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The causal relationship between gastro-oesophageal reflux disease and idiopathic pulmonary fibrosis: a bidirectional two-sample Mendelian randomisation study

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This bidirectional two-sample Mendelian randomisation study provides strong evidence that gastro-oesophageal reflux disease (GORD) increases the risk of idiopathic pulmonary fibrosis (IPF), but found no evidence that IPF increases the risk of GORD https://bit.ly/3Lde737

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Abstract

Background Gastro-oesophageal reflux disease (GORD) is associated with idiopathic pulmonary fibrosis (IPF) in observational studies. It is not known if this association arises because GORD causes IPF or because IPF causes GORD, or because of confounding by factors, such as smoking, associated with both GORD and IPF. We used bidirectional Mendelian randomisation (MR), where genetic variants are used as instrumental variables to address issues of confounding and reverse causation, to examine how, if at all, GORD and IPF are causally related.

Methods A bidirectional two-sample MR was performed to estimate the causal effect of GORD on IPF risk and of IPF on GORD risk, using genetic data from the largest GORD (78 707 cases and 288 734 controls) and IPF (4125 cases and 20 464 controls) genome-wide association meta-analyses currently available.

Results GORD increased the risk of IPF, with an OR of 1.6 (95% CI 1.04–2.49; p=0.032). There was no evidence of a causal effect of IPF on the risk of GORD, with an OR of 0.999 (95% CI 0.997–1.000; p=0.245).

Conclusions We found that GORD increases the risk of IPF, but found no evidence that IPF increases the risk of GORD. GORD should be considered in future studies of IPF risk and interest in it as a potential therapeutic target should be renewed. The mechanisms underlying the effect of GORD on IPF should also be investigated.