recurrence and slow down the rate at which sputum bacteria turn negative. This connection is more prominent in people with low vitamin D levels (Yadav et al., 2021).

Meanwhile, CYP2E1 and NAT2 polymorphisms may indirectly affect treatment success by altering plasma drug levels: Metabolic features such as rapid acetylation may lead to subtreatment exposure and be associated with an increase in persistent posipositive and recurrence rates, while insufficient metabolism may cause treatment interruption due to increased toxicity. Variations in efflux transport genes (such as *ABCG2*) may also lead to insufficient intracellular drug accumulation, which is conducive to the survival of bacteria under therapeutic stress. Overall, the interaction between pharmacogenetic factors and immunomodulatory factors provides a reasonable explanation for the heterogeneous outcomes that still occur in patients with drug-resistant tuberculosis under a uniform protocol. In the future, if the host genomic characteristics can be combined and integrated with the monitoring of therapeutic drugs and immunophenotypes, it is expected to establish more precise treatment algorithms to increase the cure rate and reduce the risk of recurrence.

7 Develop Individual Treatment Plans Based on Genetic Characteristics

7.1 Select anti-tuberculosis drugs and adjust medication based on genotypes

Everyone's genes are different, which leads to varying treatment outcomes for drug-resistant tuberculosis. The differences in drug metabolism genes can affect the concentrations of drugs such as isoniazid and rifampicin in the body. People with a slower metabolism rate of the *NAT2* gene tend to have drugs stay in their bodies for a longer time and have a greater risk of liver injury. People with fast gene metabolism have lower drug concentrations in their blood, and the possibility of developing drug resistance increases. By integrating the monitoring results of therapeutic drugs with pharmacogenomic information, more reliable medication plans can be formulated, which not only can kill bacteria more effectively but also reduce the toxic and side effects brought by drugs (Igumnova, 2025).

Genetic information can also help improve the safety of using second-line anti-tuberculosis drugs. For instance, hearing loss after taking aminoglycoside drugs may be related to the variation of the *MT-RNR1* gene. If genetic testing could be done earlier, there would be a chance to avoid irreversible damage (Igumnova, 2025). In addition, different *CYP3A4* genes can affect the metabolism of bedaquiline, making it easier for this drug to accumulate in the body and thereby increasing the risk of prolonged QT interval. Pharmacogenomics can also provide more appropriate medication guidance for new drugs like pretomanib.

7.2 Strengthen the monitoring and management methods for high-risk genotypes

Patients who are prone to treatment failure or severe side effects can be identified through genetic markers. People carrying genes related to *CYP2E1* or *NAT2* slow metabolism are more prone to drug-induced liver injury. They should enhance liver function tests and adjust the dosage in a timely manner. For individuals with mutations in the *ABCG2* and *SLCO1B1* genes, there may be insufficient drug absorption or increased toxicity, making it more suitable to use drugs flexibly based on blood drug concentration and therapeutic effect. The use of pharmacogenomic data in conjunction with routine biochemical tests can provide more timely risk warnings for clinical practice.

Therapeutic drug monitoring and population pharmacokinetic models are a good approach to managing critically ill patients. They can flexibly adjust the dosage of medication during treatment and reduce risks. Drug proteomics studies have found that biomarkers at the protein level can make up for the shortcomings of gene screening and more comprehensively reflect the differences in drug responses among different people (Kumar et al., 2025). These methods can help form a management model of "risk classification+dynamic adjustment", making the treatment process more flexible and efficient.

7.3 Application of gene and clinical comprehensive evaluation model in treatment decision-making

Putting genetic information, clinical manifestations and drug metabolism data in the same decision-making tool is a key approach to improving the accuracy of treatment for multidrug-resistant tuberculosis. Gene-clinical models can take into account gene differences such as *NAT2* and *CYP2E1* along with factors like age and comorbidities,