

## **FAQs regarding**

### **“Molecular genetic contributions to social deprivation and household income in UK Biobank”**

W David Hill, Saskia P Hagenaars, Riccardo E Marioni, Sarah E Harris, David CM Liewald, Gail Davies, Aysu Okbay, Andrew M McIntosh, Catharine R Gale, Ian J Deary.

Additional queries should be directed to W David Hill (David.Hill@ed.ac.uk) and Ian J. Deary (i.deary@ed.ac.uk).

#### **What did you do in this study?**

We performed a genome-wide association study (GWAS). Data were provided by 112,151 individuals aged 40-70 years from across the United Kingdom who are participants in a study called the UK Biobank. Our GWAS examined around 17 million points of DNA variation called single nucleotide polymorphisms (SNPs, pronounced ‘snips’). SNPs are the smallest and most common form of genetic variation found (although they are not the only way in which individuals can differ genetically). We looked at these genetic data in relation to two measures of what social scientists often call socioeconomic status (SES): social deprivation, as measured by the level of deprivation in the postcode area in which an individual lives; and household income. The Townsend Deprivation Index was used to measure social deprivation. The Townsend Deprivation Index is derived for an area and is composed of four variables: the prevalence of overcrowded housing, non-home ownership in the area, non-car ownership in the area, and unemployment.

In participants who had data on these social deprivation and income measures, and who had donated genetic material for analysis, we tested whether the level of socioeconomic status varied along with their genetic variation. First, we examined if people who were at different levels of deprivation and income were more likely to have particular version (called an allele) of a SNP in their genome. Second, we looked at how much of the SES differences between people could be accounted for by differences across the whole set of SNPs that we examined; that is, we used DNA data to examine the ‘heritability’ of these SES measures, as indicated by these SNPs.

#### **What did you find?**

Our results suggest that, as expected, the reasons that people differ in social deprivation and income are mostly environmental in origin. There was some small genetic contribution to these factors.

We found four SNPs that were statistically significantly associated with household income, but did not find any that were associated with deprivation. The SNPs that were found to be associated with household income were also found in an independent sample examining a third measure of SES, education. Each individual SNP had only a miniscule association with household income, even though it was statistically significant.

We found that variation across all the SNPs in the DNA from this sample could account for 21% of the variation in social deprivation, and 11% of the variation in household income. The rest of the variation is due to environmental factors, and some of it possibly to types of genetic differences that we didn’t measure. Therefore, the large majority of these social differences are likely to be environmental in origin.

So, at this stage, we found that a small amount of the individual differences in these measures of SES was associated with genetic differences called SNPs. We then asked if the SNPs that contributed towards these social estimates (the ones that explained 21% of social deprivation differences, and 11% of household income differences) were also associated with some of people’s differences in other areas of life, such as longevity, health, and cognitive ability. There was some overlap: SNPs

that were associated with social deprivation were also associated with 16 other traits, and SNPs that contributed towards household income were associated with 22 other traits; these are listed below<sup>1</sup>.

### **How could genetic differences be associated with something like income?**

At first this seems confusing: a person's income (and their socioeconomic status more generally) is a social variable, influenced by factors such as their parents, which part of the country they happen to live in, how the economy is doing, politics and social policies, health, education, and pure luck. How can it be associated with genetic differences?

However, there are many traits that a person has that could contribute to making them more or less likely to earn a higher or lower income. They might be more highly motivated and conscientious at work, for example, or they might be more intelligent, be less susceptible to illness, or simply more interested in the kinds of jobs that lead to higher wages. All these and other psychological and health factors might be influenced to some extent by genetics, especially if these genetic variants have effects in the brain or in other parts of the body that are important for maintaining one's health. There are some clues about the activity of these genetic variants in our study, but we need future studies in different (and even larger) samples to find out more of the details and possible mechanisms.

Note that our results imply that by far the largest influence on people's socioeconomic status is differences in environments through life, probably including demographic, political, physical, cultural, and social factors. But our findings also indicate that socioeconomic status attainment is a complex process, associated not just with differences in environmental exposures but also perhaps to a small extent by genetic differences, that probably affect our health, cognitive skills, personality, and volition. These results make a small start at unpicking this tangle of influences.

### **What's the point of doing this research?**

The prompt for the study was the interest in health inequalities and how to ameliorate them. It is well known that people with more social deprivation and lower incomes are at greater risk of poorer health than those from advantaged social backgrounds. Research into the reasons for these health differences has focussed on environmental explanations. However, previous studies have shown that many common health problems are partly due to the genes that people inherit and that a small part of the variation in social deprivation between people is also associated with differences in their genes, so we wanted to investigate whether the links between socioeconomic status and health might be partly accounted for by genes that influence both socioeconomic status and health. If politicians or others wish to make effective policies to reduce the health inequalities between people of different social backgrounds, they need to know what brings about those health inequalities. Health inequalities between people of different social background and between those living in areas with different levels of social deprivation have risen sharply in the UK over the past 30 to 40 years. The speed of this change means that the rise in health inequalities must be due to environmental factors—social, political, and economic—rather than genes, because genes cannot change so rapidly. Nonetheless, it is important to discover the extent to which genes might explain links between socioeconomic status and health because if genes do play a part—however small—it means that children born into families with a lower socioeconomic status, or who live in an area of social deprivation, face a double risk in that they not only have a genetic predisposition to ill health and other factors associated with lower socioeconomic status later in life, but they also grow up with all the environmental disadvantages that commonly accompany lower socioeconomic status and lead to worse health. Policy makers should therefore intensify their efforts to address the environmental influences on health.

### **Have you found "the income gene"?**

No. Nobody has ever found such a gene, and nor are they ever likely to. This is because the genetic contribution to factors like household income (or intelligence, personality, or many other traits with a “complex genetic architecture”) is made up of many thousands of genetic variants, each with a tiny effect that adds up; in this case, they add up to explain 11% of people’s income differences. If there was one single gene or genetic variant that had a big effect on income—“the income gene”—it would have stuck out like a sore thumb in our study, but we didn’t find anything like it.

To think about this another way, consider walking in the rain. Each individual drop has only a small effect, but the cumulative effect of being hit by many thousands of drops is what causes you to get wet. Any one of these genetic variants makes only a small difference, but the effect of many thousands of them can add up to detectable associations with factors like those we assessed here.

**Does this mean that an individual’s level of SES is determined at birth?**

No. We examined one large group of individuals and examined if differences in two SES measures might be, partly, associated with genetic differences. This does not imply that each individual is predestined to end up in a particular SES, but rather that the genetic variants people carry have some small association with their SES by the time they’re middle-aged.

As the study was examining how individuals differ, it is critical to remember that variation in both the environment and in genetic factors must be present if they are to be associated. If there were a society where everyone was raised in exactly the same environment, with exactly the same opportunities and personal and social resources, then the only reason that people would differ would be due to genetic differences. That’s not what we found here: in our study, the genetic associations were modest.

Imagine that we had found no genetic associations with these SES variables. What might this mean? It would indicate that even those born with genetic variants associated with, say, better health, higher intelligence, and greater conscientiousness would not be able to alter their SES due to environmental or social factors holding them back. As such, the finding of a genetic association with SES should be viewed as an indicator of the “meritocratic” notion that, at least within the population studied here, the individual’s level of, perhaps, health/ability/personality as partly conferred by genetic effects allows them to alter their SES to some extent. We also note that, with respect to personality traits, the best evidence we have is that genetic variation plays some part, but the environment is the major influence on why people differ.

Another important point is that the finding of genetic associations with a trait does not mean that environmental interventions cannot change them. A classic example of this is the disorder of phenylketonuria. This disorder is genetic in origin, and results in serious medical problems along with a high level of intellectual disability. However, by altering their diet from birth, individuals with this condition can lead lives that are not hampered by the disease, or by a reduction in their cognitive abilities. Or consider eyesight; having poorer eyesight is partly heritable (it’s passed down from parent to child), but these problems can be solved with an environmental intervention: spectacles. These examples show that, even if a trait is highly genetic (and recall that SES most certainly is not), it is a possibility that environmental influences can change it. Even more simply put, if a government had a huge financial windfall and decided to redistribute it equally, it could all but eliminate income differences, thus reducing genetic associations to zero.

<sup>1</sup> Social deprivation showed positive genetic correlations (indicated by a +) with 10 traits and negative genetic correlations (indicated by a -) with 6 traits. These traits were body mass index (BMI)+, height-, neuroticism+, schizophrenia+, major depressive disorder+, triglycerides+, low-density lipoprotein level+, high-density

lipoprotein level-, childhood obesity+, obesity+, smoking+, diastolic blood pressure+, longevity-, verbal numerical reasoning-, years of education-, and childhood IQ-.

Household income showed positive genetic correlations (indicated by a +) with 9 traits and negative genetic correlations (indicated by a -) with 13 traits. These traits were intracranial volume+, BMI-, infant head circumference+, height+, neuroticism-, schizophrenia-, bipolar disorder-, Alzheimer's disease-, fasting insulin level-, triglycerides-, low-density lipoprotein level-, high-density lipoprotein level+, HbA1c-, homeostatic model assessment insulin resistance-, homeostatic model assessment beta-cell function-, obesity-, smoking-, coronary artery disease-, longevity+, verbal numerical reasoning+, years of education+, and childhood IQ+.