

Leading genetics study method may need reconsideration, significant distortions discovered

April 24 2018

Many conclusions drawn from a common approach to the study of human genetics could be distorted because of a previously overlooked phenomenon, according to researchers at the Department of Genetics and Genomics Sciences at the Icahn School of Medicine at Mount Sinai and collaborators from Massachusetts General Hospital and the Broad Institute. Their conclusions and a unique method they developed to help correct for this distortion were recently published in *Nature Genetics*.

The common approach, called Mendelian randomization (MR), is a [method](#) that uses genetic variation to assess how [risk factors](#) such as obesity and lipid levels affect the likelihood of disease and mortality. The researchers found that a phenomenon called horizontal pleiotropy - in which [genetic](#) variants influence disease through pathways different from the risk factors being tested - was present in 48 percent of the MR studies they analyzed. The results were distorted, on average, by -131 to 201 percent, meaning certain exposures analyzed in these studies may have appeared to have more or less influence on disease than they actually do. They also found that widespread horizontal pleiotropy induced false positive causal relationships in up to 10 percent of results in certain tests.

As technology in genomic analysis has evolved rapidly in the past decade, researchers have developed multiple MR methods to study health and disease. A study of the validity of MR methods and

innovation to correct for factors such as horizontal pleiotropy comes at a crucial time.

"Mendelian randomization has significant implications for drug discovery and validation," said Ron Do, PhD, Assistant Professor in the Department of Genetics and Genomic Sciences at the Icahn School of Medicine. "It can be used to determine whether biomarkers are causal for [disease](#), which can determine what types of drug therapeutics may be worth exploring in clinical trials, and can potentially predict accurate dosing for drug effectiveness."

In light of these findings, the study authors stress the importance of assessing all MR studies for the occurrence of horizontal pleiotropy, and have developed open-source software to detect and correct for it, MR-PRESSO, which is available on GitHub at <https://github.com/rondolab/MR-PRESSO>

More information: Marie Verbanck et al, Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases, *Nature Genetics* (2018). [DOI: 10.1038/s41588-018-0099-7](https://doi.org/10.1038/s41588-018-0099-7)

Provided by The Mount Sinai Hospital

Citation: Leading genetics study method may need reconsideration, significant distortions discovered (2018, April 24) retrieved 4 May 2024 from <https://medicalxpress.com/news/2018-04-genetics-method-reconsideration-significant-distortions.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.