most significant locus being retained (Hutchinson et al., 2020). This treatment more adequately reflects the uncertainty of local signals and substantially reduces the risk of prioritizing false positives driven by LD structure.

More importantly, once statistical inference is advanced from significance testing to probabilistic characterization, the output of fine-mapping is no longer limited to the interpretation of local association signals, but can be further integrated with other statistical modules. PIP and credible sets can be used for functional annotation integration, support cross-population comparisons, and facilitate colocalization analysis, thereby maintaining a relatively consistent measurement basis across different data domains (Kichaev et al., 2014; Gerber et al., 2023). For this reason, fine-mapping should not be understood merely as a downstream filtering step following GWAS, but rather as an important inferential layer linking association analysis to mechanistic interpretation.

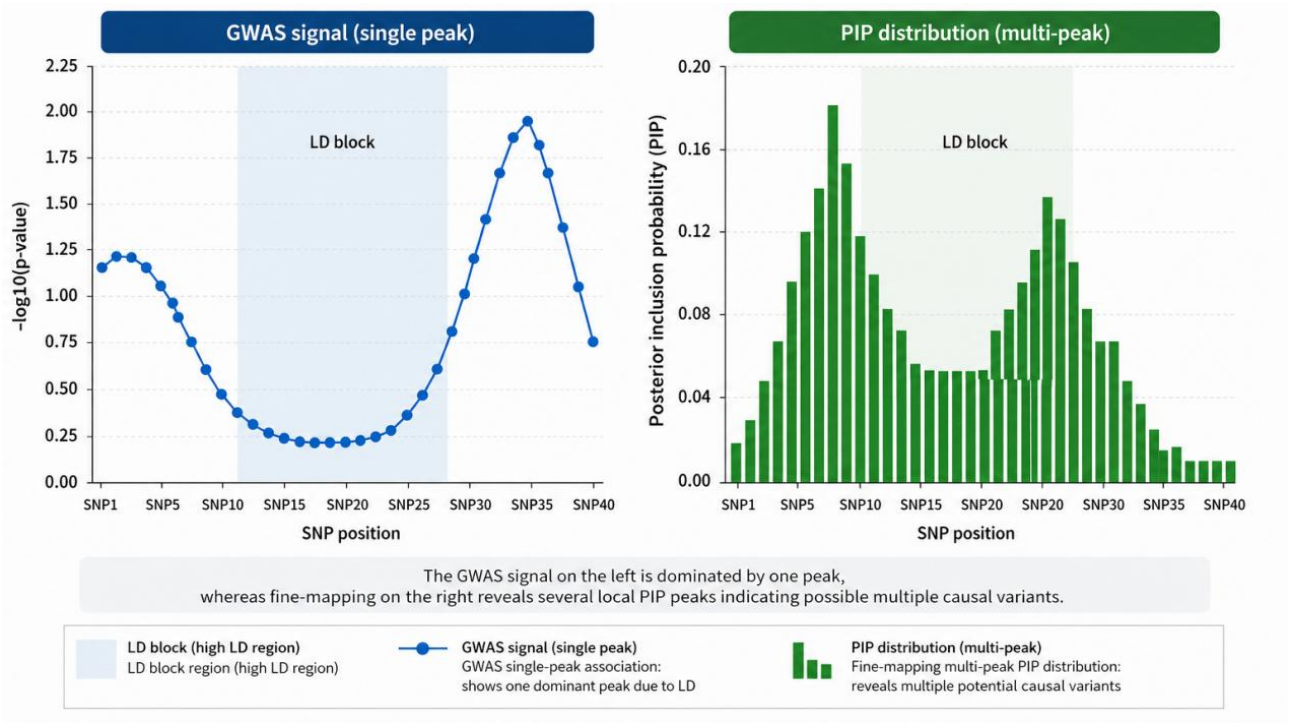

Figure 2 p-value vs PIP under an LD block: contrast between single-peak association signals and multi-peak causal probability distributions

Note: The left panel shows GWAS association signals represented by −log10(p), typically characterized by a single dominant peak within an LD block. The right panel shows the corresponding posterior inclusion probability (PIP) distribution obtained from fine-mapping, revealing multiple local peaks that reflect potential causal variants. The shaded region denotes the LD block

2.3 Theoretical implications: from point estimates to causal distributions

From a more general statistical perspective, the central significance of fine-mapping lies in its transformation of causal inference from the identification of a single locus into the estimation of a posterior distribution. A credible set can be understood as the smallest set estimator constructed under a coverage probability constraint, and this logic is highly consistent with that of interval estimation and confidence set inference (Hutchinson et al., 2019; 2020). Within this framework, the effects of LD structure and the presence of multiple causal variants are no longer treated as nuisances in the analysis, but are instead directly incorporated into the model, allowing causal inference to shift from deterministic judgment to probabilistic characterization. Compared with approaches that rely on a single significant locus to draw conclusions, this strategy more faithfully captures the uncertainty inherent in the genetic architecture of complex traits and avoids excessive simplification of local association signals.

At the same time, once causal probabilities are expressed in the form of PIP and credible sets, they can be propagated into downstream analyses, thereby providing a common probabilistic basis for integrative studies at different levels. For example, in joint analyses of GWAS and eQTL data, researchers may compare the overlap of