

Higher genetic risk of obesity means working out harder for same results, study shows

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Persons with a higher genetic risk of obesity need to work out harder than those of moderate or low genetic risk to avoid becoming obese, according to a Vanderbilt University Medical Center (VUMC) paper



published in JAMA Network Open.

Study authors used activity, clinical and genetic data from the National Institutes of Health's "All of Us" Research Program to explore the association of genetic risk of higher body mass index and the level of physical activity needed to reduce incident obesity.

"Physical activity guidelines do not account for <u>individual differences</u>," said senior author Douglas Ruderfer, Ph.D., associate professor of Medicine, Division of Genetic Medicine, and director of the Center for Digital Genomic Medicine at VUMC. "Genetic background contributes to the amount of physical activity needed to mitigate obesity. The higher the genetic risk, the more steps needed per day."

"I think an important component to this result is that individuals can be active enough to account for their genetic background, or their genetic risk for obesity, regardless of how high that risk might be," he added. "And there are many other contributors that play a role including diet and environmental factors."

Included in the study were 3,124 middle-aged participants without obesity who owned a Fitbit device and walked an average of 8,326 steps per day for a median of more than five years. The incidence of obesity over the study period increased from 13% to 43% in the lowest and highest polygenic risk score groups.

Individuals with a polygenic risk score in the 75th percentile would need to walk an average of 2,280 more steps per day (a total of 11,020 steps per day) than those in the 50th percentile to have a comparable risk of obesity, according to the study.

Persons with a baseline BMI of 22, 24, 26 and 28 who were in the 75th percentile of polygenic risk score would need to walk an additional



3,460, 4,430, 5,380 and 6,350 steps per day, respectively, to have a comparable risk of obesity to persons in the 25th percentile.

"I think it is intuitive that individuals who have a higher genetic risk of obesity might need to have more physical activity to reduce that risk, but what is new and important from this study is that we were able to put a number on the amount of activity needed to reduce the risk," said lead author Evan Brittain, MD, associate professor of Medicine in the Division of Cardiovascular Medicine at VUMC and lead investigator in Digital Health for the All of Us Research Program Data and Research Center.

"It is becoming more commonplace to know you have a genetic risk for obesity in the genomic era when genetic results are being returned directly to patients. And you can imagine a future in which that data could be integrated with someone's electronic health record and could form the basis of an individual's physical activity recommendation from their doctor."

Study authors said they now want to see if the findings generalize to more representative and diverse populations in order to determine if providing information for individual activity recommendations results in improved health and a lower likelihood of obesity.

"We would like to test whether knowledge of one's genetic risk for obesity actually has an impact on their behavior," Brittain said. "I think these findings could be empowering for patients because the current physical activity guidelines take a one-size-fits-all approach, and what we learned is that depending on your genetic risk, the guidelines may underestimate the amount of activity needed to reduce your risk of obesity.

"Most importantly, I would like for patients to know that your genetic



<u>risk</u> doesn't determine your overall risk of obesity, and you can actually overcome that risk by being more active," he added.

More information: Physical Activity and Incident Obesity Across the Spectrum of Obesity Genetic Risk, *JAMA Network Open* (2024). <u>DOI:</u> 10.1001/jamanetworkopen.2024.3821

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