to estimate drug concentrations, the risk of liver damage, and the possibility of successful treatment. Studies have found that machine learning models trained with relevant data can screen out high-risk patients with "specific genotype+liver disease", and suggest that the prognosis of such patients may be worse.

This system conforms to the host-centered precision treatment direction. Combining the genetic characteristics of patients, genetic information of pathogens and drug metabolism data can help formulate more reasonable plans and reduce the chance of drug resistance. Pharmacogenomics should also be used for the medication guidance of new drugs such as bedaquiline to improve efficacy and reduce adverse reactions (Espino-Pereiro et al., 2022; Motta et al., 2023). In the future, clinical decision-making platforms that integrate multi-omics data may shift the management approach from "dealing with problems only when they arise" to "continuous adjustment during the treatment process", thereby further promoting individualized treatment.

8 Discussion and Outlook

The results of this study and the increasing evidence worldwide both indicate that an individual's genetic status can significantly affect the therapeutic effect of drug-resistant tuberculosis (DR-TB). The differences in genes such as drug-metabolizing enzymes (such as *NAT2*, *CYP2E1*, *CYP3A4*), drug transporters (such as ABCG2, SLCO1B1), and immune-related genes (such as *PDCD1*, *VDR*, *PI3K/AKT*) It can lead to different therapeutic effects by altering the metabolism of drugs in the body, the body's tolerance to drugs, and the immune regulatory capacity. Common situations include: People with slow drug metabolism caused by the NAT2 gene are more likely to suffer liver damage due to drug accumulation in the body. For those with a fast drug metabolism, the risk of treatment failure may increase due to insufficient drug concentration in the body. At the same time, mutations in the *ABCG2* and *VDR* genes will also make people more prone to adverse drug reactions, and the speed at which sputum bacteria turn negative will also slow down. It is precisely because of these differences determined by genes that even if a uniform treatment plan is used, patients' treatment responses can still vary greatly. Overall, identifying these key genetic influencing factors can lay the foundation for formulating personalized treatment plans, help doctors assess the efficacy and drug toxicity risks before the start of treatment, and promote the development of drug-resistant tuberculosis treatment towards precision.

Although pharmacogenomics research has made considerable progress, it still faces many difficulties. Current research often leads to unstable validation results from different research teams due to issues such as small sample sizes, most of the research subjects being of the same race, and inconsistent definitions of treatment effects. Moreover, the occurrence of drug-resistant tuberculosis is the result of the combined effect of multiple factors such as the patient's genes, pathogen mutations, living environment and drug metabolism. These factors are intertwined, making it difficult to accurately calculate the independent impact of a single genetic variation on treatment failure. In practical applications, the high cost of genetic testing, the insufficient popularization of testing technology, and the lack of a unified clinical interpretation standard all limit the use of pharmacogenomics in first-line treatment. In those low-and middle-income countries where the problem of drug-resistant tuberculosis is relatively serious, local medical systems often lack the basic conditions for standardized genetic testing and drug efficacy monitoring. In addition, many of the reported associations between genes and therapeutic effects still lack verification from large-scale actual diagnosis and treatment data and long-term follow-up studies. Therefore, it is difficult to directly use these conclusions to guide clinical treatment decisions.

Future research should prioritize the integration of multiple omics and large-scale population studies, and enhance the systematic validation of genotype-phenotypic associations in clinical scenarios to screen for scalable pharmacogenomic markers. Linking the host genome, bacterial genome and pharmacokinetic data is expected to provide a more complete explanation of treatment dynamics and the mechanism of drug resistance evolution. Meanwhile, machine learning models that integrate genetic, clinical and biochemical data may also become effective decision-making tools for optimizing individualized plans. To promote the implementation in resource-limited areas, subsequent work still needs to develop more economical and rapid real-time genotyping methods and explore the connection path with the conventional monitoring system. The integration of pharmacogenomics into the national tuberculosis control program cannot be achieved without interdisciplinary