

Supplementary Online Content

Kubota Y, Heiss G, MacLehose RF, Roetker NS, Folsom AR. Association of educational attainment with lifetime risk of cardiovascular disease: the Atherosclerosis Risk in Communities study. *JAMA Intern Med*. Published online June 12, 2017. doi:10.1001/jamainternmed.2017.1877

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMETHODS

Study Design, Setting, and Population

The Atherosclerosis Risk in Communities (ARIC) Study is an ongoing population-based prospective study of cardiovascular diseases (1). In 1987–1989, the ARIC Study recruited and examined 15,792 mostly Caucasian or African American men and women aged 45–64 from 4 U.S. communities [Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and suburbs of Minneapolis, Minnesota]. The participants were re-examined in 1990–1992 (visit 2, 93% return), in 1993–1995 (visit 3, 86% return), and 1996–1998 (visit 4, 80% return). The institutional review boards of the collaborating institutions approved the study protocol, and each participant provided written informed consent.

Risk Factor Measurements

The main exposure of interest was self-reported educational attainment, ascertained at ARIC baseline, and categorized into six levels: (i) grade school, (ii) high school without graduation, (iii) high school with graduation, (iv) vocational school, (v) college with or without graduation, and (vi) graduate or professional school.

We assessed other potential CVD risk factors as follows: socioeconomic status; gender, race (white or African American), family income (under \$5,000, \$5,000–7,999, \$8,000–11,999, \$12,000–15,999, \$16,000–23,999, \$24,000–34,999, \$35,000–49,999, or over \$50,000), occupation for the longest time period [“precision jobs” (mechanic, repairman, construction worker or craftsman), “service jobs” (hairstylist, domestic, restaurant, or security), “machine operating jobs” (driver, machine operator, sanitation, laborer), “technical and sales jobs” (technician, sales or clerical), “professional and managerial jobs” and “homemaker”], parental educational attainment (the same levels as above), marital status and

health insurance (yes or no): lifestyle factors; smoking status (current, former, or never), alcohol drinking status (current, former, or never), alcohol amount (g/week), physical activity, and healthy diet score (2, 3): health conditions; obesity [body mass index ≥ 30 kg/(m)²], hypertension (systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or hypertension medication use), diabetes mellitus (a fasting blood glucose ≥ 126 mg/dl, non-fasting blood glucose ≥ 200 mg/dl, a self-reported physician diagnosis of diabetes, or use of antidiabetic medication in the past 2 weeks) (4), and hypercholesterolemia (total cholesterol ≥ 240 mg/dl or hypercholesterolemia medication use): subclinical organ damages (5); subclinical atherosclerosis defined by carotid intima media thickness > 0.9 mm or the presence of plaque, electrocardiographic left ventricular hypertrophy, and chronic kidney disease defined by estimated glomerular filtration rate < 60 ml/min/1.73m². The Baecke questionnaire asked participants to report the frequency and the number of hours of participation in walking and in as many as 4 sports in the previous year (6) As in prior ARIC studies (7, 8), each sport activity was converted into metabolic equivalents of task (METs) via the Compendium of Physical Activities (9). The reliability and validity of the Baecke questionnaire were evaluated in several populations and summarized elsewhere (1, 10–12). Those who did not engage in moderate (3-6 METs) or vigorous (> 6 METs) activities were defined as physically inactive. Diet was assessed by a 66-item Harvard food frequency questionnaire (2), and a healthy diet score was calculated by adding each point (0 or 1) of the following 5 healthy dietary metrics (3): ≥ 4.5 cups/day of fruits and vegetables (approximated as ≥ 4.5 servings/day in the ARIC study); 2 or more ≥ 3.5 -oz servings/week of fish (approximated as 3- to 5-oz servings/week); 3 or more 1-oz servings/day of whole grains (approximated as ≥ 3 servings/day); sodium ($< 1,500$ mg/day); and ≤ 36 oz/week of sugar-sweetened beverages (approximated as ≤ 4 glasses/week). A diet score ≤ 1 was defined

as an unhealthy diet. Information on occupation and parental educational attainment was not available at ARIC baseline but was obtained at visit 4.

Confirmation of Cardiovascular Disease

We defined incident CVD events as coronary heart disease, heart failure, and stroke. ARIC staff contacted participants annually by telephone to capture all hospitalizations and deaths related to possible CVD (13). They also surveyed lists of discharges from local hospitals and death certificates from state vital statistics offices for potential CVD events. Abstractors reviewed medical records and recorded information to validate CVD outcomes. Incident coronary heart disease was validated by physician review, and was defined as a definite or probable myocardial infarction, definite coronary death, or coronary revascularization procedure. Incident heart failure was defined as the first occurrence of either a hospitalization that included an International Classification of Diseases-9th Revision (ICD-9) discharge code of 428 (428.0 to 428.9) among the primary or secondary diagnoses or else a death certificate with an ICD-9 code of 428 or an ICD-10 code of I50 among the listed or underlying causes of death (14). ARIC has shown the validity of ICD-9 Code 428 to be moderately high, with a sensitivity of 93% for identifying acute decompensated heart failure (15). For patients hospitalized for potential strokes, the abstractors recorded signs and symptoms and photocopied neuroimaging (computed tomography or magnetic resonance imaging) and other diagnostic reports. Using criteria adopted from the National Survey of Stroke, definite or probable strokes were classified by computer algorithm and separate review by a physician, with disagreements resolved by a second physician (16).

Statistical Analysis

SAS version 9.3 software (SAS Institute Inc., Cary, NC) was used for statistical analyses.

We excluded participants who self-reported pre-baseline CVD (coronary heart disease, heart failure or stroke) or had electrocardiographic evidence of pre-baseline coronary heart disease (n=1,553) and participants whose data on educational attainment or outcome status were missing (n=291). After exclusions, 13,948 participants were available for these analyses.

Participants were followed from age at baseline to age at CVD event, age at last follow-up contact or December 31, 2013, whichever came first. We included the first-ever coronary heart disease, heart failure or stroke event as the incident CVD event. We estimated remaining lifetime risks of incident CVD at age 45 years through age 85 years according to educational attainment, using a modified version of survival analysis (17). This method uses survival age as the time scale, combines information on participants entering the observation periods at different ages, and accounts for varying durations of follow-up by individuals (18). In addition, it adjusts for the occurrence of competing risks of non-CVD deaths to yield an accurate estimate of cumulative incidences. In contrast, standard Kaplan-Meier cumulative incidence estimation does not properly account for competing risks, often resulting in overestimates of the remaining lifetime risk (18–21). Results unadjusted and adjusted for competing risks in relation to educational attainment and lifetime risk of CVD are shown in the eTable. We also estimated the lifetime risk of CVD according to family income, occupation and parental educational attainment—other important socioeconomic factors often closely related to participants’ educational attainment—and evaluated the associations of these variables and individual educational attainment jointly with the lifetime CVD risk. After identical exclusions as above, 13,128 participants (94%) had baseline income data. Similarly, 9,381, 9,609 and 8,963 participants who were free of CVD at that time completed the visit 4 questionnaire on income, occupation and parental education, respectively, among whom we estimated lifetime risk of CVD from age 55 years to age 85 years.

In sensitivity analyses, we also evaluated the association between educational attainment and lifetime risk of CVD by stratifying on CVD risk factors [family income (<\$35,000 vs. ≥\$35,000), occupation (occupations with the top 3 highest vs. top 3 lowest lifetime risks of CVD), parental educational attainment (non-high school graduates vs. high school graduates), marital status, smoking status (current vs. former vs. never), drinking status (current vs. former vs. never), physical inactivity, diet (healthy diet score≤1 vs. healthy diet score≥2), obesity, hypertension, diabetes, and hypercholesterolemia. Next, we estimated lifetime risks of CVD according to family income at visit 4 instead of visit 1. Finally, we also evaluated the association between educational attainment and lifetime risks of CVD by stratifying birth years [individuals born before 1935 (55–64 years at baseline) vs. after 1935 (45–54 years)] to assess birth cohort effects.

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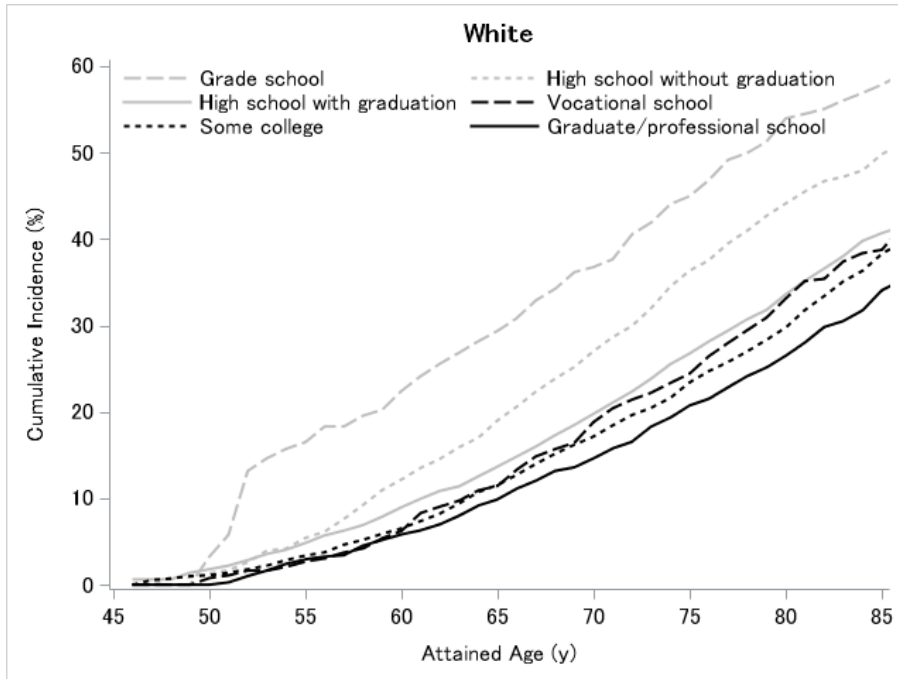
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eTable. Unadjusted and Adjusted Risk (%) of Cardiovascular Disease (95% Confidence Interval) to Various Ages According to Educational Attainment at Age 45 among all participants

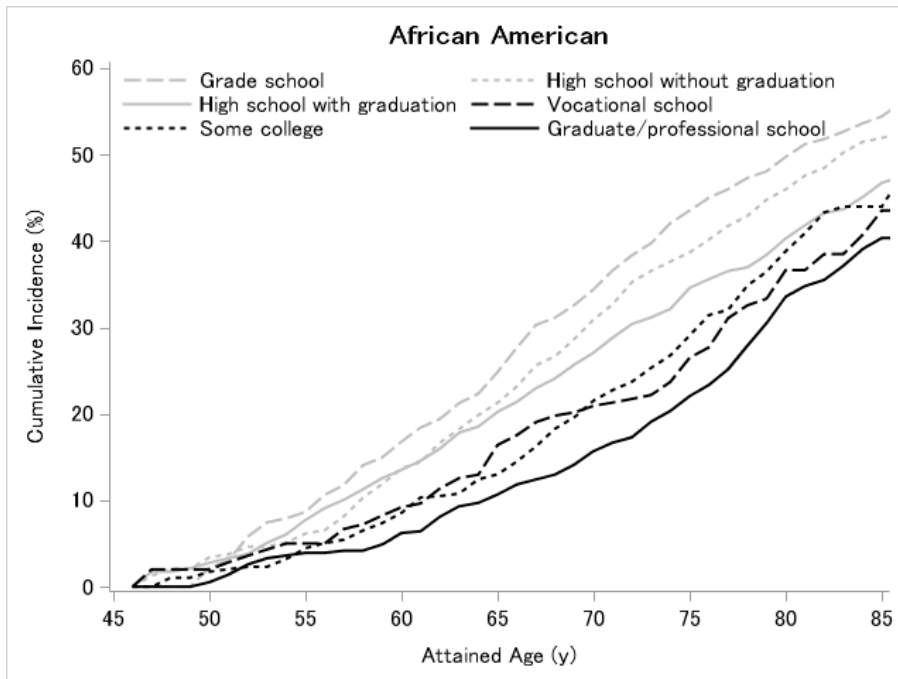
CVD risk (%) to age	Educational attainment					
	Grade school	High school without graduation	High school with graduation	Vocational school	College with or without graduation	Graduate/professional school
Unadjusted Model						
55 y	10.7 (6.3–15.1)	5.8 (3.6–8.0)	5.5 (4.1–6.9)	3.4 (1.5–5.3)	3.6 (2.6–4.7)	3.3 (2.0–4.6)
65 y	26.3 (21.9–30.6)	20.6 (18.1–23.2)	15.3 (13.7–16.9)	13.0 (10.5–15.6)	12.1 (10.7–13.5)	10.3 (8.5–12.2)
75 y	46.5 (42.6–50.3)	40.3 (37.6–42.9)	29.9 (28.2–31.6)	26.5 (23.5–29.5)	25.8 (24.1–27.4)	22.1 (19.7–24.6)
85 y (lifetime risk)	63.2 (59.6–66.8)	58.6 (55.3–61.8)	47.3 (45.1–49.6)	45.4 (41.2–49.6)	44.4 (41.8–47.0)	40.3 (36.1–44.5)
Adjusted model						
55 y	10.7 (6.3–15.1)	5.7 (3.5–7.9)	5.4 (4.0–6.9)	3.4 (1.5–5.3)	3.6 (2.6–4.7)	3.3 (2.0–4.6)
65 y	25.6 (21.2–30.0)	20.0 (17.4–22.6)	15.0 (13.4–16.6)	12.7 (10.1–15.2)	11.8 (10.5–13.2)	10.1 (8.3–12.0)
75 y	43.1 (39.3–47.0)	37.3 (34.6–39.9)	28.2 (26.5–30.0)	24.9 (22.0–27.8)	24.4 (22.7–26.0)	21.1 (18.7–23.4)
85 y (lifetime risk)	55.0 (51.4–58.6)	50.5 (47.3–53.3)	41.7 (39.5–43.8)	39.7 (35.5–43.4)	39.2 (36.6–41.4)	36.1 (31.9–39.7)

eFigure 1. Race-specific risk estimates of cardiovascular disease from age 45 to 85 years, non-high school vs. high school graduates (1987–2013)

A

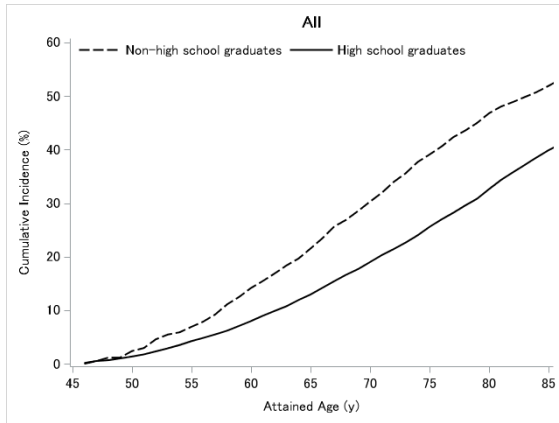


B

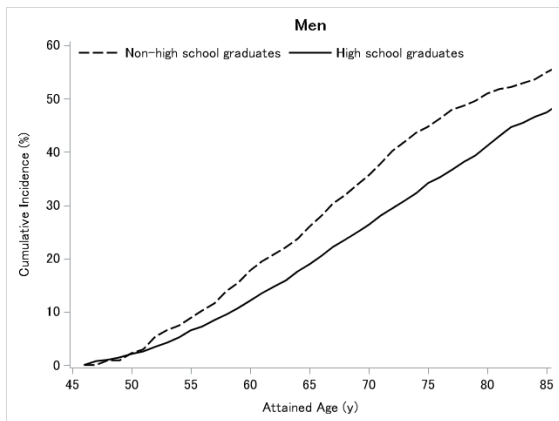


eFigure 2. Risk estimates of cardiovascular disease from age 45 to 85 years, non-high school vs. high school graduates (1987–2013)

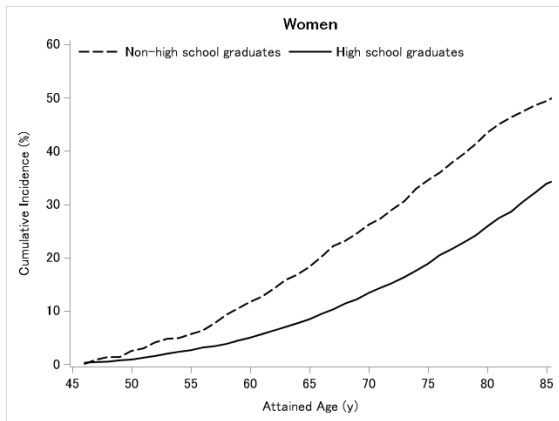
A



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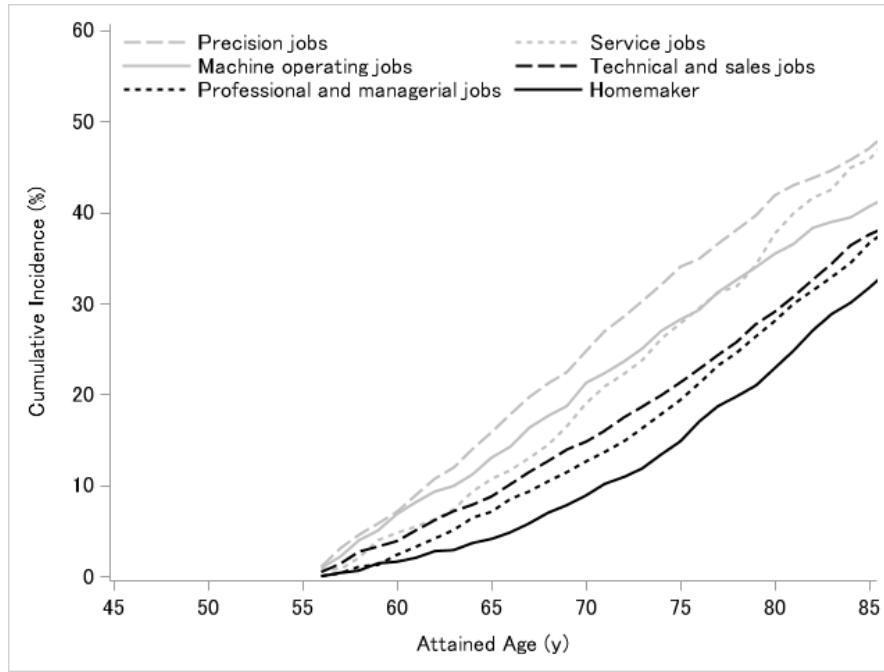


C

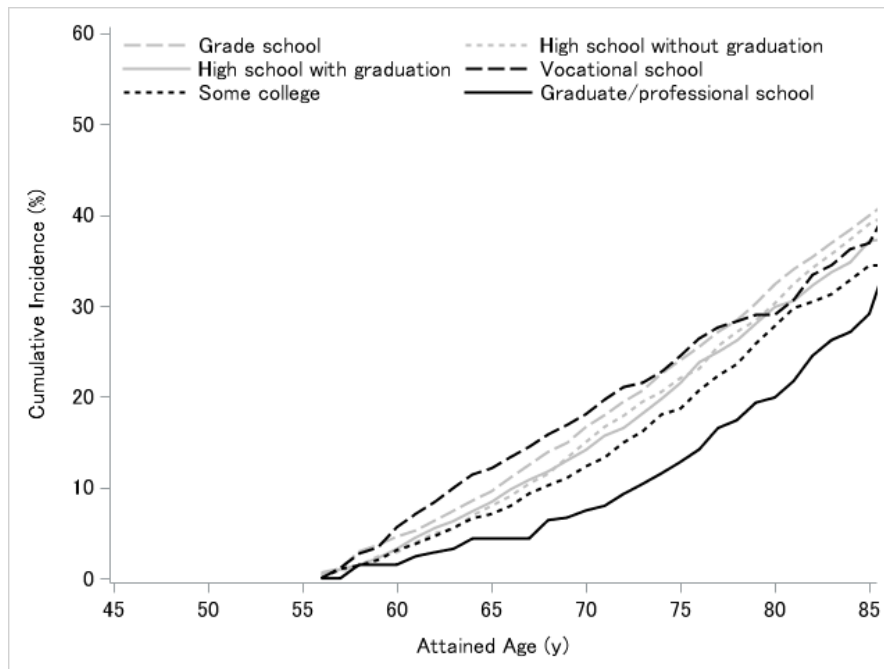


eFigure 3. Risk estimates of cardiovascular disease from age 55 to 85 years according to (A) occupations and (B) parental educational attainment (1996–2013)

A

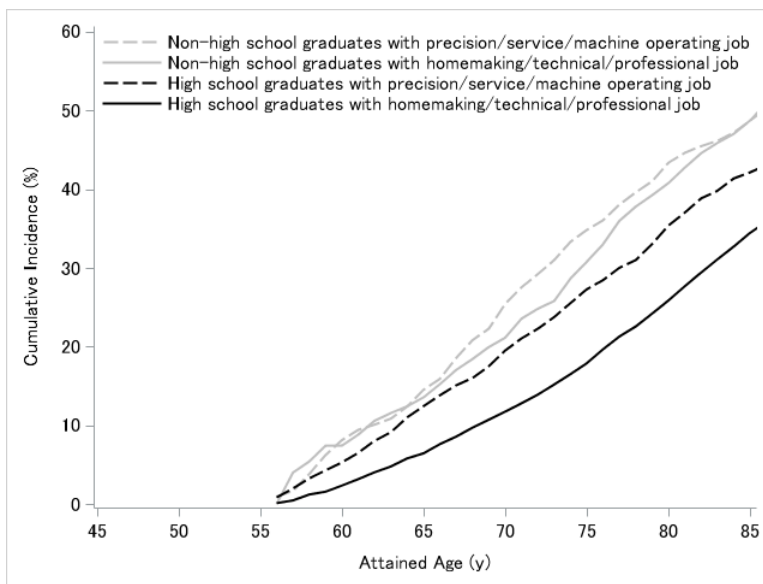


B

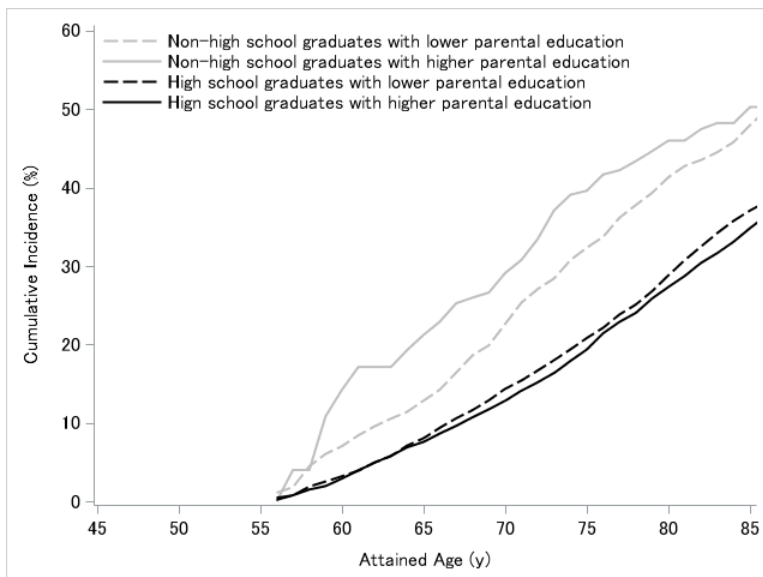


eFigure 4. Risk estimates of cardiovascular disease from age 55 to 85 years in estimated jointly by educational attainment (non-high school vs. high school graduates) and (A) occupations (precision, service or machine operating job vs. homemaking or technical and sales or professional and managerial job) or (B) parental educational attainment (non-high school vs. high school graduates) (1996–2013)

A

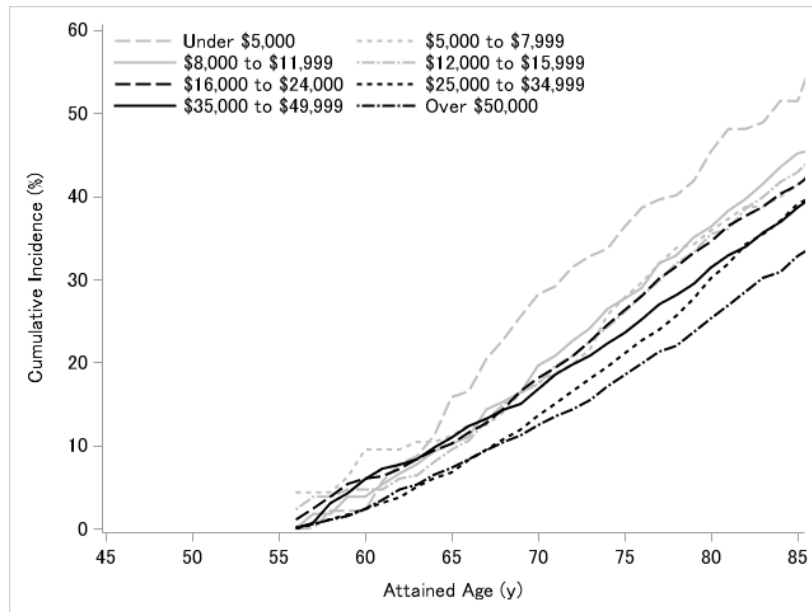


B

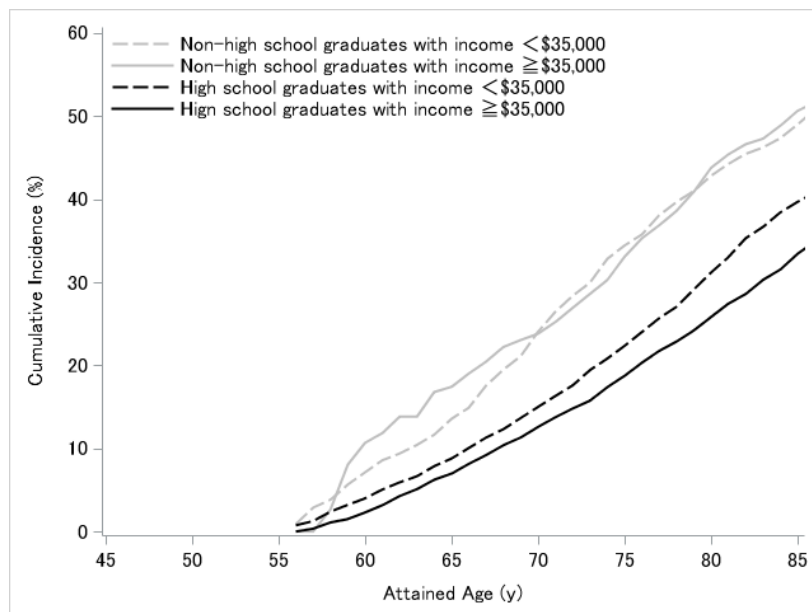


eFigure 5. Risk estimates of cardiovascular disease from age 55 to 85 years according to (A) income at visit 4, and (B) jointly by educational attainment (non-high school vs. high school graduates) and family income (<\$35,000 vs. ≥\$35,000), (1987–2013)

A

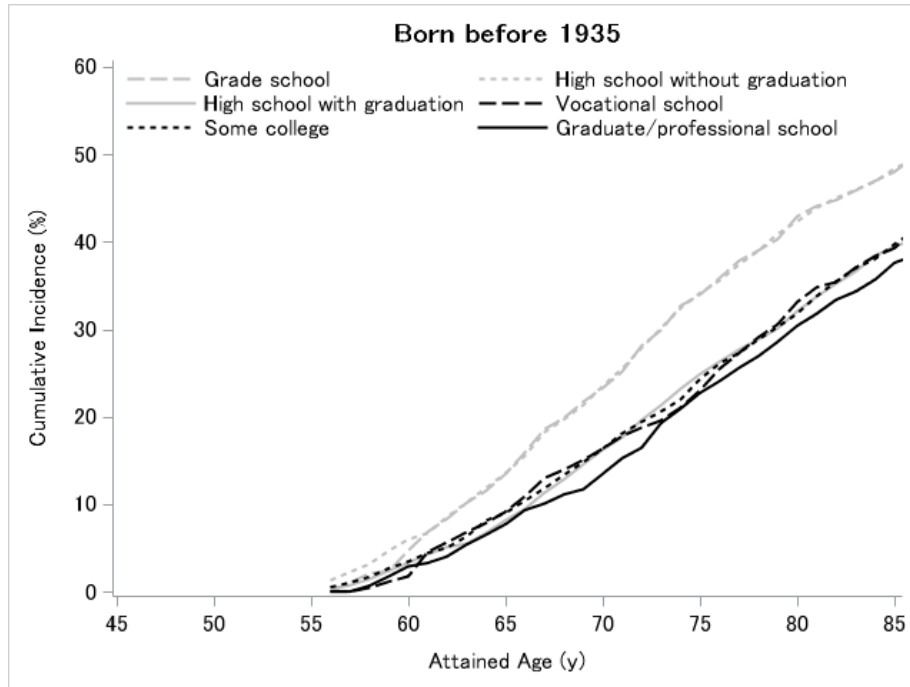


B



eFigure 6. Risk estimates of cardiovascular disease according to educational attainment for participants born (A) before and (B) after 1935

A



B

