

multidrug-resistant tuberculosis remains unsatisfactory. Globally, the cure rate of multidrug-resistant/rifampicin-resistant tuberculosis is only 60%~65%, significantly lower than that of common sensitive tuberculosis (Bartholomay et al., 2021). During the treatment process, treatment failure, loss to follow-up, and adverse reactions after medication are still relatively common. These problems are often associated with factors such as co-infection with HIV, malnutrition, previous tuberculosis history, and difficulty in controlling drug side effects (Dlatu et al., 2025). Treatment failure not only increases the risk of recurrence, severe illness and even death for patients, but also may promote the further spread of drug-resistant strains and generate new drug resistance, thereby weakening the overall effectiveness of tuberculosis prevention and control efforts (Liebenberg et al., 2022; Farhat et al., 2024). Therefore, it is of great significance to promote individualized treatment and seek reliable indicators to predict the treatment effect.

This study will explore the strain characteristics of *Mycobacterium tuberculosis* and the possible impact of human genetic factors on therapeutic effects. Some specific genetic changes in *Mycobacterium tuberculosis* may cause the bacteria to develop varying degrees of drug resistance, thereby increasing the risk of treatment failure and death. These bacterial characteristics may also interact with human genes and immune-related substances, thereby influencing disease progression and treatment outcomes. As for the specific role of human genetic background in the therapeutic effect of drug-resistant tuberculosis, further exploration is still ongoing. Due to the differences in the study population, treatment plans and diagnostic conditions, the conclusions of each study are not completely consistent. This study aims to integrate relevant research ideas, promote the application of precision medicine, form more targeted treatment strategies, increase the cure rate, and alleviate the burden brought by drug-resistant tuberculosis worldwide.

## **2 Clinical Characteristics and Causes of Treatment Failure of Drug-resistant Tuberculosis**

### **2.1 Definition, criteria and main clinical manifestations of treatment failure**

The World Health Organization (WHO) defines treatment failure for drug-resistant tuberculosis (DR-TB) as: after completing standard treatment, no pathogen is detected, the condition turns negative, and there is no significant improvement. This can usually be confirmed by sputum cultures and sputum smears that remain positive during or after treatment (Gunther et al., 2021). Common criteria for judging treatment failure include: sputum culture remaining positive after 5 months of treatment, or being negative first and then positive; Imaging studies show that the lesion and clinical condition have not improved significantly. And new drug resistance emerged during the treatment process (Gunther et al., 2021; Kherabi et al., 2025). Common symptoms are often manifested as coughing, hemoptysis, persistent fever and weight loss, etc., indicating poor disease control. Meanwhile, the imaging also shows the progression of lung lesions, such as new cavities and pleural effusion signs (Miirio et al., 2023; Li et al., 2025).

In the treatment of drug-resistant tuberculosis, there are many reasons for the failure of treatment. Some conditions are very similar to the side effects of the drugs, making it difficult to distinguish them when seeing a doctor. For patients with multidrug-resistant tuberculosis or those who have had related diseases before, the risk of treatment failure is significantly higher, with the failure rate reaching 44%, and the subsequent recovery effect is often poor (Kherabi et al., 2025). If the patient also has other diseases such as AIDS and diabetes, the possibility of treatment failure will be even greater. Doctors usually make a judgment on the condition based on the examination results and changes in symptoms, and also take into account the patient's own risk situation. Only by doing so can they have a more comprehensive understanding of the illness.

### **2.2 Non-genetic factors**

In addition to genetic factors, many non-genetic factors can also have a significant impact on the treatment outcome of tuberculosis. Failure of patients to take medicine as prescribed is a common cause of treatment failure. Long treatment cycle, a wide variety of drugs to be taken, prominent drug side effects, coupled with high economic pressure, all these make it very difficult for patients to adhere to the regular medication (Bartholomay et al., 2021). In areas with backward medical conditions, it is not uncommon and even very common for patients who have received long-term treatment to lose contact during subsequent follow-ups. Meanwhile, if the