Against this background, the probabilistic framework centered on PIP and credible sets will continue to serve as an important connecting foundation across different methods, functioning as a common language of representation and supporting the ongoing transition of statistical genetics from association analysis toward causal inference (Schaid et al., 2018).

8 Conclusion

The development of probabilistic fine-mapping marks an important shift in the research paradigm of statistical genetics. The focus of complex trait research is no longer confined to the detection of association signals, but is gradually moving toward an inferential framework centered on causal probability distributions. Within this framework, genetic variants are no longer ranked solely according to significance levels, but are instead characterized probabilistically through posterior inclusion probabilities (PIPs) and credible sets, thereby enabling a more systematic representation of uncertainty in causal inference. This shift means that research on complex traits is moving from the localization of association signals toward the analysis of causal mechanisms.

The main contribution of this study lies in its attempt to bring different fine-mapping methods into a common causal configuration framework from a unified Bayesian perspective. Although these methods differ in their implementation, they all essentially serve to constrain and characterize the same causal space. Methods that rely on functional annotations primarily improve resolution through prior information, whereas methods that rely on LD structure enhance robustness through likelihood-based modeling, and cross-study integrative methods further improve the identifiability of causal signals by expanding the data basis. Thus, the differences among these methods are better understood as arising from the way information is utilized, rather than from differences in the inferential target itself.

On this basis, the inferential framework can also be naturally extended to the multi-trait level. By modeling the probability that different phenotypes share causal variants, colocalization analysis extends causal inference from the single-trait setting to the evaluation of cross-trait causal consistency, thereby establishing a statistical connection between genetic variation and molecular mechanisms. In this way, research on complex traits gradually forms a continuous inferential path, beginning with GWAS, proceeding through fine-mapping and colocalization analysis, and ultimately moving toward functional interpretation and candidate gene identification.

From a practical perspective, method selection should be organized systematically according to inferential layers and data structure. Different methods are not simple substitutes for one another, but rather different steps designed to address different questions within the same causal inference process. Only by combining these methods appropriately in specific research contexts is it possible to achieve a balance among computational efficiency, inferential robustness, and biological interpretability, and thereby improve the overall reliability of complex trait analysis.

Author Contributions

Xuanjun Fang conducted the study, including literature review, data analysis, and drafting and revising the manuscript. The author has read and approved the final version of the manuscript.

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