Two genetic analyses to elucidate causality between body mass index and personality

Running head: Causality between BMI and personality

Kadri Arumäe, MA¹; Daniel Briley, PhD²; Lucía Colodro-Conde, PhD³; Erik Lykke Mortensen, MSc⁴; Kerry Jang, PhD⁵; Juko Ando, PhD⁶; Christian Kandler, PhD⁷; Thorkild I. A. Sørensen, MD, Dr Med Sci⁴; Alain Dagher, MD, PhD⁸; René Möttus, PhD^{9,1}; Uku Vainik, PhD^{1,8*}

1: University of Tartu

2: University of Illinois

3: QIMR Berghofer Medical Research Institute Brisbane

4: University of Copenhagen

5: University of British Columbia

6: Keio University

7: University of Bremen

8: Montreal Neurological Institute, McGill University

9: University of Edinburgh

* Corresponding author at: Institute of Psychology, Faculty of Social Sciences, University of Tartu, Näituse 2, 50409, Tartu, Estonia; uku.vainik@gmail.com; +372 737 5912

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Abstract

Background/Objectives: Many personality traits correlate with BMI, but the existence and direction of causal links between them are unclear. If personality influences BMI, knowing this causal direction could inform weight management strategies. Knowing that BMI instead influences personality would contribute to a better understanding of the mechanisms of personality development and the possible psychological effects of weight change. We tested the existence and direction of causal links between BMI and personality.

Subjects/Methods: We employed two genetically informed methods. In Mendelian randomization, allele scores were calculated to summarize genetic propensity for the personality traits Neuroticism, Worry, and Depressive Affect and used to predict BMI in an independent sample ($N=3\,541$). Similarly, an allele score for BMI was used to predict eating-specific and domain-general phenotypic personality scores (PPSs; aggregate scores of personality traits weighted by BMI). In a Direction of Causation analysis, twin data from five countries ($N=5\,424$) were used to assess the fit of four alternative models: PPSs influencing BMI, BMI influencing PPSs, reciprocal causation, and no causation.

Results: In Mendelian randomization, the allele score for BMI predicted domain-general ($\beta=0.05$; 95% CI 0.02, 0.08; $P=.003$) and eating-specific PPS ($\beta=0.06$; 95% CI 0.03, 0.09; $P<.001$). The allele score for Worry also predicted BMI ($\beta=-0.05$; 95% CI -0.08, -0.02; $P<.001$), while those for Neuroticism and Depressive Affect did not ($P\geq.459$). In Direction of Causation, BMI similarly predicted domain-general ($\beta=0.21$; 95% CI 0.18, 0.24; $P<.001$) and eating-specific personality traits ($\beta=0.19$; 95% CI 0.16, 0.22; $P<.001$), suggesting causality from BMI to personality traits. In exploratory analyses, links between BMI and domain-general personality

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43 traits appeared reciprocal for higher-weight individuals ($BMI > \sim 25$).

44 **Conclusions:** Although both genetic analyses suggested an influence of BMI on personality

45 traits, it is not yet known if weight management interventions could influence personality.

46 Personality traits may influence BMI in turn, but effects in this direction appeared weaker.

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Introduction

Excess adiposity, commonly proxied by body mass index (BMI), is a global health concern associated with increased economic¹ and disease burden². BMI, like many other health outcomes, has been robustly linked to personality traits³—individuals' behavioral, affective, and cognitive patterns. Still, it is unclear whether BMI and personality are causally associated. Even longitudinal analyses say little about their causal links as personality and BMI are both relatively stable and could be influenced by common processes⁴. If personality traits influence weight, understanding this could provide input for behavioral treatment of obesity⁵. If BMI is instead found to influence personality, this could help delineate some of the otherwise elusive mechanisms of personality development.

Understanding the causal impact of personality on body weight could also have wider implications. Personality traits are associated with a range of outcomes like mental and physical health, life events, occupational success, and longevity⁶⁻⁸. For example, personality interventions have been proposed to improve human welfare⁹, although it is still to be shown that personality traits are causal to life outcomes, including obesity. The direction of causation for body weight may generalize to other outcomes.

Much of the research regarding the links between personality and obesity has operationalized personality with five broad domains: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness. Studies have consistently reported a negative correlation between BMI and Conscientiousness, whereas associations with the other domains are less consistent^{3,10}. Each broad trait is also comprised of subtraits, facets, which can be further split into narrower traits, nuances¹¹. As with many other health-related outcomes¹², subtraits

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within the same domain often vary markedly in their associations with BMI, sometimes even in direction¹³. Representing personality trait–BMI associations with the domains may thus unduly attenuate or otherwise obscure them. While BMI–personality correlations are small, the numerous nuance-level associations can be aggregated into phenotypic personality scores (PPSs). We constructed such PPSs by weighting personality questionnaire items by their correlations with BMI (obtained from independent samples) and summing them. The PPSs, bespoke personality-based propensity scores for high BMI, provide greater statistical power to detect modestly sized associations¹³.

Beyond cross-sectional links, longitudinal studies have demonstrated that personality traits predict future BMI^{14,15} and BMI predicts future personality traits¹⁶. However, longitudinal studies have sometimes failed to predict results of randomized controlled trials because they are unable to eliminate confounding factors like alcohol abuse, socioeconomic status, or co-morbid diseases⁴. These factors could potentially influence both personality and obesity. Change in various personality traits has also been observed following bariatric surgery¹⁷, but it is uncertain whether these results could generalize to weight change that follows more traditional, non-surgical attempts or interventions. Altogether, causal links between personality and BMI remain unknown.

When randomized controlled trials are difficult or impossible to conduct, genetic methods can provide an alternative way to test causal models¹⁸. Importantly, although any one method may be fallible, converging results from different statistical approaches can increase confidence in results¹⁹. First, we used Mendelian randomization, a statistical technique where patterns of correlations between genetic propensities for phenotypes and the phenotypic outcomes

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themselves are used to assess potential causal links (see Briley et al (2018)²⁰ for a brief and Haycock et al (2016)²¹ for an in-depth overview). So far, genetic propensity for BMI has been found to track psychological distress²², lower subjective well-being²³, and ADHD²⁴ in Mendelian randomization studies. Because personality and BMI are both influenced by a high number of genetic variants^{25–27}, we summarized the genetic propensities for high BMI and, when possible, personality traits, in allele scores—aggregate scores of a person’s genetic predisposition for the traits in question.

Second, we applied a structural equation model analysis called Direction of Causation (DoC) on twin data. There, phenotypic variance in BMI and personality traits was parsed into genetic and environmental variance components and the most plausible causal model based on patterns of correlation between these components was chosen. The DoC analysis relies on the assumption that if an outcome is causally explained by a phenotype, then the phenotype’s variance components should be proportionally represented in the outcome²⁸ (see Briley et al (2018)²⁰ for a brief summary). We compared four models: 1) correlated (no causal links—a common cause for BMI and PPS), 2) reciprocal causation between PPS and BMI, 3) PPS influencing BMI, and 4) BMI influencing PPS. As personality influencing physical health is the commonly assumed causal direction⁵, we labeled personality influencing BMI the forward model; BMI influencing personality was accordingly termed the reverse model.

Materials and Methods

Participants

Mendelian randomization. Mendelian randomization was based on a subsample drawn from the Estonian Biobank²⁹, a volunteer-based sample of Estonian residents recruited by medical

personnel from among individuals visiting general practitioners and hospitals throughout the country. After giving informed consent, participants donated blood for DNA testing and underwent a standardized health examination. The data used in the current study were collected between 2002 and 2014. Analysis included individuals that had DNA, demographic, and personality data available ($N=3\,541$). Mean age of participants was 46.74 ($SD=16.97$, range 18–91) years, 2 112 (59.64%) were female. 1 174 (33.15%) participants were overweight and an additional 719 (20.30%) obese; mean BMI was 26.18 kg/m^2 ($SD=4.97$). Although men were somewhat underrepresented, the proportions of weight groups were comparable to the Estonian adult population³⁰. Exclusions and sample sizes by cohort are detailed in Supplementary Tables 1–2; sample sizes reported in the main text are after exclusions. The study was approved by Estonian Committee on Bioethics and Human Research.

Direction of Causation. The dataset for DoC analysis comprised cross-sectional twin samples from five countries: Australia, Canada, Denmark, Germany, and Japan. To obtain the data, we approached several cohorts known to have the information on both the NEO PI–R/3 and BMI and solicited access to the five datasets. Current analyses included only complete twin pairs ($N=5\,424$). Across the full DoC sample, participants’ mean age was 29.91 years ($SD=12.29$), mean BMI was 22.62 kg/m^2 ($SD=3.85$) and 3 531 (65.10%) were female; the full sample’s and the subsamples’ characteristics are expanded upon in Supplementary Table 2. Each study was approved by the local ethics committee. Informed consent was obtained from all participants.

Materials

Phenotypic personality. In all samples, personality was assessed with NEO PI–R³¹ or NEO PI–3³², comprehensive personality questionnaires measuring the five broad personality domains and

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their 30 facets with a total of 240 questions. Answers were provided on five-point Likert scales. To maximize prediction, the items were aggregated in composite PPSs, detailed in the Statistical analyses section.

Phenotypic BMI. BMI (kg/m^2) was calculated as weight in kilograms divided by height in meters squared. Height and weight were self-reported in the Japanese, as well as in part of the Australian and German samples, and measured objectively in others.

Personality and BMI allele scores. Allele scores were calculated for BMI and, where possible, personality traits, to be used in Mendelian randomization. As an aggregate score of genetic effects on a phenotypic trait, an allele score reflects an individual's genetic propensity for the trait. Calculation of the allele scores is detailed in the Statistical analyses section.

Statistical analyses

Phenotypic personality scores. For each participant in the Mendelian randomization and DoC analyses, three types of PPSs were calculated: an all-encompassing PPS_{ALL} , an eating-specific PPS_{EAT} , and a domain-general PPS_{GEN} . Namely, PPS_{ALL} was calculated from all 240 personality questions. To disentangle the links of eating-related personality from domain-general personality, we additionally created an eating-specific PPS_{EAT} from two personality items (N5.4 “Overeats favorite foods” and N5.6 “Eats excessively”) reflecting Uncontrolled Eating—a trait robustly correlated with BMI³³. We also created a domain-general PPS_{GEN} excluding these two items. This enabled us to clarify whether personality–BMI links were solely driven by the two eating-specific questions. To create the PPSs, the NEO PI items included in the scores were weighted by their empirical association with BMI (calculated in independent samples) and subsequently summed. A regression-based procedure, the least absolute shrinkage and selection operator³⁴, was

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used to calculate the weights. As a way of dealing with multicollinearity, this procedure sets the weights for some predictors to zero, effectively eliminating their contributions; the number of items remaining in the PPSs after weighting can be seen in **Table 1**. The weighting procedure is described in the Supplement; details on the weights and samples used to create them can be found in Supplementary Tables 3–6.

Prior to use in main analyses, the PPSs were validated in terms of predictive performance by regressing them on BMI—the target phenotype. The relative independence of PPS_{GEN} and PPS_{EAT} was further assessed by regressing the former on the latter. PPS validation was done on a combined sample of the Estonian Biobank and the twin samples (total $N=9\,151$).

Allele scores. Allele scores of BMI and personality traits were calculated for each individual in the Estonian Biobank from independent samples. The allele scores included single nucleotide polymorphisms (SNPs) that correlated with their target phenotype at a genome-wide significance level ($P<5\times 10^{-8}$) in UK Biobank data. To exclude the SNPs from each allele score that correlated more strongly with the outcome than with the intended phenotype, we applied a Steiger filtering procedure (detailed in the Supplement). Each trait-increasing SNP's effect on the target phenotype was multiplied by the count of the allele present in the individual. The SNPs included in each allele score are listed in Supplementary Tables 9–12. Weights were calculated from an automatic genome-wide association study (GWAS) using UK Biobank data³⁵, $N=461\,460$. Of personality traits, we were able to obtain allele scores for Neuroticism ($N=390\,278$), as well as for two narrower traits within the Neuroticism domain: Worry ($N=348\,219$) and Depressive Affect ($N=357\,957$)²⁷. Although the Neuroticism, Worry, and Depressive Affect allele scores were weighted with Eysenck's Personality Questionnaire–Revised³⁶ data, they were used to

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predict the largely overlapping NEO PI Neuroticism domain³⁷ and its facets N1 Anxiety and N3 Depression, respectively, in the Estonian Biobank. Prior to the Mendelian randomization analyses, phenotypic BMI and personality traits were regressed on their allele scores (weighted in the UK Biobank) to confirm sufficient predictive power in Estonian Biobank.

We also attempted to create allele scores for other broad personality factors based on available GWAS data³⁸. Possibly due to low sample size ($N \approx 60\,000$), these allele scores were underpowered and therefore not included in further analyses. Creation of allele scores is described in more detail in the Supplement.

Mendelian randomization. In the Mendelian randomization analysis the allele scores were used to predict relevant phenotypes in the Estonian Biobank cohort: the PPSs were regressed on BMI's allele score, and phenotypic BMI on the allele scores of Neuroticism, Worry, and Depressive Affect, controlling for age, age², sex, and 10 principal components of ancestry.

Although Mendelian randomization is often conducted using single genetic variants, combining the effects of many SNPs in allele scores was necessary to reach sufficient statistical power. To minimize potential confounders and pleiotropic effects arising from the use of many SNPs¹⁸, only GWAS-significant ($P < 5 \times 10^{-8}$) variants were included in the allele scores. Further details regarding the power considerations of Mendelian randomization can be found in the Supplement.

While Mendelian randomization analyses are less susceptible to confounding than common observational studies³⁹, the method requires the consideration of three central assumptions³⁹: (a) that the genetic instrument (here: allele score) is associated with its corresponding phenotype, (b) that the genetic instrument and the outcome do not share common

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causes, and (c) that the genetic instrument is associated with the outcome only through the intermediate phenotype (i.e, the genetic instrument does not have a direct effect on the outcome). Assumption (a) was assessed by calculating regression coefficients, partial F, and R^2 statistics between allele scores and their corresponding phenotypes (see **Table 1**). Because no testing procedure can definitively rule out common causes, assumption (b) cannot be fully assessed. However, common causes between genetic variants and outcomes can arise due to ancestry effects, which were controlled for by including 10 principal components of ancestry in the models.

As a rule, assumption (c) is the most problematic in Mendelian randomization studies as pleiotropic effects are not easy to rule out. Knowledge of the biological processes through which the genetic variants are related to the phenotypes would be required³⁹; however, such knowledge is currently unavailable and, in case of allele scores comprising large numbers of genetic variants, the information is particularly unlikely to be available. Still, a procedure known as MR-Egger regression can estimate pleiotropic effects, and was applied to statistically significant associations (detailed in the Supplement). Applying Steiger filtering and using a stringent P -value in SNP selection ($P < 5 \times 10^{-8}$) additionally decrease the likelihood of pleiotropic effects¹⁸. Yet another way to ensure robustness of the findings is to compare them to the results of complementary methods¹⁹. In the current study, this was done with DoC analyses.

Direction of Causation. With DoC models, quasi-causal effects can be tested on cross-sectional phenotypic twin data²⁸. Variance in the phenotypes of interest (BMI and the PPSs) in the combined twin sample was partitioned into additive genetic (A), common-to-siblings environmental (C), and unique-to-individual environmental (E) components based on the

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average genetic similarity between monozygotic and dizygotic twin pairs. This method assumes that a causal trait would leave a trace on the outcome trait. Namely, the variance components of the purported causal variable should be proportionally represented in the outcome: for instance, if the causal variable has a large C component, then the C component should be accordingly present in the outcome²⁰. The best-fitting causal model is chosen by comparing the observed covariance structure to those implied by different causal models. When certain assumptions are met (discussed in the Supplement), the best-fitting model implies causal associations between the traits at the phenotypic level.

For each PPS, we compared four models: 1) correlated (a common cause for BMI and PPS), 2) reciprocal causation, 3) forward causation (PPS influencing BMI), and 4) reverse causation (BMI influencing PPS). All analyses were run in Mplus⁴⁰, controlling for age, age², cohort, and sex.

Fit of the DoC models was assessed using Root Mean Square Error of Approximation (RMSEA) and the Comparative Fit Index (CFI) with RMSEA<.05 and CFI>.95 suggesting good fit^{41,42}. The fit of hierarchically nested models was compared using the χ^2 test: the reciprocal model was tested against the correlated model, and the unidirectional forward and reverse models against the reciprocal and correlated models. Where χ^2 *P*-values did not differ, the more parsimonious model was preferred. Comparison of the two non-nested unidirectional models was based on Akaike information criterion (AIC) with $\Delta\text{AIC} \geq 4$ signifying meaningfully different models⁴³.

DoC analyses also require certain considerations to be met^{28,44}. The considerations and the tests conducted to assess them are described in the Supplement; results of the tests are reported in

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Supplementary Table 7 along with power calculations in Supplementary Table 8. We found the considerations to be met. Importantly, the proportions of heritability were required to be and indeed found to be different for BMI (74%) and PPS (42%).

Test-retest reliabilities were incorporated in the models to avoid biases arising from reliability differences. Test-retest reliability was established for PPS_{ALL} from 263 assessments over 7–10 days (.89⁴⁵), and for BMI from 170 assessments over 7 days (.95⁴⁶).

To clarify whether the same causal model fit the data across all BMI levels, we ran follow-up DoC analyses with a) underweight (BMI<18.5) participants excluded, $N=4\,898$, and b) overweight (BMI $\geq$ 25) participants excluded, $N=4\,163$. As only borderline significant differences were found between alternative models in some cases, we additionally applied a local structural equation modeling (LOSEM) approach⁴⁷ to provide an additional way to compare model fit at different BMI levels. Detailed descriptions of the follow-up analyses can be found in the Supplement.

BMI was log-transformed in all analyses. The analytic process is outlined in **Figure 1**.

Code availability

Code for the analyses is available at <https://osf.io/meqxn/>.

Results

Predictive performance of allele scores and phenotypic personality scores

As specified in **Table 1**, the allele scores for BMI, Neuroticism and Worry significantly predicted their target phenotype, suggesting their suitability for use as indicators of genetic propensity for the traits. The allele score for Depressive Affect, however, fell short of statistical significance in predicting its target phenotype, suggesting that it may not be able to capture

effects on related outcomes.

Further, we found that each PPS captured additional variation in BMI after accounting for age, age², cohort, and sex, supporting their applicability as BMI-specific personality scores. Results of these regressions are detailed in **Table 1** along with allele score validation. Although significant, the association between the domain-general PPS_{GEN} and the two-item PPS_{EAT} was modest ($\beta=0.06$; $SE=0.01$; $P<.001$; $R^2=0.003$; 95% CI 0.001, 0.006) compared to the PPSs' associations with BMI, suggesting that the PPSs were largely able to isolate eating-specific from domain-general personality effects.

Mendelian randomization

Results of Mendelian randomization are shown in **Table 2**. We found a negative effect of the allele score of Worry on phenotypic BMI, while the allele scores of Neuroticism and Depressive Affect had no detectable effect; in the latter case, however, the lack of effect may be explained by the allele score's low predictive power. In the reverse direction, BMI's allele score was able to predict all three PPSs, suggesting an effect of BMI-related genetic variation on eating-specific as well as domain-general personality traits. We found no evidence for pleiotropic effects in any of the significant associations (see the Supplement for results). Altogether, this suggests that BMI may influence eating-specific as well as domain-general personality traits, whereas certain personality traits like Worry may also influence BMI.

Direction of Causation

Table 3 details fit indices and model comparison results for each PPS. Coefficients are specified in **Table 4** for the best-fitting models and in Supplementary Table 13 for the remaining models. For the eating-specific PPS_{EAT}, the reverse model fit best, and for the all-encompassing

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PPS_{ALL}, the reverse model was close in fit to the more complex reciprocal model and was preferred as the more parsimonious model. The reciprocal model fit best for the domain-general PPS_{GEN}. Interestingly, in this model, the forward direction (PPS_{GEN} influencing BMI) had a negative coefficient and the reverse direction (BMI influencing PPS_{GEN}) a positive coefficient, suggesting a negative feedback loop between BMI and PPS_{GEN}. Remarkably, the forward model had the worst fit across all three PPSs as it significantly differed from the correlated and reciprocal models in terms of χ^2 (**Table 3**). Thus, while BMI appeared to influence eating-related as well as domain-general personality traits, domain-general personality may have additionally had a comparatively smaller influence on BMI.

In the follow-up DoC analysis with underweight participants excluded, the reciprocal model fit best for PPS_{GEN} whereas the reverse model fit best for PPS_{EAT} and PPS_{ALL}. With overweight participants excluded, on the other hand, the difference between the reverse and reciprocal models was borderline significant for PPS_{EAT} ($P=.037$) while the reverse model was superior for PPS_{GEN} and PPS_{ALL} (see Supplementary Tables 14–15 for BMI subgroup analyses). The LOSEM analyses suggested influences of BMI on PPS_{EAT} across all BMI levels, and a switch from BMI unidirectionally influencing PPS_{GEN} to reciprocal influences between them at BMI $\approx$ 25 (Supplementary Figure 1). Altogether, these follow-up analyses suggest influences of BMI on the PPSs with additional reciprocal influences at higher BMI levels for domain-general personality.

Results of the main analyses are summarized in **Figure 2**.

Discussion

Two genetic analyses indicated a potential influence of BMI on personality traits. Genetic

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propensity for BMI predicted eating-related and domain-general PPSs—aggregates of BMI-related personality traits. In contrast, although genetic propensity for Worry predicted lower BMI, no such effect was detected for the broader Neuroticism domain. Analyses on twin data corroborated the effect of BMI on personality traits in all models. A reciprocal effect emerged for domain-general personality, particularly in higher-weight individuals. Namely, BMI had a positive effect on aggregate personality traits, whereas personality traits had a slightly decreasing effect on BMI in return. This suggests a compensatory effect of relevant personality traits on BMI. Notably, the reciprocal model fit best for people with BMI $\approx$ 25 and higher. As this number roughly corresponds to the lower bound of overweight, there may be something unique to excess weight that triggers effects of personality on BMI. Yet, effect sizes from DoC suggest that even in higher-weight individuals, the influence of BMI on personality may dominate over the opposite effect.

BMI influencing eating-specific personality is consistent with higher BMI leading to a higher overall energy requirement⁴⁸, thereby affecting eating behaviors like Uncontrolled Eating⁴⁹. It is unclear whether this effect is purely driven by the energy need of increased fat-free mass or also cognitions about weight status which are likely driven by fat mass. In a broader sense, the personality profile of obesity could be considered a collection of behavioral symptoms accompanying obesity. For instance, people with overweight and obesity tend to score higher than normal-weight individuals on facets of Neuroticism and lower on facets of Conscientiousness¹³—the two personality domains in which people most often wish to change⁵⁰. Although additional analyses are necessary to clarify if weight change can influence personality traits, if this is the case, maintaining or achieving a healthy BMI may influence traits favorably.

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While evidence for BMI influencing the PPSs emerged across both genetic methods employed, the results regarding Neuroticism-related traits should be interpreted more cautiously. Although similar negative relations between aspects of Neuroticism and BMI have been reported previously^{27,51,52}, positive correlations have been found elsewhere^{13,53}. Although the allele score for Depressive Affect was underpowered and may have potentially missed a link with BMI, the fact that the allele score for Worry, but not Neuroticism, negatively predicted BMI, suggests that a focus on narrower personality traits is warranted. Still, given the contradictory findings regarding Worry and similar traits in extant literature, making conclusions regarding their possible effects on body weight would be premature. Future studies could consider potential moderators to clarify the nature of their links.

Current findings also have broader implications for personality development. Although some⁵⁴ have been skeptical toward the possibility of identifying specific drivers of personality development and such effects have indeed remained elusive⁵⁵, our analyses suggest that body weight may be among the contributors to personality development. Despite the substantial genetic contribution to overweight⁵⁶, lifestyle changes—regulation of food environments⁵⁷ or physical activity⁵⁸, for instance—can to some extent override genetic propensity for high BMI. This may, in turn, affect personality, possibly through biological mechanisms or the social environment. As personality traits are linked with various mental health disorders⁶ including eating disorders⁵⁹, the potential for personality change may play a role in their development or treatment. Even beyond clinical populations, most people would like to change their personality and success in doing so is associated with increased well-being^{50,60}. Although effects may be small, having a healthy BMI could contribute to such goals.

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While strengths of the current work include the use of different statistical approaches and multiple samples, our analyses were not without limitations. First, due to the unavailability of well-powered GWASs, we were unable to test the effects of single personality traits outside the Neuroticism domain on BMI. Similarly, while using PPSs provided the necessary statistical power, this approach simultaneously limited our ability to distinguish specific traits and hindered our ability to evaluate the magnitude of effects. The results are informative about the direction of the effects of BMI and personality traits on each other, but not their magnitude; the logarithmic transformation applied to BMI should additionally be considered when interpreting the effects. Further, results of the genetic analyses do not necessarily imply that weight loss interventions lead to personality change as they may target other aspects of variance in BMI than the variance in BMI that relates to personality. Although some of the assumptions the current analyses relied upon were untestable, the convergence of results across two approaches strengthens our conclusions.

To conclude, in a novel application of two types of genetically informative analyses, BMI was found to be a potential contributor to personality differences. These findings counter common assumptions about the direction of causal effects, highlighting ways in which BMI may be relevant in mental health and well-being. While personality traits may additionally influence BMI, especially in higher-weight individuals, their combined effects appear weaker. If weight management interventions are to consider personality, knowledge of narrow traits' role in body weight is required; for instance, domain-level Neuroticism may be too broad a focus, but its facet Worry may turn out to be relevant. Although current results may not generalize to weight loss interventions, if BMI does influence personality, achieving a healthy weight may also manifest

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378 favorably in psychological traits. This remains to be clarified in future research.

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Competing interests

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The authors declare no competing financial interests.

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Figures

Figure 1. The analytic process.

Note. PPS=phenotypic personality score. PPS_{ALL} was calculated from all 240 personality items, PPS_{EAT} includes two eating-specific items and PPS_{GEN} was calculated from the remaining 238 items.

Figure 2. A graphical summary of the main findings.

Note. Panel **a** shows standardized Mendelian randomization coefficients. The forward direction represents effects of Neuroticism-related allele scores on phenotypic BMI; the reverse direction represents effects of BMI allele score on the PPSs. Panel **b** illustrates model comparison in Direction of Causation analyses. The figure specifies only *P*-values of key comparisons; the remaining significance values are indicated in **Table 3**. Correlated model=no causal effects between BMI and personality; reciprocal model=bidirectional causation between BMI and personality; forward model=personality influences BMI; reverse model=BMI influences personality. Panel **c** shows the effects between BMI and personality in Direction of Causation analyses. The best-fitting models suggest that BMI unidirectionally influences PPS_{ALL} and PPS_{EAT}, but influences between BMI and PPS_{GEN} are bidirectional. The forward direction indicates the effect of personality on BMI; the reverse direction indicates the effects of BMI on

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546 personality.

547 PPS=phenotypic personality score. PPS_{ALL} was calculated from all 240 personality items, PPS_{EAT}

548 includes two eating-specific items and PPS_{GEN} was calculated from the remaining 238 items.

549 Error bars in panels **a** and **c** represent standard errors.

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Table 1. Validation of allele scores and phenotypic personality scores

Validated score	Phenotype	Items ^a	β [95% CI]	SE	<i>t</i>	<i>P</i>	<i>R</i> ² [95% CI]	χ^2 /partial <i>F</i> ^b
Allele score								
BMI	BMI	957	0.21 [0.18, 0.23]	0.01	14.02	<.001	0.042 [0.031, 0.054]	196.44
Neuroticism	Neuroticism	109	0.07 [0.03, 0.10]	0.02	3.99	<.001	0.004 [0.001, 0.009]	15.88
Worry	N1: Anxiety	59	0.05 [0.01, 0.08]	0.02	2.79	0.005	0.002 [0.000, 0.006]	7.80
Depressive Affect	N3: Depression	61	0.03 [-0.01, 0.06]	0.02	1.52	0.129	0.001 [0.000, 0.004]	2.31
Phenotypic personality score								
PPS _{ALL}	BMI	115–156	0.18 [0.17, 0.20]	0.01	23.94	< .001	0.047 [0.039, 0.056]	551.05
PPS _{GEN}	BMI	113–154	0.12 [0.10, 0.13]	0.01	14.84	< .001	0.018 [0.013, 0.024]	217.03
PPS _{EAT}	BMI	2	0.15 [0.13, 0.17]	0.01	19.43	< .001	0.031 [0.025, 0.039]	367.22

Note. PPS=phenotypic personality score. The betas represent the change in the phenotype given a one-unit increase in the allele score or PPS, controlling for age, age², sex, and, for allele scores, 10 principal components of ancestry. The units of the PPSs are not interpretable in a straightforward manner as the scores were constructed by weighting personality item scores by their associations with BMI. Incremental *R*²s for PPSs were calculated accounting for age, age², sex, and, for allele scores, 10 principal components of ancestry. Confidence intervals were estimated using bootstrapping (1 000 iterations). Allele score weights were derived from UK Biobank data³⁵. *N*=9 151 for PPSs, *N*=3 541 for allele scores.

^a Number of personality items included in PPSs or number of SNPs included in allele scores. PPS_{ALL} was calculated from an initial set of all 240 personality items, PPS_{EAT} includes two eating-specific items and PPS_{GEN} was calculated from the remaining 238 items. The table indicates the numbers of predictors with nonzero weights included in PPS_{ALL} and PPS_{EAT} after applying the least absolute shrinkage and

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560 selection operator. Separate weights were calculated for each training subsample; ranges reflect the number of items included in the PPSs in
561 different subsamples.

562 ^b Partial F is reported for allele scores; χ^2 is reported for the PPSs as the linear models also included a random intercept for family structure
563 of the twin data.

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564 **Table 2.** Prediction of phenotypes in Mendelian randomization

Allele score	Phenotype	β [95% CI]	SE	<i>t</i>	<i>P</i>	<i>R</i> ² [95% CI]	Partial <i>F</i>
Neuroticism	BMI	-0.01 [-0.04, 0.02]	0.02	-0.74	0.459	0.000 [0.000, 0.002]	0.55
Worry	BMI	-0.05 [-0.08, -0.02]	0.02	-3.43	<.001	0.003 [0.001, 0.006]	11.79
Depressive Affect	BMI	-0.01 [-0.04, 0.02]	0.02	-0.62	0.533	0.001 [0.000, 0.002]	0.39
BMI	PPS _{ALL}	0.07 [0.04, 0.11]	0.02	4.29	<.001	0.005 [0.002, 0.011]	18.38
BMI	PPS _{EAT}	0.06 [0.03, 0.09]	0.02	3.52	<.001	0.003 [0.001, 0.008]	12.36
BMI	PPS _{GEN}	0.05 [0.02, 0.08]	0.02	2.93	0.003	0.002 [0.000, 0.006]	8.60

565 *Note.* PPS=phenotypic personality score. PPS_{ALL} was calculated from all 240 personality items, PPS_{EAT} includes two eating-specific items
566 and PPS_{GEN} was calculated from the remaining 238 items. The betas represent the change in the outcome phenotype given a one-unit increase
567 in the allele score, controlling for age, age², sex, and 10 principal components of ancestry. The betas are informative about the directions of
568 the effects and their size in comparison to other effects measured in the same units, but do not directly translate to the magnitude of the effect
569 of changes in phenotypic personality traits on BMI or vice versa. Incremental *R*²s for PPSs were calculated accounting for age, age², sex,
570 and 10 principal components of ancestry. *N*=3 541.

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571 **Table 3.** Comparison of models in Direction of Causation analyses

Model	χ^2	<i>df</i>	Compared to Correlated	Compared to Reciprocal	AIC	CFI	RMSEA
PPS _{ALL}							
Correlated	139.44	71	-	-	28 302.13	0.97	0.03
Reciprocal	139.44	72	> .999	-	28 300.13	0.97	0.03
Forward	272.61	73	< .001	< .001	28 431.30	0.92	0.06
Reverse	142.11	73	.263	.102	28 300.80	0.97	0.03
PPS _{EAT}							
Correlated	154.19	71	-	-	28 407.68	0.97	0.04
Reciprocal	154.19	72	> .999	-	28 405.68	0.97	0.04
Forward	198.23	73	< .001	< .001	28 447.72	0.95	0.04
Reverse	154.19	73	> .999	.975	28 403.68	0.97	0.04
PPS _{GEN}							
Correlated	139.65	71	-	-	28 443.97	0.97	0.03
Reciprocal	139.65	72	> .999	-	28 441.97	0.97	0.03
Forward	238.60	73	< .001	< .001	28 538.92	0.93	0.05

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Reverse	144.97	73	.070	.021	28 445.30	0.97	0.03
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572 *Note.* PPS=phenotypic personality score, correlated model=no causal effects between BMI and personality, reciprocal model=bidirectional
573 causation between BMI and personality, forward model=personality influences BMI, reverse model=BMI influences personality,
574 AIC=Akaike Information Criterion, CFI=Comparative Fit Index, RMSEA=Root Mean Square Error of Approximation. PPS_{ALL} was
575 calculated from all 240 personality items, PPS_{EAT} includes two eating-specific items and PPS_{GEN} was calculated from the remaining 238
576 items.

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577 **Table 4.** Estimates of the best-fitting Direction of Causation models for each phenotypic personality score

Phenotypic personality score	Model ^a	β [95% CI]	<i>P</i>
PPS _{ALL}	Reverse	0.28 [0.25, 0.30]	<.001
PPS _{EAT}	Reverse	0.19 [0.16, 0.22]	<.001
PPS _{GEN}	Reverse	0.21 [0.18, 0.24]	<.001
PPS _{GEN}	Reciprocal: PPS _{GEN} influencing BMI	-0.04 [-0.08, -0.01]	.022
	Reciprocal: BMI influencing PPS _{GEN}	0.26 [0.21, 0.31]	<.001

578 *Note.* Reverse model=BMI influences personality, reciprocal model=bidirectional causation between BMI and personality. PPS_{ALL} was
579 calculated from all 240 personality items, PPS_{EAT} includes two eating-specific items and PPS_{GEN} was calculated from the remaining 238
580 items.

581 ^aTwo models—reverse and reciprocal—are presented for PPS_{GEN} due to their borderline significant difference in fit ($P=0.021$). Coefficients
582 for both directions of the reciprocal model are presented.