

In applied fields such as biomedicine and crop genetics, this model-centered understanding of heritability has direct practical implications. First, it facilitates a more cautious delineation of the scope of genetic effects, enabling research conclusions to more accurately reflect the genetic architecture under specific analytical conditions. Second, by clarifying the prerequisites for comparability between estimates across studies, it enhances the reliability of cross-study integration. Furthermore, in the construction of genomic prediction models, this framework provides a more targeted basis for both model selection and parameter interpretation.

In summary, empirical analysis based on UK Biobank data demonstrates that the differences observed across methods fundamentally stem from systematic inconsistencies in their corresponding estimands (estimand mismatch). This perspective not only offers a logically coherent framework for understanding methodological discrepancies, but also establishes a clearer theoretical foundation for reconciling the statistical meaning and biological interpretation of SNP heritability.

4.6 Practical and translational implications

This study builds on the core finding that different methods correspond to different statistical objects, further demonstrating that SNP heritability does not possess a single “true value” independent of model assumptions and data structure. This conclusion is not only of methodological importance but also directly affects the fundamental logic of study design, method selection, and result interpretation in both human and crop genetics. The differences among estimation strategies do not simply arise from random error; rather, they are rooted in systematic differences in model assumptions, treatment of linkage disequilibrium (LD), and forms of data input (Hou et al., 2019; Speed et al., 2020). Therefore, SNP heritability should be understood not as a single parameter estimate, but as a conditional statistical quantity.

In human genetics, particularly in large-scale biobank studies such as the UK Biobank, SNP heritability is widely used as a key metric to quantify the genetic basis of complex traits. However, the numerical values of this metric are not directly comparable across methods. When individual-level genotype data are available, GREML-based approaches under linear mixed models (e.g., GCTA-GREML or BOLT-REML) typically provide more stable estimates. These methods explicitly model genetic relatedness among individuals and achieve a balance between statistical efficiency and model robustness (Yang et al., 2010; Hou et al., 2019). In large samples, their estimates can be interpreted as a baseline representation of the genetic variance captured by the given set of SNPs under the corresponding LD structure. In contrast, summary-statistics-based approaches such as LDSC rely more heavily on external LD reference panels, and their estimates are highly sensitive to the degree of match between the reference and the study data. Under complex genetic architectures (e.g., when effect sizes depend on LD or minor allele frequency), such methods may produce systematic biases (Bulik-Sullivan et al., 2015; Ni et al., 2018).

From this perspective, method choice itself effectively defines the concept of “heritability” being estimated. Relying on a single method for reporting can easily lead to misinterpreting methodological differences as biological differences, thereby undermining the reliability of conclusions. A more appropriate approach is to apply multiple estimation strategies within the same analytical framework and to clearly report their respective model assumptions and LD references.

Although this study is based on human data, its conclusions are equally applicable to crop genetics. Crop populations typically exhibit stronger and longer-range LD, clearer population structure, and higher marker density, all of which fundamentally influence the “capturability” of genetic variance. Under strong LD, SNP markers are more likely to tag causal variants effectively, making SNP heritability numerically closer to true heritability. This property underlies the high predictive accuracy achieved in genomic selection in breeding practice. In such contexts, standard linear mixed models are often sufficient for predicting most traits; however, when the genetic architecture shows clear dependence on MAF or LD, incorporating weighted models (e.g., LDAK) may further improve model fit and predictive performance.

At the same time, both human and crop studies face similar statistical constraints when comparing SNP heritability across populations. If marker sets, LD structures, or model specifications are not aligned, observed