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Height, social position, and coronary heart disease incidence: the contribution of genetic and environmental factors

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Abstract

Background: The associations between height, socioeconomic position (SEP) and coronary heart disease (CHD) incidence are well established, but the contribution of genetic factors to these associations is still poorly understood. We used a polygenic score (PGS) for height to shed light on these associations.

Methods: Finnish population-based health surveys in 1992–2011 (response rates 65–93%) were linked to population registers providing information on SEP and CHD incidence until 2019. The participants (N=29,996; 54% women) were aged 25–75 at baseline, and there were 1,767 CHD incident cases (32% in women) during 472,973 person years of follow-up. PGS-height was calculated based on 33,938 single nucleotide polymorphisms, and residual height was defined as the residual of height after adjusted for PGS-height in a linear regression model. Hazard ratios (HR) of CHD incidence were calculated using Cox regression.

Results: Both PGS-height and residual height showed clear gradients for education, social class and income, with a stronger association for residual height. Residual height also showed stronger association with CHD incidence (HRs per 1 SD 0.94 in men and 0.87 in women) than PGS-height (HRs per 1 SD 0.97 and 0.99, respectively). All SEP indicators showed a clear gradient for CHD incidence, but only a small fraction of the associations were statistically explained by the height indicators (6% or less).

Conclusions: Residual height shows a stronger association with SEP than PGS-height and is also more strongly associated with CHD incidence. This supports the role of material and social living conditions in childhood as contributing to the association of height with both SEP and CHD risk.

What is already known on this topic

● Height is associated with social position and CHD incidence.

What this study adds

● Genetic propensity for height – as measured by a polygenic score for height – showed a robust social gradient but only a weak association with CHD incidence.

● Height residuals adjusted for the genetic propensity showed stronger associations with social position and CHD incidence than the genetic propensity for height.

How this study might affect research

● Our results of strong associations of residual height with social position and CHD incidence are consistent with the idea that height reflects living conditions during neonatal development, childhood and adolescence.

● Even though both PGS-height and residual height showed clear SEP gradients and residual height was also associated with CHD incidence, they only made a negligible contribution to social inequalities in CHD risk.

Introduction

The higher risk of coronary heart disease (CHD) in those of lower socioeconomic position (SEP) is well established in high income societies (1). In addition to behavioral factors (2), material deprivation in childhood may affect CHD risk and thus contribute to social inequalities in CHD (3). However, since reliable direct measures of early life material deprivation are seldom available in epidemiological studies, an important part of this evidence is based on surrogate measures, such as height. At the population level, adult height has been found to strongly correlate with the standard of living and population nutrition (4). In addition, those of lower SEP have, on average, shorter stature than those of higher SEP (5). Short stature is also associated with increased CHD risk (6,7). This suggests that height can capture environmental variation that is potentially important for the explanation of social inequalities in CHD. However, a limitation in many previous studies looking at height, SEP and CHD risk is that they ignore the role of genetic factors. Between 65 to 85% of population variation in adult height at a particular place and time is explained by genetic factors when estimated using twin designs (8), and thousands of genetic variants have been identified that associate with adult stature in genome-wide-association studies (GWAS) (9). Previous studies have also shown that the polygenic score (PGS) of height is associated with SEP (10) and CHD risk (11). Thus, the contribution of genetic factors to these associations needs to be considered.

Figure 1 summarizes the underlying causal pathways behind the associations between height, SEP and CHD risk expected based on previous studies. Childhood environment can affect height (12), SEP (13) and CHD risk (3). Genetic factors can affect height directly through, e.g., growth plate chondrocytes of long bones (14) but also indirectly through influencing childhood nutrition, as indicated by genetic correlations between childhood height and skinfold thickness measures (15).

Further, genetic factors can affect SEP (10) and CHD risk (11) whereas height can affect SEP (16) which can further affect CHD risk (17).

In this study, we summarized the genetic factors affecting height as the PGS of height (hereafter referred as PGS-height). The childhood environment cannot, however, be estimated directly since it is not possible to measure all potential environmental exposures affecting height (18). Thus, we calculated the residuals of height adjusted for PGS-height (hereafter referred to as residual height), which indexes environmental variation of height, in addition to genetic height variation not captured by PGS-height and measurement error. Based on these assumptions, we made the following study hypotheses: i) Both PGS-height and residual height are associated with SEP and CHD risk. ii) These associations are stronger for residual than PGS-height indicating that environmental factors affecting growth make a major contribution to both SEP and increased CHD risk. iii) Adjusting for these height indicators will attenuate SEP inequalities in CHD risk, with greater attenuation resulting from adjustment for residual compared to PGS-height.

Data and methods

Several Finnish population-based health surveys – FINRISK surveys conducted in 1992, 1997, 2002, 2007 and 2012 and Health 2000/2011 surveys – were pooled together to create the baseline study cohort (19). The response rates in these surveys varied between 65% and 93%. Height was measured at the baseline health examinations, and at the same time the participants gave a blood sample used for genotyping and metabolic measures. PGS-height was based on the LASSO-weighted GWAS scores from the GWAS of height (20), which included 33,938 single nucleotide polymorphisms (SNP) selected using the p-value threshold of 0.05. Birth year and the square of birth year explained 8% of height variation in men and 9% in women. After these adjustments, the

PGS-height explained an additional 29% of height variation both in men and women (r^2 totaling 0.37 and 0.38). Residual height was calculated from a regression model for height with PGS-height as the independent variable for men and women separately.

The baseline measurements were linked to Finnish population registers using unique personal identification codes that were pseudonymized before releasing data to the research team. We used education, occupation-based social class and income as the SEP indicators. Education and 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). Social class was measured at the age of 40 or 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) (21). 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 non-linear associations.

We restricted the participants to those born between 1935 and 1980 due to the availability of the measures of SEP indicators given the age restrictions. Thus, the participants were between 25 and 76 years of age at baseline of each data collection. Information for education and income was available at every five years between 1970 and 1985 and yearly between 1987 and 2019. Information on social class was available at every five years between 1970 and 2005 and yearly between 2006 and 2018. Together, we had 36,418 participants in the selected birth cohorts, among whom 32,074 had genotype data available. However, 641 participants had missing information on height or on SEP indicators and were thus removed. Further, we removed randomly one individual

from pairs with identity-by-descent (IBD) value ≥ 0.178 (N=1,435), corresponding to the expected lower bound of second-degree relatives. Thus, in the analyses on the association between height and the SEP indicators, we had 29,996 participants (54% women). In the main analyses, the height indicators were standardized (mean=0, standard deviation (SD)=1) in men and women separately.

The longitudinal information on CHD incidence cases was based on the Hospital Discharge Register for non-fatal (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 whole Finnish population. When analyzing CHD incidence, we also used information on a number of risk factors of CHD. Body mass index (BMI), systolic and diastolic blood pressure, total cholesterol and high-density lipoprotein cholesterol were measured in the baseline clinical examination. Smoking classified as current, former and never smokers was asked in a self-administrated questionnaire at baseline. In these analyses, we removed additional 327 participants having pre-baseline CHD event and 200 participants having missing information on any of these risk factors of CHD. Thus, we had 29,499 participants for the CHD incidence analyses among whom there were 1767 incident CHD cases (27% fatal cases and 32% in women) during the 472,973 person years until the end of follow-up on December 31st 2019. The distributions of participants and CHD incidence by the SEP indicators are presented in Supplementary table 1 and the means of the three height indicators in Supplementary table 2.

We first estimated the associations of SEP indicators (education, social class and income) with height indicators (height, PGS-height and residual height) using linear regression models. The results can be interpreted as difference in height indicators between the SEP categories, but they do not imply causal associations between the variables. Second, we analyzed how these SEP and

height indicators were associated with CHD incidence using Cox regression. Those who died from other causes of death than CHD during the follow-up were censored at the time of death. Cox proportional hazards assumptions appeared not to be violated when examined graphically (Kaplan-Meier curves available from the corresponding author). Additionally, we calculated population attributable fractions (PAF), which indicate the proportion of CHD cases that would be avoided had the higher risk SEP categories the same CHD risk as the lowest risk SEP category.

All statistical models were adjusted for the first 10 principal components of genetic population structure, five geographic areas of residence, and the combination of baseline year and genotyping batch dummies. These adjustments help to minimize the impact of geographic differences in genetic structure, CHD incidence, height and SEP in the Finnish population. In the linear regression models, we adjusted for birth year and the square of birth year to account for the secular increase in height, change in social class structure and educational expansion in the Finnish population. In Cox regression models, the analyses were adjusted for age and squared age at baseline as well as baseline year dummies. The genetic principal components, IBD values and PGS-height were calculated by the PLink 1.9 software. The statistical models were conducted using Stata, version 16.1.

Results

Table 1 and 2 present the mean differences of height indicators in SD units between SEP categories calculated by linear regression models in men and women, respectively. Height, PGS-height and residual height were greatest in the uppermost SEP categories, i.e., in those with higher tertiary education, upper non-manual workers and the highest income quintile when adjusted for birth year and region indicators (Model 1). Generally, all height indicators showed SEP gradients

systematically decreasing to the lowest categories. However, residual height showed systematically larger differences between the SEP categories as compared to PGS-height. For example, when residual height was 0.34 SD (95% CI 0.28–0.49) higher in those men and 0.33 SD (95% CI 0.27–0.38) higher in those women having higher tertiary education as compared to the basic education category, the differences in PGS-height were only 0.18 SD (95% CI 0.12–0.24) and 0.20 SD (95% CI 0.15–0.26), respectively. Similar differences between residual height and PGS-height were found for all SEP indicators in men and women. Model 2 includes SEP indicators simultaneously adjusted with each other. The parameter estimates decreased as compared to Model 1. However, all SEP indicators still showed gradients for height, PGS-height and residual height. Also in this model, residual height showed larger SEP differences than PGS-height.

After the analyses of SEP differences of height indicators, we studied how these SEP and height indicators were associated with CHD incidence. We found that in men (Table 3) and women (Table 4) there were clear gradients in CHD incidence according to all SEP indicators. When added into the model separately, height and residual height were associated with CHD incidence with similar effect sizes among both men and women; for PGS-height, this association was weak (Model 1). The adjustment for genetic and residual height (Model 2) explained only a small fraction of social inequalities in CHD incidence (0 – 6% indexed by PAF) whereas other risk factors for CHD (Model 3) explained a more substantial proportion (19 – 39%). When all SEP indicators were included in the model (Model 4), education in men and social class in women showed the largest inequalities in CHD risk. Metabolic risk factors of CHD showed negative correlations with all height indicators (Supplementary table 3). Adjusting the results for metabolic and social risk factors of CHD diminished the associations of height and residual height with CHD incidence whereas for PGS-height the association was essentially null (Model 4).

Discussion

In this study, we found that both PGS-height and residual height, defined as the residual of height adjusting for PGS-height, showed clear gradients according to education, occupation-based social class and income. The gradients were also found when mutually adjusting for all SEP indicators suggesting that they capture different social dimensions relevant for height. Residual height was also inversely associated with CHD incidence. For PGS-height this association was weaker and totally explained by metabolic and social risk factors of CHD. Our results concerning PGS-height are consistent with the studies based on the UK Biobank also finding associations between PGS-height and several SES indicators (10). However, we could not replicate the results in the UK Biobank on the association between PGS-height and CHD incidence (11) found also within sibling pairs (22). Uniquely, we showed that these height associations were systematically stronger when measured height was adjusted for the known genetic variants for height and the residuals taken from this supporting the role of environmental factors behind the associations of height with SEP and CHD risk. It is noteworthy that PGS-height explained only around a third of height variation in men and women, which is half or less of the heritability of adult height in these birth cohorts when estimated using twin modeling (8). Residual height thus also partly reflects unknown genetic variation as well as measurement error, in addition to environmental variation. Nevertheless, the stronger residual height than PGS-height associations with SEP and CHD incidence suggest that environmental rather than genetic factors affecting growth are driving the association of height with lower SEP and increased CHD risk.

The reasons why PGS-height is associated with SEP is not clear. A large study of Swedish conscripts found that height in early adulthood predicted further achievement of higher education after adjustment for parental social position and own cognitive ability, a result which is consistent

with the causal hypothesis (16). The association between height and social position can originate from positive stereotypes related to tall stature which could help proceed in educational and occupational careers and thus create a positive correlation between height and social position; however, empirical evidence is still mixed (23). However, previous twin studies have found genetic correlations between height and cognitive ability (24–26) as well as education (27). It is thus possible that there are, for example, hormonal mechanisms jointly affecting growth and cognitive development. It is also possible that PGS-height captures environmental variation which underlines the associations with social position and CHD incidence. However, this explanation was not supported in a recent study reporting that the association between PGS-height and measured height was roughly similar within sibling pairs than it was at population level (28).

Although we could not empirically assess factors driving the associations of residual height with SEP and CHD risk, their effect is likely to start early in the life course or even prenatally. In a study including undernourished pregnant mothers, energy supplementation increased the height of neonates (29). Further, environmental factors during the first two years of life seem to be important for growth strongly affecting later height differences (30). For nutrition, protein is considered the most important macro-nutrient needed for growth, but it also requires balanced micronutrients, and childhood infections can also delay growth (12). Thus, detailed longitudinal measures of childhood nutrition and health would be crucial to better understand the environmental factors behind height variation.

Even when we found that both PGS-height and residual height showed clear SEP gradients and residual height was also associated with CHD incidence, they had only a negligible contribution to social inequalities in CHD risk. Basic metabolic risk factors and smoking measured at baseline explained nearly ten times more of SEP inequalities in CHD risk than these two height indicators

together. Thus, even when there is a large body of literature concerning social inequalities in CHD risk (1), social height differences (5), and the associations between height and CHD risk (6,7), caution is needed when evaluating whether height can provide meaningful additional information on early life to explain social inequalities in CHD risk.

Our data have both strengths and limitations. The strength of our data was the large sample size that allowed us to estimate the associations reliably. Information on all SEP indicators was register based and therefore not prone to recall bias, which may be a problem in previous studies. Our data also allowed us to index SEP at the same age, thus decreasing heterogeneity in our analyses. The main limitation of our data was that we had only information on adult stature. The association between height in childhood and CHD in adulthood becomes weaker when children become older because of higher CHD incidence among children experiencing catch-up growth (31). Thus, height measured in early childhood may capture the effect of childhood environmental factors better than adult height. Further, there is evidence that leg length is more sensitive to the effects of environmental factors (32) and predict CHD risk better than overall stature (33); thus, this information may have produced stronger associations. Since height was measured at baseline, shrinkage may have affected the results. However, only 2% of participants were older than 70 years at baseline, and only after this age is any substantial shrinking observed (34). Selective mortality according to SEP and height and typically higher participation rates of those with high SEP may have leaded to selection bias in our data (35). However, the high response rates for the baseline surveys and lack of loss to follow-up because of relying on register-based CHD incidence data helped to minimize other influences of selection bias in our study. If selection bias affects our results, it would likely decrease variation and make our results more conservative. Finally, our results should not be directly generalize to other populations having a different distribution of

stressors in childhood. Thus, replication of these results in populations with various standards of living, nutrition and other environmental factors in childhood would be important.

In conclusion, we found strong evidence that genetic polymorphisms associated with height are also associated with social position. We also found suggestive evidence that environmental factors affecting height are more common in disadvantages SEP groups and increase CHD risk. However, since these associations were not very strong, height did not explain much of the social inequalities in CHD risk. Overall, our finding of an association of residual height with social indicators and CHD is consistent with the idea that height reflects material and social living conditions in childhood.

Ethics approval

The Finnish Social and Health Data Permit Authority (Findata) has accepted the use of clinical data (THL/4725/14.02.00/2020) and the data linkage to the Finnish population registers (TK-53-876-20). All participants gave informed consent when participating in the study. The samples/data used for the research were obtained from THL Biobank (study number: THLBB2020_8). We thank all study participants for their generous participation at THL Biobank.

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Sample Data Availability Statements

The data underlying this article were provided by third party by permission. Data will be shared on request to the corresponding author with permission of third party.

Conflicts of interests

None declared.

Author contributions

All authors contributed to the study conception and design. HL performed the analyses. KS prepared the first draft of the manuscript. HL, GDS, TM and PM revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work thereby ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure legends

Figure 1. Possible pathways between height, socio-economic position (SEP) and coronary heart disease (CHD).

Table 1. Differences by 1 standard deviation of height, PGS-height and residual height between classes of social position indicators in men.

	Model 1									Model 2								
	Height			PGS-height			Residual height			Height			PGS-height			Residual height		
	β	95% CI		β	95% CI		β	95% CI		β	95% CI		β	95% CI		β	95% CI	
		LL	UL		LL	UL		LL	UL		LL	UL		LL	UL		LL	UL
Education																		
Basic	0.00			0.00			0.00			0.00			0.00			0.00		
Secondary	0.10	0.06	0.14	0.07	0.03	0.11	0.07	0.03	0.11	0.08	0.04	0.13	0.07	0.03	0.11	0.06	0.02	0.10
Lower tertiary	0.28	0.23	0.32	0.16	0.11	0.21	0.23	0.18	0.27	0.19	0.14	0.25	0.15	0.09	0.20	0.13	0.08	0.19
Higher tertiary	0.38	0.32	0.44	0.18	0.12	0.24	0.34	0.28	0.40	0.24	0.17	0.31	0.13	0.06	0.20	0.20	0.13	0.27
Social class																		
Manual	0.00			0.00			0.00			0.00			0.00			0.00		
Lower non-manual	0.12	0.07	0.16	0.01	-0.03	0.05	0.13	0.09	0.17	0.02	-0.03	0.06	-0.05	-0.10	-0.01	0.05	0.01	0.10
Upper non-manual	0.30	0.26	0.35	0.14	0.10	0.19	0.27	0.23	0.31	0.11	0.05	0.16	0.03	-0.03	0.09	0.11	0.05	0.16
Entrepreneurs	0.08	0.02	0.14	0.08	0.02	0.14	0.04	-0.01	0.10	0.05	-0.01	0.11	0.06	0.00	0.12	0.02	-0.04	0.08
Farmers	0.13	0.07	0.19	0.12	0.06	0.19	0.08	0.01	0.14	0.16	0.09	0.22	0.14	0.07	0.21	0.10	0.03	0.16
Income																		
Lowest quintile	0.00			0.00			0.00			0.00			0.00			0.00		
4. quintile	0.00	-0.07	0.06	-0.01	-0.07	0.05	0.00	-0.06	0.06	0.01	-0.05	0.07	0.00	-0.06	0.07	0.01	-0.05	0.07
3. quintile	0.00	-0.06	0.06	-0.01	-0.07	0.05	0.01	-0.05	0.06	0.03	-0.03	0.09	0.02	-0.04	0.08	0.02	-0.04	0.08
2. quintile	0.11	0.06	0.16	0.05	-0.01	0.10	0.10	0.05	0.15	0.12	0.06	0.17	0.07	0.01	0.13	0.09	0.04	0.15
Highest quintile	0.26	0.21	0.31	0.12	0.06	0.17	0.23	0.18	0.28	0.17	0.12	0.23	0.09	0.04	0.15	0.15	0.09	0.20

Model 1: SEP indicators separately adjusted by year of birth (1935=0), year of birth squared, region of residence, ten first principal components of the genetic structure and genotyping batch-data collection round combination. Model 2: Model 1+ education, social class and income.

Table 2. Differences by 1 standard deviation of height, genetic height and residual height between classes of social position indicators in women.

	Model 1									Model 2								
	Height			PGS-height			Residual height			Height			PGS-height			Residual height		
	β	95% CI		β	95% CI		β	95% CI		β	95% CI		β	95% CI		β	95% CI	
		LL	UL		LL	UL		LL	UL		LL	UL		LL	UL		LL	UL
Education																		
Basic	0.00			0.00			0.00			0.00			0.00			0.00		
Secondary	0.12	0.08	0.16	0.08	0.04	0.13	0.09	0.05	0.13	0.11	0.07	0.15	0.08	0.04	0.12	0.08	0.03	0.12
Lower tertiary	0.28	0.23	0.32	0.14	0.09	0.19	0.24	0.20	0.29	0.22	0.17	0.26	0.13	0.08	0.18	0.17	0.13	0.22
Higher tertiary	0.39	0.33	0.44	0.20	0.15	0.26	0.33	0.27	0.38	0.27	0.20	0.34	0.17	0.10	0.24	0.21	0.14	0.28
Social class																		
Manual	0.00			0.00			0.00			0.00			0.00			0.00		
Lower non-manual	0.13	0.10	0.17	0.06	0.03	0.10	0.12	0.08	0.15	0.06	0.02	0.09	0.03	-0.01	0.07	0.04	0.01	0.08
Upper non-manual	0.29	0.24	0.33	0.13	0.09	0.18	0.26	0.21	0.30	0.10	0.04	0.15	0.05	-0.01	0.10	0.09	0.03	0.14
Entrepreneurs	0.15	0.08	0.21	0.10	0.04	0.17	0.11	0.04	0.17	0.11	0.04	0.18	0.09	0.02	0.16	0.07	0.00	0.14
Farmers	0.04	-0.03	0.11	0.08	0.01	0.15	-0.01	-0.08	0.07	0.05	-0.02	0.12	0.09	0.01	0.16	0.00	-0.07	0.07
Income																		
Lowest quintile	0.00			0.00			0.00			0.00			0.00			0.00		
4. quintile	0.04	0.00	0.08	0.02	-0.02	0.07	0.03	-0.01	0.07	0.04	0.00	0.08	0.03	-0.01	0.08	0.03	-0.01	0.07
3. quintile	0.12	0.07	0.16	0.04	-0.01	0.08	0.11	0.07	0.16	0.08	0.04	0.13	0.03	-0.02	0.07	0.08	0.04	0.12
2. quintile	0.20	0.15	0.24	0.04	-0.01	0.09	0.21	0.16	0.25	0.11	0.06	0.16	0.00	-0.05	0.05	0.13	0.08	0.18
Highest quintile	0.30	0.25	0.36	0.14	0.08	0.19	0.27	0.22	0.33	0.16	0.10	0.22	0.06	0.00	0.13	0.15	0.08	0.21

Model 1: SEP indicators separately adjusted by year of birth (1935=0), year of birth squared, region of residence, ten first principal components of the genetic structure and genotyping batch-data collection round combination. Model 2: Model 1+ education, social class and income.

Table 3. Hazard ratios (HR) of social position indicators, genetic height and residual height for coronary heart disease incidence in men.

	Model 1			Model 2			Model 3			Model 4		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
		LL	UL		LL	UL		LL	UL		LL	UL
Education												
Basic	1.88	1.44	2.47	1.86	1.41	2.44	1.49	1.13	1.96	1.46	1.05	2.03
Secondary	1.71	1.31	2.24	1.69	1.29	2.21	1.41	1.07	1.85	1.39	1.01	1.92
Lower tertiary	1.21	0.91	1.62	1.20	0.90	1.61	1.07	0.80	1.43	1.11	0.81	1.50
Higher tertiary	1.00			1.00			1.00			1.00		
PAF[a]	0.38	0.21	0.51	0.37	0.20	0.51	0.26	0.05	0.42	0.25	0.01	0.44
Social class												
Manual	1.46	1.23	1.73	1.44	1.21	1.71	1.26	1.06	1.51	0.97	0.77	1.22
Lower non-manual	1.12	0.91	1.37	1.11	0.90	1.35	1.02	0.84	1.25	0.89	0.71	1.11
Upper non-manual	1.00			1.00			1.00			1.00		
Entrepreneurs	1.47	1.14	1.88	1.45	1.13	1.86	1.26	0.98	1.62	0.95	0.72	1.26
Farmers	1.25	0.96	1.61	1.23	0.95	1.59	1.19	0.92	1.54	0.80	0.59	1.08
PAF[a]	0.22	0.11	0.32	0.21	0.10	0.31	0.14	0.01	0.25	-0.06	-0.28	0.12
Income												
Lowest quintile	1.79	1.49	2.15	1.77	1.47	2.13	1.57	1.31	1.89	1.47	1.20	1.80
4. quintile	1.42	1.17	1.72	1.39	1.15	1.70	1.28	1.06	1.56	1.18	0.95	1.45
3. quintile	1.16	0.97	1.39	1.15	0.96	1.37	1.06	0.89	1.27	0.96	0.79	1.16
2. quintile	1.25	1.07	1.46	1.24	1.06	1.45	1.18	1.01	1.38	1.09	0.92	1.28
Highest quintile	1.00			1.00			1.00			1.00		
PAF[a]	0.18	0.11	0.25	0.18	0.10	0.24	0.14	0.06	0.21	0.08	-0.01	0.17
Height[b]	0.94	0.88	1.00							0.98	0.92	1.04
PGS-height[b]	0.99	0.93	1.05							1.02	0.96	1.08
Residual height[b]	0.94	0.88	1.00							0.97	0.91	1.03

Model 1: SEP and height indicators added into the model separately+ age at baseline + age at baseline squared region of residence + ten first principal components of the genetic structure + genotyping batch-data collection round (=baseline year) combination. Model 2: Model 1 + PGS-height + residual height. Model 3: Model 2 + smoking status+ body mass index + systolic blood pressure + diastolic blood pressure + high-

density lipoprotein (HDL) cholesterol + total cholesterol. Model 4: Model 3+all SEP indicators (height indicators)/all SEP indicators+PGS-height+residual height (SES indicators)

[a] Population attributable fractions for CHD incidence for the socio-economic variables indicate the proportion of CHD cases that would be avoided had the higher risk SEP categories the same CHD risk as the lowest risk SEP category.

[b]HRs calculated per 1 standard deviation.

Table 4. Hazard ratios (HR) of social position indicators, genetic height and residual height for coronary heart disease incidence in women.

	Model 1			Model 2			Model 3			Model 4		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
		LL	UL		LL	UL		LL	UL		LL	UL
Education												
Basic	1.85	1.21	2.83	1.77	1.16	2.71	1.44	0.94	2.22	0.98	0.58	1.68
Secondary	1.44	0.94	2.20	1.40	0.91	2.13	1.20	0.79	1.84	0.84	0.50	1.41
Lower tertiary	1.07	0.68	1.67	1.06	0.67	1.66	0.98	0.62	1.54	0.78	0.47	1.30
Higher tertiary	1.00			1.00			1.00			1.00		
PAF[a]	0.33	0.01	0.54	0.31	-0.02	0.53	0.20	-0.18	0.46	-0.12	-0.81	0.31
Social class												
Manual	1.96	1.40	2.72	1.88	1.35	2.62	1.65	1.18	2.30	1.43	0.94	2.18
Lower non-manual	1.62	1.18	2.22	1.58	1.15	2.18	1.45	1.05	2.00	1.34	0.91	1.98
Upper non-manual	1.00			1.00			1.00			1.00		
Entrepreneurs	1.41	0.86	2.32	1.37	0.83	2.26	1.16	0.70	1.92	1.06	0.62	1.84
Farmers	1.90	1.26	2.88	1.83	1.21	2.77	1.63	1.07	2.48	1.47	0.90	2.41
PAF[a]	0.39	0.20	0.53	0.38	0.18	0.52	0.31	0.10	0.48	0.25	-0.06	0.47
Income												
Lowest quintile	1.64	1.08	2.50	1.58	1.04	2.41	1.43	0.94	2.17	1.19	0.74	1.92
4. quintile	1.83	1.21	2.78	1.76	1.16	2.67	1.61	1.06	2.44	1.33	0.82	2.14
3. quintile	1.58	1.03	2.42	1.54	1.01	2.36	1.45	0.95	2.23	1.25	0.78	2.01
2. quintile	1.19	0.74	1.89	1.17	0.74	1.87	1.12	0.70	1.79	1.03	0.63	1.69
Highest quintile	1.00			1.00			1.00			1.00		
PAF[a]	0.36	0.08	0.56	0.35	0.05	0.55	0.29	-0.03	0.51	0.18	-0.26	0.46
Height[b]	0.87	0.79	0.96							0.91	0.82	1.00
PGS-height[b]	0.97	0.89	1.06							0.99	0.91	1.09
Residual height[b]	0.87	0.79	0.95							0.90	0.82	0.99

Model 1: SES and height indicators added into the model separately+ age at baseline + age at baseline squared region of residence + ten first principal components of the genetic structure + genotyping batch-data collection round (=baseline year) combination. Model 2: Model 1 + PGS-height + residual height. Model 3: Model 2 + smoking status+ body mass index + systolic blood pressure + diastolic blood pressure + high-

density lipoprotein (HDL) cholesterol + total cholesterol. Model 4: Model 3+all SEP indicators (height indicators)/all SEP indicators+PGS-height+residual height (SEP indicators)

[a] Population attributable fractions for CHD incidence for the socio-economic variables indicate the proportion of CHD cases that would be avoided had the higher risk SEP categories the same CHD risk as the lowest risk SEP category.

[b]HRs calculated per 1 standard deviation.