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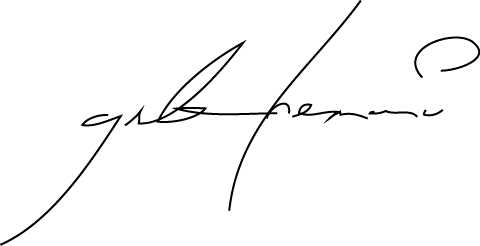
Dear Editor

We are delighted to submit our paper “Orienting the causal relationship between imprecisely measured traits using genetic instruments” for your consideration.

Combining ‘omic’ data with genetic associations is of particular current interest, particularly for inferring causal relationships. However, there are many dangerous pitfalls to which current methodology is liable, which can result in erroneous causal inference. This paper describes these pitfalls, and introduces new methodology to improve reliability, and crucially, to assess the potential unreliability of empirical estimates of inferred causal relationships.

The methods are applied to systematically infer the causal relationships between DNA methylation and gene expression levels.

Yours sincerely,



Dr. Gibran Hemani, on behalf of Kate Tilling and George Davey Smith