

regulatory processes. Mendelian randomization, in turn, builds on this information to evaluate potential directionality and effect magnitude. Rather than acting as independent components, these approaches are linked through intermediate steps—most notably colocalization—which help align signals across datasets and establish continuity between different layers of evidence.

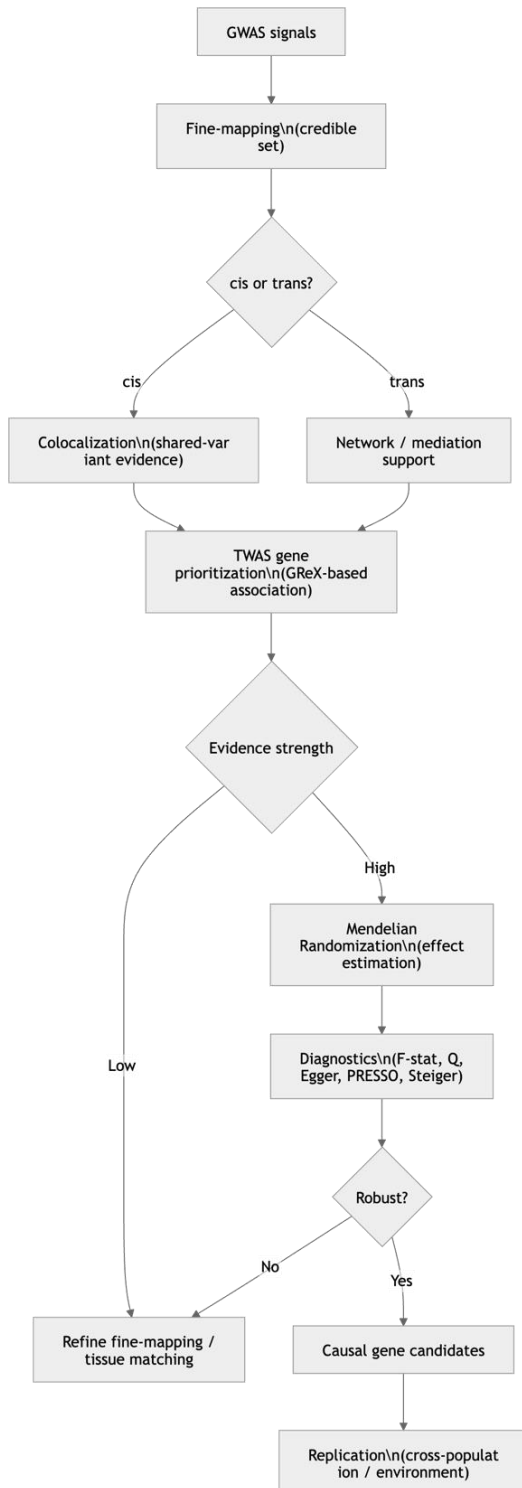


Figure 3 An integrative framework for causal inference in statistical genetics

In practice, locally acting regulatory signals, particularly cis-eQTLs derived from trait-relevant tissues, tend to be more stable and interpretable. TWAS further aggregates these signals into gene-level associations, narrowing the pool of candidates. However, such associations remain statistical in nature. Colocalization provides a way to