Determining the stability of genome-wide factors in BMI between ages 40 to 69 years.

Amanda Elswick Gentry¹, Nathan A Gillespie¹², Robert M Kirkpatrick¹, Hermine H Maes³, Chandra A Reynolds⁴, Ravi Mathur⁵, Kenneth S Kendler¹, Roseann E. Peterson¹ & Bradley T. Webb¹⁵

¹ Virginia Institute for Psychiatric and Behavior Genetics, Department of Psychiatry, Virginia Commonwealth University, Richmond VA, USA.
² QIMR Berghofer Medical Research Institute, Herston, Queensland 4006, Australia.
³ Virginia Institute for Psychiatric and Behavior Genetics, Department of Human and Molecular Genetics & Massey Cancer Center, Virginia Commonwealth University, Richmond VA, USA.
⁴ Department of Psychology, University of California, Riverside CA 92521
⁵ GenOmics, Bioinformatics, and Translational Research Center, Biostatistics and Epidemiology Division, RTI International, Research Triangle Park, NC, USA.

KEYWORDS: BMI, GWAS, genomic SEM, longitudinal, genetic

ABSTRACT:
Genome-wide association studies (GWAS) have successfully identified common variants associated with BMI. However, the stability of genetic variation influencing BMI from midlife and beyond is unknown. By analyzing BMI data collected from 165,717 men and 193,073 women from the UKBiobank, we performed BMI GWAS on six independent five-year age intervals between 40 and 73 years. We then applied genomic structural equation modeling (gSEM) to test competing hypotheses regarding the stability of genetic effects for BMI. LDSR genetic correlations between BMI assessed between ages 40 to 73 were all very high and ranged 0.89 to 1.00. Genomic structural equation modeling revealed that genetic variance in BMI at each age interval could not be explained by the accumulation of any age-specific genetic influences or autoregressive processes. Instead, a common set of stable genetic influences appears to underpin variation in BMI from middle to early old age in men and women alike.