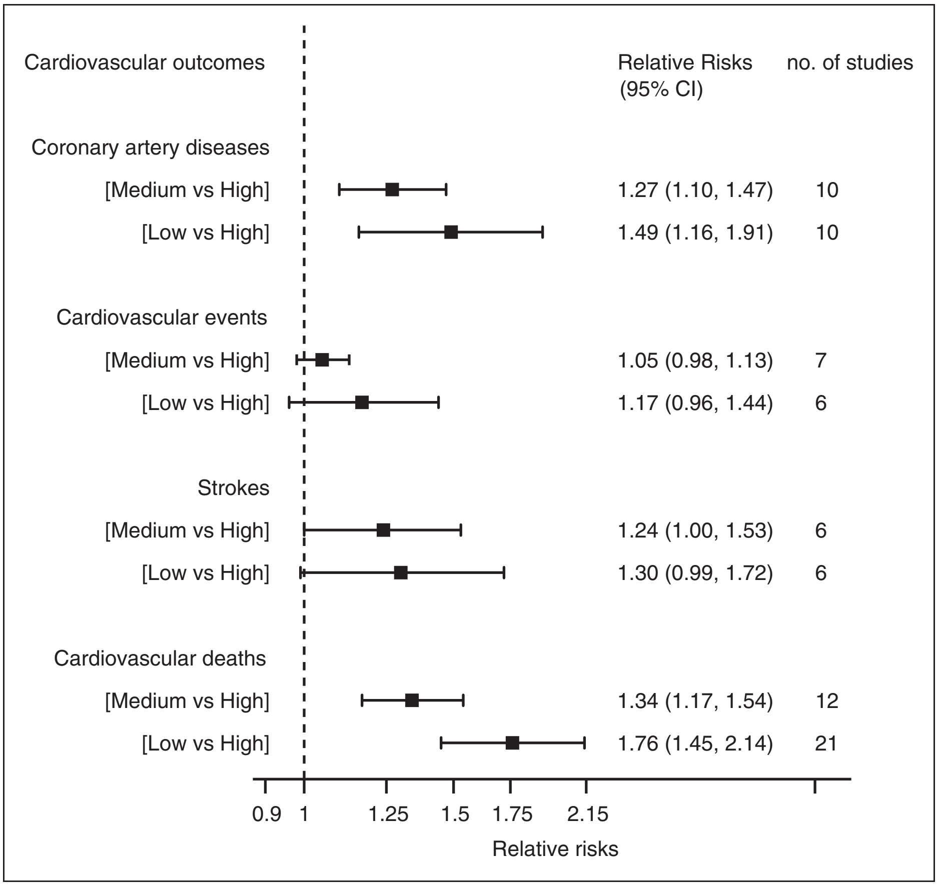

Figure 3. Pooling effects of incomes on cardiovascular outcomes (co-variate adjusted studies only).
CI: confidence interval.

combined and should not be interchangeable,[52] because they may affect CVD outcomes through different, potentially independent, causal pathways. For example, Ahmed et al.[53] found low income was a significant independent predictor of HF regardless of education level in community-dwelling older population age $\geq$65 years population. To test this hypothesis, individual patient data containing education and income variables are required, and mediation analysis applied.

Many studies[52,54] assessed education/income effect by comparing highest and lowest strata, which could not demonstrate dose-response effects.[10,55,56] To increase comparability across the studies and exposure gradient, the medium-level education and income categories were maintained. This confirmed the social gradient effect of education and income. Although there was high heterogeneity in the results, statistical significance was seen, except for effects of income on CVE and stroke outcomes. This may result from different definitions and classifications of education and income categories between individual studies, and between different geographical regions, economies, educational systems, and cultures. Differences in study periods over time could lead to variability in scales used to classify the exposure.

Strengths and limitations

Our meta-analysis has some strengths. We believe, it is the first meta-analysis assessing levels of education and income effects on major CVD outcomes. To increase comparability across studies and study social gradient effects, three strata of education/income were categorized into three groups to yield more details than previously.[23,27] Effects of education/income were simultaneously pooled using multivariate meta-analyses. In addition, only cohort studies providing more reliable effects of education and income on CVD outcomes were included. This review followed PRISMA guidelines.[36]

However, our study also has some limitations. Pooled estimates were affected by high heterogeneity, from differences in characteristics of the study populations, differences in definitions and classifications of education and income in both developed and developing countries, and differences in measurement timing of education and income categories across studies. Although many efforts were made to explore the heterogeneity, we could not identify sources. We also did not have access to primary data and many studies did not adjust and report confounding variables, so estimated risks might be confounded.

Clinical implications and further research

Braveman et al.[52] explained educational influence on general and health-related knowledge, health literacy, and problem-solving skills, which can change health outcome. The results of our meta-analysis provide some evidence of effects of education and income on CVD outcomes. However, whether education or income is directly associated with CVD outcomes,[50] or education is indirectly associated with CVD outcomes through income as mediator,[57] or both education and income are indirectly associated with CVD outcomes through other risk factors such as BMI,[58] diabetes, or smoking as mediators has not been clearly answered in studies. Further research should focus on the causal pathway between education and income on CVD outcomes with more advanced statistical models, such as mediation/moderation analysis.[59]

Conclusion

In conclusion, low/medium education and income increase the risks of CAD, CVE, stroke and cardiovascular death. Further studies should be conducted to assess causal pathway of education/income on cardiovascular outcomes to confirm our findings, especially in Asian countries.

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Author contribution

WK, SAV, and AT contributed to the conception and design, data analysis, and interpretation of data, WK and SAV contributed to study selection, risk of bias assessment, and data extraction, WK, SAV, JA, MM, and AT contributed to drafting the manuscript, critical revision of the manuscript for important intellectual content, and final approval of the version to be published. All authors gave final approval.

Declaration of conflicting interests

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