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Education and Coronary Heart Disease Risk Associations May Be Affected by Early Life Common Prior Causes: A Propensity Matching Analysis

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Abstract

PURPOSE—Education is inversely associated with coronary heart disease (CHD); however whether this is due to causal effects of schooling rather than potential confounders existing prior to school entry (e.g. childhood intelligence, childhood economic circumstances, childhood chronic illness, parental mental health) remains unknown. We evaluated whether education is associated with 10-year CHD risk independent of 21 prospectively assessed childhood conditions, in participants aged 38-47.

METHODS—Linear regression analyses evaluated associations of education with 10-year CHD risk, the latter calculated using the validated Framingham risk algorithm incorporating diabetes, blood pressure, total and HDL cholesterol, smoking, age and sex. Propensity score matching incorporated 21 early life potential confounders.

RESULTS—Regression analyses demonstrated college graduation was associated with -27.9% lower (95% CI:-36.2,-18.6%) 10-year CHD risk compared with ≤high school after matching on propensity score that included age, sex and race (n= 272); addition of 21 early life potential confounders resulted in effect size of -13.1% (95% CI:-33.4,13.4; mean n=110).

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CONCLUSIONS—Participants with college degree had substantially lower CHD risk (27.9%) after accounting for demographics; addition of early life potential confounders resulted in a moderate effect size (13.1%), suggesting potential importance of early life factors in explaining observed associations between education and CHD risk.

Keywords

socioeconomic factors; social class; educational status; coronary heart disease; longitudinal studies

INTRODUCTION

The potentially causal relationship between socioeconomic position (e.g. education, income occupation) and health is of great interest to many health professionals and policy makers (1). In developed nations, education has been shown to be inversely associated with coronary heart disease (CHD) (2-5) and CHD risk factors such as smoking, blood pressure, obesity and diabetes (6-9) in a great number of observational studies. However, the issue of causality remains a concern. Specifically, there may be common prior causes to both education and CHD that occur in early life, such as childhood intelligence, childhood socioeconomic circumstances, parental mental illness, childhood chronic health conditions, birth weight, amongst others, which may confound the observed associations between education and CHD risk. This issue has been addressed in very few studies (6, 10-12).

Given that CHD is among the most widespread and costly health challenges, significant investments are being made in prevention and early treatment (13). Yet without knowing whether educational differences reflect the protective effects of schooling or other factors such as the long-term reach of early childhood conditions, it remains unclear where to target intervention (14). If schooling were found to offer protection against CHD, there would be public health rationale to expand educational opportunities. In contrast, evidence that educational inequalities in CHD are more attributable to early childhood conditions than to the beneficial effects of schooling would argue in favor of further support for early childhood interventions (15-17). Consequently, the primary objective was to test the hypothesis that education is associated with lower 10-year risk for CHD (using the validated Framingham risk algorithm), independent of a wide range of early childhood conditions. The secondary objective was to evaluate associations of educational attainment with individual modifiable CHD risk factor components of the Framingham algorithm (i.e. smoking, total cholesterol, HDL cholesterol, systolic blood pressure, diastolic blood pressure, and diabetes) to identify if any aspects of CHD risk are particularly strongly associated with education.

METHODS

Sample

Study participants were from the New England Family Study (NEFS), which is comprised of 17,921 offspring of pregnant women in the Collaborative Perinatal Project (CPP) at the Providence, Rhode Island and Boston, Massachusetts sites (United States) between 1959 and 1974 (18). The current NEFS sub-study named the EdHealth Study was comprised of participants selected with preference for racial/ethnic minorities, low or high educational attainment, and assessed during 2005-2007. There were 914 participants selected, of which 898 were eligible (e.g. living, not incarcerated), and 618 participated. We excluded 42 participants who were not interviewed in person (and did not complete physiological assessments), 5 who reported angina or myocardial infarction, and 18 participants missing ≥3 Framingham risk algorithm components. Accordingly, the sample size for current analyses was 553.

For primary analyses using propensity score matching, we used a 0.10 caliper width and 1:1 matching (described in more detail below in the Analytic Approach section), which resulted in a mean sample size (across 5 multiply imputed datasets) of n=214 (107 matched pairs) for analyses on participants with ≤high school vs. some post-secondary training, and n=110 (55 matched pairs) for analyses on participants with ≤high school *vs.* college graduation. A comparison within the 618 participants of those included (n=553) *vs.* excluded found included participants were younger (42.3 *vs.* 43.7 years, p<0.0001). There were no significant differences between included and excluded participants for gender, race/ethnicity, education, smoking status, or diabetes. Further included *vs.* excluded comparisons were performed for each of the two comparison samples above (i.e. (1) ≤high school *vs.* college degree and (2) ≤high school *vs.* some post-secondary training), selected based on education level and propensity score caliper matching, summarized in **Appendix Table A**. The study protocol was approved by the institutional review board of the Harvard School of Public Health.

Primary Exposure Variable

Education was determined as self-reported highest degree completed, categorized as: ≤high school (<high school, high school degree or GED), some post-secondary training (participants with any schooling after high school that did not result in a bachelor's degree or higher, including those who completed some college course work for credit, technical/trade/vocational school, associate's degree or certificate program), and college degree (e.g. bachelor's degree, graduate degree). There were only 30 participants with <high school, which would have resulted in low statistical power if it were a comparison group on its own. Consequently the educational groupings were performed as shown above.

Outcome Variables

The 10-year risk of CHD was calculated as a percentage, separately for men and women, using the validated Framingham risk algorithm (19). This algorithm uses sex-specific Cox regression models that incorporate diabetes, total and HDL cholesterol, systolic and diastolic blood pressure, smoking age and sex, described in detail elsewhere (19). The c-statistic for prediction of CHD events in the Framingham Heart Study is 0.74 in males and 0.77 in females, suggesting good predictive validity (19). External validity tests on white and black participants perform reasonably well (20).

Current smoking was based on self-report (yes/no). Lipids were measured in non-fasting plasma samples at CERLab (Harvard Medical School, Boston, MA) using a Hitachi 911 analyzer, and participating in the CDC/NHLBI Lipid Standardization Program. Total cholesterol (CV=1.7%) and HDL cholesterol (CV=3.3%) were measured enzymatically as described elsewhere (21, 22). Presence of diabetes was assessed by self-report as ever having been told by a doctor or health professional that participant has diabetes (other than gestational diabetes). Five systolic and diastolic blood pressure were obtained over one-minute intervals in participants seated, after 5 minutes rest, in the right arm at heart level, using automated blood pressure monitors (VSMedTech BpTru, Coquitlam, BC, Canada) demonstrated to have good validity and reliability compared with the auscultation method (23). Systolic and diastolic blood pressure values were calculated as the mean of the lowest three systolic or diastolic blood pressure readings, excluding the first recorded blood pressure.

Childhood Determinants of Educational Attainment

Early childhood determinants of educational attainment were obtained as part of the CPP, which followed participants prenatally through age 7 years. Measures of early childhood social conditions included parental socioeconomic position, using a weighted percentile of

both parents' educational attainment, occupation, and income relative to the US population prenatally and at age 7 (24); father's absence from household at birth or age 7; household crowding (>1.5 persons/room) prenatally and age 7; number of moves between birth and age 7; maternal employment status; and mother's and father's education. Mother's and father's education were included in particular, in addition to the weighted socioeconomic position index described above, as parental education is particularly strongly associated with offspring education (25, 26). Parental demographic factors included age at birth, and marital status at birth and age 7. Mothers' and fathers' treatment for psychiatric and substance use disorders were obtained by mother's self-report during pregnancy and at offspring age 7. Childhood health status was assessed based on exposure to maternal smoking during pregnancy (27); birth weight (grams), and chronic medical conditions identified between birth and age 7. Childhood chronic medical conditions were derived from physical examinations by CPP pediatricians at ages 1 and 7 years, obtained via mothers' reports at each visit, and extracted from medical records at ages 1 and 7. Summaries of childhood health conditions were compiled by CPP pediatricians. The current study used a summary score of number of chronic physical health conditions (including abnormalities of the liver, cardiovascular conditions, hematologic conditions (e.g. anemia), lower respiratory tract abnormality (e.g. asthma), neoplastic disease, neurologic abnormality, and prolonged/ recurrent hospitalization) that excluded psychological or behavioral problems, coded for analytic purposes as 0 or ≥1 medical conditions. Childhood intellectual development at age 7 was defined using the Full-Scale Intelligence Quotient (IQ) score from the Wechsler Intelligence Scale for Children, and the Wide Range Achievement Test (28, 29).

Analytic Methods

We used propensity score matching to compare 10-year risk of CHD in relation to participants' education. The conceptual similarity between this approach and a randomized controlled trial is that both study designs attempt to overcome problems of confounding bias by obtaining samples that differ only with respect to educational attainment (30). We conducted analyses for both of the comparisons (i.e. "treatments") of interest (some post-secondary training *vs.* ≤high school, and college degree *vs.* ≤high school) separately, thereby allowing the predictors of (and thus the propensity score for) each educational milestone to vary. The propensity scores were the predicted probabilities, estimated from a logistic regression model, of either some post-secondary training or a college degree. The propensity score models included as predictors all of the childhood social and biological factors described above.

In propensity score matching, treated individuals are matched with an untreated comparison group of individuals with an equivalent (within caliper) probability of receiving 'treatment'. Specifically, this means higher educated individuals are matched to a sample of lower educated individuals who are similar with respect to the set of childhood background characteristics described above. We used what is known as "caliper matching" to construct the matched samples, in which participants are randomly sorted, and then each higher educated individual is matched to the lower educated individual with the closest propensity score, as long as their propensity scores are within 10 percentage points of one another (i.e. caliper width of 0.10) (31, 32). Higher educated participants who were unable to be matched to a lower educated control according to these criteria were excluded from analyses.

In the primary analyses, we utilized two propensity models. The first model included only age, sex and race/ethnicity. The second model included age, sex, race/ethnicity, and the childhood determinants of education described above. This enabled analyses to estimate additional contributions of childhood factors over and above demographic factors. In terms of interpretation, the CHD risk associated with, for example college degree vs. ≤high school, can be interpreted as the difference in CHD risk between individuals who are identical in all

measured respects (i.e. the parental and childhood covariates in the propensity score model) except educational attainment (i.e. college degree vs. ≤high school).

The 10-year risk of CHD was analyzed using linear regression, with the matching by propensity scores incorporated in analyses by including in the regression models an indicator variable for each matched pair. The distribution of the 10-year CHD risk variable was skewed, and consequently log (natural) transformed. In order to maintain the original units of the CHD risk algorithm (units are % risk for incident CHD during the upcoming 10 years), regression coefficients were exponentiated and reported as the percent change in untransformed calculated CHD risk per categorical increase in education [(exp(β)-1)×100]. Analyses used generalized estimating equations to account for clustering by family (33).

Multiple imputation was used to address issues of missing data (as described above, participants were included if they were missing ≤2 of the Framingham algorithm components) (34). Five multiply-imputed datasets were generated using the method of chained equations as implemented in IVEWare (35); all analyses were conducted separately within each imputed dataset, and results combined across datasets using the MIANALYZE procedure in SAS which accounts for sampling variability across imputations.

RESULTS

Descriptive characteristics of the 553 participants (age 38-47 years) categorized by level of educational attainment, are shown in **Table 1**. In unadjusted analyses, participants with a college degree had lower calculated 10-year CHD risk, smoking, systolic blood pressure, diastolic blood pressure, and higher HDL cholesterol, compared with participants with ≤high school. There were no associations between education and age, sex, race/ethnicity, diabetes, or total cholesterol.

An important step in propensity score analyses is to demonstrate that the matched samples are similar (i.e. balanced) with respect to the variables included in the propensity score models. Starting out in the overall sample, there were substantial differences in the childhood background variables between higher *vs.* lower educated individuals (**Table 2, Appendix Figure A**). The propensity score matched samples matched had markedly improved balance on the childhood covariates (**Figure 1**), and substantially reduced standardized differences between propensity score components (extensive bias reduction for most propensity score components shown in **Table 2**).

In the first propensity score analyses incorporating only age, race/ethnicity and sex, linear regression analyses demonstrated that college graduation was associated with 27.9 (95% CI:-36.2,-18.6)% lower 10-year CHD risk compared with ≤high school (**Table 3**). In the second propensity score analyses that further incorporated the early life potential confounders (i.e. early childhood social conditions, parental demographic factors, parental psychiatric health history, childhood health status, and childhood intellectual development), college graduation was associated with 13.1 (95% CI:-33.4,13.4)% lower 10-year CHD risk *vs.* ≤high school (**Table 3**). No associations were found between some post-secondary training versus ≤high school (**Table 3**).

Sensitivity analyses were performed varying caliper widths from 0.01 to 0.20 in analyses matched on age, race/ethnicity, sex and all early life confounders, and found the following effect sizes (for college vs. ≤high school): Caliper width 0.01, β=-12.0 (95% CI:-32.7,15.2)%, n=90; caliper width 0.05, β=-11.0 (95% CI:-35.2,22.2)%, n=107; caliper width 0.20, β=-15.9 (95% CI:-37.3,12.8)%, n=121, where n represents mean sample size across 5 multiply imputed datasets.

In order to evaluate which components of the 10-year CHD risk algorithm may be driving observed associations with education, propensity score analyses incorporating age, sex and race/ethnicity were performed and demonstrated that college degree was associated with lower systolic blood pressure, diastolic blood pressure and smoking, and higher HDL cholesterol, compared with ≤high school (**Table 3**). Further incorporation of all early life factors into the propensity score reduced association strengths, which became statistically non-significant.

DISCUSSION

This study found that participants with a college degree had substantially lower CHD risk (27.9% lower risk) after accounting for traditional confounders (age, sex and race/ethnicity). Further addition of early life potential confounders (such as childhood intelligence, maternal mental health, childhood illness and childhood economic circumstances, amongst others) resulted in a moderate effect size (13.1% lower CHD risk). This suggests the potential importance of early life factors in explaining observed associations between education and CHD.

Most studies find consistent associations of education with CHD (2-5) and CHD risk factors such as blood pressure (7) and smoking (6). However despite these observed associations, very few studies have accounted for the wide range of early life potential confounders adjusted for in the current study. Some studies adjusted for a small number of early life variables or other common prior causes such as intelligence (36, 37), and childhood socioeconomic position (4, 38, 39), however there is very little information available on whether the association of education with CHD risk exists after a large number of the above potential common prior causes have been accounted for (12). This study suggests that early life conditions explain a substantial amount of the association.

Stringent tests of causality between education and health outcomes that account for the wide range of plausible early life confounders are rare, but preliminary findings to date call into question the strength of evidence for education causally influencing health (associations with CHD risk in particular have been minimally assessed). For example, twin and sibling studies (twin/sibling participants share similar family environment and genes) performed by our group and others, demonstrate that twins or siblings discordant in education have little difference in health outcomes such as mortality (11), health behaviors (6, 10) and self-rated health (10). Most of these studies, with the exception of one (11), have low statistical power and it is not clear whether the null findings are due to a lack of effect and/or lack of power. Studies that statistically account for a wide range of early life potential confounders are very rare. In our study, after adjusting for the early life factors, the effect size was reduced in half and was not statistically significant. However, with the relatively small number of participants in the college *vs.* ≤high school analyses (mean n=110), these results need to be interpreted with the understanding that there may be limited statistical power. Furthermore, some studies demonstrated that a change in government policies that altered mandatory number of years of school were related to health outcomes such as mortality and self-rated health (40, 41), while others demonstrated no effect on mortality of similar policies (42). Overall, these results suggest that some controversy over the causal role of education in influencing health. Many studies to date are substantially limited by statistical power, and the evidence base will be greatly helped by large cohort studies with ability to control for early life factors.

Education is typically associated with risk factors for coronary heart disease (CHD), however controversy still exists on whether the relationship between education and CHD risk factors is independent of infrequently measured confounders (6, 10-12). Studies often

show reductions in effect size of education with CHD after adjustment for conventional CHD risk factors such as blood pressure, diabetes, and obesity, suggesting these may be part of the explanatory pathway (3, 4). Education is typically associated with protective health behaviors such as fruit/vegetable consumption (43), and non-smoking (44), suggesting these may also be mechanisms. Adjusting for time-dependent covariates appears to provide substantial reductions in association between education and mortality (45). However, it is important to reflect on the possibility that associations between education and CHD risk factors are due to common prior causes, rather than the effects of education on these CHD risk factors (11, 12, 44). Other potential explanatory mechanisms are more poorly understood, including literacy (46), time preference (47, 48) and sense of control (49), which may influence people's abilities to understand health messages, plan ahead for their health, and have a sense of control over their lives enough to change behaviors to become more health-promoting, respectively.

Strengths and Limitations

With regard to limitations, a substantial number of participants were excluded from analyses due to non-matching within the caliper width of 0.10, which could have resulted in exclusion bias (50). In order to evaluate the potential importance of this bias, we varied the caliper widths from 0.01 to 0.20, with resulting mean sample sizes of 90 to 121 participants. The magnitude of the point estimates was not substantially affected by the caliper width or sample size, however lack of generalizability remains a valid concern for propensity score matching analyses such as these, when a substantial portion of the study population is excluded based on matching participants with different exposure levels, yet similar propensity scores. Further considerations of generalizability include that as this study preferentially selected participants from the original Collaborative Perinatal Project data collection who were racial/ethnic minorities, and who went on to have high or low educational attainment, we gained larger numbers of participants in these categories. Because race/ethnicity was included in the propensity score, and education was the exposure variable, this enabled greater statistical power given the relatively small sample size, including racial/ethnic minorities. However, with regard to generalizability, given that the study population was about 80% white race/ethnicity, and the major statistically significant findings were for those with college degree vs. ≤high school, the study findings pertain primarily to white race/ethnicity for those with college degree or ≤high school. Furthermore, as the study sample was born in the Boston, MA or Providence, RI in the United States, findings pertain more to urban-born participants of the northeast region of the United States. Future larger, more representative studies of larger populations will provide more generalizable information. An additional study weakness is the CHD risk algorithm is not as accurate a measure of CHD as the measurement of CHD events themselves. However, given the relatively young age of the participants (38-47 years), it is too early in the life course to evaluate associations with CHD events in this study. Educational attainment may have an effect on a wide range of CHD risk factors. Consequently by utilizing a validated CHD prediction algorithm (19, 20) that encompasses a variety of CHD risk factors, it allows for the evaluation of a variety of systems that may be simultaneously influenced by education. The relations between education and the individual components of the CHD risk algorithm provide additional, more specific information on the association of education with each individual CHD risk factor. It should be noted that as is this still a relatively young cohort (38-47 years of age), effects of education may manifest more strongly in later ages, and through unmeasured pathways such as inflammation, obesity, and lipids other than those measured (total and HDL cholesterol). An additional potential confounder not accounted for in these analyses are genetic factors that may be common prior causes to education and CHD. Twin studies have evaluated potential contributions of genetic confounding to the relation of education with mortality (11) and self-reported health constructs (10), and found

evidence of genetics as a plausible confounder. A limitation of propensity matching analysis is that it can only balance covariates on observed variables. The method does not take account of confounding by unobserved variables, such as genetic factors. Strengths of the study include accurate measurement of biological measures (including cholesterol, blood pressure, and BMI), using substantial internal and external quality control protocols. Furthermore, the birth cohort study design offered a unique ability to statistically account for directly assessed uncommonly measured prior common causes such as childhood intelligence, childhood socioeconomic position, childhood illness and parental mental health, amongst others.

Conclusions

This study found that participants with a college degree had lower CHD risk (27.9% lower CHD risk) after accounting for demographic factors. Further statistical accounting for early life potential confounders (such as intelligence, childhood economic circumstances, childhood chronic illness, parental mental health) resulted in a moderate effect size (13.1% lower risk), suggesting the potential importance of early life factors in explaining observed associations between education and CHD. These results provide some suggestion that a reasonable amount of the observed educational disparities in CHD risk found in observational studies may be due to factors occurring earlier in the life course.

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LIST OF ABBREVIATIONS AND ACRONYMS

CHD	Coronary heart disease
CPP	Collaborative Perinatal Project
GED	General equivalency diploma
HDL	High density lipoprotein
NEFS	New England Family Study

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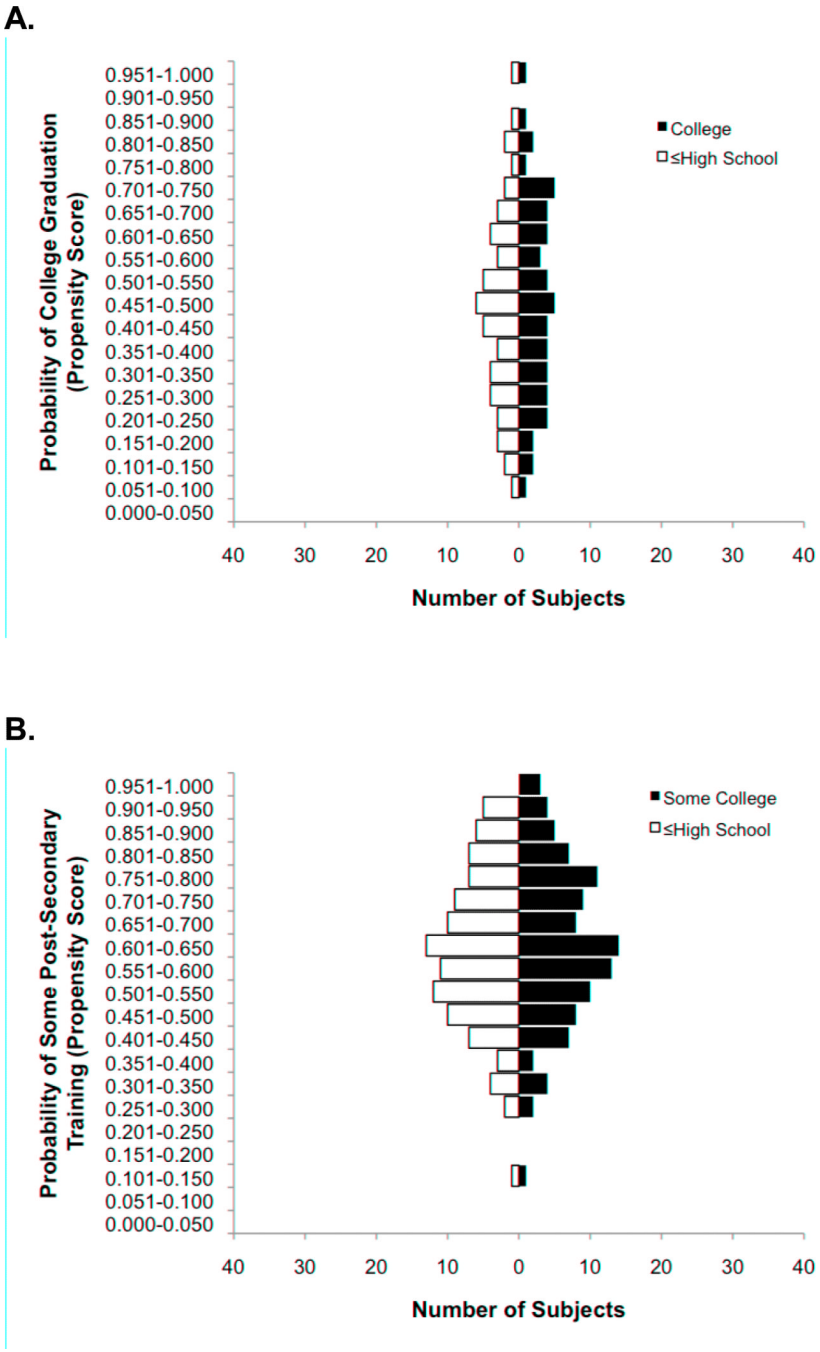

Figure 1.

Participant (n) overlap in propensity scores according to education level, after propensity score caliper matching. **A.** College degree *vs.* ≤high school (mean n across 5 multiple imputations = 110; 55 matched pairs). **B.** Some post-secondary training *vs.* ≤high school (mean n across 5 multiple imputations = 214; 107 matched pairs).

Table 1

Descriptive statistics (means or proportions, 95% confidence intervals) stratified by education.

	Educational Attainment			
	Overall (n=553)	**≤High School (n=136)**	**Some PS Training (n=278)**	**College Graduate (n=139)**
10-year CHD risk, %	4.2 (3.9, 4.5)	4.7 (4.1, 5.3)	4.3 (3.9, 4.7)	3.5 (3.0, 4.0)
Current smoker, %	27.5 (23.8, 31.2)	33.8 (25.8, 41.9)	32.7 (27.2, 38.3)	10.8 (5.6, 16.0)
Total cholesterol, mg/dl	199.1 (195.6, 202.6)	200.5 (193.4, 207.6)	198.5 (193.6, 203.3)	198.8 (191.5, 206.4)
HDL cholesterol, mg/dl	50.1 (48.7, 51.4)	47.9 (45.3, 50.6)	50.2 (48.2, 52.3)	51.8 (49.3, 54.3)
Systolic blood pressure, mmHg	113.4 (112.1, 114.6)	115.2 (112.6, 117.8)	114.5 (112.6, 116.4)	109.2 (106.9, 111.5)
Diastolic blood pressure, mmHg	74.6 (73.6, 75.5)	76.3 (74.4, 78.2)	74.9 (73.6, 76.3)	72.2 (70.5, 73.8)
Diabetes, %	4.2 (2.5, 5.8)	4.4 (0.9, 7.9)	5.0 (2.4, 7.6)	2.2 (0.0, 4.6)
Age, years	42.3 (42.2, 42.5)	42.1 (41.8, 42.4)	42.5 (42.3, 42.7)	42.2 (41.9, 42.5)
Sex, % male	40.5 (36.4, 44.6)	45.6 (37.1, 54.1)	37.8 (32.0, 43.5)	41.0 (32.7, 49.3)
Race/ethnicity, % white	80.3 (77.0, 83.6)	82.4 (75.9, 88.8)	78.4 (73.6, 83.3)	82.0 (75.5, 88.5)

CHD, coronary heart disease; PS, post-secondary

Table 2

Covariate balance across exposure groups prior to, and after, propensity score matching.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)		
Covariate	**≤High School (n=136)**	**Some PS Training (n=278)**	**College (n=139)**	**≤HS vs. Some PS Standardized Difference: Before Matching**	**≤HS vs. College Standardized Difference: Before Matching**	**≤High School (n=126)**	**Some PS Training (n=126)**	**≤HS vs. Some PS Standardized Difference: After Matching**	**≤High School (n=55)**	**College Graduate (n=55)**	**≤HS vs. College Standardized Difference: After Matching**	**≤HS vs. Some PS % Bias Reduction**	**≤HS vs. College % Bias Reduction**
	mean	**mean**	**mean**	**(1) vs. (2)**	**(1) vs. (3)**	**mean**	**mean**	**(6) vs. (7)**	**mean**	**mean**	**(9) vs. (10)**	**(4) vs. (8)**	**(5) vs. (11)**
Early childhood social conditions													
Parental SES index	48.6	53.0	63.2	-23.3	-72.7	49.5	48.2	7.0	54.7	53.4	7.4	69.8	89.8
Change in parental SES index, birth to age 7	-0.9	-1.9	2.5	5.7	-20.7	-1.2	-2.6	8.1	2.2	5.7	-21.8	-42.8	-5.2
Father absent from the household, %	17	12	3.6	13.3	47.3	11	13	-7.2	5.4	5.4	0.0	45.6	100.0
Household crowding													
<1 person/room	0.3	0.2	0.2	16.8	26.3	0.3	0.2	22.5	0.3	0.1	35.3	-33.8	-34.3
1-1.5 persons/room	0.2	0.2	0.2	9.2	17.7	0.2	0.2	2.0	0.2	0.1	4.9	78.5	72.1
1.5+ persons/room	0.5	0.6	0.7	-21.8	-36.4	0.5	0.6	-20.8	0.6	0.7	-33.6	4.5	7.7
No. moves between birth and age 7	1.6	1.4	1.3	22.2	27.3	1.6	1.5	5.9	1.3	1.4	-3.2	73.2	88.1
Maternal employment status, % employed	11	12	22	-3.7	-29.0	12	11	2.5	14	16	-4.9	33.7	83.0
Maternal education, years	10.3	11.0	11.9	-33.3	-68.7	10.4	10.4	0.0	10.9	11.2	-15.0	99.9	78.1
Paternal education, years	10.5	11.2	12.4	-29.4	-66.6	10.5	10.4	6.7	11.1	11.4	-11.8	77.2	82.2
Parental demographic factors													
Maternal age, years	24.5	25.2	26.7	-11.7	-37.7	24.3	24.0	4.5	25.2	24.9	5.7	61.7	84.8
Paternal age, years	26.3	28.2	29.7	-29.4	-52.0	26.7	27.1	-6.4	27.7	27.4	4.3	78.2	91.8
Parental marital status at birth, % married	85	87	96	-7.1	-39.3	87	86	2.3	93	93	0.0	67.9	100.0
No. changes in marital status, birth to age 7	0.4	0.3	0.2	17.8	36.6	0.4	0.3	10.3	0.3	0.2	5.7	42.2	84.5
Parental psychiatric health history													
Maternal psychiatric history, % mental illness	2.9	5.4	1.4	-12.4	10.4	3.2	4.8	-8.1	1.8	1.8	0.0	34.3	--
Paternal psychiatric history, % mental illness	8.1	6.8	2.2	4.8	28.3	7.9	7.1	3.0	1.8	1.8	0.0	37.1	100.0
Childhood health status													
Maternal smoking during pregnancy													
0 cigarettes	36	43	54	-13.9	-36.5	36	41	-11.4	46	48	-3.5	17.8	90.3
1-9 cigarettes/day	14	11	9.4	8.5	14.4	14	13	2.3	7.1	11	-12.5	73.1	13.4
10-19 cigarettes/day	8.8	13	12	-14.4	-8.9	8.7	7.1	5.9	8.9	7.1	6.5	59.2	26.6
≥20 cigarettes/day	41	33	25	17.5	34.4	41	38	6.5	38	34	7.4	63.1	78.5
Birth weight, grams	3212	3258	3309	-8.4	-17.7	3208	3192	2.8	3267	3346	-14.7	67.1	17.1

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)		
Covariate	**≤High School (n=136)**	**Some PS Training (n=278)**	**College (n=139)**	**≤HS vs. Some PS Standardized Difference: Before Matching**	**≤HS vs. College Standardized Difference: Before Matching**	**≤High School (n=126)**	**Some PS Training (n=126)**	**≤HS vs. Some PS Standardized Difference: After Matching**	**≤High School (n=55)**	**College Graduate (n=55)**	**≤HS vs. College Standardized Difference: After Matching**	**≤HS vs. Some PS % Bias Reduction**	**≤HS vs. College % Bias Reduction**
	mean	**mean**	**mean**	**(1) vs. (2)**	**(1) vs. (3)**	**mean**	**mean**	**(6) vs. (7)**	**mean**	**mean**	**(9) vs. (10)**	**(4) vs. (8)**	**(5) vs. (11)**
Childhood chronic medical conditions	0.2	0.2	0.2	20.5	11.8	0.2	0.2	5.7	0.3	0.2	12.8	71.9	-8.3
Childhood intellectual development at age 7													
IQ, WISC	95.7	100.0	108.8	-32.3	-98.9	96.5	96.9	-3.0	101.2	103.0	-16.7	90.8	83.2
WRAT: Reading score	98.8	103.5	112.6	-30.0	-78.3	99.0	99.3	-1.7	105.2	105.8	-3.9	94.3	95.0
WRAT: Spelling score	95.5	100.1	107.3	-34.9	-78.7	95.9	96.9	-7.8	101.9	102.1	-1.7	77.7	97.8
WRAT: Math score	95.5	99.3	103.0	-36.3	-80.2	96.2	96.6	-4.4	100.4	99.9	6.8	87.9	91.5
Adult demographic factors													
Age, years	42.1	42.5	42.2	-23.5	-7.2	42.0	42.4	-22.1	42.4	42.4	0.0	6.1	100.0
Sex, % male	46	38	41	-15.9	9.2	46	46	0.0	45	45	0.0	100.0	100.0
Race/ethnicity, % white	82	78	82	9.9	0.9	81	80	2.0	84	82	4.7	79.8	-434.9
Propensity Score													
Some College	0.58	0.71	N/A	-79.2	N/A	0.6	0.6	-11.7	N/A	N/A	N/A	85.2	N/A
College	0.28	N/A	0.73	N/A	-180.9	N/A	N/A	N/A	0.5	0.5	-3.8	N/A	97.9

Note: Results presented for the comparison of the matched samples using the first imputed file.

IQ, intelligence quotient; N/A, not applicable; No., number; SES, socioeconomic status; WISC, Wechsler Intelligence Scale for Children; WRAT, Wide Range Achievement Test.

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Table 3

Regression analyses using propensity score matching, demonstrating associations of education with change in calculated 10-year coronary heart disease (CHD) risk and CHD risk factors. Point estimates represent odds ratios (for smoking) or regression coefficients (for all other variables) for college degree *vs.* ≤high school, or some post-secondary (PS) training *vs.* ≤high school.

	Age, Gender, Race/Ethnicity in Propensity Score[†]		All Variables in Propensity Score[††]	
	β or OR	**95% CI**	**β or OR**	**95% CI**
College degree vs. ≤high school				
10-year CHD risk, %	**-27.9**	**-36.2, -18.6**	-13.1	-33.4, 13.4
Systolic blood pressure, mmHg	**-6.1**	**-8.6, -3.7**	-4.7	-11.6, 2.2
Diastolic blood pressure, mmHg	**-4.4**	**-6.1, -2.7**	-4.0	-8.0, 0.1
Total cholesterol, mg/dL	0.8	-7.2, 8.8	2.5	-17.1, 22.2
HDL cholesterol, mg/dL	**4.3**	**1.2, 7.4**	1.5	-5.9, 9.0
Smoker[‡]	**0.1**[‡]	**0.1, 0.3**	0.5[‡]	0.1, 1.6
Some PS training vs. ≤high school				
10-year CHD risk, %	2.0	-9.5, 14.9	3.9	-11.8, 22.5
Systolic blood pressure, mmHg	**-6.1**	**-8.6, -3.7**	1.4	-1.9, 4.7
Diastolic blood pressure, mmHg	-0.6	-2.3, 1.2	-0.2	-2.7, 2.3
Total cholesterol, mg/dL	-0.3	-7.3, 6.7	-2.8	-20.0, 14.3
HDL cholesterol, mg/dL	0.5	-2.6, 3.7	1.3	-2.0, 4.6
Smoker[‡]	1.0[‡]	0.6, 1.7	1.2[‡]	0.6, 2.4

Due to low sample size, models for diabetes could not be estimated.

β, regression coefficient; CHD, coronary heart disease; HDL, high-density lipoprotein; OR, odds ratio PS, Post-Secondary

[†] n= 272 participants (136 matched pairs) for analyses comparing college to ≤ high school; n=272 participants (136 matched pairs) for analyses comparing some PS training to ≤high school.

[††] "All variables" include age, gender, race/ethnicity and all measured early life potential confounders, including early childhood social conditions, parental demographic factors, parental psychiatric health history, childhood health status, and childhood intellectual development. Sample size ranges between 108 and 112 (54 to 56 matched pairs) for analyses comparing college to ≤high school; n ranges between 174 and 258 participants (87 to 129 matched pairs) included in the analyses comparing some PS training to ≤high school.

[‡] Due to low sample size and large number of adjustment variables, smoking analyses were performed using logistic regression on pairs discordant for smoking; point estimates and 95% CI are odds ratios.