Personalized treatment for liver fat needed after discovery of new link to cardiovascular diseases, cancer

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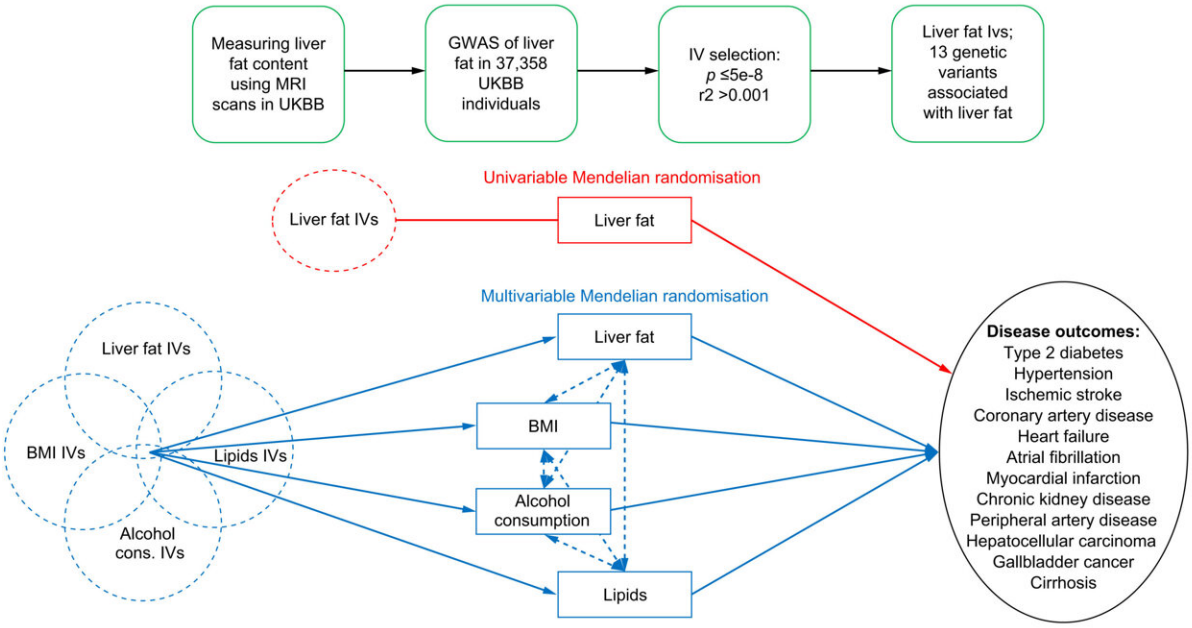

Study design. Credit: *Journal of Hepatology* (2024). DOI: 10.1016/j.jhep.2024.06.030

New research led by Hanieh Yaghootkar, Senior Lecturer in Precision Health at the University of Lincoln, U.K., challenges the belief that liver fat is an independent risk factor for cardiovascular disease.

Dr. Yaghootkar's research delves into the intricate mechanisms connecting fatty liver (steatotic liver disease) with cardiovascular and cancer outcomes, areas that have previously been poorly understood. The work is published in the *Journal of Hepatology*.

Dr. Yaghootkar, who leads the Precision Health research group, explained, "Our research shows that fatty liver is not just one disease; different mechanisms can cause fat to build up in the liver. Some of these mechanisms raise liver fat and the risk of cardiovascular disease, while others increase liver fat but lower cardiovascular disease risk.

"This is important because a new drug for fatty liver might also raise the risk of heart disease if it increases plasma lipid levels through higher export of fat from the liver into the bloodstream. We also found that more fat in the liver, no matter the cause, raises the risk of liver cirrhosis and cancer.

"These findings highlight the need for personalized treatment and better risk assessment. It also suggests that reducing liver fat, perhaps through weight loss, could help prevent liver fibrosis and cancer."

Using magnetic resonance imaging (MRI)-derived measures of liver fat from the UK Biobank study, the research team identified 13 different genetic variants associated with liver fat, each exhibiting different impacts on health outcomes.

Some of these genetic variants showed liver fat-increasing alleles to correspond with a reduced risk of coronary artery disease but an elevated risk of type 2 diabetes. However, some variants associated with enhanced de novo lipogenesis (a complex metabolic pathway that converts excess carbohydrates into fatty acids) showed liver fat-increasing alleles to be linked to a higher risk of coronary artery disease.

Dr. Yaghootkar's research provides detailed insights into the unique effects of the 13 identified genetic variants, underscoring the importance of Precision Health. A key conclusion of the study is that excess liver fat , regardless of the underlying mechanism, is causally linked to liver cirrhosis and cancers in a dose-dependent manner.

More information: Altayeb Ahmed et al, Differing genetic variants associated with liver fat and their contrasting relationships with cardiovascular diseases and cancer, *Journal of Hepatology* (2024). DOI: 10.1016/j.jhep.2024.06.030

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