Confounding Fuels Misinterpretation in Human Genetics

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Abstract

The scientific literature has seen a resurgence of interest in genetic influences on human behavior and socioeconomic outcomes. Such studies face the central difficulty of distinguishing possible causal influences, in particular genetic and non-genetic ones. When confounding between possible influences is not rigorously addressed, it invites over- and misinterpretation of data. We illustrate the breadth of this problem through a discussion of the literature and a reanalysis of two examples. Clark (2023) suggested that patterns of similarity in social status between relatives indicate that social status is largely determined by one's DNA. We show that the paper's conclusions are based on the conflation of genetic and non-genetic transmission, such as wealth, within families. Song & Zhang (2024) posited that genetic variants underlying bisexual behavior are maintained in the population because they also affect risk-taking behavior, thereby conferring an evolutionary fitness advantage through increased sexual promiscuity. In this case, too, we show that possible explanations cannot be distinguished, but only one is chosen and presented as a conclusion. We discuss how issues of confounding apply more broadly to studies that claim to establish genetic underpinnings to human behavior and societal outcomes.

Introduction

People vary remarkably in behavior and social outcomes. This variation sparks curiosity about its causes, and for the past 150 years, scholars have debated the extent to which it arises due to underlying genetic differences. In the 19th century, Galton (*1*) found strong resemblance between parents and their offspring in measures of social status and on that basis inferred that genetics is the most likely root cause, a school of thought described broadly as "hereditarianism" (see *2*). As is now well appreciated, Galton's inference dismissed the fact that parents transmit not only genetic material to their offspring, but also wealth, place of residence, knowledge, religion, culture, and more. For such attributes, transmission within families can parallel genetic transmission (**Fig. 1a**) (*3–20*), often leading genetic and non-genetic transmission to be indistinguishable in observational data. A long history of scholarship has highlighted this type of confounding and how it impedes inference of the causes of phenotypic variation, especially when molecular genetic data are unavailable (*21–28*).

Here, we demonstrate how confounding is frequently overlooked or downplayed in contemporary reports about genetic causes of human behavior and socioeconomic outcomes. We begin with a reanalysis of data from a recent publication that made claims about genetic determinism of social status (*29*). We then discuss how confounding can pervasively impact inferences based on genome wide association studies (GWAS) for behavior and social outcomes. Lastly, we illustrate the impacts of a broader category of confounding and errors in causal inference, stemming from data preparation and other analysis choices, in a recent study (*30*) that purported to explain the evolutionary maintenance of genetic variation affecting bisexual behavior.

Confounding fuels hereditarian fallacies

A recent publication (*29*) analyzed familial correlations in a dataset of socioeconomic measures (e.g., occupational status, house value, literacy) from a selection of records spanning the 18th to 21st centuries in England. (*29*) fits a quantitative genetic model to these observed correlations [(*31*, *32*); **Supplementary Note 1**]. Based on this fit, (*29*) infers that social status persists intergenerationally because of strong assortative mating on a status-determining genotype (or "social genotype" as the author has used in previous work (*33*)). Further, the paper argues that because mates share the genes underlying social status to such a high degree, the persistence

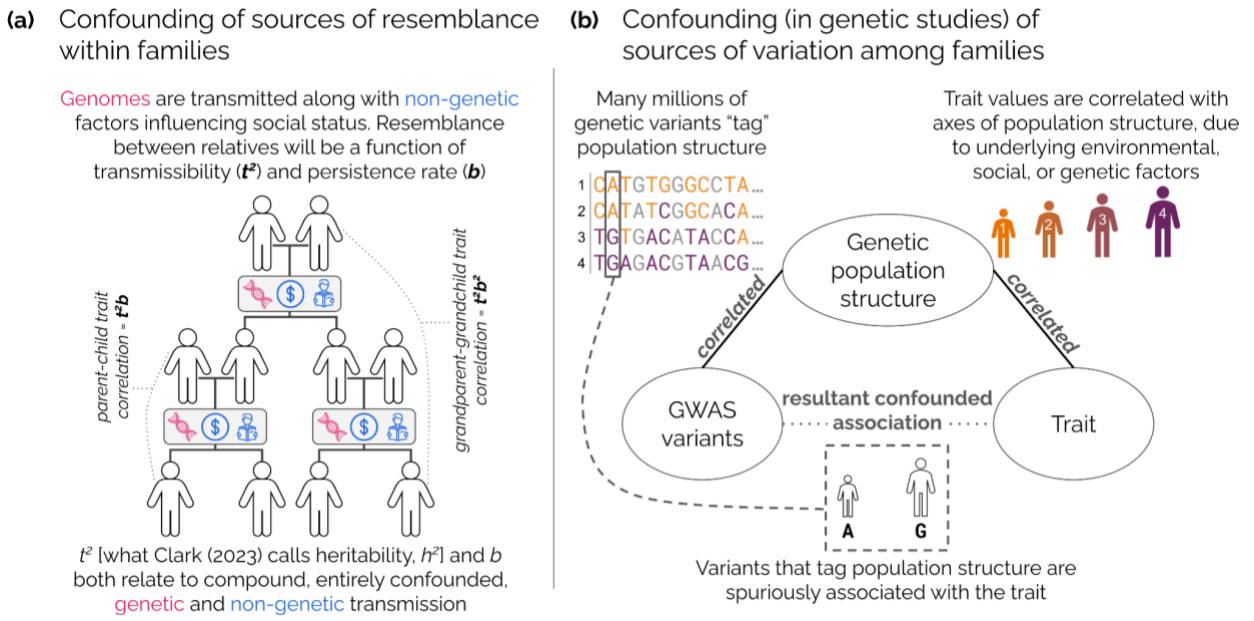

Figure 1. Confounding between genetic and non-genetic factors influencing traits. (a) Confounding within families. Non-genetic transmission can parallel genetic transmission, and their respective effects are confounded in observational data. Illustrated is a model where a trait value is the sum of an inherited component from parents and random noise. Under this model, the expected resemblance between relatives depends on transmissibility (t^2, the portion of trait variation attributable to the transmitted component) and a rate of decay across genealogical distance (the "persistence rate," *b,* which increases with increasing degree of assortative mating). Ignoring the confounding of genetic and non-genetic transmission in the data, Clark (2023) misassigns all transmission as genetic heritability and all assortative mating to be on a latent "social genotype". **(b) Confounding among families induces biases in GWAS.** "Population structure confounding" in genomic data relates to correlations between the structure of genetic relatedness in a GWAS sample (exemplified by the orange-to-purple gradient) and the phenotype studied. Here we show genetic sequences from individuals 1-4 at top left, with their attendant phenotypes (height) at top right. For a given genetic variant, individuals with purple alleles will tend to be taller than those with orange alleles, regardless of the variant's causal effect on height. This confounding affects any variants that reflect this axis of genetic population structure—typically many millions of variants. While researchers often use methods that adjust for population structure in an attempt to avoid spurious associations, the extent of residual confounding in GWAS remains unclear.

of social status within families—and persistence of differences in status among families—have been largely unaffected by changes in social policy in the last four centuries. In a subsequent commentary about this work (*34*), the author presents the results of (*29*) as providing strong support for a hereditarian interpretation. In doing so, he appeals to the metaphor of a "genetic lottery" underlying social outcomes.

Here, we discuss the failure to account for the confounding of genetic and non-genetic transmission (**Fig. 1a**) that, together with other core flaws of the analysis (**Fig. 2a-b**), fuels the hereditarian claims in (*29*) (see our discussion of other misinterpretations, errors, and incongruencies in (*29*) in **Supplementary Notes 2-7**; **Tables S1-S3**; **Figs. S1-S13**). We also

demonstrate that familial status correlations varied substantially over the time period examined, generally decreasing (**Fig. 2c**). This finding contrasts with the paper's conclusion, based on the same data, that social mobility has been stagnant. As we show below, the analyses in (*29*) do not establish the contribution of genetics to social status.

Confounding between genetic and non-genetic transmission. Inferences in (*29*) are based on a linear regression model derived from quantitative-genetic theory developed by R.A. Fisher (*31*, *32*) (**Supplementary Note 1**) and the model

$$P = G + E \qquad \text{Eq. 1}$$

where an individual's phenotype, P, is the sum of separable genotypic (G) and environmental (E) influences on it. Since genotypes are transmitted from parents to offspring, genetic parameters can be inferred from correlations between relatives, so long as environmental influences are independent and random with respect to genotypes. Fisher (1918) formally showed that under this model, the expected correlation in a trait between pairs of individuals of a defined relationship is a function of the genealogical relationship between the relatives, the trait's heritability (h^2), and the extent of assortative mating in the population (b). (h^2 is the fraction of phenotypic variance due to additive genetic variance, commonly referred to as "narrow-sense" heritability.)

Crucially, to interpret the model parameters h^2 and b as relating to genetic effects, Fisher's model assumes that there are no non-genetic (material, environmental, or cultural) influences on a trait that are systematically shared or transmitted between relatives. This assumption is valid in an experimental setting, for instance, in which genotypes are randomized with regard to environment. However, in humans that assumption is nonsensical. Non-genetic transmission is ubiquitous for social and behavioral traits. Traits may be transmitted directly between relatives (e.g., literate parents teaching their children how to read) (*5*), or via indirect mechanisms such as "ecological inheritance," where the trait value of an offspring is influenced by the environmental conditions bestowed by their parents (e.g., familial wealth influencing educational opportunities) (*8*, *35*). When genotypes cannot be randomized over environments, true genetic effects are much more difficult to separate from other factors underlying phenotypic resemblance between relatives (*22*). In (*29*), for instance, the assumption of no systematic non-genetic transmission implies that similarity in house value among relatives (one of the measures of social status analyzed) is solely due to shared genes, and does not arise from similarity in parental wealth, the inheritance of wealth or property, or having learned from one's relatives about investment.

In fact, we found signals of strong confounding between genetic and non-genetic contributions to familial resemblance in the data used in (*29*). The paper acknowledges the inheritance of material wealth from one's parents as an example of non-genetic transmission only when treating wealth itself as the focal status measure. For other measures studied, the effect of familial wealth on social status is ignored. Yet familial wealth can obviously influence a wide range of conditions that affect offspring (e.g., healthcare, place of residence, access to tutors, social circles, etc.) (*36–40*). Consistent with this intuition, we found that all seven status measures analyzed in (*29*) are substantially correlated with an individual's father's wealth (Pearson *r* ranging from 0.19 - 0.66; mean *r* = 0.36; all $P < 2 \times 10^{-16}$; **Table S2**; **Fig. 2a**). Closer relatives tend to have more similar paternal wealth, and the similarity in paternal wealth between relatives predicts their similarity in occupational status extremely well (Pearson *r* = 0.91; **Fig. 2a; inset**). Thus, there is clear confounding in these data between transmission of genes and the effects of parental wealth on familial similarity in social status. Apart from wealth, numerous other non-genetic factors may contribute to familial correlations (*41*, *42*). (*29*) presents two post hoc analyses in an attempt to rule out non-genetic contributors to familial resemblance in social status. In **Supplementary Note 4**, we detail why these analyses are uninformative as to the strength of non-genetic effects on resemblance in social status between relatives (**Fig. S1**).

The confounding of genetic and non-genetic transmission in these data invalidates the interpretation of the model parameters offered in (*29*) as pointing to identifiable genetic contributions (**Supplementary Note 1**). In particular, in the presence of such confounding, the interpretation of *G* and *E* in **Eq. 1** as transmissible genetic (heritable) and random non-genetic effects on a phenotype, respectively, no longer holds. Instead, they can be interpreted as a transmissible component and a random, non-transmissible component. Consequently, the parameter interpreted in (*29*) as narrow-sense heritability, h^2, is in fact an estimate of the "total transmissibility" of a trait, t^2, the proportion of trait variance attributable to an unknown compound of transmissible influences on the traits, including genes, culture, wealth, environment, etc. (*10*, *12*). The second key parameter, m, which (*29*) interpreted as the "spousal correlation in the underlying genetics," does not represent a genetic correlation between mates. It is instead the spousal correlation in the transmissible component of the trait. m is derived from the "intergenerational persistence rate," $b = \frac{1+m}{2}$, estimated from the regression model. The expected correlation for a given kinship pair is equal to $t^2 b^n$, where n denotes genealogical distance (**Fig. 1a**). (Note that the parameterization of b for father-son and grandparent-grandchild relationships

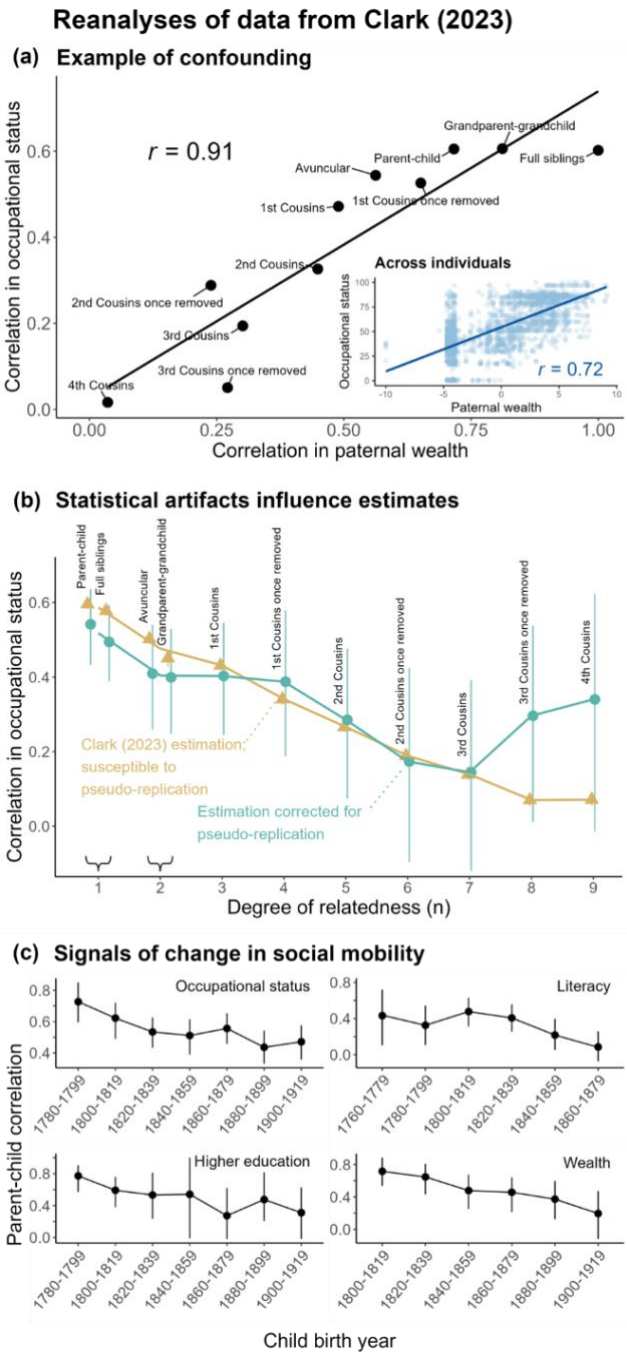

Figure 2. Reanalyses of data from Clark (2023) challenge the paper's claims. (a) Example of confounding between genetic and non-genetic transmission. Relationships between social status measures and paternal wealth suggest at least one potential source of confounding between genetic and non-genetic transmission. Across relative pairs, correlation in occupational status is highly correlated (Pearson's r = 0.91) with those relatives' correlation in paternal wealth. Inset shows that individual occupational status is strongly correlated (Pearson's r = 0.72) with father's wealth. Plots show data for 13,030 individuals born 1780-1859 and their fathers. ((*29*) estimated wealth from probate records. The log of estimated wealth was mean-centered with respect to 5-year bin means. Individuals not probated due to insufficient wealth were assigned a value of half the minimum probate requirement for the time period.) **(b) Pseudoreplication distorted estimates of familial correlations.** Familial correlations (95% CI) in occupational status (1780-1859) using the approach employed by (*29*) (in gold) involved pervasive, non-uniform pseudoreplication (Supplementary Note 6). For example, the (1780-1859) occupational status correlation for fourth cousins is calculated from 17,382 pairs, derived from only 1,878 unique individuals. In teal we show conservative estimates using only a single relative pair per surname [means and 95% CI over 1000 bootstrap samples are plotted for each familial correlation], which are therefore not susceptible to pseudoreplication. Distant cousins show dramatically higher correlations after adjusting for pseudoreplication. **(c) Signals of change in social mobility.** Parent-offspring correlations in multiple status measures generally decrease over time in (*29*)'s data, in contrast to claims of stagnant social mobility made in the original paper. To mitigate pseudoreplication, we calculated correlations using one pair from each surname [as in (b)]. Shown are average correlations (95% CI) across 500 bootstrap iterations of correlation estimation. Fig. S13 shows two complementary analyses estimating correlations either without accounting for pseudoreplication, or using percentile ranks—both result in similar trends.

also depends on the degree of assortative mating with respect to the focal trait itself; see **Supplementary Note 1**.) The conflation of genetic and non-genetic transmission helps to explain why the model parameters estimated in (*29*), which are claimed to represent quantitative genetic parameters, h^2 and m, are much higher than estimates of these same parameters from studies that attempt to account for confounding (e.g. (*19*, *43*, *44*)).

Conclusions in (*29*) about the insensitivity of social standing to policy and sociopolitical context rest on the similarity of estimates of the parameter b across status measures and across time. (*29*) argues that this stability is due to strong assortative mating on a genetic factor for "social ability". However, given that both genetic and non-genetic factors are transmitted within families, it follows that m tells us nothing about genetic versus non-genetic contributions to assortment, and b tells us nothing about the cause of within-family persistence of social status (**Fig. 1a; Supplementary Note 1**).

Regardless of whether due to genetic causes or not, a striking report of (*29*) is that "*The vast social changes in England since the Industrial Revolution, including mass public schooling, have not increased, in any way, underlying rates of social mobility*". In point of fact, we found that the estimates of familial correlations in (*29*), and, in turn, estimates of the persistence rate, are heavily affected by statistical artifacts (**Fig. 2b; Supplementary Note 6**). Furthermore, we show that across status measures, parent-offspring correlations — an established measure of social mobility (*45*, *46*) — generally decrease over time (**Fig. 2c; Supplementary Note 7**). How could the new measure, "persistence rate", used by (*29*) lead to such contrasting conclusions? (*29*) offers neither justification for why this measure reflects social mobility, nor explanation for the discrepancies with established measures of mobility used in other literature (e.g., *47*) and applied to the same data.

Some readers have already taken arguments in (*29*) as compelling evidence that social status is largely caused by genetic factors (*48–52*). Yet the assumptions and interpretations in (*29*) ignore a century of quantitative-genetic theory, previous empirical evidence for confounding, and the fallacies that arise when confounding is ignored (*13*, *17*, *21*, *22*, *26*, *42*, *53–60*), as well as patterns in the paper's own data that conflict with the interpretations presented. In this regard, we emphasize that (*29*) does not merely overstate the findings: the model parameters are misconstrued and the pervasive confounding of genetic and non-genetic transmission not addressed.

Are modern genomic studies less susceptible to confounding?

In relying solely on observational phenotypic data and assuming that transmission in families is solely genetic, (*29*) is similar in spirit to studies carried out by Francis Galton a century and a half ago. One might hope that the inferential flaws described above are addressed in studies that use

large genomic datasets and employ state-of-the-art statistical methods to adjust for confounding. As we outline, however, the same concerns remain broadly applicable, as confounding is still poorly understood and often underplayed in the literature.

Confounding in genomic studies is poorly understood. Human geneticists have long appreciated that there are myriad ways by which a genetic variant may be associated with a trait or outcome (*26*, *61*, *62*). A key example is "population stratification" in genomic data (e.g., in GWAS) wherein patterns of genetic similarity in a sample are correlated with the phenotype studied (**Fig. 1b**). Possible reasons for this correlation include social, environmental, or genetic factors, contemporary and historical. Typically, the specific causes are unknown. These same axes of genetic similarity ("population structure") are reflected in the frequencies of numerous genetic markers that may be tested for association with a trait in a GWAS. Consequently, any such markers will tend to be correlated with the trait, even if only a subset (or in fact none) of the variants causally affect it (**Fig. 1b**).

Consider, for example, a GWAS aimed to identify genetic risk factors for asthma in a sample of people from the US of either primarily European American genetic ancestry or African American genetic ancestry. There are many millions of variants in the genome that significantly differ in frequency between these groups. At the same time, African Americans in the US are systematically exposed to higher levels of air pollution (*63*), an environmental risk factor for asthma. If confounding is not adequately addressed, the GWAS would then lead us to conclude erroneously that "African American genetics" predispose one for asthma. More generally, the contributors to the correlation between axes of population structure and a phenotype may be partly or entirely genetic. Regardless, they will drive confounded associations in numerous genetic markers that tag these axes of population structure (**Fig. 1b**).

Human geneticists use various methods to adjust for confounded associations. However, confounding may persist, despite application of these methods (residual confounding). In 2019, we and other researchers discovered that genetic effect estimates in the largest GWASs for height—the most extensively studied polygenic trait of humans—were biased due to residual confounding (*58*, *59*). It became clear that the bias for each individual genetic variant was slight, but it was systematic across variants. Consequently, when researchers summed over signals from many genetic variants, they also summed over systematic biases. This led to erroneous conclusions in many studies (as detailed in *17*, *58*, *59*). Further research has demonstrated that

residual confounding may affect many GWASs, in particular for social outcomes and traits that are heavily influenced by social context (*26*, *60*, *62*, *64–66*).

Confounding in genomic studies is downplayed. Studies often imply that confounding is completely remedied by current methods, despite ample evidence to the contrary (*58–60*, *62*, *64*, *66–75*). Sometimes, methods to estimate genetic parameters grow in popularity even after they are shown to be susceptible to confounding, with this susceptibility rarely mentioned as a caveat (see, e.g., discussions in *58*, *65*, *66*, *70*, *76*, *77*). In other cases, confounding is acknowledged as a potential limitation, but its impact on the reported results (and their interpretation) is downplayed or obscured (see, for instance, (*78*, *79*)).

As one example, consider the reporting of evidence for genetic effects from standard GWASs versus family-based studies. Family studies identify genotype-trait associations within, instead of among, families. This approach greatly mitigates many sources of confounding (*60*, *62*, *80*). Family studies have yielded estimates of genetic effects on behavior or social outcomes that are substantially weaker than those estimated from standard GWASs (*43*, *60*, *64*, *66*, *81–84*). Reporting practices tend to downplay this point by instead emphasizing that there exists a true genetic effect based on evidence from family studies, while continuing to rely on the magnitude of those effects estimated in a standard GWAS (*55*). Such reporting choices mislead by presenting signals susceptible to confounding as measures of genetic causality.

Confounding in complex traits: death by a thousand cuts. Quantitative geneticists acknowledge residual confounding as an unsolved problem. But in practice, researchers face incentives to publish their inferences of genetic associations that are vulnerable to confounding. In the case of polygenic (or “complex”) traits, the usual focus of these studies, genetic contributions to trait variation are largely due to numerous genetic variants with individually small effects. Researchers often wish to leverage weaker and weaker genetic associations to capture these highly polygenic signals. At the same time, confounding tends to be aggravated as more weakly associated variants are considered (*60*, *74*). Thus, in the pursuit of understanding polygenic effects, researchers may face a tradeoff between explaining a smaller part of the phenomenon under study in a causally rigorous way, versus accounting for a seemingly larger part, at the price of unknown biases introduced by confounding.

An example of this tradeoff lies in genetic trait prediction with so-called "polygenic scores" (*85*). Polygenic scores based on more variants, including weakly-associated ones, may be preferred by researchers because they often attain higher prediction accuracy than polygenic scores that are limited to confident associations. However, polygenic scores that include many weakly-associated variants are plausibly more susceptible to underappreciated axes of confounding (*60*, *74*, *86*). Subsequent "consumers", including clinicians, researchers, policymakers, and the general public, may then assume these polygenic scores capture strictly direct genetic effects; the possibility of confounding is rarely acknowledged. Consider, for instance, an hypothetical preimplantation genetic testing using a polygenic score based on the asthma GWAS we described above. In this extreme, embryos would mistakenly be prioritized for implantation according to whether or not they share genetic variants with people exposed to higher levels of air pollution in a previous generation.

Similarly, popular methods to estimate genetic correlations (the correlation between two groups of individuals in genetic effects on a trait, or the correlation in genetic effects on two traits) often indiscriminately aggregate across genome-wide associations (*87*, *88*). Such methods are useful for characterizing how the genetic bases of complex traits are intertwined. However, they may inadvertently mask (or even introduce) additional axes of confounding (e.g., confounding that is shared between groups or traits) (*60*, *70*, *76*, *89*, *90*) and their uses in causal inference remain controversial (*70*, *91*). Yet when a study reports conclusions based on *genetic correlations*, it is likely to be interpreted—particularly by non-experts—as unambiguously reflecting genetic causality.

Confounding and further pitfalls in causal inference

Such unknown axes of confounding are plausibly a concern in a recent study that, based on an analysis of genetic correlations, purported to resolve an evolutionary paradox, why alleles associated with same-sex sexual behavior are maintained, despite being "reproductively disadvantageous" (*30*). In what follows, however, we focus on other forms of confounding and errors in causal inference in (*30*) confusing model assumptions with evidence, ignoring the compatibility of data with confounded explanations, and the introduction of confounding through researchers' analysis choices. We posit that, while these problems are not unique to genomic studies, they can evade attention when couched in reports about how behaviors and outcomes are *genetically correlated*.

Confusion of assumptions with evidence. (*30*) defined a measure of bisexual behavior based on questionnaire data about total lifetime number of sexual partners and same-sex sexual partners (hereafter, we refer to this measure as BSB; see (*92*) and (*93*) for discussion of shortcomings of such measures). (*30*) reports a significant positive genetic correlation between BSB in males and the number of children. But when adjusting this genetic correlation for genetic correlations of each measure with self-assessment as a "risk-taker", the adjusted (or "partial") genetic correlation between BSB in males and number of children was statistically indistinguishable from zero (**Fig. 3a**). (*30*) interpret this finding as evidence that "the current genetic maintenance of male BSB is a by-product of selection for male risk-taking behavior." (*30*) does not explain the hypothesized mechanism by which risk-taking behavior increases the number of offspring, but in subsequent news coverage, one of the authors is quoted as stating that, "self-reported risk-taking [likely] includes unprotected sex and promiscuity, which could result in more children" (*94*).

The study presents the contrast between these unadjusted and partial genetic correlations as support for a causal claim. However, the causal model is assumed *a priori*, and no evidence supporting this model is provided. Even under the assumption that the three measures considered are the only ones at play—and some causally affect others—the evidence is equally consistent with contradictory causal hypotheses (e.g., different directions of causality, arrows in Fig. 2b of (*30*) and **Figs. 3a**, **S14** here; **Supplementary Note 8**; c.f. (*95*)).

Furthermore, the study did not evaluate the support for any alternative model involving other factors, observed or latent. The authors justify their focus on risk-taking as a mechanistic explanation for the genetic maintenance of same-sex sexual behavior by citing previous reports of genetic correlations of same-sex sexual behavior and risk-taking (*96*, *97*). However, these studies (and others (*98*)) reported multiple measures with similar (or even stronger) genetic correlations with same-sex sexual behavior than risk-taking (*96*) (**Supplementary Table 5**). Sexual behavior aside, (*30*) neither cite nor offer any evidence for the alleles associated with risk-taking being maintained over long evolutionary timescales. Additionally, this association is based on an answer to a single questionnaire question, "Would you describe yourself as someone who takes risks?" (*99*). It is possible that responses to this question reflect a tendency towards practicing unprotected sex and promiscuity, and that they simultaneously correlate with risk-taking tendencies that have been relevant for fitness throughout recent human evolution and across evolving societies; but, as acknowledged in (*30*), these key assumptions are hard to evaluate.

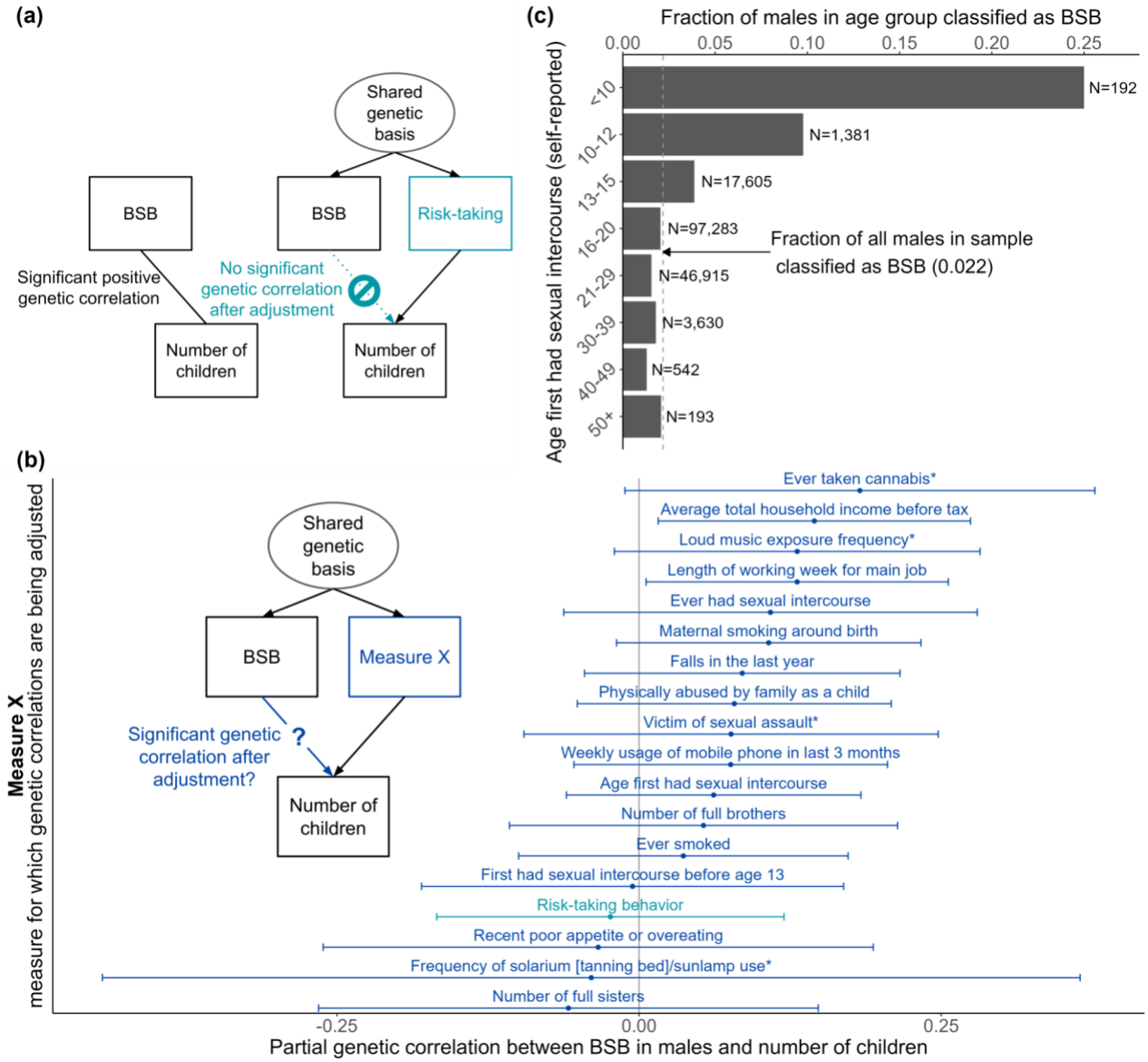

Figure 3. (a) Song and Zhang (2024) show that the estimated genetic correlation between BSB (a measure of bisexual behavior) in males and number of children is significantly different from zero (left diagram). They hypothesized the causal structure shown in the right diagram: Genetic variants affecting BSB affect the number of children only through their simultaneous effect on risk-taking behavior. When adjusting for genetic effects on risk-taking behavior, the residualized (or "partial") genetic correlation between BSB and number of children is no longer significantly nonzero. They take this observation as evidence for their hypothesis. **(b)** However, when we repeat this analysis but replace risk taking with a variety of other measures (blue in causal diagram), 16/18 measures yield a partial genetic correlation between BSB in males and number of children that is consistent with zero (measures we considered are shown in blue in the plot on the right; error bars indicate 95% confidence intervals). Asterisks indicate the four measures without a significant partial genetic correlation with number of children (Fig S16). **(c)** Male participants in the study sample who reported having first had sex before age 13 (including victims of childhood sexual assault, many of which would have had same-sex perpetrators) are likelier to be classified as BSB by the criteria used in Song and Zhang (2024). N, total number of males in each group.

For these reasons, we asked: Is there unique support for the assumed mechanistic model, in particular the role of risk-taking behavior as a mediator? To answer this question, we considered models wherein a measure other than risk-taking mediates the genetic correlation between BSB and number of children ("Measure X" in blue in **Fig. 3b**). If adjusting for this measure also results in a partial genetic correlation between BSB and number of children that is not significantly different from 0, the data are equally compatible with the hypothesis that there is a reproductive advantage for BSB-affecting alleles because of their simultaneous effect on Measure X. We implemented this strategy with 18 measures, selected based on prior evidence of high genetic correlations with same-sex sexual behavior, risk-taking behavior, and/or number of children (*98*) (**Supplementary Tables 4-5**; **Supplementary Note 8**). All but two of these models yielded a partial genetic correlation between BSB and number of children that was not significantly different from 0 (Genomic SEM (*100*) P-value >0.05 before applying any correction for multiple testing) (**Fig. 3b**). Hence, other causal narratives that do not involve risk taking could just as easily be constructed: the data are equally consistent with the hypothesis that genetic variants driving BSB are maintained through evolution as a byproduct of selection on the number of falls in the last year, weekly usage of cell phone, or any of these measures (**Fig. 3b; Fig. S15**).

Confounding introduced by researchers' analysis choices. Measures relating to having experienced some form of nonconsensual sex ("victim of sexual assault" and "first had sex before age 13") exhibited some of the strongest genetic correlations with BSB in males (**Fig. S15**). This observation led us to be concerned about the ascertainment choices made in (*30*). Indeed, we found that classification as a BSB individual is highly enriched among males who reported having first had sex before age 13 (in this regard, we note that children under this age are not legally capable of consenting to any sexual activity in the UK (*101*)) (**Fig. 3c**). Whereas 2.2% of males in the sample considered were classified as "BSB individuals," this classification rate increased to 9.8% among those who reported first having sex between ages 10-12 (inclusively), and 25% among those who reported first having had sex before age 10. Though we do not know, for this dataset, the age at which males classified as BSB first had same-sex sexual intercourse, or what fraction of victims of sexual assault had a perpetrator of the same sex, the majority of reported sexual assaults on prepubescent male victims are carried out by male perpetrators (*102–105*). This aggravates the concern that the BSB classification used in (*30*) conflated voluntary sexual behavior and sexual assault, undermining the study's stated aim of advancing our understanding of human sexual preferences. Taken together, our reanalysis of (*30*) cautions yet again against

causal inference based on preferential attention towards sensational hypotheses and analyses that seemingly support them.

Conclusion. The study of the genetics underlying human behavior and social outcomes, with its fraught history and heightened potential for misinterpretation and misappropriation (*55*, *56*, *65*, *92*, *106*, *107*), demands the utmost rigor. The failure to reckon with confounding fuels misinterpretation of genetics research and impedes scientific progress. We are therefore concerned that a publishing culture that rewards sensationalism may instead promote a decline in standards (*108*, *109*). In that respect, everyone has a role to play: it is crucial that researchers, reviewers, and editors uphold the highest standards in their handling of these complex, far-reaching issues.

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Data availability. All code for reproducing our analyses is available at https://github.com/harpak-lab/confounding.

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