

## SHORT COMMUNICATION

# Provider bias as a function of patient genotype: polygenic score analysis among diabetics from the Health and Retirement Study

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## Summary

### Objective

Poor patient–provider interactions due to provider bias are associated with worse physiological and behavioural health outcomes for patients. Prior research has shown that patients with obesity perceive less favourable interactions compared with those with lower weights. This paper explores whether this association depends on patients' cumulative polygenic score with respect to genes linked to obesity (i.e. a single variable quantifying the individual's genome-wide risk factors for high body mass index [BMI] or genetic liability) and whether providers react differentially to patients whose obesity is more genetic in nature compared with patients with diabetes caused by environmental factors.

### Methods

The association between patients' BMI category, their polygenic score for high BMI and their interaction was assessed for two measures of the patient–provider interaction within a sample of 521 older patients with diabetes from the Health and Retirement Study.

### Results

Particularly for patients with obesity, the quality of the patient–provider interaction depended on genetic liability for high BMI controlling for demographic and clinical covariates. Providers responded less favourably to patients with diabetes influenced by environmental factors compared with individuals with high genetic liability.

### Conclusions

Results of this study suggest that a patient's genotype may elicit particular responses from their healthcare provider. When a provider judges a patient's high BMI to be environmentally driven rather than genetically oriented, patients receive reduced quality of care.

**Keywords:** Body mass index (BMI), genotype, patient provider, weight-related discrimination.

## Introduction

Obesity is highly stigmatized in the USA (1); with common stereotypes being that people with obesity are lazy, lacking discipline and competency, and are sloppy (2). These widespread attitudes and beliefs can lead to prejudice and discrimination in many domains such as employment, educational settings, the legal system and in health care (1,2). Specifically in health care settings, obesity stigma has been associated with inequities in utilization,

length of visits, quality and overall satisfaction with health care, which may result in worse physiological and behavioural health outcomes (3,4).

Relatedly, stereotype or stigma can activate provider bias based on observable characteristics of the patient, wherein internalized negative attitudes about groups alter provider behaviour (2). Obesity stigma is a common source of provider bias (3), as many healthcare workers also hold negative attitudes and beliefs about patients with obesity (4). In one study, a majority of first-year

medical students endorsed far more negative explicit attitudes towards people with obesity than towards members of other marginalized groups (5). Specifically, provider bias may result in differential treatment when physicians associate the patient's obesity with laziness, lack of discipline and a poor lifestyle. Physicians may treat patients as if obesity and related morbidities such as diabetes are 'their fault', whether or not they are aware that they hold these common negative biases. Effects of obesity stigma on provider bias are widespread, even among providers specializing in treatment of obesity and related morbidities (6).

Less positive patient-provider interactions are one proposed mechanism by which obesity stigma and provider bias may lead to worse physiological and behavioural health outcomes (7). Indeed, many dimensions assessing the quality of the patient-provider interaction have been shown to impact health outcomes (i.e. physiological, functional and subjective) for a range of chronic diseases (8). For example, worse outcomes for patients with diabetes have been associated with poor patient-provider interactions (8-10). Specifically, deficits in several dimensions of patient-provider interactions, including provider communication with the patient and shared decision-making regarding treatment plans, predicted worse overall diabetes self-management (e.g. monitoring blood sugar and sores, maintaining exercise and diet regimens) (11). Finally, worse patient-provider interactions can occur when providers assume their patients will not be compliant with treatment plans (12).

This study proposes an important extension to the provider related obesity stigma. Specifically, it is possible that providers' bias depends upon judgments about the underlying cause of a patient's diabetes. Across patients with comparably high body mass index (BMI), some individuals may have high genetic liability (i.e. many genome-wide risk factors that predict increased risk for obesity), whereas others may have low genetic liability (i.e. thus, risk factors must be environmental in nature). These forms are hereinafter referred to as genetically oriented or environmentally driven obesity. Observable cues such as a patient's educational attainment, presentation of health or even family history may influence a provider's judgment about the patient's form of obesity. Even when accounting obvious cues, it is possible that providers are picking up on subtle biological differences across patients. Given this, obesity stigma research suggests that providers should hold more negative attitudes towards patients who they judge to have environmentally driven obesity compared with genetically oriented obesity. From the perspective of providers, culpability of obesity and subsequent health problems for patients with genetically oriented

obesity lies outside the control of the patient, but the opposite is true for those with environmentally driven obesity. Thus, genetic differences across participants with comparable morbidities and comorbidities may contribute to differential patient-provider interactions.

In sum, provider bias is hypothesized to be related to the underlying cause of a patient's BMI, will influence the patient-provider interaction and reduce quality of care for patients without a high genetic liability for obesity. This effect should be stronger in patients with diabetes and high BMI, compared with those who have maintained a normal weight. The use of a sample of patients with diabetes is pertinent, as management of weight and high BMI is inextricably linked to the management and care of this chronic condition.

## Methods

This study uses data from the Health and Retirement Study, a biannual, longitudinal assessment survey of individuals over 50 years old and their spouses from 1992 to 2014 (13,14). Analyses were limited to participants who completed the 2003 Diabetes Study supplemental survey ( $n = 1,901$ ), who had genotype data collected between 2006 and 2008 (484 participants excluded), who were of non-Hispanic European descent (179 participants excluded) and who were non-missing on key variables (717 participants excluded).

The following validated scales of provider-provider interaction were used: thoroughness of information provision or physician communication (PCOM) and participation in decision-making (PDM) (11,15). Five items of PCOM (e.g. how well the provider explained treatment alternatives, side effects of medications and so on) were rated on a 5-point scale from poor to excellent, whereas the seven items of PDM (were assessed in terms of frequency (e.g. how often provider provided treatment choices, helped set specific health goals and so on) on a 5-point scale from never to very often (16). Standardized mean scores were created using all available information, which resulted in standardized scores with high internal consistency (i.e.  $\alpha = 0.94$  for PCOM and  $\alpha = 0.93$  for PDM). Higher scores indicated better reported patient-provider interactions (i.e. better PCOM or more frequent inclusion of the patient treatment decision-making).

Genotypes were assessed using the Illumina HumanOmni2.5 BeadChips (HumanOmni2.5-4v1, HumanOmni2.5-8v1, Illumina, Inc., San Diego, CA, USA), which assessed over 1,900,000 single nucleotide polymorphisms (SNPs), or base pair differences across the genome, after standard quality control procedures were applied (17). Effect sizes for each SNP were

estimated in a discovery sample, which was a large-scale study of BMI over 300,000 participants of European genetic ancestry (18). Using these effects as weights, polygenic scores (PGS) were calculated by taking the weighted sum of all SNP effect sizes. These scores more accurately reflect the nature of genetic variance of complex traits; the PGS reflects genome-wide liability for high BMI by capturing the aggregate effects of genetic variants with both large and small effects (19). For example, approximately 2.7% of BMI can be explained by SNPs that reached a stringent cut-off for statistical significance in the discovery sample; however, aggregating signal across the genome (e.g. using all available SNPs) can explain over 20% of variation in BMI (18). Higher scores indicate greater genetic liability for high BMI.

A series of multilevel linear models were fit, which included a random intercept for household and sample weights that adjust for the likelihood of being selected into the diabetes study. As such, estimates control for assortative mating for BMI (20) and were representative of the full US population with diabetes born in 1948 or earlier (21).

All models included demographic covariates (i.e. age, gender and educational attainment) and standard categories of BMI (22). Additional models controlled for number of comorbid diagnoses, self-reported health, self-reported memory, smoking status (e.g. current and past), depression, length of relationship with provider, patient-driven discussion regarding treatment and diabetes type. Raw scores for demographic and clinical covariates are shown in Table 1. All variables were standardized in regression models for ease of interpretation. Statistical

analyses were conducted using R (version 3.4.1, Project for Statistical Computing) (23).

## Results

Full data were available for 521 older patients with diabetes. Model 1 estimated the effects of BMI category on the patient-provider interaction measures (Table 2) while adjusting for sociodemographic background. The results provided evidence for lower levels of provider communication among patients with extreme obesity ( $\beta = -0.38$ ,  $p < 0.049$ ) and lower levels of patient decision-making among patients with overweight ( $\beta = -0.19$ ,  $p < 0.041$ ) compared with patients with normal weight. Model 2 in Table 2 included the BMI PGS, and for both outcomes, there is no consistent or statistically significant association with this main effect. That is, on average, there was no association between a patients PGS score and their interactions with their physicians. Model 3 in Table 2 presents the results of the primary research question. That is, did the effect of BMI category depend on the patients' BMI PGS? Based on the results, the answer is yes. In line with the hypothesis, we showed that for both PCOM and PDM, patients with obesity reported more positive communication and increased role in decision-making with their physicians if their BMI PGS scores were relatively high (Figure 1). To rule out other mediating mechanisms, a host of other observable health factors and other indicators of interactions were controlled for in Model 4, and the results remain virtually identical. Additional analyses controlled for the first five principal components calculated from genome-wide data to control for influence of

**Table 1** Sample characteristics

Measure	Mean (SD) or %	Scale
Age	69.21 (8.19)	Years
Gender	48.56	% Female
Educational attainment	12.81(2.6)	Years
BMI	30.04 (6.05)	kg/m <sup>2</sup>
Self-rated health	3.08 (0.83)	(1) Excellent, (2) very good, (3) good, (4) fair, (5) poor
Comorbid diagnoses	2.96 (1.19)	0–6 diagnoses <sup>†</sup>
Smoker now	87.29	% Yes
Smoker ever	59.88	% Yes
Diabetes type	97.30	% Type II
Self-rated memory	2.88 (0.83)	(1) Excellent, (2) Very Good, (3) Good, (4) Fair, (5) Poor
Self-rated depression	1.38 (1.80)	0–8 items endorsed on CESD <sup>‡</sup>
Patient-driven treatment discussion	2.44 (0.97)	(1) Never, (2) rarely, (3) sometimes, (4) often, (5) very often
Patient-provider relationship length	3.34 (0.82)	(1) Less than 6 months, (2) 6 months to 1 year, (3) 1 year to 5 years, (4) 5+ years

<sup>†</sup>Comorbid diagnoses include high blood pressure, cancer, lung disease, heart disease, stroke and arthritis.

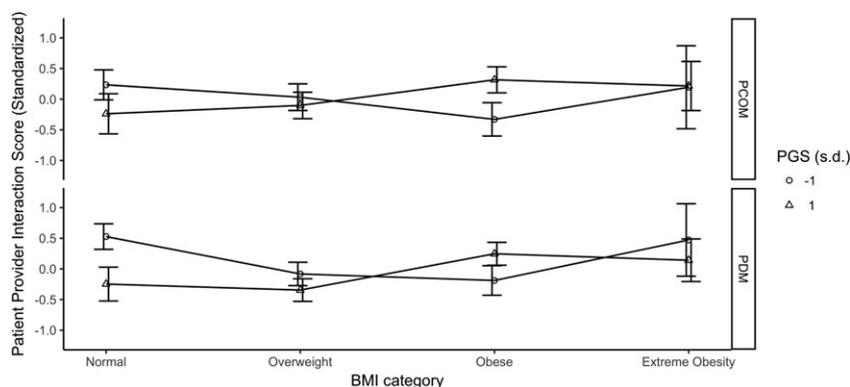
<sup>‡</sup>CESD items include feeling depression, that everything is effortful, sleep is restless, feeling alone, feeling sad and trouble getting going as how often they felt happy or enjoyed life (reverse coded).

BMI, body mass index; CESD, Center for Epidemiologic Studies Depression; SD, standard deviation.

Table 2 Patient-provider interaction in relation to BMI, PGS and covariates

	PCOM				PDM			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Intercept	-0.07 (-0.28, 0.13)	-0.05 (-0.27, 0.18)	-0.21 (-0.44, 0.03)	0.54 (-0.14, 1.23)	0.18 (-0.02, 0.38)	0.11 (-0.12, 0.33)	-0.17 (-0.39, 0.04)	0.09 (-0.54, 0.72)
Age (years)	-0.07 (-0.18, 0.05)	-0.07 (-0.18, 0.05)	-0.04 (-0.16, 0.07)	-0.07 (-0.18, 0.03)	-0.01 (-0.13, 0.11)	-0.01 (-0.12, 0.11)	0.01 (-0.10, 0.11)	-0.12 (-0.22, -0.03)
Female	<b>0.25 (0.12, 0.39)</b>	<b>0.24 (0.09, 0.38)</b>	<b>0.31 (0.17, 0.46)</b>	0.10 (-0.07, 0.27)	<b>-0.22 (-0.35, -0.10)</b>	<b>-0.18 (-0.32, -0.05)</b>	-0.04 (-0.17, 0.09)	<b>-0.18 (-0.32, -0.03)</b>
Education (years)	<b>0.17 (0.07, 0.26)</b>	<b>0.17 (0.08, 0.26)</b>	<b>0.14 (0.04, 0.23)</b>	<b>0.14 (0.05, 0.23)</b>	0.07 (-0.02, 0.16)	0.07 (-0.03, 0.16)	-0.03 (-0.12, 0.05)	0.04 (-0.04, 0.12)
Weight (Normal)								
Overweight	0.07 (-0.12, 0.27)	0.05 (-0.16, 0.26)	0.21 (0.00, 0.43)	-0.10 (-0.33, 0.13)	<b>-0.19 (-0.37, -0.01)</b>	-0.13 (-0.33, 0.07)	0.15 (-0.05, 0.35)	<b>-0.32 (-0.52, -0.13)</b>
Obese	-0.05 (-0.29, 0.19)	-0.08 (-0.33, 0.18)	-0.06 (-0.31, 0.19)	-0.09 (-0.34, 0.16)	0.09 (-0.13, 0.32)	0.16 (-0.08, 0.40)	<b>0.25 (0.02, 0.48)</b>	-0.11 (-0.33, 0.11)
Obese II+	<b>-0.38 (-0.77, 0.00)</b>	<b>-0.40 (-0.79, -0.01)</b>	-0.30 (-0.72, -0.12)	0.16 (-0.27, 0.58)	-0.29 (-0.64, 0.07)	-0.26 (-0.62, 0.10)	-0.16 (-0.53, 0.21)	0.17 (-0.19, 0.53)
PGS								
PGS * Overweight		0.03 (-0.07, 0.13)	<b>-0.24 (-0.43, -0.06)</b>	<b>-0.20 (-0.38, -0.01)</b>		-0.07 (-0.17, 0.03)	<b>-0.70 (-0.87, -0.53)</b>	<b>-0.45 (-0.60, -0.29)</b>
PGS * Obese I and II			0.19 (-0.05, 0.43)	0.12 (-0.12, 0.36)			<b>0.79 (0.57, 1.01)</b>	<b>0.32 (0.12, 0.53)</b>
PGS * Obese III			<b>0.69 (0.42, 0.96)</b>	0.51 (0.25, 0.77)			<b>1.05 (0.80, 1.30)</b>	<b>0.65 (0.43, 0.88)</b>
Self-rated health			0.32 (-0.14, 0.78)	0.19 (-0.24, 0.61)			<b>0.68 (0.23, 1.14)</b>	0.25 (-0.13, 0.63)
Comorbid diagnoses				0.02 (-0.08, 0.13)				0.09 (-0.54, 0.72)
Smoker now				<b>0.14 (0.05, 0.23)</b>				<b>0.13 (0.04, 0.22)</b>
Smoker ever				0.24 (-0.18, 0.66)				<b>0.08 (0.00, 0.17)</b>
Diabetes type				-0.09 (-0.28, 0.10)				0.00 (-0.38, 0.39)
Self-rated memory				-0.51 (-1.17, 0.15)				0.13 (-0.03, 0.30)
Self-rated depression				<b>-0.30 (-0.39, -0.22)</b>				0.04 (-0.56, 0.65)
Discussion				<b>-0.19 (-0.29, -0.09)</b>				<b>-0.12 (-0.19, -0.05)</b>
Relationship length				<b>0.15 (0.07, 0.24)</b>				<b>-0.24 (-0.33, -0.16)</b>
				0.01 (-0.08, 0.10)				<b>0.39 (0.32, 0.46)</b>

Data presented as the regression coefficient  $\beta$  (95% CI) for the fixed effects in a linear model. Males treated as reference group. BMI classified as follows: normal weight (reference), <25; overweight, 25–29.9; obese, 30–39.9 (Class I and II); and extreme obesity (Class III), >40. Bold indicates significance at  $p < 0.05$ . BMI, body mass index; PCOM, physician communication; PDM, participation in decision-making; PGS, polygenic scores.



**Figure 1** Marginal means for patient-provider interaction scores across body mass index (BMI) categories and polygenic scores (PGS) level, controlling for demographic, clinical and patient-provider interaction covariates. PCOM, physician communication; PDM, participation in decision-making.

population stratification, or spurious association due to non-casual allele frequency differences across ancestry groups (24), and the results remained the same.

## Discussion

While previous work exploring the patient-provider interaction for diabetes care has explored how demographic characteristics of the patient is associated with reductions in quality of care, this study is the first to explore how a patient's genotype may lead to differential treatment in healthcare settings.

The quality of patient-provider interactions were hypothesized to be linked to patient's BMI, and the strength of this link was expected to depend on the patient's genetic liability for high BMI. While previous work suggested that providers would react negatively to patients with overweight or obesity, there was inconsistent evidence for effects of obesity stigma. However, the sample was selected for diabetes diagnoses and had a higher mean BMI than Centers for Disease Control and Prevention estimates of the US population (22). These sample characteristics may have restricted the range of BMI and associated clinical features that may occur in other studies of obesity stigma.

However, there was an effect of the PGS that depended on BMI category. Particularly for patients with Class I or II obesity (i.e. BMI between 30.0–39.9.0), there was an impoverished patient-provider interaction when obesity was attributable to socio-environmental causes rather than genetic influences. Given the obesity stigma, it is possible that providers are blaming these patients for their high BMI and deeming them less competent to understand or participate in their own treatment. Genetically influenced obesity may elicit better patient-provider

treatment because providers judge high BMI to be 'out of the patient's control'.

Surprisingly, participants with higher genetic liabilities for obesity who were able to maintain a normal BMI reported being less involved in their treatment decision-making compared with those with lower genetic liability. Given that patients in this category are in a healthier BMI category, there is less reason to make judgments about the underlying cause of a patients' weight status. Instead, a low PGS may signal that patients have modifiable risk factors for diabetes that could be alleviated through better PCOM.

Importantly, providers are not responding directly to their patient's genotypes, as the use of the BMI PGS is relatively recent and would not have been available to providers at the time of data collection. Rather, providers may be responding to other observable phenotype cues that are correlated with genetic or environmental-oriented obesity. As such, it is possible that the PGS is capturing important differences in a patient's presentation of BMI. Providers may make implicit judgments about the source of a patient's diabetes that cannot be accounted for by educational attainment (e.g. proxy for socioeconomic status) or other observable health cues; thus, they are detecting and responding to a patient's underlying biological risk factors. Implicit biases activated by stigma or stereotypes alters behaviour even in the absence of explicit negative attitudes about groups (25). Thus, genotype-based provider bias can operate even if providers are unaware they are making judgments about the source of a patient BMI and even if they are unaware they hold implicit negative attitudes about patient with environmentally driven BMI.

The novel use of a PGS raises several important considerations. As previously stated, the PGS is predictive

of quality of patient–provider interactions in patients with obesity despite that this score is unknown to both the patient and provider. In the coming decades, it is feasible that genetic information or a PGS may become more common in healthcare settings. As this information becomes more accessible to both patients and providers, could this effect become magnified? In this case, genotype-based provider bias would no longer depend on a providers' ability to 'pick up on' cues about the source of BMI. To the extent that providers hold beliefs about genetic determinism, the use of these scores could exacerbate existing disparities in patient–provider interactions. A second consideration is that the accuracy of a BMI PGS, which depends on several characteristics of the sample (26). Further, the predictive power of any given loci might vary across BMI categories (27). This study did not attempt to predict BMI with the PGS; rather, the study asked whether two individuals with the same BMI and different genetic risk factors were treated differently by physicians. Thus, whether the score has the same predictive accuracy across weights is less of a concern than if the score points to something meaningful about individuals within a BMI category.

Several limitations should be considered when interpreting the results. Patient–provider interactions were assessed by the patient only. Such measures may suffer from ceiling effects or reflect patient held biases (28). Though the patient's weight status was controlled for, it is possible that other unmeasured factors contributing to internalized self-stigma may influence patient's perceptions of the provider's PCOM and PDM. Future studies would benefit from the use multiple raters (i.e. patient, provider and objective reviewer), especially if the design allows assessment of the provider in multiple patient–provider interactions. Additionally, the predictive power of the PGS is optimized for use in non-Hispanic samples with European ancestry. As the accuracy of these scores are limited by lack of diverse discovery samples, the results should not be extended to other populations. Future work exploring how racial ethnicity interacts with genotype-based provider bias is warranted. Finally, the results are representative of older patients with diabetes, and caution should be taken when generalizing to younger cohorts or patients without diabetes.

In conclusion, this study is the first to demonstrate that patient's genotype may elicit particular responses from their healthcare provider. Specifically, provider bias based on the underlying cause of diabetes may contribute to reduced quality of patient–provider interactions.

## Conflict of interest statement

The authors declared no conflict of interest.

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## References

1. Puhl RM, Andreyeva T, Brownell KD. Perceptions of weight discrimination: prevalence and comparison to race and gender discrimination in America. *International Journal of Obesity* 2008; **32**: 992–1000.
2. Puhl RM, Heuer CA. The stigma of obesity: a review and update. *Obesity* 2009; **17**: 941–964.
3. Puhl RM, Heuer CA. Obesity stigma: important considerations for public health. *American Journal of Public Health* 2010; **100**: 1019–1028.
4. Phelan SM, Burgess DJ, Yeazel MW, Hellerstedt WL, Griffin JM, van Ryn M. Impact of weight bias and stigma on quality of care and outcomes for patients with obesity. *Obesity Reviews* 2015; **16**: 319–326.
5. Phelan SM, Dovidio JF, Puhl RM, et al. Implicit and explicit weight bias in a national sample of 4,732 medical students: the medical student CHANGES study. *Obesity* 2014; **14**: 1201–1208.
6. Schwartz MB, Chambliss HO, Brownell KD, Blair SN, Billington C. Weight bias among health professionals specializing in obesity. *Obesity* 2003; **11**: 1033–1039.
7. Phelan S, Lynch B, Blake KD, et al. The impact of obesity on perceived patient-centered communication. *Obesity Science & Practice* 2018 <https://doi.org/10.1002/osp4.276>.
8. Kaplan SH, Greenfield S, Ware JE Jr. Assessing the effects of physician–patient interactions on the outcomes of chronic disease. *Medical Care* 1989; **27**: S110–S127.
9. Nam S, Chesla C, Stotts NA, Kroon L, Janson SL. Barriers to diabetes management: patient and provider factors. *Diabetes Research and Clinical Practice* 2011; **93**: 1–9.
10. Heisler M, Bouknight RR, Hayward RA, Smith DM, Kerr EA. The relative importance of physician communication, participatory decision making, and patient understanding in diabetes self-management. *Journal of General Internal Medicine* 2002; **17**: 243–252.
11. Heisler M, Cole I, Weir D, Kerr EA, Hayward RA. Does physician communication influence older patients' diabetes self-management and glycemic control? Results from the Health and Retirement Study (HRS). *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 2007; **62**: 1435–1442.
12. Sabin JA, Marini M, Nosek BA. Implicit and explicit anti-fat bias among a large sample of medical doctors by BMI, race/ethnicity and gender. *PLoS One* 2012; **7**: e48448.
13. Juster FT, Suzman R. An overview of the Health and Retirement Study. *Journal of Human Resources* 1995; **30**: S7–S56.
14. Sonnega A, Faul JD, Ofstedal MB, Langa KM, Phillips JW, Weir DR. Cohort profile: the health and retirement study (HRS). *International Journal of Epidemiology* 2014; **43**: 576–585.

15. Glasgow RE, Wagner EH, Schaefer J, Mahoney LD, Reid RJ, Greene SM. Development and validation of the patient assessment of chronic illness care (PACIC). *Medical Care* 2005; **43**: 436–444.
16. Health and Retirement Study. 2003 Mail survey on diabetes. <http://hrsonline.isr.umich.edu/modules/meta/diabetes/qnaire/diab2003qnaire.pdf> Accessed, March 6, 2018.
17. Health and Retirement Study. HRS Polygenic Scores 2006–2010 Data. <http://hrsonline.isr.umich.edu/modules/meta/year/pgs/desc/PGENSCORES.pdf> Accessed March 6th, 2018.
18. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; **518**: 197–206.
19. Dudbridge F. Polygenic epidemiology. *Genetic Epidemiology* 2016; **40**: 268–272.
20. Robinson MR, Kleinman A, Graff M, et al. Genetic evidence of assortative mating in humans. *Nature Human Behaviour* 2017; **1**: 0016.
21. Health and Retirement Study. 2003 Diabetes Study Version 2.0, April 2007. <http://hrsonline.isr.umich.edu/modules/meta/diabetes/desc/diab2003dd.pdf> Accessed, November 7, 2017.
22. Centers for Disease Control and Prevention. Healthy weight, overweight, and obesity among U.S. adults. <https://www.cdc.gov/nchs/data/nhanes/databriefs/adultweight.pdf>. Accessed December 24, 2017.
23. R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.r-project.org/>.
24. Patterson N, Price AL, Reich D. Population structure and eigenanalysis. *PLoS Genetics*. 2006; **2**: e190.
25. Chapman EN, Kaatz A, Carnes M. Physicians and implicit bias: how doctors may unwittingly perpetuate health care disparities. *Journal of General Internal Medicine* 2013; **28**: 1504–1510.
26. Wray NR, Yang J, Hayes BJ, Price AL, Goddard ME, Visscher PM. Pitfalls of predicting complex traits from SNPs. *Nature Reviews Genetics* 2013; **14**: 507–515.
27. Abadi A, Alyass A, du Pont SR, et al. Penetrance of polygenic obesity susceptibility loci across the body mass index distribution: an update on scaling effects. *BioRxiv* 2017 Jan; **1**: 225128.
28. Rosenthal GE, Shannon SE. The use of patient perceptions in the evaluation of health-care delivery systems. *Medical Care* 1997; **35**: NS58–NS68.