Supplemental Materials to DW Belsky et al. The Genetics of Success: How SNPs Associated with Educational Attainment Relate to Life-Course Development

SUPPLEMENTAL METHODS

<u>Sample Description.</u> Participants are members of the Dunedin Study, a longitudinal investigation of health and behavior in a complete birth cohort. Study members (N=1,037; 91% of eligible births; 52% male) were all individuals born between April 1972 and March 1973 in Dunedin, New Zealand (NZ), who were eligible based on residence in the province and who participated in the first assessment at age 3. The cohort represents the full range of socioeconomic status on NZ's South Island and matches the NZ National Health and Nutrition Survey on key health indicators (e.g., BMI, smoking, GP visits) (1). The cohort is primarily white; fewer than 7% self-identify as having non-Caucasian ancestry, matching the South Island (1). Assessments were carried out at birth and ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and, most recently, 38 years, when 95% of the 1,007 study members still alive took part. At each assessment, each study member is brought to the research unit for a full day of interviews and examinations. The Otago Ethics Committee approved each phase of the study and informed consent was obtained from all study members.

<u>Genotyping and Imputation</u>. We used Illumina HumanOmni Express 12v1.1 BeadChip arrays (Illumina CA, USA) to assay common Single Nucleotide Polymorphism (SNP) variation in the genomes of our cohort members. We imputed additional SNPs using the impute2 software (version 2.3.1, <u>https://mathgen.stats.ox.ac.uk/impute/impute_v2.html</u>, (2)) and 1000 Genomes version 3 reference panel. Imputation was conducted on autosomal SNPs appearing in dbSNP (v140) that were called in >98% of the Dunedin Study samples. Invariant SNPs were excluded. Pre-phasing and imputation were conducted using a 50M base-pair sliding window. The resulting genotype database included genotyped SNPs and SNPs imputed with 90% probability of a specific genotype among the non-Maori members of the Dunedin cohort (n=918) and in Hardy-Weinberg equilibrium (p>0.01 for all).

Polygenic Scoring. We calculated polygenic scores according to the method described by Dudbridge (*3*) using the PRsice software (v1.22, <u>http://prsice.info/</u>, (*4*)).To calculate the polygenic score for educational attainment, we matched genotypes from our data with GWAS results for educational attainment reported by the Social Science Genetic Association Consortium (*5*) and used the approximately 2.3 million matched genotypes to 'score' each of our Study members' genetic predisposition to educational attainment. For each genotype, we counted the number of education-associated alleles (0, 1, or 2) and multiplied this count by the

effect-size estimated in the original GWAS. (Most genotypes had effect sizes very near zero.) We then summed weighted counts across all genotypes to calculate each Study member's score. Scores ranged from -30.51-73.77 and were normally distributed in the Dunedin birth cohort (M=17.73, SD=17.94). We standardized scores to have M=0, SD=1 for analysis (**Figure S1**). Based on the original GWAS results, Study members with polygenic scores greater than zero would be expected to complete more years of schooling and Study members with polygenic scores below zero would be expected to complete fewer years of schooling. We used this same method to calculate polygenic scores for height, this time using the results from the GIANT Consortium's most-recent GWAS of height (*6*).

Principal Components Analysis of Genome-wide SNP data. Polygenic score values may be influenced by subtle differences in ancestry, even among individuals in a European-descent cohort such as ours. To account for ancestry-related genome-wide patterns of allele-frequency differences, we conducted a principal components analysis of our genome-wide SNP database using the EIGENSOFT smartPCA tool (7, 8). We extracted the first ten principal components from the genome-wide SNP data (EIGENSOFT's default). The first principal component explained ~2% of the variance in the education polygenic score. Other principal components explained <1% of variance. Together, the 10 principal components explained 3% of the variance in the education polygenic score.

To correct for any potential population stratification, association analyses were conducted with statistical adjustment for the first 10 principal components estimated from the genome-wide SNP data. Analysis results without this adjustment are reported in **Table S2**.

Parents' Socioeconomic Status (SES). The socioeconomic statuses of cohort members' families were measured using a 6-point scale that assessed parents' occupational statuses, defined based on average income and educational levels derived from the New Zealand Census. Parents' occupational statuses were assessed when Study members were born and again at subsequent assessments up to age-15 years. The highest occupational status of either parent was averaged across the childhood assessments (*9*).

Educational Attainment. We measured educational attainment as the highest degree a Study member had completed through the time of the age-38 assessment. For the 1972-73 birth cohort we studied, compulsory education ended at age 15 years, at which point students could elect to sit for a School Leaving Certificate exam. 15% of our sample obtained no educational credential. 15% obtained the School Leaving Certificate but did not progress further. 42% completed 6th form or Bursary Certificates (roughly equivalent to a full high school diploma in the United States). 29% completed a university degree. Translated to the International Standard Classification of Education (ISCED) (*10*), the distribution of educational attainment in

the cohort was as follows: 30% attained ISCED Level-2 (lower secondary education). 42% attained ISCED Level-3 (upper secondary education). 29% attained ISCED Level-5 (Bachelor's or equivalent level).

<u>Adult Attainment.</u> Study members reported their income, assets, credit problems, and difficulties paying expenses to trained Study staff during structured in-person interviews (11).

Occupational prestige. We measured Study members' occupational prestige from self-reported occupation according to the New Zealand Socioeconomic Index (NZSEI-06), a 6-point scale that assessed self-reported occupational status and allocates each occupation to 1 of 6 categories (1 = unskilled laborer, 6 = professional) (*12*). Homemakers and those not working were pro-rated based on their occupation at the previous interview (when they were aged 32 years). The mean occupational prestige score in the cohort was 3.77 (SD=1.44).

Income. Following the New Zealand Census, Study members were asked to list their sources of income and given the choice of 13 different income categories to report their total pre-tax annual income from all sources in their own currency. For Study members living outside of New Zealand, income was converted from local currency to NZD. For the cohort, mean income was NZD 62,434 (SD=44,013).

Assets. Study members were asked to estimate the value of each of a series of assets (savings, property, vehicles, homes, etc.) in local currency. For Study members living outside of New Zealand, income was converted from local currency to NZD. For the cohort, mean assets were NZD 603,042 (SD=946,575).

Difficulty paying expenses. Study members were asked about difficulties paying for each of food and necessities, housing, household bills, entertainment, holidays, property upkeep, family obligations, physician visits, and medication costs. They were also asked if they lived paycheck to paycheck, if they had needed to borrow money from family and friends, and if they had needed to take money out of a savings or retirement account to make ends meet. The count of positive response formed the Difficulty Paying Expenses scale (M=5.06, SD=5.76).

Social welfare benefit use. We measured the length of time that Study members drew on government welfare benefits by conducting record linkage with the New Zealand Ministry of Social Development (13). Data on welfare benefit receipt were available from 1 January 1993, with this date marking the beginning of reliable electronic data capture in New Zealand, allowing us to measure duration of benefit use from ages 21-38 years. We obtained information about incident spells and monthly duration of the following New Zealand government benefits: Unemployed Benefit, Invalids Benefit, Sickness and Emergency Benefits, Domestic Purposes Benefit-Sole Parent and Emergency Maintenance Allowance, Training Benefit, Emergency Benefit (for those who do not usually meet entitlement conditions). Only one benefit can be received at any given time. The mean number of months of benefit receipt among cohort members was 23 (SD=43). **Credit problems.** Study members were asked about each of a series of credit problems (Have you been turned down for a credit card? Have you defaulted on a credit card payment? Have you missed a bill, mortgage, or loan payment? Have you sold an asset to pay a bill? Have you sold any of your belongings to a pawnbroker? Have you been declared bankrupt? Have you had a house foreclosed on or sold at mortgagee auction by the bank? Have you had something repossessed? (like a car, T.V., or furniture?)) The count of positive response formed the Credit Problems Scale (M=0.43, SD=0.89).

Credit scores. Credit scores were acquired at the age-38 assessment phase from the Veda Company (*14*). The Veda credit score algorithm is proprietary. Scores are based on 5-year histories of consumer credit activity and include the following factors: the number and types of credit applications and inquiries, age of credit file, residential stability, adverse information such as payment defaults and judgments, and the existence of any current or prior insolvency information. Factors such as race, national origin, marital status, occupation, salary, employment history, medical or academic records are not included in Veda scoring. The mean VEDA score among cohort members was 678 (SD=166).

Adult Attainment Factor. To calculate the Adult Attainment Factor, we conducted a confirmatory factor analysis (CFA) in MPlus v7.3 (*15*). We categorized severely skewed variables (occupational prestige, credit problems, value of assets, personal income, benefit days) and treated these variables as ordinal in the CFA; VEDA credit scores were divided by 100 (model convergence is facilitated when all items are scaled similarly). Data for 6 or more of the 7 attainment measures were available for 97% of the cohort. Missing data was imputed using Full Information Maximum Likelihood. The model fit well: χ^2 (N = 971, df = 14) = 130.080, p = 0.00; RMSEA = 0.092 (90% CI: 0.078, 0.107); CFI = 0.933, TLI = 0.900. Standardized factor loadings (95% CI) are presented in **Table S3**. Individual factor scores were output and used in subsequent analyses. The factor score was standardized to have mean=0 SD=1 for analysis (**Figure S2**). **Figure S3** shows effect-sizes for associations between the polygenic score and the attainment factor and each of its components. The figure shows effect-sizes before and after adjustment for educational attainment.

Developmental Milestones. When Study members were aged 3 years, their mothers were interviewed about the age at which their child had reached each of a series of developmental milestones. Mothers reported the age at which their child first smiled, when the child began to walk, defined as taking 6 steps, when the child began feeding himself/herself with a spoon without requiring assistance, when the child began to talk, defined as using 6 words appropriately, when the child began to potty train during the day, defined as staying dry all day 6 out of 7 days per week, when the child began to communicate using sentences, and when the child began to potty train at night, defined as staying dry all night 3 out of 4 nights. **Figure S4**

shows survival curves illustrating when Dunedin Study members reached each of these milestones.

Reading. We measured the development of reading skills using repeated assessments of the Burt Reading Test (*16*). At ages 7, 9, 11, 13, 15, and 18 years, children were tested according to a standard protocol by a trained staff member. We used multilevel longitudinal growth models (*17*) to analyze children's development of reading skills. We set the model intercept at the age-7 baseline measurement. Because Burt scores show a curvilinear development trajectory (**Figure S5**), we modeled both linear and quadratic slopes. The intercept captured the cohort mean Burt score at age 7 (b=30.50). The linear slope term captured average annual change in reading score across the age 7-18 interval (b=12.50). The quadratic slope term captured deceleration of change, that is, the convexity of the trajectory across childhood (b=-0.60). All model terms were statistically significant (p<0.001). We tested genetic influence on growth by modeling intercept and slope terms of the growth curve as functions of the polygenic score and covariates. Polygenic score coefficients measure the effect of a 1-SD difference in polygenic score from age 7-18 (linear slope), and on the deceleration of that change with increasing age (quadratic slope).

<u>Aspirations.</u> When they were aged 15 years, Study members completed a questionnaire about their educational and occupational aspirations (*18*). They indicated how far they wanted to go in school and what type of occupation they hoped to hold as an adult. Occupational responses were coded according to the Elley and Irving occupational prestige scale (*19*).

Standardized Testing. In New Zealand, at the time Dunedin Study members were in high school, standardized exams were administered during 5th, 6th, and 7th forms (ages 15-17 years). For the 1972-73 birth cohort, the age-15 "Certificate" exam was required to earn a School-Leaving Certificate (the minimum secondary education credential at the time); the age-16 Sixth-Form Certificate was used for entry to various tertiary institutions; the age 17 "Bursary" exam was the method through which the government allocated funds ("bursaries") to support room and board costs during university. Study members brought their official exam records to the research unit and their scores were recorded.

Geographic Mobility. We measured geographic mobility from Study members' reports about their place of residence and work, recorded to monthly resolution, during Life History Calendar interviews at ages 26, 32, and 38 years (*20*). We measured whether study members had spent at least one continuous year living and working outside of New Zealand and Australia, commonly referred to as "The Big OE" for "overseas experience" (*21, 22*). We also identified

those Study members who had been living and working outside of New Zealand for at least the past year at the time of the age-38 assessment.(gave

Financial Planfulness. We measured Study members' financial planfulness from informant reports about their ability to manage money and from interviews with the Study members themselves about financial building blocks and savings behavior.

Money Management. At the age 32 and 38 assessments, we mailed a brief questionnaire to people nominated by the Study member as knowing him/her well (informants included friends, partners, and family members). Full details of the Dunedin Study informant rating system are provided elsewhere (*23*). Information from informants was available for 96% of Study members. Informants rated the Study member on two items ("poor money manager," "lacks enough money to make ends meet") using a 3-point scale (0=not a problem, 1=bit of a problem, 2=yes, a problem). Scale scores were averaged across ages 32 and 38 to calculate the Money Management Difficulties index (M=0.67, SD=0.84).

Financial Planfulness. At the age-32 and -38 assessments, Study members were interviewed about financial building blocks and about their savings behavior. They were asked if they had investments such as stocks or business investments, and if they had a retirement plan. We counted the number of these building blocks across the two measurement ages to create a 0-4 Financial Building Blocks scale (M=2.24, SD=1.27). Study members' attitudes toward saving and saving behaviors were assessed with seven questions: "Is saving for the future important to you?", "Do you save money to buy expensive items by putting money away and not touching it?", "Do you make regular savings into a special bank account?", "Do you think that saving money makes people more independent?", "Were you encouraged to save money as a child?", "Are you often puzzled by where your money goes?", "Do you think it is important to live within your budget?" (*24*). Scale scores were averaged across ages 32 and 38 to form the final Saving Behavior scale (M=4.11, SD=1.09). We computed the final Financial Planfulness index by standardizing the Financial Building Blocks and Savings Behavior scales and averaging.

Mate Selection. At the age-38 assessment, Study members were interviewed about their romantic relationships. Most Study members (89%) reported being in a serious relationship. These Study members were further asked about the highest educational degree their partner had completed and what their income was. We used these data to classify partners according to whether they had completed a university degree and if their income was above the national median for their sex. Reports of partner income for Study members living outside of New Zealand were converted from local currency to NZD. National age-specific median incomes were queried from Statistics New Zealand (*25*) to form cut points. We then classified partners as low, middle, and high SES according to whether they met none (31%), one (49%), or both (20%) of these criteria.

Life satisfaction. When they were aged 38 years, Study members completed the 5-item Satisfaction with Life Scale (*26*) (e.g., In most ways my life is close to ideal, So far I have gotten the important things I want in life). The scale was converted to a Z-score, mean=0, SD=1.

Cognitive Ability. We measured children's cognitive ability from intelligence tests administered by trained psychometrists at ages 3, 5, 7, 9, 11, and 13 years. At age 3, children completed the Peabody Picture Vocabulary Test (*27*). At age 5, children completed the Stanford-Binet IQ test (*28*). At ages 7-13, children completed the Wechsler Intelligence Test for Children (WISC-R) (*29*).

Cognitive Development. We measured children's cognitive development from repeated assessments of mental age made with the Wechsler Intelligence Scale for Children (WISC-R) (29) at ages 7, 9, 11, and 13. Mental age scores express the child's level of performance as the chronological age for which his/her score is normative. (For example, although Sara is 10 years old, her mental age is 12.) Mental age can be used to monitor each child's intra-individual development over time (*30*). (For example, a 10-year-old child with an IQ score equal to the average score for 12-year olds would have a mental age of 12.) We used multilevel longitudinal growth models (*17*) to analyze children's cognitive development, i.e. the "growth" of their mental age. The model intercept captured the cohort mean mental age at chronological age 7 years (b=7). The linear slope term captured average annual change in mental age (b=1). Model terms were statistically significant (p<0.001). We tested genetic influence on growth by modeling intercept and slope terms of the growth curve as functions of the polygenic score and covariates. Polygenic score coefficients measure the effect of a 1-SD difference in polygenic score and mental age at chronological age 7 (intercept), and on the linear change per year in mental age from chronological age 7-13 (linear slope).

Self-Control Skills. Children's self-control during their first decade of life was measured using a multioccasion/multi-informant strategy, as previously described (*11*). Briefly, the composite score includes nine measures: observational ratings of children's lack of control (at 3 and 5 years of age), parent and teacher reports of impulsive aggression, hyperactivity, lack of persistence, inattention, and impulsivity (at 5, 7, 9, and 11 years of age), and self-reports at age 11 years.

Interpersonal Skill. We measured children's interpersonal skill from reports made by trained research workers following standardized testing sessions when the children were aged 3, 5, 7, and 9 years (*31*). At each age, research workers gave children binary ratings for being friendly (rated as "very friendly" or "extremely friendly"), confident (rated as "more than usual confidence" or "very self-confident"), cooperative (rated as "reasonably cooperative" or

"accepts directions more easily"), and communicative (rated as "readily answers questions, may elaborate" or "answers freely"). Children were given a score ranging 0-100 based on the percent of items endorsed by the research workers (M=52, SD=16).

Childhood Physical Health. As described previously (32), we measured childhood health from medical exams, anthropometry, lung function testing, and clinical interviews with parents at assessments spanning birth to age 11 years. Motor development was assessed at ages 3, 5, 7, and 9 using the Bailey Motor Scales (age 3) (33), McCarthy Motor Scales (34) (age 5) and Basic Motor Ability Test (35) (ages 7 and 9) (36). Children's overall health at ages 3, 5, 7, 9, and 11 years was rated by two Unit staff members based on review of birth records and assessment dossiers including clinical assessments and reports of infections, diseases, injuries, hospitalizations, and other health problems collected from children's mothers during standardized interviews. Ratings were made on a five-point scale (inter-rater agreement=0.85). Body mass index was calculated from height and weight measurements taken at ages 5, 7, 9, and 11 years. In addition, tricep and subscapular skinfold thicknesses were measured at ages 7 and 9 years by trained anthropometrists (37). (For calculation of the overall measure, tricep and subscapular skinfold thicknesses were averaged to create a single score.) Systolic and diastolic blood pressure were measured at ages 7, 9, and 11 years using a London School of Hygiene and Tropical Medicine blind mercury sphygmomanometer (Cinetronics Ltd., Mildenhall, United Kingdom) (38). Fixed expiratory volume in one second (FEV₁) and the ratio of FEV₁ to forced vital capacity (FVC) were measured at ages 9 and 11 using a Godart water spirometer (39). To calculate the childhood health measure, assessments were standardized to have mean=0 SD=1 within age and sex specific groups. Cross-age scores for each measure were then computed by averaging standardized scores across measurement ages. The final childhood health score was calculated by taking the natural log of the average score across all measures, resulting in a normally distributed childhood health index.

Mediation Analysis. For each potential mediator (cognitive ability, self-control skills, interpersonal skill), we tested associations between the polygenic score and the mediator; we tested associations between the mediator and the educational attainment and Adult Attainment Factor score outcomes; and we tested the association between polygenic score and each outcome, including the mediator as a covariate. We used the system of equations described by Baron and Kenny (*40*) and the methods described by Preacher et al. (*41, 42*) to calculate total, direct, and indirect effects, and to estimate the proportion of the genetic effect mediated by each of the mediators (**Figure S7**). We also fitted a multiple mediator model in which all three mediators were included as covariates in the final regression. Results are reported in **Table S5**. **Figure S8** shows results for multiple mediator analyses of attainment (left side) and pathways to success measures (right side).

Data Sharing. The Dunedin Study has not sought informed consent for unrestricted data sharing because data from the Dunedin study have historically been deemed by the Duke and Otago Institutional Review Boards (IRBs) as being in a high-risk category that precludes making the data set available for unrestricted, unsupervised open-access data sharing. Consent documents for the study used over the past 40 years have informed each study member that "...all the information obtained by the researchers at the Dunedin Multidisciplinary Health and Development Research Unit will be treated as STRICTLY CONFIDENTIAL to members of the research team," and "Only approved Dunedin Study researchers will have access to your data." These consent documents were last signed by Study members at the age-38 assessment, which ended in 2012. This means that the Dunedin Study participants have not at this point given their informed consent for unrestricted data sharing, and therefore data deriving from their participation cannot be made available for unrestricted use.

<u>Our data-sharing policy</u> provides for researchers outside the Study to access data used in a published paper by becoming "honorary" staff members of the Dunedin Unit, so they can access the data via collaboration (policy on the Dunedin Study website [http://dunedinstudy.otago.ac.nz]). Applicant investigators are invited to submit a concept paper describing the data analysis project they wish to carry out.

<u>Access requirements in a nutshell.</u> Proposed data-analysis projects from qualified scientists must have a concept paper describing the purpose of data access, IRB approval at the applicants' university, and provision for secure data access. We offer secure access on the Duke and Otago campuses.

All scripts and analysis files for Dunedin Study published papers are available.

Our data-sharing policy was last approved in 2015 by NIA as part of a review of Dunedin Study competing-renewal funding.

References

- 1. R. Poulton, T. E. Moffitt, P. A. Silva, The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future. *Soc. Psychiatry Psychiatr. Epidemiol.* **50**, 679–693 (2015).
- 2. B. N. Howie, P. Donnelly, J. Marchini, A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *Plos Genet.* **5**, e1000529 (2009).
- 3. F. Dudbridge, Power and predictive accuracy of polygenic risk scores. *PLoS Genet.* **9**, e1003348 (2013).
- 4. J. Euesden, C. M. Lewis, P. F. O'Reilly, PRSice: Polygenic Risk Score software. *Bioinforma. Oxf. Engl.* **31**, 1466–1468 (2015).
- 5. C. A. Rietveld *et al.*, GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science*. **340**, 1467–71 (2013).
- 6. A. R. Wood *et al.*, Defining the role of common variation in the genomic and biological architecture of adult human height. *Nat. Genet.* **46**, 1173–1186 (2014).
- 7. A. L. Price *et al.*, Principal components analysis corrects for stratification in genome-wide association studies. *Nat. Genet.* **38**, 904–909 (2006).
- 8. N. Patterson, A. L. Price, D. Reich, Population structure and eigenanalysis. *PLoS Genet.* **2**, e190 (2006).
- 9. R. Poulton *et al.*, Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. *Lancet.* **360**, 1640–1645 (2002).
- OECD/Eurostat/UNESCO Institute for Statistics, "ISCED 2011 Operational Manual: Guidelines for Classifying National Education Programmes and Related Qualifications" (OECD/Eurostat/UNESCO Institute for Statistics, 2015), (available at http://dx.doi.org/10.1787/9789264228368-en).
- 11. T. E. Moffitt *et al.*, A gradient of childhood self-control predicts health, wealth, and public safety. *Proc. Natl. Acad. Sci.* **108**, 2693–8 (2011).
- 12. B. J. Milne, U. Byun, A. Lee, *New Zealand socio-economic index 2006.* (Statistics New Zealand, Wellington, NZ, 2013).
- 13. S. J. Goldman-Mellor *et al.*, Suicide attempt in young people: a signal for long-term health care and social needs. *JAMA Psychiatry*. **71**, 119–127 (2014).

- 14. S. Israel *et al.*, Credit scores, cardiovascular disease risk, and human capital. *Proc. Natl. Acad. Sci.*, 201409794 (2014).
- 15. L. K. Muthen, B. O. Muthen, MPLUS (L.K. Muthen & B.O. Muthen, Los Angeles, 1998).
- 16. Scottish Council for Research in Education, The Burt Word Reading Test (1976).
- 17. J. D. Singer, J. B. Willett, *Applied Longitudinal Data Analysis* (Oxford University Press, New York, 2003).
- 18. P. A. Silva, 4000 Otago Teenagers: A Preliminary Report from the Pathways to Employment *Project* (The Dunedin Multidisciplinary Health and Development Research Unit, Dunedin, NZ, 1987).
- 19. W. B. Elley, I. C. Irving, A socio-economic index for New Zealand based on levels of education and income from the 1966 census. *N. Z. J. Educ. Stud.* **7**, 153–167 (1972).
- A. Caspi *et al.*, The life history calendar: A research and clinical assessment method for collecting retrospective event-history data. *Int. J. Methods Psychiatr. Res.* 6, 101–114 (1996).
- 21. B. J. Milne, R. Poulton, A. Caspi, T. E. Moffitt, Brain drain or OE? Characteristics of young New Zealanders who leave. *N. Z. Med. J.* **114**, 450–453 (2001).
- 22. Overseas experience. *Wikipedia Free Encycl.* (2014), (available at http://en.wikipedia.org/w/index.php?title=Overseas_experience&oldid=633298303).
- T. E. Moffitt, A. Caspi, H. Harrington, B. J. Milne, Males on the life-course-persistent and adolescence-limited antisocial pathways: Follow-up at age 26 years. *Dev. Psychopathol.* 14, 179–207 (2002).
- 24. A. Furnham, M.-P. Goletto-Tankel, Understanding Savings, Pensions and Life Assurance in 16-21-Year-Olds. *Hum. Relat.* **55**, 603–628 (2002).
- 25. Statistics New Zealand, "New Zealand Income Survey: June 2014 quarter" (Statistics New Zealand), (available at http://www.stats.govt.nz/browse_for_stats/income-and-work/Income/NZIncomeSurvey_HOTPJun14qtr/Tables.aspx).
- 26. W. Pavot, E. Diener, Review of the Satisfaction With Life Scale. *Psychol. Assess.* **5**, 164–172 (1993).
- 27. L. Dunn, *The Peabody Picture Vocabulary Test* (American Guidance Service, Minneapolis, 1965).
- 28. L. M. Terman, M. A. Merrill, *Stanford-Binet Intelligence Scale: Manual for the third revision, Form L-M* (Houghton Mifflin, Oxford, England, 1960), vol. xi.

- 29. D. Wechsler, *Wechsler Intelligence Scale for Children* (Harcourt Assessment, San Antonio, TX, 4th (UK Version)., 2003).
- 30. Lezak, DM, Howieson, DB, Loring, DW, Hannay, HJ, Fischer, JS, *Neuropsychological Assessment* (Oxford University Press, ed. 4, 2004).
- 31. A. Caspi, B. Henry, R. O. McGee, T. E. Moffitt, P. A. Silva, Temperamental origins of child and adolescent behavior problems: from age 3 to age 15. *Child Dev.* **66**, 55–68 (1995).
- 32. D. W. Belsky *et al.*, Cardiorespiratory fitness and cognitive function in midlife: Neuroprotection or neuroselection? *Ann. Neurol.* **77**, 607–617 (2015).
- 33. N. Bayley, *The Bayley Scale of Infant Development* (Psychological Corp, New York, NY, 1969).
- 34. D. McCarthy, Scales of Children's Abilities. (Psychological Corp, New York, NY, 1972).
- 35. D. Arnheim, S. W. Sinclair, *The Clumsy Child* (VC Mosby Co, St Louis Mo, 1974).
- M. Cannon *et al.*, Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder Results from a longitudinal birth cohort. *Arch. Gen. Psychiatry*. 59, 449–456 (2002).
- D. W. Belsky *et al.*, Polygenic Risk, Rapid Childhood Growth, and the Development of Obesity: Evidence from a 4-Decade Longitudinal Study. *Arch. Pediatr. Adolesc. Med.* 166, 515–521 (2012).
- S. Williams, R. Poulton, Birth Size, Growth, and Blood Pressure between the Ages of 7 and 26 Years: Failure to Support the Fetal Origins Hypothesis. *Am. J. Epidemiol.* 155, 849–852 (2002).
- 39. M. R. Sears *et al.*, A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N. Engl. J. Med.* **349**, 1414–22 (2003).
- R. M. Baron, D. A. Kenny, The Moderator Mediator Variable Distinction in Social Psychological-Research - Conceptual, Strategic, and Statistical Considerations. *J. Pers. Soc. Psychol.* 51, 1173–1182 (1986).
- 41. K. J. Preacher, A. F. Hayes, Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods*. **40**, 879–91 (2008).
- 42. K. J. Preacher, K. Kelley, Effect size measures for mediation models: Quantitative strategies for communicating indirect effects. *Psychol. Methods*. **16**, 93–115 (2011).

 D. P. Mackinnon, J. H. Dwyer, Estimating mediated effects in prevention studies. *Eval. Rev.* 17, 144–158 (1993).



Figure S1. Distribution of the polygenic score for educational attainment in the Dunedin cohort. The x-axis of the figure shows polygenic score z-scores (one unit corresponds to one standard deviation).



Figure S2. Distribution of the Adult Attainment Factor score in the Dunedin cohort. The x-axis of the figure shows Attainment Factor z-scores (one unit corresponds to one standard deviation).



	Estimate Adjusted for						
	Unadjusted Estimate			Educational Attainment			
	<u>r</u>	<u>(SE)</u>	<u>p-value</u>	<u>r</u>	<u>SE</u>	<u>p-value</u>	<u>N</u>
Adult Attainment Factor	0.13	(0.03)	1.18E-04	0.07	(0.03)	0.035	901
Occupational Prestige	0.15	(0.03)	7.30E-06	0.05	(0.03)	0.089	866
Personal Income (NZD)	0.08	(0.03)	0.006	0.03	(0.03)	0.283	882
Assets (log NZD)	0.06	(0.03)	0.059	0.02	(0.03)	0.644	889
Difficulty Paying Expenses Scale	-0.12	(0.03)	3.97E-04	-0.09	(0.03)	0.009	887
Social Welfare Benefit Use (log days)	-0.07	(0.03)	0.034	-0.04	(0.03)	0.226	897
Credit Problems Scale	-0.08	(0.03)	0.010	-0.06	(0.03)	0.062	887
Credit Score (Veda Corp.)	0.12	(0.04)	0.001	0.09	(0.04)	0.014	803

Figure S3. Effect-size estimates for genetic associations with the adult attainment measures before and after adjustment for educational attainment. Effect-size estimates are standardized regression coefficients (equivalent to Pearson's r). All models included sex and the first ten principal components estimated from the genome-wide SNP data as covariates.

Unadjusted estimates are shown with dark blue bars. Estimates adjusted for educational attainment are shown with light blue bars. Adjusting for educational attainment reduced genetic effect sizes by 25-70%.



Figure S4. Genetic and social inheritance combine to influence life attainments. The heat map shows variation in adult attainment (low to high attainment scaled from blue to red on the color axis) across the distributions of social inheritance (x-axis) and polygenic scores (y-axis). The clustering of blue toward the bottom left and of red toward the upper right illustrates and additive combination of genetic and social inheritance influencing life attainments.



Figure S5. Survival curves illustrating when Dunedin Study members reached each of a series of developmental milestones.



Figure S6. Development of reading skill from age 7 to 18 years in the Dunedin Cohort. The box plots show distributions of Burt Reading Test scores in the Dunedin cohort when Study members were ages 7, 9, 11, 13, 15, and 18 years.



Figure S7. Path diagram of mediation analysis. The path diagram is a graphical representation of the mediation analysis. We analyzed two attainment outcomes, educational attainment and adult socioeconomic attainment (measured as the adult attainment factor score). In addition to the multiple mediator model depicted below, we also conducted single-mediator analyses in which each candidate mediator was analyzed on its own (see Table S3). Indirect effects were estimated as the products of 'a' and 'b' paths. Direct effects were estimated as the 'c' paths.



Figure S8. Mediation of genetic associations with adult attainments and pathways to success by cognitive ability, self-control skills, and interpersonal skill. The figure graphs effect estimates from multiple-mediator models of genetic associations with attainments and pathways to success. Bar height gives the total effect estimate. Colored segments of bars show the indirect effects of cognitive ability (light blue), self-control skills (dark blue), and interpersonal skill (pink), and the portion of the total effect not explained by these mediators (lavender). Estimates for dichotomous dependent variables (OE, Migration) were derived using the method described by Mackinnon and Dwyer (*43*).

Table S1. Effect-size estimates for genetic associations with adult attainments, pathways to success, and abilities and skills: Models without adjustment for principal components estimated from the genome-wide SNP data and models with adjustment for principal components. Effect-size estimates are standardized coefficients (denoted as 'r') from linear regressions, hazard ratios (denoted as 'HR') from Cox models, relative risks (denoted as 'RR') from from Poisson models, odds ratios (denoted 'OR') from ordered logistic models, and unstandardized coefficients (denoted as 'b') from mixed-effects growth models. All models included sex as a covariate. Models under the heading "Base Model" were additionally adjusted for the first ten principal components estimated from the genome-wide SNP data. Stars next to coefficients indicate p-values *** <0.001, ** <0.01, *<0.05. 95% Confidence intervals are provided for relative risks and odds ratios. Confidence intervals that do not include 1 are statistically significant at the α =0.05 level. Confidence intervals that include 1 are denoted with gray text.

Principal ComponentsBase ModelEducational Attainmentr0.14 ***0.15 ***Adult Attainmentr0.15 ***0.12 ***	
Educational Attainmentr0.14 ***0.15 ***Adult Attainmentr0.15 ***0.12 ***	
Adult Attainment - 0.15 *** 0.13 ***	
Pathways to Success	
Milestones	
Smiling HR 0.99 [0.94-1.05] 1.00 [0.95-1.0	6]
Sitting Up HR 1.00 [0.94-1.05] 1.00 [0.94-1.0	6]
Walking HR 1.01 [0.95-1.06] 1.01 [0.95-1.0	6]
Talking HR 1.11 [1.05-1.18] 1.12 [1.05-1.	.9]
Feeding Self HR 0.98 [0.93-1.04] 0.98 [0.92-1.0	4]
Potty Training (day) HR 1.03 [0.97-1.09] 1.02 [0.96-1.0	9]
Potty Training (night) HR 0.95 [0.88-1.02] 0.95 [0.88-1.0	3]
Communicating in Sentences HR 1.06 [1.00-1.13] 1.06 [1.00-1.1	.2]
Reading	-
Reading: Intercept (age 7) b 2.69 *** 2.79 ***	
Reading: Linear Slope b 0.25 * 0.25 *	
Reading: Quadratic Slope b -0.03 ** -0.03 **	
Aspirations	
Educational Aspirations r 0.15 *** 0.15 ***	
Aspiration to University Degree RR 1.23 [1.11-1.36] 1.24 [1.11-1.37]	
SES Aspiration r 0.12 *** 0.12 ***	
Aspiration to Professional Occupation RR 1.15 [1.05-1.25] 1.16 [1.06-1.27]	
Standardized Testing	
No Educational Certification RR 0.80 [0.68-0.94] 0.78 [0.66-0.93	
Testing level OR 1.33 [1.17-1.52] 1.36 [1.18-1.56	
School Certificate Exam Score r 0.24 *** 0.24 ***	
Form 6 Exam Score r 0.21 *** 0.19 ***	
Bursary Exam Score r 0.19 * 0.19 *	
Geographic Mobility	
OF RR 1 18 [1 05-1 32] 1 17 [1 05-1 32]	
Migration RR 1 18 [1 05-1 32] 1 18 [1 05-1 32]	
Financial Planfulness	
Financial Problems r -0.09 ** -0.08 *	
Financial Planfulness r 0.10 ** 0.09 **	
Mating	
Partner SES r 0.09 * 0.09 *	
Life Satisfaction r 0.04 0.04	
Abilities and Skills	
Cognitive Ability	
Peabody IO r 0.06 0.05	
Stanford-Binet IO r 0.15 *** 0.13 ***	
WISC-B ID (age 7) r 0.13 ***	
WISC-R IQ (age 9) r 0.14 *** 0.16 ***	
WISC-R IQ (age 11) r 0.10 0.10 0.10 0.10	
WISC-R IQ (age 13) r 0.10 0.10 0.10	
Cognitive Development	
Mental Age: Intercent (age 7) b 0.14 *** 0.13 ***	
Montal Age: Intercept (age 7) 0 0.14 0.15	
Non-Cognitive Skills	
Solf-Control Skills r 0.11 *** 0.10 **	
Internersonal Skill r 0.11 0.10	
Interpersonal Skii I 0.11 0.10 Physical Health r -0.01 0.01	

Measure	Categorization	Loading	95% CI
Occupational Prestige	6 Categories	0.48	[0.42, 0.55]
Personal Income	10 Categories	0.51	[0.46, 0.57]
Value of Assets	10 Categories	0.71	[0.66, 0.75]
Difficulty Paying Expenses		-0.60	[-0.66, -0.55]
Benefit Days	8 Categories	-0.66	[-0.71, -0.61]
Credit Problems	7 Categories	-0.66	[-0.73, -0.60]
Credit Score (VEDA)	÷ 100	0.53	[0.47, 0.59]

Table S2. Standardized factor loadings for adult attainment indicators.

Table S3. Effect-size estimates for genetic associations with adult attainments, pathways to success, and abilities and skills. Effect-size estimates are standardized coefficients (denoted as 'r') from linear regressions, hazard ratios (denoted as 'HR') from Cox models, relative risks (denoted as 'RR') from Poisson models, odds ratios (denoted 'OR') from ordered logistic models, and unstandardized coefficients (denoted as 'b') from mixed-effects growth models. All models included sex and the first ten principal components estimated from the genome-wide SNP data as covariates. Models under the heading "Adjusted for Childhood SES" were additionally adjusted for childhood SES (9). Stars next to coefficients indicate p-values *** <0.001, ** <0.01, *<0.05. 95% Confidence intervals are provided for relative risks and odds ratios. Confidence intervals that do not include 1 are statistically significant at the α =0.05 level. Confidence intervals that include 1 are denoted with gray text.

		Base Model	Adjusted for Childhood SES
Educational Attainment	r	0.15 ***	0.10 **
Adult Attainment	r	0.13 ***	0.11 **
Pathways to Success			
Milestones			
Smiling	HR	1.00 [0.95-1.06]	1.00 [0.94-1.05]
Sitting Up	HR	1.00 [0.94-1.06]	0.99 [0.94-1.06]
Walking	HR	1.01 [0.95-1.06]	1.01 [0.95-1.06]
Talking	HR	1.12 [1.05-1.19]	1.11 [1.05-1.18]
Feeding Self	HR	0.98 [0.92-1.04]	0.97 [0.92-1.03]
Potty Training (day)	HR	1.02 [0.96-1.09]	1.03 [0.96-1.09]
Potty Training (night)	HR	0.95 [0.88-1.03]	0.96 [0.88-1.04]
Communicating in Sentences	HR	1.06 [1.00-1.12]	1.04 [0.98-1.11]
Reading			
Reading: Intercept (age 7)	b	2.79 ***	2.27 ***
Reading: Linear Slope	b	0.25 *	0.15
Reading: Quadratic Slope	b	-0.03 **	-0.02 *
Aspirations	-		
Educational Aspirations	r	0.15 ***	0.12 ***
Aspiration to University Degree	RR	1.24 [1.11-1.37]	1.18 [1.06-1.32]
SES Aspiration	r	0.12 ***	0.10 **
Aspiration to Professional Occupation	RR	1.16 [1.06-1.27]	1.13 [1.03-1.24]
Standardized Testing			
No Educational Certification	RR	0.78 [0.66-0.93]	0.86 [0.72-1.02]
Testing Level	OR	1.36 [1.18-1.56]	1.23 [1.06-1.42]
School Certificate Exam Score	r	0.24 ***	0.19 ***
Form 6 Exam Score	r	0.19 ***	0.16 ***
Bursary Exam Score	r	0.19 *	0.18 *
Geographic Mobility	·	0.20	0.20
OE	RR	1.17 [1.05-1.32]	1.13 [1.00-1.27]
Migration	RR	1.18 [1.05-1.32]	1.17 [1.05-1.32]
Financial Planfulness			
Financial Problems	r	-0.08 *	-0.06
Financial Planfulness	r	0.09 **	0.07 *
Mating			
Partner SES	r	0.09 *	0.07
Life Satisfaction	r	0.04	0.03
Abilities and Skills			
Cognitive Ability			
Peabody IQ	r	0.05	0.02
Stanford-Binet IQ	r	0.13 ***	0.09 **
WISC-R IQ (age 7)	r	0.13 ***	0.08 *
WISC-R IO (age 9)	r	0.16 ***	0.11 ***
WISC-R IO (age 11)	r	0.18 ***	0.13 ***
WISC-R IO (age 13)	r	0.16 ***	0.11 ***
Cognitive Development			
Mental Age: Intercept (age 7)	b	0.13 ***	0.09 *
Mental Age: Linear Slope	b	0.05 ***	0.03 **
Non-Cognitive Skills	~		
Self-Control Skills	r	0.10 **	0.07 *
Interpersonal Skill	r	0.10 **	0.09 *
Physical Health	r	0.01	0.02
,	·		

Table S4. Mediation analysis results. The table shows standardized estimates of total, direct, and indirect effects from mediation models. 95% Confidence intervals are percentile based, estimated from 500 bootstrap repetitions.

Educational Attainment Adult Attainment F Est. SE p-value 95% CI Est. SE p-value Multiple Mediator Model (Cognitive Ability, Self-Control Skills, Social Skills) Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.04) <0.001	actor <u>95% Cl</u> [0.07-0.20] [0.00-0.14] [0.04-0.09]
Est. SE p-value 95% CI Est. SE p-value Multiple Mediator Model (Cognitive Ability, Self-Control Skills, Social Skills) Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.04) <0.001	95% Cl [0.07-0.20] [0.00-0.14] [0.04-0.09]
Multiple Mediator Model (Cognitive Ability, Self-Control Skills, Social Skills)Total Effect0.15(0.03)<0.001[0.09-0.22]0.14(0.04)<0.001	[0.07-0.20] [0.00-0.14] [0.04-0.09]
Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.04) <0.001	[0.07-0.20] [0.00-0.14] [0.04-0.09]
Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.04) <0.001	[0.07-0.20] [0.00-0.14] [0.04-0.09]
	[0.00-0.14] [0.04-0.09]
Direct Effect 0.06 (0.03) 0.037 [0.00-0.12] 0.07 (0.03) 0.025	[0.04-0.09]
Total Indirect Effect 0.09 (0.02) <0.001 [0.06-0.13] 0.06 (0.01) <0.001	
% Mediation 60% 47%	
Individual Mediator Models	
IQ	
Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.03) <0.001	[0.07-0.20]
Direct Effect 0.07 (0.03) 0.022 [0.01-0.13] 0.08 (0.03) 0.010	[0.02-0.14]
Indirect Effect 0.09 (0.02) <0.001 [0.05-0.12] 0.06 (0.01) <0.001	[0.03-0.08]
% Mediation 57% 41%	
Self-Control Skills	
Total Effect 0.15 (0.03) <0.001 [0.09-0.22] 0.14 (0.03) <0.001	[0.07-0.20]
Direct Effect 0.11 (0.03) <0.001 [0.05-0.18] 0.10 (0.03) 0.001	[0.04-0.16]
Indirect Effect 0.04 (0.01) 0.002 [0.02-0.07] 0.03 (0.01) 0.004	[0.01-0.06]
% Mediation 27% 24%	
Interpersonal Skill	
Total Effect 0.15 (0.03) <0.001 [0.08-0.21] 0.14 (0.03) <0.001	[0.07-0.20]
Direct Effect 0.14 (0.03) <0.001 [0.06-0.20] 0.13 (0.03) <0.001	[0.06-0.19]
Indirect Effect 0.02 (0.01) 0.011 [0.01-0.03] 0.01 (0.01) 0.021	[0.00-0.02]
% Mediation 10% 9%	