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Genetic contributions to the educational inequalities in coronary heart disease incidence: a population-based study of 32000 middle-aged men and women

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ABSTRACT

Background: The background of educational disparities in coronary heart disease (CHD) risk is still not well understood. We utilized a polygenic score for education (PGS_{EDU}), socioeconomic indicators, and indicators of CHD risk to investigate whether these disparities result from causality or are influenced by shared factors.

Methods: Population-based health surveys including baseline measures on cardiometabolic risk factors at 25 – 70 years of age (N=32,610) and PGS_{EDU} were conducted in Finland between 1992 and 2011. Longitudinal information on education, social class, income, and CHD incidence (1716 CHD cases up to 2019) were based on national registers. Linear regression, Poisson regression, Cox regression, and linear structural equation models were used.

Results: Education and PGS_{EDU} were inversely associated with body mass index (BMI), systolic and diastolic blood pressure, total cholesterol and CHD incidence and positively associated with high-density lipoprotein cholesterol in men and women. Part of the associations of PGS_{EDU} with CHD incidence (57% in men and 28% in women) and cardiometabolic factors (30 – 55% and 31% – 92%, respectively) were mediated by education, social class, and income, but a substantial part of them was independent of socioeconomic factors. These associations were consistent across different levels of education.

Conclusion: PGS_{EDU} captures CHD risk that is not solely attributable to education and other socioeconomic indicators. This suggests that not only causality affects the educational disparities of CHD risk, but also factors reflected by PGS_{EDU} can contribute to them. Identifying these factors can help to understand and reduce socioeconomic health disparities.

KEY MESSAGES

● What is already known on this topic?

The polygenic score for education is associated with the risk of coronary heart disease, but it remains uncertain whether this association is solely due to education or if there are other mechanisms explaining it.

● What this study adds?

The polygenic score for education was found to be associated with the incidence of coronary heart disease and key cardiometabolic risk factors, but only a portion of these associations could be explained by measured education, social class, and income.

● How this study might affect research, practice or policy?

Genetic variants related to education provide insight into the risk of coronary heart disease that is not fully captured by direct measures of socioeconomic position.

INTRODUCTION

Cardiovascular diseases (CVD) are strongly socially patterned (1), and in Northern Europe, they account for a significant proportion of socioeconomic mortality inequalities (2). Behavioral factors, such as smoking, excessive alcohol consumption, and an unhealthy diet, play a crucial role in mediating the link between low social position and a higher risk of CVD, particularly in Northern Europe and North America (3). The impact of health behavior on the social disparities in CVD risk underscores the potential importance of education, as it can improve health through, for example, better health literacy (4). This hypothesis is supported by a natural experiment in the UK, which found that a legislation reform to raise the minimum school leaving age resulted in a lower CVD risk, decreased blood pressure, and reduced smoking rates (5,6). However, no reduction in CVD mortality was observed following a similar school reform in Sweden (7). Therefore, further research is needed to understand the underlying mechanisms linking education and CVD risk.

Recent advancements in genetic epidemiology provide new opportunities to gain insight into the associations between education and CVD. Previous studies have shown that genetic predisposition to education, as measured by a polygenic score (PGS_{EDU}), is associated with CVD incidence (6,8). However, aside from the direct influence of education on CVD risk, there are mechanisms that may explain this association. Education is a multifactorial trait influenced by genetic and environmental factors (9). PGS_{EDU} correlates with cognitive outcomes (10), and the expression of candidate genes associated with education is enriched in brain tissue (11). Additionally, there is a significant overlap in genetic polymorphisms associated with education between European and East Asian populations (11). This suggests a neurophysiological basis for these genetic influences that is not limited to the Western social context. In addition to IQ, genetic factors associated with education can also be linked to personality factors (12). Since both IQ (13,14) and personality (15) can explain

socioeconomic inequalities in CHD risk, they offer plausible pathways for how PGS_{EDU} can impact CHD risk. PGS_{EDU} can also reflect social factors, including childhood family through shared parent-offspring genetic effects, that can operate indirectly through pathways such as parental education (16), one's own family through assortative mating (17), or surrounding environment through selective migration (18). However, associations between PGS_{EDU} and different health outcomes have also been found within siblings, suggesting that this association is not solely explained by the childhood family environment (19,20). Furthermore, external factors that promote or hinder participation in education can explain the associations between education and CHD risk. These can be, for example, related to poor material resources leading to lower education than predicted by cognitive skills. Thus, it is important to consider mechanisms other than the direct impact of education that contribute to the association between education and CHD risk.

We aim to analyze the association between PGS_{EDU} and coronary heart disease (CHD) risk, both before and after adjusting for measured education. We present the following hypotheses regarding the relationship between education and CHD risk: i) If the association is solely due to the direct effect of education, PGS_{EDU} is not associated with CHD risk after adjusting for education. ii) If cognitive and other factors represented by PGS_{EDU} contribute to this association, PGS_{EDU} adjusted for education is inversely associated with CHD risk. iii) If external factors that either promote or hinder education contribute to this association, PGS_{EDU} adjusted for education is positively associated with CHD risk. Our results can help to untangle various biases that can affect the phenotypic level associations between education and CHD risk found in observational studies and thus contribute to the triangulation of these findings (21). We will also adjust the results for other social indicators, as they can capture different aspects of social variation than education (22). Additionally, we will analyze whether the effect of PGS_{EDU} varies across educational categories.

CHD risk is assessed using CHD incidence and cardiometabolic risk factors allowing us to consider the role of potentially preventable risk factors behind CHD incidence.

DATA AND METHODS

Data source

Finnish population-based health surveys (FINRISK 1992, 1997, 2002, 2007, and 2012 surveys, Health 2000 and 2011 surveys, and FinHealth 2017 survey) with the proportions of respondents ranging from 65% to 93% were combined (23). During the baseline examination, participants had their body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP) measured. They also provided blood samples for genotyping and assessment of total cholesterol and high-density lipoprotein (HDL) cholesterol levels and self-reported their smoking status (never smoker, former smoker, current smoker) and the number of alcoholic drinks consumed per week. Alcohol consumption was converted to pure alcohol and categorized as 0, 1–47, 48–191, and more than 191 grams of pure alcohol per week (24). These baseline data were linked to several population-based registers. Due to restrictions on register coverage for socioeconomic indicators, we selected participants born between 1935 and 1980. After this restriction, all participants were 25 years of age or older at the time of the clinical examination. Participants older than 70 years (N=1567) were removed to make the data more homogeneous by age. Following these adjustments, the study cohort consisted of 35,413 participants.

The longitudinal information on CHD incident cases was obtained from the Hospital Discharge Register for non-fatal cases (ICD-9 codes 410 or 4110 and ICD-10 codes I20.0 and I21 – I22) and the National Mortality Register for fatal cases without previous hospitalization (ICD-9 codes 410 –

414 and 798, excluding 7980A and ICD-10 codes I20 – I25, I46, R96 and R98), covering the entire Finnish population. We excluded individuals with pre-baseline CHD events (N=464), as well as those with missing data (N=68) or outlier measures (N=521) of the cardiometabolic factors. Additionally, we randomly removed one individual from pairs with an identity-by-descent (IBD) value≥0.178 (N=1750), indicating at least second-degree relatives. Our final sample size used in all analyses was 32,610 participants (17,474 women). Participants with missing information on smoking (N=175) and alcohol consumption (N= 592) were removed from analyses adjusted for health behavior. By the end of follow-up on December 31, 2019, we had 1716 CHD cases during the 479,248 person-years.

Education and occupation-based social class were derived from the Finnish population register. Education was based on the highest completed degree up to the end of 2019 and classified into four categories: basic, secondary, lower tertiary, and higher tertiary education. Secondary education was the largest category for both men (42%) and women (38%), while a minority of participants (11% of men and 13% of women) had higher tertiary education (Supplementary table 1). Social class was measured at the age of 40 or, if missing, at the most recent previous measurement when the individual was employed and classified into five categories (manual workers, lower non-manual workers, upper non-manual workers, entrepreneurs, and farmers). Income was based on personal taxable income from the Tax register. We first calculated the yearly income percentiles among the 35 – 40-year-old population for each year an individual belonged within this age group. Then, we took the mean of these percentile ranks and split them further into quintiles to also allow for non-linear associations. Information for education and income was available every 5-years between 1970 and 1985 and yearly between 1987 and 2019. Information on social class was available every 5-years between 1970 and 2005 and yearly between 2006 and 2018. For social class and income, 4055 persons had missing values and were removed from analyses adjusted for these variables.

We calculated PGS_{EDU} using the summary scores from the genome-wide association (GWA) study conducted by Okbay and colleagues (10). Participants in the 23andMe data collection were excluded from these summary scores due to privacy policies. Additionally, individuals overlapping with our analysis sample were also excluded to prevent overfitting of PGS_{EDU}. PGS_{EDU} was defined by SBayesR, which generates linkage disequilibrium-weighted scores using the summary GWA scores and an external banded linkage disequilibrium matrix from HapMap3 single nucleotide polymorphisms with a minor allele frequency of at least 0.01 in our data (25). Linkage disequilibrium adjustment of PGS_{EDU} GWA scores was conducted with GCTB 2.03 and genetic principal components, genetic relatedness, and PGS_{EDU} with PLINK 1.9–2.0 software. In our data, the correlation between PGS_{EDU} and education was 0.28 in men and 0.27 in women. Furthermore, we observed that PGS_{EDU} was 0.05 standard deviations (SD) higher in men than in women (95% confidence intervals (CI) 0.03 – 0.08), suggesting that men are more selected than women in these cohorts.

Statistical modeling

We initiated the statistical modeling by analyzing the associations between measured education and cardiometabolic factors (BMI, SBP, DBP, HDL cholesterol, and total cholesterol) using linear regression and CHD incidence using Poisson regression model. All results were adjusted for age at baseline, region of residence, the first 10 principal components of genetic population structure, and the survey round-genotyping batch combination to account for possible population stratification or subtle differences between genotyping and data collection rounds. Next, we examined the association between PGS_{EDU} and cardiometabolic factors first at the population level and then stratified by education. Subsequently, we adjusted the results for education, social class, and

income. We extended these analyses to examine CHD incidence using the Cox proportional hazards regression model. In these longitudinal analyses, we initially adjusted the models for age and population structure indicators, followed by education, social class, and income, then for cardiometabolic risk factors, and finally for smoking and alcohol consumption as indicators of health behavior. Given the correlation between SBP and DBP (0.59 in men and 0.60 in women when adjusted for age and age square) and the weak association of DBP with CHD incidence in the model including SBP (p=0.726 and 0.515, respectively), we only included SBP in the models to avoid multicollinearity. Following these analyses, we quantified the direct and indirect effects of PGS_{EDU} (i.e., effects mediated via observed education) on cardiometabolic factors and CHD risk using structural equation methodology (Supplementary figure 1). The modeling was performed using Stata 16.1 statistical software. Huber-White standard errors were utilized to address potential heteroscedasticity of residuals in the regression models. P-values were calculated using the goodness of fit statistics of the nested models.

RESULTS

Table 1 presents the means of cardiometabolic traits and CHD incidence by education and sex adjusted for age and population stratification (the unadjusted statistics are available in Supplementary tables 1 and 2). Women had healthier cardiometabolic values (lower BMI, blood pressure, and total cholesterol and higher HDL-cholesterol) and lower CHD incidence compared to men. In both men and women, those with higher education had a lower risk of CHD. When all educational coefficients were tested together, they showed associations with cardiometabolic factors ($p<0.00001$) and CHD incidence ($p<0.00001$ in men and $p=0.0002$ in women). However, these social gradients were more pronounced in women than in men, as indicated by the interaction effects between sex and education used as a categorized variable ($p<0.00001$ for BMI and blood

pressure, p=0.030 for total cholesterol, and p=0.0803 for HDL-cholesterol; the interaction parameters are available in Supplementary table 3).

Table 2 presents the mean differences of cardiometabolic traits per 1 SD of PGS_{EDU} (for HDL and total cholesterol, the regression coefficients were multiplied by 100 to reduce the number of decimals). Higher PGS_{EDU} was associated with healthier cardiometabolic values (lower BMI, blood pressure, and total cholesterol and higher HDL-cholesterol) in both men and women (Model 1). When comparing the regression coefficients of PGS_{EDU} between sexes and testing for interaction effects, the associations with PGS_{EDU} were stronger for women than for men in BMI ($p<0.0001$) and HDL-cholesterol (p=0.0039). Sex interactions for SBP and DBP were small and could be attributed to sampling error. For total cholesterol, the association with PGS_{EDU} was slightly stronger in men than in women (p=0.0600). After adjusting for education, social class, and income (Model 2), the associations between PGS_{EDU} and cardiometabolic traits decreased by 31% to 52% but remained statistically significant. The only exception was total cholesterol in women, where the association was almost fully explained (92%). PGS_{EDU} was associated with cardiometabolic traits across all educational categories (Model 1) without significant differences between them (p-values of the interactions between classified education and PGS_{EDU} 0.0316 – 0.9351). Adjustments for social class and income explained a portion of the associations in analyses stratified by education (Model 2), but the decrease in the estimates was generally smaller than what was found in the analyses including all men and women.

Next, we analyzed how PGS_{EDU} was associated with CHD incidence (Table 3). Higher PGS_{EDU} was found to be associated with a lower risk of CHD, with hazard ratios per 1 SD of PGS_{EDU} being consistent in both men (HR=0.86) and women (HR=0.86) (p-value of the interaction between sex and PGS_{EDU} 0.6566) (Model 1). When studying all participants, adjustments for education, income,

and social class explained a portion of this association (57% in men and 28% in women), yet PGS_{EDU} remained associated with CHD incidence (Model 2). Further adjustments for cardiometabolic factors (Model 3) weakened these associations (additional 15% in men 21% in women compared to Model 1). Finally, the adjustments for smoking and alcohol consumption fully explained the association between PGS_{EDU} and CHD incidence in men (Model 4). When stratified by education, PGS_{EDU} showed a weak association with CHD (Model 1). The associations between PGS_{EDU} and CHD incidence were consistent across educational categories, with the p-values of interaction effects between PGS_{EDU} and categorized education not reaching statistical significance (p=0.6315 – 0.8130). Adjustments for income and social class (Model 2) and cardiometabolic factors (Model 3) further reduced the associations between PGS_{EDU} and CHD incidence and the adjustments for smoking and alcohol consumption fully explained them in men (Model 4) when stratified by education.

Finally, we estimated the direct and indirect effects of PGS_{EDU} (mediated via observed education) on cardiometabolic factors and CHD risk (Table 4) using structural equation modeling (Supplementary figure 1). The proportions of mediated influences of PGS_{EDU} varied from 20% for DBP in females to 84% for total cholesterol in females. However, both the direct and indirect influences of PGS_{EDU} were statistically significant.

DISCUSSION

Main findings

In this large population-based study, we found that genetic liability for higher education, as measured by PGS_{EDU}, was associated with lower CHD incidence and healthier cardiometabolic risk

profiles. These associations were partially explained by measured education, occupational-based social class, and income, but they persisted even after these adjustments. PGS_{EDU} was also associated with CHD incidence and cardiometabolic risk factors in a similar way across different levels of education. The adjustment for metabolic and behavioral risk factors of CHD largely explained the association between PGS_{EDU} and CHD incidence supporting the idea that behavioral factors are important mediators between genetic liability for education and CHD risk. Previous studies have shown associations between PGS_{EDU} and CHD risk (6,8), and similar associations between PGS_{EDU} and various health outcomes have also been found within sibling pairs (19,20). Our results suggest that the associations from PGS_{EDU} to CHD risk are not solely through education or other socioeconomic indicators associated with education, but rather there may be additional mechanisms mediating these associations. Genetic variants related to education, and more broadly socioeconomic status, can thus provide new insights into the mechanisms mediating the impact of low socioeconomic status on adverse health outcomes that have been discussed for decades (26).

Possible explanations

PGS_{EDU} reflects psychological and social factors that likely contribute to the direct effect of PGS_{EDU} on CHD risk. In contrast, external factors that hinder or promote education do not seem to affect CHD risk. PGS_{EDU} is associated with cognitive outcomes (10), and the expression of candidate genes related to education is enriched in brain tissue suggesting that cognitive factors play a significant role (11). Additionally, personality can explain the genetic liability of education (12). Both IQ (13,14) and personality (15) are linked to CHD risk, supporting their contribution to the association between PGS_{EDU} and CHD risk. We also found that the association between PGS_{EDU} and CHD risk remains consistent across all levels of educational classification including those with only basic education. This aligns with a previous study indicating that IQ measured in early

childhood was associated with CHD mortality across various levels of parental education, own education, and social class (27). PGS_{EDU} can also reflect social factors, especially the childhood home (16), one's own family (17), and the neighborhood of residence (18), all of which can impact CHD risk (28). While we cannot separate these social effects from individual-level psychological factors, our results indicate that if they have impact on CHD risk, these associations can be independent of education and other social indicators. It is also possible that educational classification may not capture all variation in education that could lead to lower CHD risk. For instance, high family social position increases the likelihood of studying fields like law, economics, and medicine in Finland, which typically result in high social status (29). However, even after adjusting for occupation-based social position and incomes, PGS_{EDU} remained associated with CHD risk.

Sex differences

Even though educational disparities in CHD incidence and cardiometabolic factors were evident in both sexes, these associations were systematically stronger in women than in men. Previous studies have shown that while social differences in smoking (30) and alcohol consumption (31) are larger in men than in women, social differences in obesity are typically larger in women (32). Thus, the sex interactions with social indicators can vary between health outcomes. Interestingly, we found that when using PGS_{EDU}, the sex interactions were not as consistent as those found for education, and stronger associations in women were evident only for BMI and HDL-cholesterol. These findings may reflect lower statistical power for PGS_{EDU} compared to observed education, but they may also indicate real differences in the background of educational health inequalities between men and women. For example, it is possible that in women, education is more directly associated with CHD risk than in men due to stronger cultural pressure on health-related behaviors among highly

educated women. This has been observed in relation to BMI (32), but solid evidence is still lacking for other potential health behaviors affecting CHD risk, such as diet and physical exercise.

Strengths and limitations

Our data have both strengths and limitations. The strengths of our data include a large sample size that allowed us to reliably estimate the associations between PGS_{EDU} and CHD risk, as well as the high response rates for the baseline surveys that reduced biases related to participant selectivity. All social indicators were register-based eliminating recall bias. Additionally, we were able to reduce measurement heterogeneity by assessing social position at the same age. Our register-based follow-up of fatal and non-fatal CHD incidence minimized bias due to selective drop-out. However, despite the high response rates, there is likely selection bias in our data, as participation rates are higher among those with higher education (33). This bias may be more pronounced in men, as we observed slightly higher PGS_{EDU} in men. The correlation between PGS_{EDU} and education was lower in our data than in the original GWA study (10), which may be because of genetic differences between Finnish and other European populations (34).

CONCLUSIONS

We found that PGS_{EDU} is associated with CHD incidence and cardiometabolic factors. These associations are only partially mediated by education itself or other indicators of social position. While educational gradients were steeper in women compared to men, there was less evidence for sex interactions with PGS_{EDU}. Our results suggest that PGS_{EDU} captures CHD risk that is not solely attributable to education or other socioeconomic indicators. This suggests that PGS_{EDU} may capture residual variation in social position that is not measured by available socioeconomic indicators, but

it can also indicate different mechanisms than causal effects contributing to educational disparities in CHD risk. Genetic-level data may provide new insights into the underlying mechanisms of social disparities in CHD incidence.

Ethical approval: This study involves human participants. The Statistics Finland Board of Ethics (TK/2041/07.03.00/2023) and the Finnish Social and Health Data Permit Authority Findata (THL/706/14.06.00/2024) have accepted the use of clinical data and the data linkage to the Finnish population registers. All participants gave informed consent when participating in the study. The samples/data used for the research were obtained from THL Biobank (study number: THLBB2023_51).

Data availability statement: The data underlying this article were provided by third party by permission and is not publicly available. Data will be shared on request to the corresponding author with permission of third party.

Author contributions: All authors contributed to the study conception and design. KS performed the analyses and prepared the first draft of the manuscript. HL created the polygenic risk score and helped in the genetic part of the analyses. HL, KK, TTM and PM revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript are agree to be accountable for all aspects of the work. KS acts as the guarantor for the paper.

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References

1. Veronesi G, Ferrario MM, Kuulasmaa K, Bobak M, Chambless LE, Salomaa V, et al. Educational class inequalities in the incidence of coronary heart disease in Europe. Heart. 2016;102(12):958–65.
2. Kulhánová I, Bacigalupe A, Eikemo TA, Borrell C, Regidor E, Esnaola S, et al. Why does Spain have smaller inequalities in mortality? An exploration of potential explanations. Eur J Public Health. 2014;24(3):370–7.
3. Petrovic D, de Mestral C, Bochud M, Bartley M, Kivimäki M, Vineis P, et al. The contribution of health behaviors to socioeconomic inequalities in health: A systematic review. Prev Med. 2018;113:15–31.
4. Sørensen K, Pelikan JM, Röthlin F, Ganahl K, Slonska Z, Doyle G, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health. 2015;25(6):1053–8.
5. Davies NM, Dickson M, Davey Smith G, van den Berg GJ, Windmeijer F. The causal effects of education on health outcomes in the UK Biobank. Nat Hum Behav. 2018 Feb;2(2):117–25.
6. Davies NM, Dickson M, Davey Smith G, Windmeijer F, van den Berg GJ. The causal effects of education on adult health, mortality and income: evidence from Mendelian randomization and the raising of the school leaving age. Int J Epidemiol. 2023;52(6):1878–86.
7. Lager ACJ, Torssander J. Causal effect of education on mortality in a quasi-experiment on 1.2 million Swedes. Proc Natl Acad Sci U S A. 2012;109(22):8461–6.
8. Tillmann T, Vaucher J, Okbay A, Pikhart H, Peasey A, Kubinova R, et al. Education and coronary heart disease: mendelian randomisation study. BMJ. 2017;358:j3542.
9. Silventoinen K, Jelenkovic A, Sund R, Latvala A, Honda C, Inui F, et al. Genetic and environmental variation in educational attainment: an individual-based analysis of 28 twin cohorts. Sci Rep. 2020;10(1):12681.

10. Okbay A, Wu Y, Wang N, Jayashankar H, Bennett M, Nehzati SM, et al. Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. Nat Genet. 2022 Apr;54(4):437–49.

11. Chen TT, Kim J, Lam M, Chuang YF, Chiu YL, Lin SC, et al. Shared genetic architectures of educational attainment in East Asian and European populations. Nat Hum Behav. 2024 Mar;8(3):562–75.

12. Starr A, Riemann R. Common genetic and environmental effects on cognitive ability, conscientiousness, self-perceived abilities, and school performance. Intelligence. 2022;93:101664.

13. Batty GD, Der G, Macintyre S, Deary IJ. Does IQ explain socioeconomic inequalities in health? Evidence from a population based cohort study in the west of Scotland. BMJ. 2006 Mar 11;332(7541):580–4.

14. Batty GD, Shipley MJ, Dundas R, Macintyre S, Der G, Mortensen LH, et al. Does IQ explain socio-economic differentials in total and cardiovascular disease mortality? Comparison with the explanatory power of traditional cardiovascular disease risk factors in the Vietnam Experience Study. Eur Heart J. 2009 Aug;30(15):1903–9.

15. Nabi H, Kivimäki M, Marmot MG, Ferrie J, Zins M, Ducimetière P, et al. Does personality explain social inequalities in mortality? The French GAZEL cohort study. Int J Epidemiol. 2008;37(3):591–602.

16. Wang B, Baldwin JR, Schoeler T, Cheesman R, Barkhuizen W, Dudbridge F, et al. Robust genetic nurture effects on education: A systematic review and meta-analysis based on 38,654 families across 8 cohorts. Am J Hum Genet. 2021;108(9):1780–91.

17. Gonggrijp BMA, Silventoinen K, Dolan CV, Boomsma DI, Kaprio J, Willemsen G. The mechanism of assortative mating for educational attainment: a study of Finnish and Dutch twins and their spouses. Front Genet. 2023;14:1150697.

18. Abdellaoui A, Dolan CV, Verweij KJH, Nivard MG. Gene-environment correlations across geographic regions affect genome-wide association studies. Nat Genet. 2022;54(9):1345–54.

19. Howe LJ, Rasheed H, Jones PR, Boomsma DI, Evans DM, Giannelis A, et al. Educational attainment, health outcomes and mortality: a within-sibship Mendelian randomization study. Int J Epidemiol. 2023;52(5):1579–91.

20. Ericsson M, Finch B, Karlsson IK, Gatz M, Reynolds CA, Pedersen NL, et al. Educational influences on late-life health: genetic propensity and attained education. J Gerontol B Psychol Sci Soc Sci. 2024;79(1):gbad153.

21. Lawlor DA, Tilling K, Davey Smith G. Triangulation in aetiological epidemiology. Int J Epidemiol. 2016 Dec 1;45(6):1866–86.

22. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. Br Med Bull. 2007;81–82:21–37.

23. Paalanen L, Härkänen T, Tolonen H. Protocol of a research project "Projections of the burden of disease and disability in Finland - health policy prospects" using cross-sectional health surveys and register-based follow-up. BMJ Open. 2019;9(6):e029338.

24. Salonsalmi A, Laaksonen M, Lahelma E, Rahkonen O. Drinking habits and sickness absence: the contribution of working conditions. Scand J Public Health. 2009 Nov;37(8):846–54.

25. Lloyd-Jones LR, Zeng J, Sidorenko J, Yengo L, Moser G, Kemper KE, et al. Improved polygenic prediction by Bayesian multiple regression on summary statistics. Nat Commun. 2019 Nov 8;10(1):5086.

26. Batty GD. We must move on: taking stock (yet again) of the evidence for socio-economic differentials in health. J Epidemiol Community Health. 2011 Nov;65(11):947–8.

27. Silventoinen K, Modig-Wennerstad K, Tynelius P, Rasmussen F. Association between intelligence and coronary heart disease mortality: a population-based cohort study of 682 361 Swedish men. Eur J Cardiovasc Prev Rehabil. 2007 Aug;14(4):555–60.

28. Teshale AB, Htun HL, Owen A, Gasevic D, Phyo AZZ, Fancourt D, et al. The role of social determinants of health in cardiovascular diseases: an umbrella review. J Am Heart Assoc. 2023;12(13):e029765.

29. Lehti H, Kinnari H. Student's cultural and economic family background and duration of university studeis in Finland. European Education. 2024;56:32–49.

30. Silventoinen K, Piirtola M, Jelenkovic A, Sund R, Tarnoki AD, Tarnoki DL, et al. Smoking remains associated with education after controlling for social background and genetic factors in a study of 18 twin cohorts. Sci Rep. 2022;12(1):13148.

31. Bloomfield K, Grittner U, Kramer S, Gmel G. Social inequalities in alcohol consumption and alcohol-related problems in the study countries of the EU concerted action "Gender, Culture and Alcohol Problems: a Multi-national Study." Alcohol Alcohol Suppl. 2006;41(1):i26-36.

32. McLaren L. Socioeconomic status and obesity. Epidemiol Rev. 2007;29:29–48.

33. Reinikainen J, Tolonen H, Borodulin K, Härkänen T, Jousilahti P, Karvanen J, et al. Participation rates by educational levels have diverged during 25 years in Finnish health examination surveys. Eur J Public Health. 2018;28(2):237–43.

34. Lek M, Karczewski KJ, Minikel EV, Samocha KE, Banks E, Fennell T, et al. Analysis of protein-coding genetic variation in 60,706 humans. Nature. 2016;536(7616):285–91.

Table 1. Model based means of cardiometabolic factors and coronary heart disease incidence by education and sex.

	BMI (kg/m^2)[1]	SBP (mmHg)[1]	DBP (mmHg)[1]	HDL-cholesterol (mmol/L)[1]	Total cholesterol (mmol/L)[1]	CHD incidence cases/1000 person years[2]
	mean (95% CI)	mean (95% CI)	mean (95% CI)	mean (95% CI)	mean (95% CI)	rate (95% CI)
Men						
All	27.1 (27.0, 27.1)	135 (135, 135)	83.1 (83.0, 83.3)	1.30 (1.30, 1.31)	5.54 (5.53, 5.56)	2.85 (1.92, 4.24)
Basic	27.5 (27.4, 27.7)	137 (136, 137)	83.9 (83.5, 84.2)	1.29 (1.28, 1.30)	5.63 (5.60, 5.67)	3.77 (2.29, 6.20)
Secondary	27.2 (27.1, 27.3)	135 (135, 136)	83.3 (83.0, 83.5)	1.30 (1.29, 1.31)	5.58 (5.55, 5.60)	3.37 (2.06, 5.51)
Lower tertiary	27.0 (26.8, 27.1)	135 (134, 135)	83.3 (82.9, 83.6)	1.30 (1.29, 1.31)	5.50 (5.46, 5.53)	2.43 (1.47, 4.03)
Higher tertiary	26.1 (26.0, 26.3)	133 (132, 134)	82.0 (81.5, 82.5)	1.33 (1.32, 1.35)	5.42 (5.37, 5.46)	1.73 (1.00, 2.99)
p-value education[3]	<0.00001	<0.00001	<0.00001	<0.00001	<0.00001	<0.00001
Women						
All	26.3 (26.3, 26.4)	130 (130, 130)	78.7 (78.5, 78.8)	1.57 (1.56, 1.58)	5.46 (5.45, 5.48)	1.15 (0.77, 1.71)
Basic	27.3 (27.1, 27.5)	132 (132, 133)	79.3 (78.9, 79.7)	1.54 (1.53, 1.56)	5.54 (5.51, 5.58)	1.45 (0.72, 2.94)
Secondary	26.6 (26.5, 26.7)	130 (130, 131)	78.7 (78.4, 78.9)	1.56 (1.55, 1.57)	5.47 (5.45, 5.50)	1.28 (0.64, 2.55)
Lower tertiary	25.9 (25.8, 26.0)	129 (128, 129)	78.4 (78.1, 78.6)	1.58 (1.57, 1.59)	5.39 (5.37, 5.42)	0.87 (0.43, 1.76)
Higher tertiary	24.9 (24.8, 25.1)	127 (126, 128)	77.6 (77.2, 78.0)	1.62 (1.61, 1.64)	5.39 (5.35, 5.43)	0.74 (0.34, 1.61)
p-value education[3]	<0.00001	<0.00001	<0.00001	<0.00001	<0.00001	0.0002
p-value sex*education[4]	<0.00001	<0.00001	<0.00001	0.0803	0.0303	0.4428

[1]Values based on linear regression models holding control variables (age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch) at their observed values.
[2]Values based on Poisson regression model holding control variables (age centralized as mean age of population, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch) at their observed values.
[3]P-value of the main effect of education used as a categorized variable.
[4]P-value of the interaction effect between sex and education used as a categorized variable.
Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval, DBP, diastolic blood pressure; HDL, high density lipoprotein; LL, lower limit; SBP, systolic blood pressure; UL, upper limit

Table 2. The regression coefficients (β) per one standard deviation of PGS of education on cardiometabolic factors stratified by education and sex.[1]

	Model 1			Model 2		
	Men	Women	p-value	Men	Women	p-value
	β (95% CI)	β (95% CI)	sex*PGS[2]	β (95% CI)	β (95% CI)	sex*PGS[2]
BMI (kg/m^2)						
All	-0.28 (-0.35, -0.22)	-0.50 (-0.57, -0.43)	<0.00001	-0.19 (-0.27, -0.12)	-0.34 (-0.42, -0.27)	<0.00001
Basic	-0.15 (-0.29, -0.01)	-0.48 (-0.65, -0.30)	0.0082	-0.13 (-0.28, 0.01)	-0.45 (-0.63, -0.27)	0.0172
Secondary	-0.19 (-0.29, -0.08)	-0.32 (-0.44, -0.20)	0.0690	-0.21 (-0.32, -0.10)	-0.33 (-0.45, -0.20)	0.0946
Lower tertiary	-0.19 (-0.33, -0.05)	-0.32 (-0.45, -0.19)	0.4147	-0.19 (-0.34, -0.04)	-0.34 (-0.48, -0.19)	0.3154
Higher tertiary	-0.35 (-0.53, -0.17)	-0.18 (-0.34, -0.01)	0.1424	-0.30 (-0.49, -0.11)	-0.24 (-0.41, -0.07)	0.5009
p-value education*PGS[3]	0.1879	0.2186		0.3980	0.5720	
SBP (mmHg)						
All	-0.87 (-1.13, -0.62)	-1.07 (-1.31, -0.83)	0.3613	-0.61 (-0.90, -0.32)	-0.63 (-0.89, -0.36)	0.7302
Basic	-0.12 (-0.69, 0.46)	-0.26 (-0.87, 0.35)	0.9537	-0.07 (-0.69, 0.54)	-0.11 (-0.76, 0.54)	0.6489
Secondary	-0.74 (-1.15, -0.34)	-0.68 (-1.09, -0.27)	0.3178	-0.67 (-1.10, -0.23)	-0.59 (-1.02, -0.15)	0.3370
Lower tertiary	-1.02 (-1.59, -0.45)	-0.91 (-1.35, -0.47)	0.2664	-1.16 (-1.77, -0.55)	-0.84 (-1.31, -0.38)	0.1226
Higher tertiary	-0.76 (-1.56, 0.04)	-0.95 (-1.58, -0.32)	0.6354	-0.82 (-1.69, 0.06)	-1.04 (-1.71, -0.37)	0.5605
p-value education*PGS[3]	0.0883	0.1860		0.0698	0.0986	
DBP (mmHg)						
All	-0.31 (-0.47, -0.14)	-0.49 (-0.63, -0.35)	0.1879	-0.19 (-0.38, 0.00)	-0.39 (-0.55, -0.23)	0.2343
Basic	0.16 (-0.19, 0.52)	-0.17 (-0.51, 0.17)	0.2274	0.19 (-0.18, 0.56)	-0.17 (-0.53, 0.20)	0.2679
Secondary	-0.22 (-0.48, 0.05)	-0.38 (-0.63, -0.14)	0.7567	-0.15 (-0.44, 0.14)	-0.38 (-0.64, -0.12)	0.5311
Lower tertiary	-0.57 (-0.95, -0.19)	-0.41 (-0.70, -0.13)	0.2466	-0.65 (-1.06, -0.24)	-0.41 (-0.71, -0.11)	0.2428
Higher tertiary	-0.28 (-0.81, 0.25)	-0.71 (-1.11, -0.32)	0.2716	-0.40 (-0.99, 0.19)	-0.69 (-1.11, -0.26)	0.5136
p-value education*PGS[3]	0.0316	0.1886		0.0339	0.2419	
HDL-cholesterol (100*mmol/L)						
All	0.69 (0.17, 1.22)	1.72 (1.18, 2.26)	0.0039	0.45 (-0.14, 1.04)	1.19 (0.58, 1.81)	0.0042

Basic	0.24 (-0.89, 1.38)	1.52 (0.21, 2.82)	0.1061	0.19 (-1.02, 1.40)	1.29 (-0.10, 2.69)	0.1204
Secondary	0.32 (-0.50, 1.15)	0.82 (-0.10, 1.75)	0.2573	0.36 (-0.55, 1.26)	0.96 (-0.04, 1.96)	0.2097
Lower tertiary	0.67 (-0.48, 1.82)	1.60 (0.52, 2.67)	0.2632	0.58 (-0.68, 1.85)	1.59 (0.44, 2.74)	0.2775
Higher tertiary	0.30 (-1.42, 2.02)	0.76 (-0.77, 2.29)	0.5462	0.54 (-1.28, 2.37)	1.02 (-0.64, 2.69)	0.5653
p-value education*PGS[3]	0.8334	0.6663		0.8471	0.8214	
Total cholesterol (100*mmol/L)						
All	-3.51 (-5.14, -1.87)	-2.00 (-3.41, -0.59)	0.0600	-1.59 (-3.42, 0.23)	-0.17 (-1.76, 1.42)	0.0338
Basic	-0.47 (-3.95, 3.01)	-2.88 (-6.30, 0.55)	0.8468	-0.86 (-4.59, 2.87)	-1.78 (-5.41, 1.85)	0.5422
Secondary	-2.11 (-4.76, 0.53)	1.36 (-1.05, 3.78)	0.0023	-1.80 (-4.65, 1.05)	1.13 (-1.47, 3.74)	0.0060
Lower tertiary	-2.77 (-6.35, 0.80)	-0.99 (-3.72, 1.73)	0.1220	-2.07 (-5.95, 1.80)	-0.15 (-3.10, 2.81)	0.1717
Higher tertiary	-2.06 (-7.00, 2.89)	-1.98 (-6.00, 2.03)	0.5375	-0.96 (-6.26, 4.35)	-1.23 (-5.56, 3.09)	0.7481
p-value education*PGS[3]	0.7906	0.1376		0.9351	0.3259	

Model 1= age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch

Model 2=Model 1 + education (only for the analyses including all men and women) + occupational based social class + incomes

[1]A separate model was conducted for each cardiometabolic outcome.

[2]P-value of interaction between sex and PGS_{EDU} within each educational category.

[3]P-value of interaction between categorical education and PGS_{EDU}.

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval, DBP, diastolic blood pressure; HDL, high density lipoprotein; LL, lower limit; PGS, polygenic score; SBP, systolic blood pressure; UL, upper limit

Table 3. Hazard ratios (HR) of coronary heart disease incidence for one SD change of PGS of education and sex.

	Men	Women	p-value
	HR (95% CI)	HR (95% CI)	sex*PGS[1]
Model 1			
All	0.88 (0.83, 0.94)	0.86 (0.79, 0.94)	0.6566
Basic	0.93 (0.85, 1.02)	0.95 (0.82, 1.09)	0.6011
Secondary	0.92 (0.83, 1.01)	0.85 (0.73, 1.00)	0.5656
Lower tertiary	0.95 (0.81, 1.12)	0.89 (0.70, 1.14)	0.4422
Higher tertiary	0.99 (0.72, 1.36)	0.79 (0.48, 1.30)	0.5373
p-value education*PGS[2]	0.8130	0.7538	
Model 2			
All	0.95 (0.89, 1.01)	0.90 (0.82, 0.99)	0.4529
Basic	0.95 (0.87, 1.05)	0.96 (0.83, 1.11)	0.7247
Secondary	0.92 (0.83, 1.02)	0.86 (0.73, 1.00)	0.5063
Lower tertiary	0.97 (0.82, 1.14)	0.89 (0.69, 1.14)	0.2894
Higher tertiary	1.08 (0.77, 1.53)	0.84 (0.50, 1.14)	0.3224
p-value education*PGS[2]	0.6918	0.6751	
Model 3			
All	0.97 (0.91, 1.03)	0.92 (0.83, 1.01)	0.4760
Basic	0.97 (0.88, 1.06)	0.97 (0.84, 1.12)	0.6965
Secondary	0.93 (0.84, 1.04)	0.87 (0.74, 1.02)	0.4518
Lower tertiary	1.00 (0.85, 1.18)	0.89 (0.70, 1.15)	0.2168
Higher tertiary	1.06 (0.74, 1.52)	0.87 (0.50, 1.51)	0.3244
p-value education*PGS[2]	0.6245	0.6928	
Model 4			
All	0.99 (0.93, 1.05)	0.92 (0.84, 1.02)	0.4206
Basic	0.99 (0.90, 1.09)	0.99 (0.85, 1.15)	0.7808
Secondary	0.96 (0.87, 1.07)	0.87 (0.74, 1.02)	0.3242
Lower tertiary	0.99 (0.84, 1.17)	0.87 (0.68, 1.13)	0.2737
Higher tertiary	1.11 (0.75, 1.62)	0.85 (0.47, 1.54)	0.2919
p-value education*PGS[2]	0.7935	0.6132	

Model 1=age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch

Model 2=Model 1 + education (only for the analyses including all men and women) + occupational based social class + incomes

Model 3=Model 2 + BMI + SBP + HDL-cholesterol + total cholesterol

Model 4=Model 2 + BMI + SBP + HDL-cholesterol + total cholesterol + smoking status + alcohol consumption

[1]P-value of interaction between sex and PGS_{EDU} within each educational category.

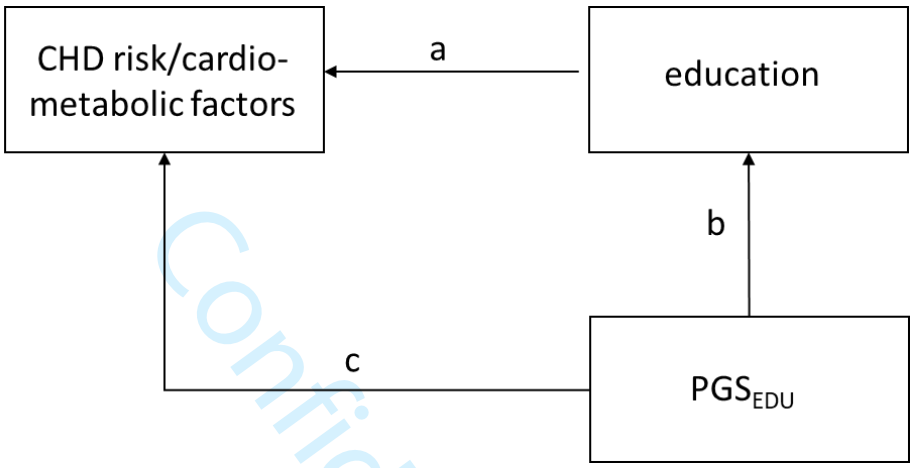
[2]P-value of interaction between categorical education and PGS_{EDU}.

Abbreviations: BMI, body mass index; CI, confidence interval, DBP, diastolic blood pressure; HDL, high density lipoprotein; LL, lower limit; PGS, polygenic score; SBP, systolic blood pressure; UL, upper limit

Table 4. Direct and indirect effects of the PGS of education on cardiometabolic factors and CHD risk.[1]

	Education (mediator)	PGS_{EDU}		
	Effect on outcome	Direct effect on outcome	Indirect effect on outcome via mediator	%[3]
	β/HR[2] (95% CI)	β/HR[2] (95% CI)	β/HR[2] (95% CI)	
Males				
BMI	-0.36 (-0.43, -0.29)	-0.19 (-0.26, -0.13)	-0.09 (-0.11, -0.07)	32
SBP	-1.20 (-1.49, -0.90)	-0.57 (-0.83, -0.30)	-0.29 (-0.37, -0.22)	34
DBP	-0.48 (-0.67, -0.28)	-0.19 (-0.36, -0.01)	-0.12 (-0.16, -0.07)	39
HDL cholesterol	0.98 (0.38, 1.58)	0.44 (-0.10, 0.98)	0.24 (0.09, 0.39)	35
Total cholesterol	-7.70 (-9.60, -5.80)	-1.50 (-3.22, 0.21)	-1.89 (-2.37, -1.41)	56
CHD risk[4]	0.85 (0.83, 0.87)	0.92 (0.90, 0.94)	0.96 (0.95, 0.97)	51
Females				
BMI	-0.66 (-0.74, -0.58)	-0.33 (-0.40, -0.26)	-0.17 (-0.19, -0.14)	34
SBP	-1.57 (-1.86, -1.28)	-0.67 (-0.92, -0.42)	-0.40 (-0.47, -0.32)	37
DBP	-0.40 (-0.57, -0.22)	-0.39 (-0.54, -0.23)	-0.10 (-0.14, -0.06)	20
HDL cholesterol	2.00 (1.35, 2.65)	1.21 (0.64, 1.77)	0.50 (0.34, 0.67)	29
Total cholesterol	-6.43 (-8.14, -4.72)	-0.32 (-1.81, 1.16)	-1.62 (-2.06, -1.18)	84
CHD risk[4]	0.75 (0.73, 0.76)	0.95 (0.93, 0.97)	0.93 (0.92, 0.94)	59

[1]All variables are adjusted for age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch. See Supplementary figure 1 for the model used to estimate direct and indirect effects.
[2]β-coefficients for cardiometabolic factors and HRs for CHD risk.
[3]The proportion of indirect effect in relation to total effect.
[4]CHD risk is estimated by using log-hazards in the statistical model and then taking antilogarithm to produce HR.
Abbreviations: BMI, body mass index; CHD, coronary heart disease, CI, confidence interval, DBP, diastolic blood pressure, HR, hazard ratio; LL, lower limit, PGS, polygenic score, SBP, systolic blood pressure UL, upper limit



Supplementary figure 1. Structural equation model used to estimate direct and indirect effects of PGS_{EDU} and education on cardiometabolic factors and CHD risk. Estimating effects: the direct effect of education=a, the direct effect of PGS_{EDU}=c, the indirect effect of PGS_{EDU}=b*a. All variables are adjusted for age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch (not shown in the figure).

Supplementary table 1. Distribution of participants, person follow-up years, coronary heart disease incidence cases and incidence ratios by education and sex.

	Men				Women			
	%	person years	CHD cases	cases/1000 person years	%	person years	CHD cases	cases/1000 person years
All	100	216509	1193	5.51	100	262739	523	1.99
Basic	24	53624	516	9.62	20	57197	229	4.00
Secondary	42	89403	438	4.90	38	98411	193	1.96
Lower tertiary	23	49139	184	3.74	29	74367	79	1.06
Higher tertiary	11	24344	55	2.26	13	32764	22	0.67

Supplementary table 2. Descriptive statistics of cardiometabolic factors by education and sex.

	Men		Women	
	mean	SD	mean	SD
BMI (kg/m^2)				
All	27.1	4.01	26.3	4.90
Basic	27.8	4.20	27.8	5.11
Secondary	27.1	4.05	26.6	4.95
Lower tertiary	26.9	3.77	25.7	4.66
Higher tertiary	25.9	3.56	24.4	4.02
SBP (mmHg)				
All	135	16.7	130	18.6
Basic	140	18.1	138	19.9
Secondary	135	16.2	130	18.3
Lower tertiary	134	16.0	127	17.0
Higher tertiary	131	14.8	122	15.7
DBP (mmHg)				
All	83.3	10.94	78.6	10.51
Basic	85.0	10.98	81.3	10.48
Secondary	83.0	11.02	78.7	10.48
Lower tertiary	83.0	10.73	77.7	10.33
Higher tertiary	81.0	10.37	75.8	10.07
HDL cholesterol (mmol/L)				
All	1.30	0.33	1.57	0.37
Basic	1.28	0.34	1.55	0.38
Secondary	1.30	0.33	1.56	0.37
Lower tertiary	1.30	0.32	1.58	0.37
Higher tertiary	1.33	0.32	1.62	0.35
Total cholesterol (mmol/L)				
All	5.55	1.08	5.45	1.03
Basic	5.72	1.11	5.80	1.06
Secondary	5.56	1.08	5.47	1.03
Lower tertiary	5.47	1.03	5.31	0.98
Higher tertiary	5.33	1.02	5.18	0.93

Supplementary table 3. Interaction parameters of regression and Poisson regression models using men and basic education as the reference categories.

	Estimate	95% confidence intervals	
		LL	UL
BMI[1] (kg/m^2)			
Secondary	-0.52	-0.78	-0.26
Lower tertiary	-1.02	-1.29	-0.74
Higher tertiary	-1.28	-1.59	-0.97
SBP[1] (mmHg)			
Secondary	-2.53	-3.52	-1.54
Lower tertiary	-3.47	-4.53	-2.41
Higher tertiary	-4.24	-5.46	-3.02
DBP[1] (mmHg)			
Secondary	-0.55	-1.14	0.04
Lower tertiary	-0.85	-1.49	-0.20
Higher tertiary	-0.45	-1.21	0.32
HDL cholesterol[1] (mmol/L)			
Secondary	-0.01	-0.03	0.01
Lower tertiary	0.02	-0.01	0.04
Higher tertiary	0.02	0.00	0.05
Total cholesterol[1] (mmol/L)			
Secondary	-0.17	-0.23	-0.11
Lower tertiary	-0.17	-0.23	-0.11
Higher tertiary	-0.13	-0.20	-0.05
CHD incidence[2] (cases/1000 persons years)			
Secondary	0.87	0.69	1.09
Lower tertiary	0.80	0.59	1.08
Higher tertiary	0.89	0.53	1.50

[1]Regression coefficients based on regression models adjusted for the control variables (age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch)
[2]Incident rate ratios based on Poisson regression models adjusted for the control variables (age, age squared, 10 first principal components of population structure, region of residence, and the combination of data collection and genotyping batch)