

Birth weight and adult income: An examination of mediation through adult height and body mass

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Abstract

This paper examines the causal links between early human endowments and socioeconomic outcomes in adulthood. We use a genotyped longitudinal survey (Cardiovascular Risk in Young Finns Study) that is linked to the administrative registers of Statistics Finland. We focus on the effect of birth weight on income via two anthropometric mediators: body mass index (BMI) and height in adulthood. We find that (i) the genetic instruments for birth weight, adult height, and adult BMI are statistically powerful; (ii) there is a robust total effect of birth weight on income for men but not for women; (iii) the total effect of birth weight on income for men is partly mediated via height but not via BMI; and (iv) the share of the total effect mediated via height is substantial, of approximately 56%.

KEYWORDS

birth weight, body mass index, height, income, mediation, multivariable Mendelian randomization, polygenic instrument

1 | INTRODUCTION

Birth weight is a widely used measure of the early health status of infants (e.g., Corman et al., 2017). Low birth weight has been linked to poor health outcomes. The literature documents associations between low birth weight and various health concerns, ranging from infant illnesses to adult heart disease (e.g., Almond et al., 2018; Barker, 1995; Fonseca et al., 2019). Low birth weight has also been linked to poor cognitive performance and educational disadvantages in

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childhood (e.g., Cheadle & Goosby, 2010; Figlio et al., 2014; Maruyama & Heinesen, 2020) and to weaker educational and labor market outcomes in adulthood (e.g., Behrman and Rosenzweig, 2004; Black et al., 2007; Cook & Fletcher, 2015).

The direct economic costs of low birth weight to society are large. Preterm and low birthweight infants incur some of the highest healthcare expenditures of any population. For example, Beam et al. (2020), using data on 763,566 infants, documented that infants with a preterm status (<37 weeks) or low birthweight status (<2500 g) incurred expenditures of approximately \$76,000 and \$114,000 during the first 6 months of life, respectively. Later-life economic costs of low birth weight for an individual may also be substantial and long-lasting, though these concerns have not received much attention in prior research. Notably, an examination of possible pathways that mediate the effect of birth weight on long-term economic outcomes have not received attention, though the identification of these pathways could provide policy-relevant information for interventions.

The effect of birth weight on later-life socioeconomic outcomes is not straightforward to identify for two reasons. First, the birth weight of a child depends on the environment provided by the mother, which may affect the child's later life outcomes. This could confound the relationship between birth weight and outcomes in adulthood (Brooks et al., 1995; Kramer, 1998). Second, variations in early endowments, such as birth weight, influence later life outcomes through their effects on individuals' development of traits and behaviors. The pathways that mediate the effects over the life course are numerous, and the gene–environmental interplay potentially complicates the picture (e.g., Belsky et al., 2019; Brumpton et al., 2020; Mills & Tropf, 2020).

To address the confounding problem, a method called Mendelian randomization (MR) uses genetic markers as instruments for potentially endogenous variables (e.g., Davey Smith & Hemani, 2018; Lawlor et al., 2008). This method has gained growing interest in economic research, as genome-wide association studies (GWASs) have identified significant correlations between genetic variants and observable traits (e.g., Horikoshi et al., 2016; Belsky et al., 2016; Okbay et al., 2016). Because genetic variants are randomly assigned at conception, this “randomization by nature” leads to exogenous variations in observable traits and, under certain identification assumptions, enables causal inference (e.g., Fletcher, 2011; von Hinke et al., 2016). The research on causal effects using genetic information has inspired a multivariable Mendelian randomization (MVMR) method that uses genetic markers as instruments for the exposure and factors that may operate as mediators between exposure and later life outcomes (e.g., Burgess et al., 2015; Sanderson et al., 2019; Zheng et al., 2017).

In this paper, we build on the recent advances in MR modeling by examining the association between birth weight and later life economic success, measured by earnings during prime working-age. To this end, we use a genotyped Finnish longitudinal survey (Cardiovascular Risk in Young Finns Study [YFS]) that we link to the administrative registers of Statistics Finland. Using linked data, we contribute to the literature on two frontiers. First, we examine whether birth weight has a causal effect on labor income. As such, our study contributes to earlier sibling and twin studies on the US (Behrman & Rosenzweig, 2004), Norway (Black et al., 2007), and Japan (Nakamuro et al., 2013). Second, MVMR provides a novel method for examining the possible pathways that mediate the effect of birth weight on income. Two mediators are considered: adult body mass index (BMI) and adult height. This approach allows us to contribute to earlier research examining how the anthropometric traits of an individual track from birth weight to adulthood (e.g., Dubois et al., 2012; Ward et al., 2017) and how these traits are rewarded in the labor market (e.g., Averett, 2011; Cawley, 2015; Norton & Han, 2008; Tyrrell et al., 2016).

Our results show that the genetic instruments for birth weight and potential mediators are statistically powerful and that there is a robust effect of birth weight on income for men that is partly mediated via height. These results are robust to numerous specification checks.

2 | DATA, VARIABLES, AND METHODS

2.1 | Data

The YFS consists of randomly chosen children and adolescents from 5 university hospital districts and their rural surroundings in six age cohorts (aged 3, 6, 9, 12, 15, and 18 years in 1980). This ongoing epidemiological study began in 1980 with 3596 subjects who participated in several follow-up evaluations (Raitakari et al., 2008). The data were collected from questionnaires and physical measurements and included information regarding the participants' weight at birth. Using unique personal identifiers, we linked the YFS data to two registers of Statistics Finland: the Finnish Longitudinal Employer-Employee Data (FLEED) and the Longitudinal Population Census (LPC). The use of the linked YFS-FLEED-LPC

data was approved by Statistics Finland (permission TK-53-673-13). In the linked data, $N = 3577$, because 19 participants denied linking their YFS information to register data. The FLEED data include information on labor market outcomes, and the LPC contains information on the participants' parental backgrounds (family income and education). Appendix 1 presents the summary statistics of the study sample. Due to missing information in some variables, the size of the study sample is 1703. Appendix 2 compares the summary statistics for the total linked sample and the study sample. The proportion of individuals born in 1962 (1974) is lower (higher) in the study sample. In addition, the individuals in the study sample had, on average, higher education and earnings in 2001.

2.2 | Variables

2.2.1 | Birth weight, height, BMI, and labor market income in prime working age

Information on the YFS participants' birth weights was based on parental reports. The mean birth weight in the study sample was 3.50 kg, with a standard deviation of 0.541 kg (see Appendix 1). The average birth weight varied between 3.46 and 3.55 kg among the cohorts. The fraction of low-birth-weight children (less than 2.5 kg) was 3.6%. The fraction of high-birth-weight children (more than 4.5 kg) was 2.9%. The YFS participants' birth weights are representative of the Finnish population (National Institute for Health and Welfare, 2014). Height and weight measurements were conducted by healthcare professionals in 2001 when the participants were between 24 and 39 years of age. Using these measures, the BMI was calculated as weight (kg)/squared height (m^2).

Income is measured as the logarithm of the average annual wage and salary earnings over the 2001–2012 period. The register-based income measure is not top coded and does not suffer from underreporting or recall error. The aggregated measure is also less likely to suffer from idiosyncratic variation, which characterizes cross-sectional measures of income (Dahl et al., 2011). Information on prime working-age individuals (age ranging from 24–50 years) extends the earlier literature that has used data on middle-aged workers (Cook & Fletcher, 2015) or young adults (Black et al., 2007).

2.2.2 | Genetic instruments for birth weight and mediators

The polygenic scores (PGSs) that we use as instruments to identify causal effects are calculated as a sum of several genetic variants (single nucleotide polymorphism [SNP]) that are related to the potentially endogenous phenotype.¹ In this study we use weighted PGSs that were calculated by summing the risk alleles for each independent SNP, weighted by its effect size from the GWAS.² To maximize the strength of the instrument, we used PGSs that are based on a lenient significance threshold ($p < 0.01$). The PGS for birth weight in the YFS data is based on the GWAS of Warrington et al. (2019).³ The PGSs for height and BMI are based on the GWASs of Wood et al. (2014) and Locke et al. (2015), respectively.

2.2.3 | Additional control variables

The information on parental background (family income measured in euros, mother's years of education, and father's years of education) was drawn from the LPC from 1980. As additional control variables, we used the following biomarkers and their PGSs: waist-to-hip ratio (WHR) (Shungin et al., 2015), triglycerides, LDL cholesterol, and HDL cholesterol (Willer et al., 2013). These biomarkers were based on anthropometric measures or blood tests conducted in 2001. The information on years of education was obtained from the register-based FLEED in 2001, and its PGS was based on the GWAS of Okbay et al. (2016).

We also used the following self-reported measures of health and health behavior in the analyses: the number of chronic conditions based on physician diagnoses, the smoking status based on pack-years, and an indicator for excessive drinking pattern equal to one if the subject had suffered from a hangover at least once a month during the past year. These measures also refer to the year 2001.

2.3 | Methods

The MR method is a special case of the instrumental variables method, which uses genetic markers as instruments for potentially endogenous variables. The MR analysis is based on the assumption that genetic instruments are robustly related to the exposure (the relevance assumption) and that they are not associated with any confounders of the exposure–outcome relationship (the independence assumption). The independence assumption could be violated because of population stratification (the allele frequencies differ between population subgroups), genetic nurturing (the parental genotype indirectly affects offspring's phenotype by influencing parent's phenotype), or assortative mating (the selection of partners based on phenotype) (e.g., Brumpton et al., 2020). The third assumption, exclusion restriction, could be violated if genetic instruments affect the outcome via multiple pathways or if they are in linkage disequilibrium (i.e., co-inherited) with other genetic variants that affect the outcome via other pathways (e.g., Hemani et al., 2018; von Hinke et al., 2016).

In this paper, we identify the total effect of birth weight (BW) on income (INC) using a PGS (PGS_{BW}) as an instrument for birth weight. The MR model is estimated using the two-stage least squares (2SLS) regression consisting of the first-stage equation (Equation 1) and the second-stage structural equation (Equation 2). Omitting any additional controls, the model can be written as:

$$BW = \lambda_0 + \lambda_1 PGS_{BW} + v_1 \quad (1)$$

$$INC = \gamma_0 + \gamma_1 BW + v_2 \quad (2)$$

where the total effect of birth weight on income is given by γ_1 .

Figure 1, together with equations (1)–(5), illustrates the MVMR setup used for mediation analysis. The MVMR approach is useful in settings where the exposures of interest may be correlated and if the purpose is to examine whether one of the exposures mediates the effect of the other on the outcome (Sanderson et al., 2019, p. 715). The total effect of birth weight on income is decomposed into a direct and an indirect effect. The direct effect is the effect of birth weight on income after accounting for the mediated effects via a mediator ($M = \text{BMI, height}$). The mediation model, based on genetic instruments (PGS_{BW} for birth weight and PGS_M for the mediator) and omitting any additional controls, can be parametrized as:

$$BW = \pi_0 + \pi_1 PGS_{BW} + \pi_2 PGS_M + v_3 \quad (3)$$

$$M = \alpha_0 + \alpha_1 PGS_{BW} + \alpha_2 PGS_M + v_4 \quad (4)$$

$$INC = \beta_0 + \beta_{BW} BW + \beta_M M + v_5 \quad (5)$$

Using 2SLS, the PGSs for birth weight and the mediator are used to predict the exposure in the first-stage (Equations 3 and 4). In the second-stage (Equation 5), the outcome is regressed on the predicted values of each exposure. The direct effect of birth weight on income after controlling for the mediated effect is given by β_{BW} . The indirect effect can be calculated by the difference method by subtracting the direct effect of birth weight from the total effect ($\gamma_1 - \beta_{BW}$) (Carter et al., 2021). The confidence intervals for the indirect effects in this paper are based on bootstrapping with 1000 replications. The birth weight, mediators, and income are log-transformed; therefore, the dependent variable can be interpreted as the percentage change for a 1% increase in the independent variable.

The research design based on PGSs, anthropometric exposures, and MVMR has advantages that may mitigate the problems of MR. First, PGSs may enhance the strength of the instruments over individual SNPs. This may limit the finite sample bias toward the observational estimate (Hemani et al., 2018). A weak instrument also tends to increase biases, which stem from violations of other MR assumptions; consequently, using PGS instead of individual SNPs may alleviate this problem (Belsky, 2013). Second, MVMR allows exposure and a mediator to share some of the same genetic variables, thus reducing bias due to potential pleiotropy—the phenomenon of a genetic variant influencing multiple traits (Sanderson et al., 2019; Carter et al., 2021). Third, anthropometric measures that are obtained by healthcare professionals together with register data on income minimize measurement errors. This coupled with statistically strong instruments, mitigates concerns related to the small study sample. According to Brion et al. (2013), the MR sample should be $1/R^2$ times higher than in a non-MR study, where R^2 is the variation explained in the exposure by the genetic variable. Furthermore,

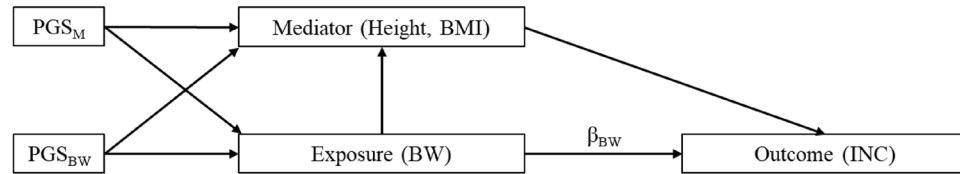
Total effect**Mediaton analysis**

FIGURE 1 A multivariable Mendelian randomization (MVMR) model for total effect and mediation analysis. γ_1 depicts the total effect of birth weight (BW) on income (INC). β_{BW} is the remaining direct effect after controlling for the mediated effect. The indirect effect is obtained by subtracting the direct effect of birth weight from the total effect ($\gamma_1 - \beta_{BW}$)

an anthropometric mediator may be less vulnerable to gene–environmental confounding than, for example, educational attainment or health behavior (McMartin and Conley, 2020; Mills and Tropf, 2020).

Following Sanderson et al. (2019) and Carter et al. (2021), we examined the causal links in each step of the mediation path. We present evidence of the total effect and the causal links between the exposure and mediators and between the mediators and outcome. We report MVMR estimates for the indirect and direct effects and examine their robustness. The results are for both men and women. Although MVMR based on PGSs attenuates concerns related to confounding, we augment the baseline model with cohort indicators and covariates that describe the participants' family backgrounds during childhood in 1980—that is, prior to the participants' entry into the labor market. Furthermore, we control for the potential effect of assortative mating with an interaction variable (mother's years of education \times father's years of education).

3 | RESULTS

3.1 | Descriptive evidence

Figure 2 depicts the relationship between birth weight and income in the study sample. The graph indicates that a higher birth weight is associated with higher income. Although the estimates are noisy for the very low and very high birth weights and potentially subject to confounding, the graph provides an indicative benchmark to further analyze causality and mediation. Furthermore, the graphs in Figure 3 (Panels A, B, and C), based on non-parametric kernel-weighted local polynomial regression, show that higher values of birth weight, BMI, and height are positively associated with higher values of their PGSs. As expected, the correlations (Appendix S1) between the PGSs are weak, especially for PGS_{BMI} and PGS_{BW} ($r = -0.002$; $p = 0.948$) and for PGS_H and PGS_{BMI} ($r = -0.097$; $p < 0.01$). The correlation between PGS_H and PGS_{BW} is stronger and statistically significant ($r = 0.205$; $p < 0.01$). This indicates that the PGSs may have overlapping SNPs. Consequently, they may be invalid instruments for MR, although they do validate the use of MVMR (Sanderson et al., 2019; Carter et al., 2021).

3.2 | MR estimates

3.2.1 | Total effect of birth weight on income

Table 1 documents the total effect of birth weight on income in adulthood. The model uses a PGS for birth weight as an instrument. We utilized a logarithmic specification, following Black et al. (2007), and controlled for cohort effects. We report the pooled (column 1) and sex-stratified estimates (column 2 for men and column 3 for women). First, we found

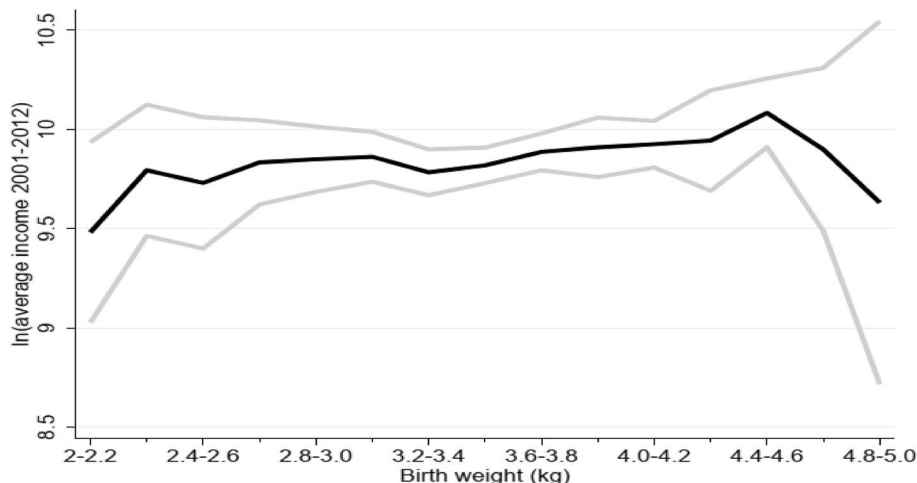


FIGURE 2 Log of the average working-age income by birth weight. Notes: $N = 1,703$. Income is measured as the log-transformed average annual earnings during the 2001–2012 period in the birth weight bins with 95% confidence intervals. The width of a bin is 0.200 kg. The participants whose birth weights were below 2 kg or above 5 kg were excluded from the analysis

that the first-stage F-statistics support the strong instrument assumption ($F = 523.87$ for pooled, $F = 204.70$ for men, and $F = 324.94$ for women). Second, the PGS explains the variation in birth weight well (partial $R^2 = 0.211$ for pooled, 0.201 for men, and 0.221 for women). This reduces the concern that the analysis is insufficiently powered (Brion et al., 2013; Carter et al., 2021; Pierce et al., 2011). Third, there is a non-zero total effect of birth weight on income for men ($\beta = 1.117$; $p = 0.002$), but not for women ($\beta = -0.157$; $p = 0.740$) or for the pooled data ($\beta = 0.422$; $p = 0.165$). A lack of evidence for a non-zero total effect suggests that either the birth weight has no causal effect on income for women or the analysis lacks statistical power.

3.2.2 | Univariable MR estimates on causal mediation

The MR estimates (Table 2) provide evidence of the causal relationship between birth weight and mediators. The standard F-statistics for instrument strength are well above the rule of thumb cut-off of 10 (Staiger & Stock, 1997) and the much more conservative cut-off of 50 for genetic instruments proposed by Lee et al. (2020). The inclusion of parental covariates leaves the estimates intact. The estimates (columns 2 and 4) show that men and women with higher birth weights have a higher probability of being taller ($\beta = 0.130$; $p < 0.01$ for men and $\beta = 0.099$; $p < 0.01$ for women). The effect of birth weight on BMI differs by sex. A higher birth weight increases the probability of having a higher BMI among men ($\beta = 0.124$; $p = 0.051$) but not among women ($\beta = 0.018$; $p = 0.812$).

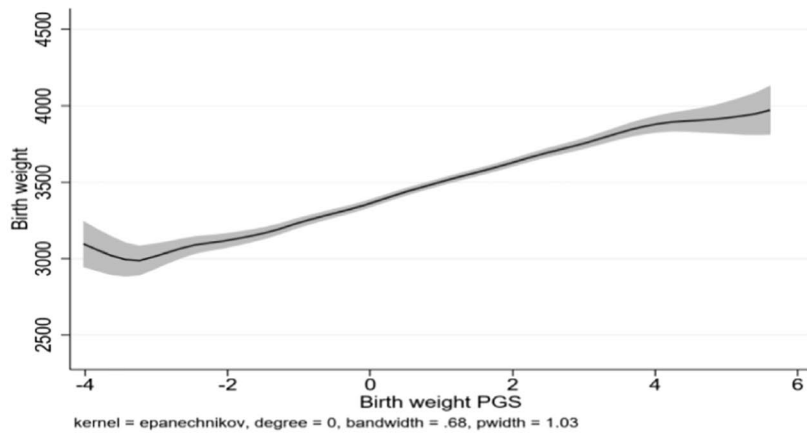
The MR estimates for the mediators (Table 3) show further differences between men and women. First, height (Panel A) is causally linked to income for men ($\beta = 4.841$; $p < 0.01$) but not for women ($\beta = 0.155$; $p = 0.909$). Second, the BMI (Panel B) has a weak causal link to income for men ($\beta = 1.195$; $p = 0.098$) but not for women ($\beta = -0.799$; $p = 0.125$). For men, the association is positive, while for women, it is negative. In brief, the MR estimates show evidence of causal mediation via height for men but not for women, while the evidence of causal mediation via BMI remains weak.

3.2.3 | MVMR estimates of the direct and indirect effects

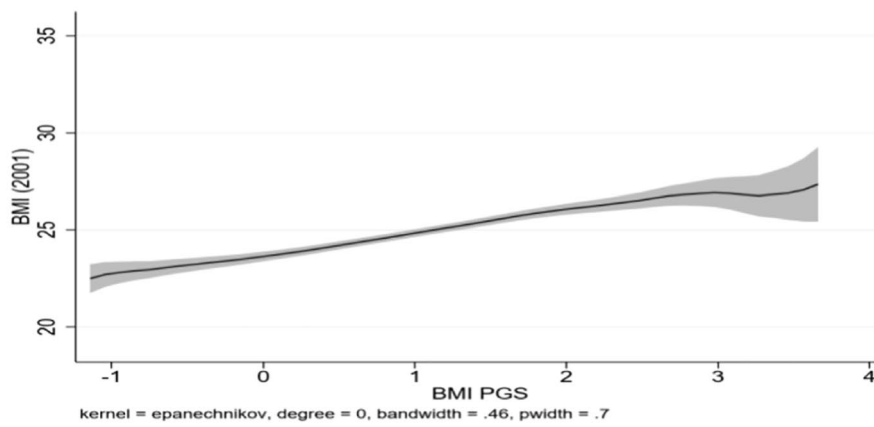
The standard F-statistics (Table 4) show that the instruments strongly predict both exposure and mediators. The Sander-son-Windmeijer multivariate F-test of excluded instruments shows that the instruments have sufficient strength to jointly predict the exposure and mediator. In fact, the MVMR estimation increases the power of the instruments. As for the MR analysis, the inclusion of parental controls left the point estimates intact.

The MVMR estimates for men show an indirect effect of birth weight on income via height ($\beta = 0.627$; $p = 0.020$) but not via BMI ($\beta = 0.146$; $p = 0.264$). For women, there is no evidence of an indirect effect via height ($\beta = 0.030$; $p = 0.847$) or via BMI ($\beta = -0.014$; $p = 0.849$). The estimates are thus consistent with the MR estimates in Tables 2 and 3. Using

Panel A



Panel B



Panel C

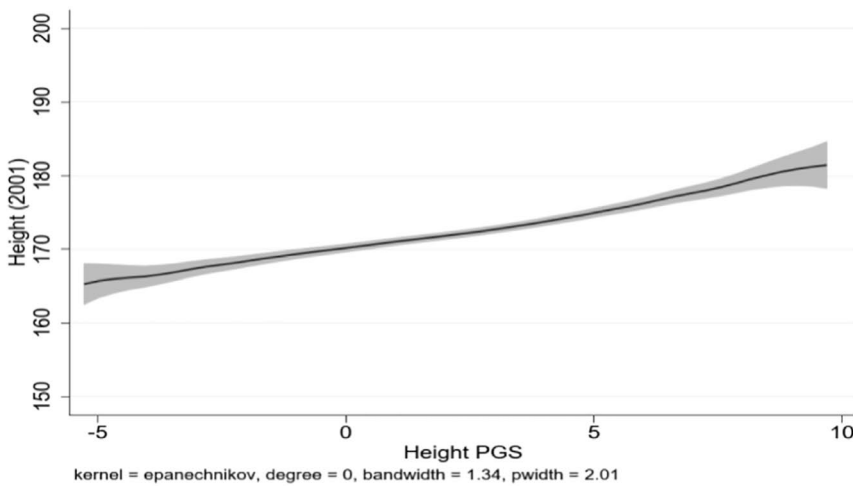


FIGURE 3 Associations between birth weight and PGS_{BW} (Panel A), BMI and PGS_{BMI} (Panel B), and height and PGS_H (Panel C). Note: Individuals whose BMI, height, or birth weight was in the top/bottom 2.5% of the corresponding distribution were excluded from the figure

TABLE 1 The total effect of birth weight on Income. Univariable MR estimates

Outcome	ln(Income)		
	Pooled	Men	Women
ln(BW)	0.422 (0.304) [0.165]	1.117*** (0.365) [0.002]	-0.157 (0.473) [0.740]
Partial-R ²	0.211	0.201	0.221
F-statistics	523.78	204.70	324.94
N	1,703	765	938

Notes: Standard errors in parentheses; *p*-values in square brackets. Significant at the *10%, **5%, and ***1% level. All models control for birth cohort. The pooled model also controls for sex.

TABLE 2 The effect of birth weight on the mediator. Univariable MR estimates for men and women

Outcome	ln(Height)		ln(BMI)	
	(1)	(2)	(3)	(4)
Panel A: Men				
ln(BW)	0.132*** (0.019) [0.000]	0.130*** (0.019) [0.000]	0.133** (0.064) [0.039]	0.124* (0.064) [0.051]
Controls for SES	No	Yes	No	Yes
Instrument	PGS _{BW}	PGS _{BW}	PGS _{BW}	PGS _{BW}
F-statistics	204.70	208.25	204.70	208.25
N	765	765	765	765
Panel B: Women				
ln(BW)	0.100*** (0.015) [0.000]	0.099*** (0.015) [0.000]	0.010 (0.075) [0.894]	0.018 (0.074) [0.812]
Controls for SES	No	Yes	No	Yes
Instrument	PGS _{BW}	PGS _{BW}	PGS _{BW}	PGS _{BW}
F-statistics	324.94	323.95	324.94	323.95
N	938	938	938	938

Notes: Standard errors in parentheses; *p*-values in square brackets. Significant at the *10%, **5%, and ***1% level. All models control for birth cohort. Controls for socio economic status (SES): log of family income in 1980, mother's years of education in 1980, father's years of education in 1980, and interaction term: mother's years of education × father's years of education.

Abbreviations: BMI, body mass index; BW, birth weight.

the total effect estimate from Table 1, the estimate for the share mediated via height for men is 56% (0.627/1.117). The result of no indirect effect via BMI for men is consistent with a statistically strong estimate for the remaining direct effect ($\beta = 0.968$; $p = 0.013$). For women, the results of no indirect effect via BMI or via height are similarly consistent with a statistically weak estimate for the remaining direct effect for height ($\beta = -0.185$; $p = 0.658$) and for BMI ($\beta = -0.141$; $p = 0.720$), together with the result of no total effect from birth weight to income ($\beta = -0.157$; $p = 0.740$).

3.2.4 | Robustness of the MVMR estimates for men

To control for any possible confounding, Appendix S2 augments the baseline model with several additional covariates. We controlled for years of education, three biomarkers (triglycerides, HDL, and LDL cholesterol), and their PGSSs. Furthermore, we estimate the model with height as mediator with weight-related traits (BMI and WHR and their PGSSs) and with BMI as mediator with height and its PGS. The estimates are consistent with the baseline: the instruments jointly strongly predict both birth weight and height, and the estimate of the indirect effect via height for men remains significant ($p < 0.10$). The results for BMI remain similarly unaltered—there is no indirect effect on income via BMI. However, the additional covariates reduced the estimate for the remaining direct effect, indicating that auxiliary pathways may mediate the total effect of birth weight on income. Further analysis based on a slightly smaller sample (Appendix S3) or inverse probability weighting (Appendix S4) are similarly consistent with the baseline results.⁴ The former analysis augments the baseline with variables related to the participants' health and health behavior (i.e., number of chronic conditions, smoking status, or drinking patterns). Probability weights, in turn, account for any possible non-random

TABLE 3 The effect of the mediator on income. Univariable MR estimates for height and BMI by sex

Outcome Sex	ln(Income)			
	Men		Women	
	(1)	(2)	(3)	(4)
Panel A:				
ln(Height)	5.275*** (1.643) [0.001]	4.841*** (1.633) [0.003]	0.494 (1.326) [0.710]	0.155 (1.359) (0.909)
Controls for SES	No	Yes	No	Yes
Instrument	PGS _H	PGS _H	PGS _H	PGS _H
F-statistics	257.12	255.13	338.73	327.91
N	765	765	938	938
Panel B:				
ln(BMI)	1.098 (0.721) [0.128]	1.195* (0.721) [0.098]	-0.848* (0.503) [0.092]	-0.799 (0.521) [0.125]
Controls for SES	No	Yes	No	Yes
Instrument	PGS _{BMI}	PGS _{BMI}	PGS _{BMI}	PGS _{BMI}
F-statistics	99.44	99.89	148.75	141.79
N	765	765	938	938

Notes: Standard errors in parentheses; *p*-values in square brackets. Significant at the *10%, **5%, and ***1% level. All models control for birth cohort. Controls for SES: log of family income in 1980, mother's years of education in 1980, father's years of education in 1980, and interaction term: mother's years of education × father's years of education.

TABLE 4 Indirect and direct effects of birth weight on income. Multivariable MR estimates by mediator and sex

Outcome Mediator Sex	ln(Income)							
	ln(Height)				ln(BMI)			
	Men		Women		Men		Women	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Indirect effect for mediator	0.630** (0.267) [0.018]	0.627** (0.269) [0.020]	0.066 (0.147) [0.655]	0.030 (0.156) [0.847]	0.142 (0.125) [0.253]	0.146 (0.130) [0.264]	-0.008 (0.076) [0.911]	-0.014 (0.074) [0.849]
Direct effect for birth weight	0.487 (0.458) [0.287]	0.555 (0.451) [0.219]	-0.222 (0.417) [0.594]	-0.185 (0.418) [0.658]	0.975** (0.394) [0.013]	0.968** (0.390) [0.013]	-0.148 (0.396) [0.708]	-0.141 (0.392) [0.720]
Controls for SES	No	Yes	No	Yes	No	Yes	No	Yes
Instruments	PGS _{BW} PGS _H	PGS _{BW} PGS _H	PGS _{BW} PGS _H	PGS _{BW} PGS _H	PGS _{BW} PGS _{BMI}	PGS _{BW} PGS _{BMI}	PGS _{BW} PGS _{BMI}	PGS _{BW} PGS _{BMI}
F-statistics								
*BW	95.26	95.13	132.08	132.62	94.96	94.90	131.86	132.48
*Mediator	157.56	154.94	175.07	164.37	51.82	51.32	66.00	62.73
S-W F-statistics								
*BW	118.94	119.81	232.88	226.57	177.49	179.40	263.38	264.60
*Mediator	157.92	158.28	297.23	271.34	99.82	99.53	131.92	125.38
N	765	765	938	938	765	765	938	938

Notes: Standard errors in parentheses; *p*-values in square brackets. Significant at the *10%, **5%, and ***1% level. Indirect effects are calculated using the difference method (Carter et al., 2021). All models control for birth cohort. Controls for SES: log of family income in 1980, mother's years of education in 1980, father's years of education in 1980, and interaction term: mother's years of education × father's years of education. S-W F-statistics refers to the Sanderson-Windmeijer multivariate *F*-test of excluded instruments.

attrition bias in the sample study. As previously, the instruments jointly strongly predict both birth weight and height, and the estimate of the indirect effect via height for men remains significant ($p < 0.05$). The specification that accounts for non-random attrition implicates a slightly larger estimate of the share mediated by adult height (approximately 66%). However, the estimate is well within the 95% confidence intervals of the baseline estimate.

4 | DISCUSSION

In this paper, we examine the association between birth weight and later-life economic success, measured by earnings during prime working-age. To this end, we use a genotyped Finnish longitudinal survey that we link to the administrative registers of Statistics Finland. The state-of-the-art MVMR approach based on strong genetic instruments provides a credible research design to examine causal links over the course of a person's life. Furthermore, the setting provides an intuitively clear and consistent ordering of the exposure, mediators, and outcome: individuals who have a higher genetic propensity for a high birth weight are heavier at birth, and these children have a higher probability of being taller and having higher BMI values in adulthood, factors that may be later rewarded or penalized in the labor market.

The main findings of the study, based on a sample of prime working-age individuals in Finland and their wider relevance with respect to earlier research, can be summarized as follows. First, we show that birth weight matters. The genetic instrument for birth weight is strong, and we identified a nonzero total effect of birth weight on labor income for men. The pooled estimate, although imprecise, implies that a 10% increase in birth weight leads to 4–5% higher long-term income. This estimate can be compared to that of Black et al. (2007) and Cook and Fletcher (2015). The former, using twin data from Norway, showed that a 10% increase in birth weight is associated with a 1% increase in full-time earnings. The latter, using a sample of 469 sibling pairs in the US, reported an estimate of 5%. Furthermore, our study shows that sex matters: we do not detect a statistically significant total effect for women. The result is consistent with earlier findings. Nakamuro et al. (2013) reported similar results in a twin study for Japan. By contrast, Behrman and Rosenzweig (2004), using US data on female twins, found a significant effect for women. According to their study, an increase in birth weight by 1 lb. (approx. 450 g) increases adult earnings by 7%.

Second, the MR estimates on causal links are consistent with empirical findings on tracking: traits inherited at birth are likely to be associated with traits later in life (Couto Alves et al., 2019; Dubois et al., 2012; Ward et al., 2017). Our estimates differ by sex and mediator. The estimate for height is similar for men and women: a 10% (approx. 350 g) increase in birth weight increases height by around 1% (approx. 2 cm). The estimates for BMI differ notably by sex. There is no statistically strong effect for women, whereas a 10% increase in birth weight for men translates into an increase in BMI of around 1.3% (approx. 0.3 BMI units). The estimates are consistent with, although larger than, the twin-fixed effects estimates by Black et al. (2007) for men and Behrman and Rosenzweig (2004) for women: a 10% increase in birth weight is translated into 0.6 extra cm of height for men in Norway and 0.3 extra cm of height for women in the US. Consistent with our estimates, the latter found no effect for BMI, while the former reported a statistically strong estimate for men (approx. 0.11 BMI units).

Third, approximately 56% of the total effect of birth weight on men's income is mediated via adult height. The estimate is robust: it remains intact with respect to the inclusion of additional phenotype mediators, including BMI, WHR, educational attainment, health-related covariates, and health behavior indicators. The height premium estimate for men (approx. 2.8% per extra cm using the MR results)⁵ may occur for a variety of reasons, including differences in productivity (Lakdawalla & Philipson, 2007), cognitive ability (Case & Paxson, 2008), or discrimination against short people. Our estimate is consistent with the empirical results summarized in Hübler (2016) and the evidence provided by Böckerman and Vainiomäki (2013) and Böckerman et al. (2017) for the case of Finland. Using twin data, Böckerman and Vainiomäki (2013) reported a statistically strong ordinary least square estimate of 3.3% per cm but a statistically weak instrumental variable estimate of 12.3%. Böckerman et al. (2017) reported a statistically weak instrumental variable estimate of 0.9% for both sexes. Our results are also qualitatively similar to those of Tyrrell et al. (2016) for UK data, which showed two times stronger effects for men than women. Our finding of no mediation via height for the women in the study sample may be partly explained by strong occupational segregation; in Finland, women are more often employed in the public sector and in occupations where physical productivity gains have a minor role in remuneration and wage premiums for leadership are negligible (e.g., Emerek, 2008).

We stress that MVMR is based on strong assumptions that PGSs need to satisfy. Furthermore, statistical power (as determined by the sample size), the causal effect size, and the proportion of variance in the exposure explained by a genetic instrument are additional concerns. The possible limitations of our study are related to these concerns. First, the

empirical analysis may not be sufficiently statistically powered, which may explain the null results. However, this issue is counterbalanced by two facts: we use high-quality register data that reduce measurement errors, and the PGSs used in the analysis explain over 20% of the variations in birth weight. Thus, the sample fulfils a rough rule of thumb for the relevance assumption in MR studies.

Second, MVMR is based on a sample of unrelated individuals, although recent research indicates that MR is most effectively applied within the family unit (Brumpton et al., 2020; Selzam et al., 2019). For example, Brumpton et al. (2020) showed that the effect of BMI and height on educational attainment decreases after accounting for the family effect. However, this limitation applies to almost all MR studies, and a recent study by Cawley et al. (2019) on peer effects in BMI showed no evidence of genetic nurture within families. Furthermore, we used covariates for the parental environment (income and education) to account for any possible confounding. Consequently, the concerns related to our research design should not be overstated.

Third, anthropometric mediators can be regarded a priori as not relevant to public policy because they provide limited opportunities for interventions. However, these mediators do offer an intuitively clear causal ordering of exposure and outcome and may contain fewer elements of environmentally-mediated genetic effects (e.g., Belsky et al., 2019). This may facilitate interpretation and increase the precision of the estimates. Furthermore, the mediators allow us to contribute to earlier research that has examined how the anthropometric traits of an individual track from birth weight to later life (e.g., Couto Alves et al., 2019) and how these traits are rewarded in the labor market (e.g., Averett, 2011; Cawley, 2015; Norton & Han, 2008).

Fourth, the local average treatment effect that we identified captures the average treatment effect for compliers. Consequently, the result of no indirect effect via BMI applies to those whose birth weight is higher due to genetic inheritance. The finding broadens the picture given by earlier research (e.g., Brunello & D'Hombres, 2007; Cawley, 2004; Lindeboom et al., 2010) that used the BMI of biological relatives (parents, siblings, or children) as an instrument. For example, using US data and a biological sibling as an instrument for BMI, Cawley (2004) found that the effect of weight on wages varies by gender and race, with the greatest impact on white females. In short, our results suggest that differences in genetic inheritance may have different impacts on wages than differences driven by maternal nutrition or the parental environment in general. We also stress that earlier findings suggest that the effect of weight on wages can also be non-linear (e.g., Caliendo & Gehrsitz, 2016; Han et al., 2011; Royer, 2009). Using US data, Han et al. (2011) reported that the indirect wage penalty via education and occupation occurs at the upper tail of the BMI distribution for both men and women. However, the MR setup is based on the linearity assumption and does not allow us to focus on the tails of the BMI distribution in the study sample.

Our results show that early human endowments have long-lasting effects on socioeconomic outcomes. Although MVMR alleviates problems related to unobserved confounders, we caution against the interpretation that our results are strictly causal estimates of how an individual's physical traits are rewarded or penalized in the labor market. We also stress that gene–environment (GE) correlations, such as evocative rGEs (in which individuals' genetics induce environmental responses) or passive rGEs (environments with shared genetic variation), may be country-specific—GE correlations vary with the availability of resources and opportunities (McMartin & Conley, 2020). In this respect, data from a country such as Finland, which has narrow income inequality and comprehensive public services, is an advantage. On the other hand, this may limit the generalization of the results to other institutional contexts.

We emphasize that there are several extensions that could be addressed in future studies. For example, there are plenty of opportunities for comparisons between other mediating pathways. One potentially interesting mediator is childhood health. The effect of birth weight may be mediated through poor health in childhood, which, in turn, may have an impact on school absences or the ability to learn, thus leading to poorer education and income. There is also a need to consider the factors that may enhance or weaken the mediation pathways. However, in addition to the complexity of the pathways, such an analysis requires large samples, a family-based research design, and valid instruments that may be difficult to obtain.

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CONFLICT OF INTEREST

All authors declare that they have no relevant or material financial interests that relate to the research described in this paper.

ETHICS STATEMENT

All participants of the Young Finns Study provided written informed consent, and the study was approved by local institutional review boards (ethics committees of the participating universities). Parents or guardians provided written informed consent on behalf of the under aged children enrolled in the study. The study does not disclose information concerning individual persons. The linked data have been approved for research purposes by Statistics Finland (SF), under the ethical guidelines of the institution which comply with the national standards.

DATA AVAILABILITY STATEMENT

The study dataset comprises health related participant data and their use is therefore restricted under the regulations on professional secrecy (Act on the Openness of Government Activities, 612/1999) and on sensitive personal data (Personal Data Act, 523/1999, implementing the EU data protection directive 95/46/EC). Also the informed consents for the original study must be taken into consideration. In addition, data have also been obtained from registry authorities with permission to use them for the original research only. After appraising the request, the Ethics committee concludes that under applicable law, the data from this study cannot be stored in public repositories or otherwise made publicly available. The data controller (=this means the YFS investigators) may permit access on case by case basis for scientific research, not however to individual participant level data, but aggregated statistical data, which cannot be traced back to the individual participants' data.

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ENDNOTES

¹ YFS participants (1,123 males and 1,319 females, including 546,776 SNPs) were genotyped in 2009. The genotypes were called up using the Illumina clustering algorithm (Teo et al., 2007). Quality control was performed using the Sanger genotyping QC pipeline, and individuals with possible relatedness were removed. Genotype imputation was conducted with the SHAPEIT v1 and IMPUTE 2 software (Delaneau et al., 2012), and the 1000 Genomes Phase I Integrated Release version 3 (March 2012 haplotypes) was used as a reference panel (Howie et al., 2009; Altshuler, Durbin and Abecasis 2010).

² The independent effect SNPs on birth weight was identified by double-clumping with LD threshold $R^2 = 0.1$; see Vösa et al., (2018) for technical details.

³ Because the analyses include the YFS as one of the data sources, they may suffer from over-predictions (Wray et al., 2013). However, this error is very unlikely in our research setting due to the very small contribution of the YFS data to the GWAS.

⁴ The inverse probability weights were constructed as follows: First, to obtain predicted probability for being in the estimation sample (p) a logit model where an indicator for being in the estimation sample was regressed on the following covariates separately for women and men: birth cohort, birth month, indicator for having university-level education in 2001, income in 2001, region of residence in 2001 (4 indicators). Then, the inverse probability weight for participants who were in the estimation sample was calculated as $1/(p)$ and these weights were used in the MVMR to control for potential attrition bias.

⁵ The average height among men was 180 cm. Since a 1% (1.8 cm) increase in height was associated with about a 5% increase in income (see Table 3), a 1 cm increase in height is associated with about a 2.8% ($=5/1.8$) increase in income.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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APPENDIX 1: Summary statistics

Variable	Mean	Standard deviation	N
Children's characteristics (1962–1977)			
Birth weight (kg)	3.501	0.541	1,703
Low birth weight (<2500 g, fraction)	0.036	0.186	1,703
High birth weight (>4500 g, fraction)	0.029	0.167	1,703
Sex (females, fraction)	0.551	0.498	1,703
Adulthood characteristics			
Adult height (cm)	172.274	9.240	1,703
Adult BMI in 2001	25.047	4.366	1,703
Family background (1980)			
Years of education, mother	11.076	2.457	1,703
Years of education, father	11.308	2.792	1,703
Log of family income (euros, annual)	9.321	0.866	1,703
Long-term outcomes			
Log of average income (euros, 2001–2012)	9.817	0.973	1,703
Risk scores			
Birth weight (PGS _{BW})	1.121	1.508	1,703
BMI (PGS _{BMI})	0.987	0.716	1,703
Height (PGS _H)	2.112	2.501	1,703

Notes: To minimize the amount of missing information, adult height was obtained from either the 2001, 2007, or 2011 survey. In 2001, the participants were at least 24 years old.

APPENDIX 2: Comparison of the total linked YFS-FLEED sample ($N = 3,577$) and the study sample ($N = 1,703$)

	Original sample mean	Estimation sample mean	Difference	z-statistics (t-statistics)
Female	0.509	0.551	-0.042	-2.84**
Cohort 1974	0.161	0.181	-0.020	-1.83*
Cohort 1962	0.149	0.122	0.028	2.71***
High education (2001)	0.188	0.224	-0.036	-3.00***
Earnings (2001)	19,804.48	20,719.81	-915.333	(-2.224**)

Notes: The table reports only variables whose means differ based on the two-sample test of proportions (indicator variables) or the two-sample *t*-test (continuous variables) at least at a 10% level. Statistically significant differences were not observed in terms of the following dimensions: cohorts born in 1965, 1968, 1971, and 1977; birth month; and region of residence in 2001 (4 indicators). Information on education and earnings in 2001 was available for 3,464 participants. Statistically significant at the *10%, **5%, and ***1% level.