**2025年第40周**

**中国大陆学者发表的结核病英文文章摘要**

**（26篇）**

**PubMed Publication date: 2025/9/29---2025/10/5**

**(tuberculosis[Title/Abstract]) AND (English[Language]) AND (China[Affiliation])**

**1. Talanta. 2025 Sep 26;298(Pt A):128909. doi: 10.1016/j.talanta.2025.128909.**

**Online ahead of print.**

Multiplex biosensing platform for simultaneous and precise evaluation of dual

tuberculosis biomarkers.

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A multiplex electrochemiluminescence (ECL) biosensing platform utilizing a

potential-resolved pattern was constructed for precise evaluation of dual

tuberculosis (TB) biomarkers, interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α). In the study, the synthesized carbon quantum dot (CQD) and gold

nanocluster (AuNC) were successively combined on gold nanoparticle (AuNP) and

magnetic bead (MB) to construct signal-amplifying and potential-resolved ECL

complex probes. Primary antibody (Ab1) to IFN-γ and TNF-α was modified onto

double distinct regions of patterned indium tin oxide electrodes for capturing

TB biomarkers. Then, the captured IFN-γ and TNF-α was recognized by

corresponding secondary antibody (Ab2)-functionalized ECL complex probes. The

binding events generated two distinct and well-resolved ECL peaks in a single

potential scan. The intensity of ECL peaks correlated linearly with IFN-γ and

TNF-α concentrations over the range of 0.01-1500 pg mL-1. The multiplex

biosensing platform enabled simultaneous and precise evaluation of dual TB

biomarkers in serum, potentially establishing a faster and more reliable TB

diagnostic technology.

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**2. Ann Clin Microbiol Antimicrob. 2025 Sep 26;24(1):52. doi:**

**10.1186/s12941-025-00822-7.**

Innowave MTB/RIF/INH facilitates timely and accurate diagnosis of multiple-drug

resistant tuberculosis as a near POCT technique: a multicenter prospective

on-site performance evaluation study.

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**BACKGROUND:** Many rifampicin (RIF)-resistant (RR) tuberculosis (TB) patients

remain sensitive to isoniazid (INH), which challenges the strategy of using RR

as an instant indicator of multiple-drug resistance tuberculosis (MDR-TB). A

molecular test capable of concurrently detecting RIF and INH resistance is

urgently needed.

**METHODS:** The performance of a novel rapid molecular test, Innowave MTB/RIF/INH

(InnowaveDX) was evaluated prospectively in three tertiary hospitals. Its

capability of detecting resistance to RIF and INH was assessed.

**RESULTS:** In 767 pulmonary tuberculosis (PTB) patients, InnowaveDX showed

significantly higher sensitivity than the Xpert MTB/RIF assay (Cepheid, USA)

(74.97% versus 68.18%; p = 0.003, χ2 = 8.664). This difference was particularly

notable in culture-negative PTB cases (52.73% versus 41.29%; p = 0.001,

χ2 = 10.565). Both tests demonstrated high specificity in 286 non-TB patients.

The overall consistency in RIF susceptibility prediction between InnowaveDX and

the Xpert assay was 97.3% (505/519). InnowaveDX identified 83.05% (98/118) of

INH-resistant cases as predicted by phenotypic drug susceptibility testing

(pDST) and 95.45% (105/110) by another molecular method (MeltPro, Zeesan, China)

for INH resistance detection on isolates. In addition, InnowaveDX showed a

99.35% consistency (154/155) with katG, inhA, and ahpC sequencing on sputum

samples. The consistency rate for MDR-TB prediction between InnowaveDX and pDST

was 93.25% (332/356). The accuracy of using RR to predict MDR-TB varied between

64.1 and 80.5%, depending on the reference method.

**CONCLUSION:** InnowaveDX is an easy, rapid, and sensitive molecular test for PTB

diagnosis that can detect INH and RIF resistance within 3 h, facilitating MDR-TB diagnosis on the first day of hospital admission.

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**3. BMC Infect Dis. 2025 Sep 26;25(1):1139. doi: 10.1186/s12879-025-11505-1.**

Association between neutrophil-lymphocyte ratio and latent tuberculosis

infection in the United States: a cross-sectional study from NHANES 2011-2012.

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**BACKGROUND:** Latent tuberculosis infection (LTBI) breeds community-wide

tuberculosis (TB). Early detection is the key to TB control. A novel

inflammatory measure, the neutrophil-lymphocyte ratio (NLR), may be essential in

this regard. However, the relationship between NLR and LTBI remains uncertain.

This study aimed to investigate the association between neutrophil-lymphocyte

ratio (NLR) and latent tuberculosis infection (LTBI).

**METHODS:** This cross-sectional study utilized data from the United States

National Health and Nutrition Examination Survey (NHANES) conducted in

2011-2012. Curve fitting was performed to examine the association between the

NLR and LTBI. Logistic regression analysis was applied to further elucidate this

relationship. In addition, stratified analyses were conducted considering

various blood indicators, clinicodemographic characteristics, and other relevant

variables to account for potential confounders.

**RESULTS:** A total of 2,609 subjects were included, in which the prevalence of

LTBI was 17.44% (455/2,609). Multivariate regression modeling showed that after

trichotomizing for the NLR and adjusting for all covariates, the association

between the NLR and LTBI in the T3 group compared with the T1 and T2 groups

reached 1.79 (95% confidence interval [CI]: 1.36 to 2.37, p < 0.001) and 1.47

(95% CI: 1.11 to 1.96, p < 0.001), respectively. In subgroup analyses, the

effect size of NLR in the presence of LTBI in subgroups was robust.

**CONCLUSION:** In patients with LTBI, the NLR was negatively associated with LTBI.

Assessment of NLR may be a valuable part of prevention and diagnosis in patients

with LTBI.

© 2025. The Author(s).

DOI: 10.1186/s12879-025-11505-1

PMID: 41013264 [Indexed for MEDLINE]

**4. Respir Med. 2025 Sep 24:108377. doi: 10.1016/j.rmed.2025.108377. Online ahead of print.**

Artificial Intelligence Chest CT Imaging for the Diagnosis of

Tuberculosis-Destroyed Lung with PH.

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Liu E(1), Jin X(1), Liu S(1), Li C(3), Zhu Z(4).

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**OBJECTIVE:** Explore the clinical characteristics of Tuberculosis Destroyed Lung

(TDL) with pulmonary hypertension. Use Artificial Intelligence (AI) CT Imaging

for the Diagnosis of TDL Patients with PH.

**METHODS:** 51 cases of TDL patients. Based on the results of the right heart

catheterization examination, the patients were divided into two groups: TDL with

group (n=31) and TDL Non-PH (n=20). The original chest CT data of the patients

were reconstructed, segmented, and rendered using AI, and lung volume-related

data were calculated. The differences in clinical data, hemodynamic data, and

lung volume-related data between the two groups of patients were compared.

**RESULTS:** The proportion of TDL patients with PH is significantly higher than

those without TDL (61.82% vs. 22.64%, P<0.01). There were significant

differences between the two groups of patients in terms of pulmonary function,

PCWP/PVR, PASP/TRV and total volume of destroyed lung tissue (VTDLT) (P<0.05),

and VTDLT is positively correlated with mean pulmonary arterial pressure (mPAP).

Combined Diagnosis (VTDLT + PSAP): The area under the AUC was 0.917 (95%CI:

0.802-1), with a predicted probability of 0.51 and a Youden index of 0.789. The

sensitivity was 90% and specificity was 88.9%.

**CONCLUSIONS:** Patients with TDL accompanied by pulmonary hypertension are related

to restrictive disorders. The VTDLT is positively correlated with mPAP. By

calculating the VTDLT and combining it with the estimated PASP from

echocardiography, it assists in the diagnosis of PH in these patients.

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PMID: 41005682

**5. Eur J Vasc Endovasc Surg. 2025 Sep 24:S1078-5884(25)00930-X. doi:**

**10.1016/j.ejvs.2025.09.043. Online ahead of print.**

Carotid Pseudoaneurysm as a Rare Tuberculosis Complication.

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DOI: 10.1016/j.ejvs.2025.09.043

PMID: 41005647

**6. Trop Med Int Health. 2025 Sep 25. doi: 10.1111/tmi.70039. Online ahead of print.**

Genetic Insights Into Depression Induced by Tuberculosis via Mediating Roles of

Interleukins: Evidence From Mendelian Randomization.

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**BACKGROUND:** Tuberculosis and depression frequently coexist, with

interleukin-associated inflammation recognised as a potential mechanistic link.

Nevertheless, the precise causal relationships and mechanisms underlying the

associations between tuberculosis, interleukins and their receptors, and

depression remain incompletely elucidated.

**METHOD:** We analysed summary statistics from European individual genome-wide

association studies (GWAS) to analyse the genetic causal relationships between

tuberculosis (FinnGen), 216 interleukins and receptors (IEU OpenGWAS) and

depression (UK Biobank). The genetic causality between tuberculosis and

depression was explored by applying bidirectional Mendelian Randomization

analysis, supplemented by two-step and multivariate Mendelian Randomization

mediation analysis to identify potential mediating interleukins. Inverse

variance weighting regression served as the primary method for estimating causal

effects. In addition, heterogeneity tests, horizontal pleiotropy tests and

sensitivity analyses were performed to validate the robustness of the results.

**RESULTS:** A significant genetic causal effect (βtotal = 0.015 [0.004, 0.026]) was

demonstrated between tuberculosis and depression. Only one mediating pathway,

involving the interleukin receptor interleukin-1R2, was identified linking

tuberculosis to depression. The causal effect size from tuberculosis to

interleukin-1R2 in the upstream causal pathway was 0.032 [0.002, 0.062], and the

multivariate Mendelian Randomisation effect size from interleukin-1R2 to

depression in the downstream causal pathway was 0.023 [0.003, 0.043]. The

mediation proportion of interleukin-1R2 was 7.30% [0.27%, 15.44%]. None of the

identified causal associations exhibited reverse Mendelian Randomisation

relationships.

**CONCLUSION:** Interleukin-1R2 may mediate depressive symptoms in tuberculosis

patients, potentially through specific inhibition of interleukin-1-related

inflammatory signalling. These findings elucidate genetic mechanisms underlying

tuberculosis-depression comorbidity and suggest novel targets for preventive and

therapeutic interventions.

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PMID: 40996096

**7. Br J Hosp Med (Lond). 2025 Sep 25;86(9):1-14. doi: 10.12968/hmed.2025.0235. Epub 2025 Sep 15.**

Thymosin α1 Combined With 2HRZE/4HR Regimen as a Potential Treatment of

Pulmonary Tuberculosis: An Analysis of Immune Function, Pulmonary Function and

Inflammatory Response.

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**Aims/Background** Immunotherapy plays a critical role in the clinical treatment of

tuberculosis, an infectious disease caused by Mycobacterium tuberculosis, in

which immune damage promotes the occurrence and development of the disease. This

study aimed to investigate the efficacy of thymosin α1 combined with the

2HRZE/4HR (2 months of isoniazid, rifampin, pyrazinamide, and ethambutol

followed by 4 months of isoniazid and rifampin) in the treatment of pulmonary

tuberculosis and its effect on immune function and inflammatory factors. **Methods**

A retrospective analysis was conducted on 106 pulmonary tuberculosis patients

treated between October 2022 and June 2024. The patients were divided into two

groups based on their treatment regimens: the control group (n = 47) received

the 2HRZE/4HR treatment, while the observation group (n = 59) received thymosin

α1 in addition to the 2HRZE/4HR treatment. All patients underwent a 6-month

treatment course. Clinical efficacy was evaluated 6 months after treatment based

on clinical symptoms and sputum smear results. The study compared foci

resorption rates, cavity closure rates, and changes in pulmonary function

indices, immune function indices, and inflammatory factor levels before and

after treatment between the two groups. Adverse reactions were also recorded and

analyzed. **Results** The total effective rate and the rate of foci resorption and

cavity closure of the observation group were higher than the control group (p <

0.05). After 6 months of treatment, forced expiratory volume in one second

(FEV1), forced vital capacity (FVC), FEV1/FVC, and peak expiratory flow (PEF) of

the observation group were higher compared to the control group (p < 0.05).

Compared with the control group, the observation group exhibited lower mRNA

expression of T-cell immunoglobulin mucin-1 (TIM-1) and TIM-3; reduced levels of

immunoglobulin E (IgE), sputum supernatant, serum interleukin-4 (IL-4) and tumor

necrosis factor-alpha (TNF-α); but higher interferon-gamma (IFN-γ) levels (p <

0.05). There was no significant difference in the incidence of adverse reactions

between the two groups (p > 0.05). **Conclusion** Thymosin α1 combined with the

2HRZE/4HR regimen holds promise as an effective treatment of pulmonary

tuberculosis by improving immune function and pulmonary function of patients

while attenuating the inflammatory response.

DOI: 10.12968/hmed.2025.0235

PMID: 40994373 [Indexed for MEDLINE]

**8. mSphere. 2025 Sep 22:e0051325. doi: 10.1128/msphere.00513-25. Online ahead of print.**

TAK1 phosphorylation mediates macozinone (PBTZ169) induced innate immune

activation against tuberculosis.

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The management of tuberculosis (TB), particularly drug-resistant variants,

presents enduring clinical challenges characterized by complex therapeutic

regimens, prolonged treatment durations, suboptimal success rates, and

significant adverse effects, issues that have persisted as critical concerns in

global healthcare. Current TB drug development predominantly focuses on novel

compounds and combination therapies targeting pathogen-specific pathways while

overlooking the influence of different drugs on host immunity, which is indeed a

key factor affecting treatment-related tissue damage and treatment time. In this

study, we evaluated the effects of important anti-TB drugs and candidate drugs

on host innate immunity and found that PBTZ169 showed potent innate immunity

activator, which is a promising drug for the treatment of drug-sensitive and

-resistant TB. The expression of cytokines and type I interferon was strongly

upregulated by PBTZ169 under lipopolysaccharide (LPS) stimulation and

PBTZ169-resistant strain infection, and the innate immune activation enhanced

antibacterial activity in macrophages. Mechanistically, PBTZ169 upregulated the

NF-kB and MAPK signaling pathways by activating the phosphorylation of TAK1.

TAK1 knockdown abrogated PBTZ169-mediated immune activation and antibacterial

effects. We thus demonstrate for the first time that PBTZ169 up-regulates NF-κB

and MAPK innate immune signaling pathways via activating TAK1 phosphorylation,

which may inform clinical deployment strategies and patient

selection.

**IMPORTANCE** Maintaining immune homeostasis is paramount for efficient

Mycobacterium tuberculosis (Mtb) clearance and tissue repair. Current

therapeutic strategies, however, predominantly focus on achieving maximal

bacterial suppression within compressed timelines while overlooking the

immunomodulatory consequences of anti-tuberculosis agents. This critical

knowledge gap underscores the urgent need for mechanistic investigations to

establish evidence-based frameworks for optimizing drug combinations and

integrating therapies with host-directed approaches.

DOI: 10.1128/msphere.00513-25

PMID: 40980904

**9. mSystems. 2025 Sep 22:e0089825. doi: 10.1128/msystems.00898-25. Online ahead of print.**

Ongoing evolution of PE/PPE genes in Mycobacterium tuberculosis associated with

drug resistance and host immune response.

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The Proline-Glutamate/Proline-Proline-Glutamate (PE/PPE) gene family comprises

approximately 10% of the Mycobacterium tuberculosis (Mtb) genome and is

characterized by GC-rich, highly repetitive sequences. As a result, these genes

are usually excluded from short-read-based whole-genome sequencing analyses,

leaving their sequence diversity and evolutionary dynamics poorly characterized.

Recently, a genome masking approach demonstrated that roughly 54% of PE/PPE

sequences are recoverable from short-read data, providing an opportunity to

examine the evolution of this gene family at a population level. Here, we

analyzed 51,229 Mtb genomes to characterize sequence diversity and selection

pressures across the PE/PPE gene family. Overall, we observed that PE/PPE genes

are under relaxed purifying selection compared to other gene categories, as

evidenced by higher ratios of nonsynonymous to synonymous polymorphisms (pNpS)

and greater mutation burdens. We identified 12 PE/PPE genes with signatures of

positive selection and 7 with selective pressure associated with antibiotic

resistance. Among these genes, PPE51 exhibited selection favoring

loss-of-function mutations, which occurred only in Mtb strains that were already

multidrug-resistant (MDR). This pattern suggests either compensatory evolution

or adaptation related to resistance against second-line or newly introduced

drugs. Additionally, we identified T-cell epitopes in six PE/PPE genes that were

subject to diversifying selection, suggesting immune-driven adaptation.

Collectively, this work provides a baseline characterization of genetic

diversity in PE/PPE genes and highlights specific genes that may be involved in

adaptation to host immunity and antibiotic pressure and represent candidates for

further investigation.IMPORTANCETuberculosis remains a significant global health

challenge, partly due to Mycobacterium tuberculosis (Mtb)'s remarkable

evolutionary adaptation to antibiotics and human immune responses. Around 10% of

its genome comprises PE/PPE genes, whose functions and evolutionary dynamics are

poorly understood due to their repetitive sequences and high GC content. In this

study, we analyzed 51,229 global Mtb genomes using an advanced genome-masking

method, revealing numerous PE/PPE genes under positive selection, potentially

facilitating antibiotic resistance and immune evasion. Notably, PPE51 often

loses its function in strains resistant to multiple antibiotics, suggesting a

role in bacterial survival during drug treatment. Additionally, we identified

mutation-prone regions within six PE/PPE genes, highlighting potential targets

for future vaccine development. Collectively, our findings underscore the

crucial role of PE/PPE genes in Mtb evolution and drug resistance, providing

valuable insights to inform novel therapeutic and vaccine strategies.

DOI: 10.1128/msystems.00898-25

PMID: 40980874

**10. Tuberculosis (Edinb). 2025 Sep 19;155:102693. doi: 10.1016/j.tube.2025.102693.**

**Online ahead of print.**

Knockdown of argininosuccinate lyase influences the growth of Mycolicibacterium

smegmatis in vitro and in vivo.

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The rising prevalence of drug-resistant tuberculosis (DR-TB), coupled with

stagnation in the development of novel therapeutics, underscores the urgent need

for new drug targets and innovative anti-tuberculosis agents. In this study, we

demonstrate that CRISPR interference-mediated knockdown of argH, a nitrogen

metabolism-associated gene encoding argininosuccinate lyase, significantly

impairs the growth of Mycolicibacterium smegmatis (formerly Mycobacterium

smegmatis). This growth defect was alleviated in a concentration-dependent

manner by arginine supplementation. In a goldfish infection model, argH

knockdown led to a marked reduction in bacterial burden within both liver and

kidney tissues. Notably, bacitracin and 5-fluorouracil exhibited synergistic

effects when combined with argH knockdown. Metabolomic profiling revealed

significant perturbations in multiple amino acids, as well as in succinyl-CoA

and lactate levels, suggesting that suppression of argH impairs M. smegmatis

proliferation by disrupting amino acid homeostasis and interfering with aerobic

respiration.

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PMID: 40992203

**11. Tohoku J Exp Med. 2025 Sep 25. doi: 10.1620/tjem.2025.J111. Online ahead of**

**print.**

Inhibition of miR-199b-5p Suppresses the Tuberculosis-Induced Inflammation in

Spinal Tuberculosis via Targeting Gcnt2.

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DOI: 10.1620/tjem.2025.J111

PMID: 40993090

**12. BMC Infect Dis. 2025 Oct 2;25(1):1225. doi: 10.1186/s12879-025-11566-2.**

Global burden of MDR-TB and XDR-TB: trends, inequities, and future implications

for public health planning.

Tan EL(#)(1), Qin Y(#)(2), Yang J(2), Li XJ(2), Liu TQ(2), Yang GB(3), Li YJ(3),

Zhang ZZ(4), Lu ZH(5), Wang JC(6), Zheng JX(7)(8), Zhang SX(9)(10).

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**BACKGROUND:** Drug-resistant tuberculosis (TB) remains a major global health

threat, reflecting disparities in healthcare capacity, access, and socioeconomic

development. Previous research often lacks geographic breadth. This study

provides a comprehensive assessment of the global, regional, and national burden

of Multidrug-resistant TB without extensive drug resistance (MDR-TB) and

extensively drug-resistant TB(XDR-TB) from in Global Burden of Disease Study

(GBD) 2021 Study 1990 to 2021, with a focus on distributional inequities. The

findings aim to guide resource prioritization, inform targeted interventions,

and reduce the burden in high-risk populations.

**METHODS:** We systematically assessed the global, regional, and national burden of

MDR-TB and XDR-TB, along with their change trends from 1990 to 2021, using data

from the GBD 2021 database. The indicators included age-standardized incidence

rate (ASIR), prevalence rate (ASPR), mortality rate (ASMR), and

disability-adjusted life-years rate (ASDR). ASDR was analyzed in conjunction

with the sociodemographic index (SDI) for a comprehensive assessment. Health

inequalities were quantified using the slope index of inequality (SII) and

concentration index (CCI). Frontier analysis estimated the achievable outcomes

across different development levels, while decomposition analysis identified the

key factors driving changes in disease burden.

**RESULTS:** In 2021, the global ASIR of MDR-TB was 5.42 per 100,000 population [95%

uncertainty interval(UI): 3.17, 9.34]), and the ASIR of XDR-TB was 0.29 per

100,000 population (95% UI: 0.21, 0.42). From 1990 to 2021, the ASIR of MDR-TB

[AAPC = 0.14%, 95% confidence interval (CI): 0.13, 0.14] and XDR-TB

(AAPC = 0.01%, 95% CI: 0.01, 0.02) both showed an increasing trend. The ASIR and

ASMR of MDR-TB increased in low and low-middle SDI regions. Similarly, the ASIR

and ASMR of XDR-TB increased in all five SDI regions. The ASIR of MDR-TB

increased in 155 countries, with the largest increase observed in Somalia

(AAPC = 1.79%, 95% CI: 1.67, 1.92). The ASIR of XDR-TB increased in all

countries. From 1990 to 2021, both absolute and relative health inequalities in

the ASDR of MDR-TB and XDR-TB have grown. In addition, the ASIR and incidence of

MDR-TB and XDR-TB are negatively correlated with SDI.

**CONCLUSION:** The burden of MDR-TB/XIDR-TB is projected to increase, with

persistent disparities concentrated in low-SDI settings. Targeted public health

strategies-including improved resource allocation, infrastructure development,

and community health education-are essential to reduce inequities. Strengthening

these efforts may enhance global TB control and advance progress toward health

equity.

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**13. BMC Public Health. 2025 Oct 1;25(1):3282. doi: 10.1186/s12889-025-24575-2.**

Analyzing factors affecting tuberculosis incidence in various mainland Chinese

economic regions and predicting trends: a comprehensive regression study.

Lv H(#)(1)(2)(3), Chen H(#)(1), Zhang X(#)(4), Li X(5), Liu L(5), Dang C(1)(3),

Liu X(6), Zhao C(1)(3), Zhang X(1)(3), Bai J(1)(3), You S(1)(3), Zhang W(7)(8),

Xu Y(9)(10).

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**BACKGROUND:** The tuberculosis (TB) burden differs significantly across various

regions of China, and these differences influence the effort focused on

eradicating TB nationwide. The main factors influencing variations in TB

incidence rates between different regions remain unclear. Therefore, the aim of

this study was to analyze the factors influencing TB rates in different economic

regions of China as well as determine the actual TB incidence rates during the

COVID-19 pandemic and to project 2025 rates.

**METHODS:** This study was based on the surveillance data of TB incidence from the

Chinese Center for Disease Control and Prevention. Joinpoint regression analysis

was employed to analyze the temporal trends of the TB incidence rate, and a

generalized additive model was used to analyze the influencing factors and their

differences in distribution in China and different economic zones. The machine

learning models were used to determine the actual incidence of TB in China

during the COVID-19 pandemic and forecast the incidence rate up to 2025.

**RESULTS:** From 2004 to 2020, the incidence rate of TB increased in all areas,

except for Xizang. Other provinces in China showed a downward trend, and the

inflection point of the decline appeared near 2008. Western China had a notably

higher incidence rate than other regions. The number of medical and health

institutions, the number of health personnel, and gross domestic product per

capita were negatively correlated with the incidence rate, especially in the

western region. The seasonal autoregressive integrated moving average model

achieved the optimal fit. Through this model, the following predictions were

made: the incidence of TB in central, western, northeastern, and eastern China

will be 52.460/100,000, 81.438/100,000, 59.152/100,000, and 52.401/100,000,

respectively, with all incidence rates higher than the TB incidence rates

reported during COVID-19 pandemic in 2020.

**CONCLUSION:** Except in the eastern region, China is unlikely to achieve its 2025

goals. Regional economic disparities coupled with strained medical resources

during the COVID-19 crisis have hindered TB control efforts. To address this

issue, it is recommended that the central and western regions prioritize

optimizing health resource allocation and strengthening the management of

patients with TB.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

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PMCID: PMC12487523

PMID: 41034927

**14. ACS Infect Dis. 2025 Oct 1. doi: 10.1021/acsinfecdis.5c00192. Online ahead of print.**

Rv2647-Mediated NLRP3 Ubiquitination Inhibits Macrophage Pyroptosis and Promotes

Mycobacterium tuberculosis Survival.

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Inflammasome-mediated pyroptosis and cytokine release are crucial host defenses

against intracellular pathogens. Mycobacterium tuberculosis (M. tb) is a

successful intracellular pathogen, and it is largely unclear how it evades

immune clearance and persists in macrophages. This study investigated whether

the Rv2647 protein acts as a key virulence factor of M. tb and explored the

potential mechanism of inhibiting macrophage pyroptosis and promoting M. tb

survival. The results showed Rv2647 promoted NLRP3 degradation via enhancing its

ubiquitination, which led to the inactivation of NLRP3/caspase-1/GSDMD and

reduction of IL-1β secretion, thereby inhibiting macrophage pyroptosis and

facilitating M. tb survival. Furthermore, Rv2647-mediated enhancement of NLRP3

ubiquitination and degradation depended on its binding to ISG15, competitively

inhibiting ISGylation of NLRP3. The study identified Rv2647 as the key virulence

factor that promoted M. tb survival by inhibiting macrophage pyroptosis, whose

mechanism was to competitively inhibit the ISGylation of NLRP3 and enhance its

ubiquitination, thus suppressing NLRP3/caspase-1/GSDMD-mediated pyroptosis. This

finding highlighted Rv2647 as a promising drug target or vaccine antigen for

tuberculosis prevention and control.

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PMID: 41032685

**15. Microbiol Spectr. 2025 Oct 1:e0110125. doi: 10.1128/spectrum.01101-25. Online**

**ahead of print.**

Discrepancies in isoniazid susceptibility profiles: Bactec MGIT 960-resistant

but GenoType MTBDRplus-susceptible Mycobacterium tuberculosis strains in Hunan,

China.

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Discordant drug susceptibility testing (DST) results between the Bactec MGIT 960

system (MGIT) and the GenoType MTBDRplus assay (MTBDRplus) for isoniazid (INH)

complicate clinical decision-making. In this study, we performed minimum

inhibitory concentration (MIC) assays and whole-genome sequencing (WGS) on 53

Mycobacterium tuberculosis strains identified as INH-resistant by MGIT but

INH-susceptible by MTBDRplus. The variants conferring INH resistance were

evaluated by the WHO mutation catalogue. Our results showed that only five

strains carried variants classified as "associated with resistance" (Group 1/2),

including katG Trp39STOP, katG Ser315Asn, inhA -154G>A, and inhA Ser94Ala. In

addition, 44 strains carried 70 variants classified as "Group 3: Uncertain

significance" across nine genes, including katG, ahpC, inhA, Rv0010c, Rv1129c,

Rv2752c, mshA, dnaA, and Rv1258c. The remaining four strains carried no variants

(Groups 1-3) linked to INH resistance. No significant difference in the

prevalence of high-level INH resistance was observed between lineage 2 and

lineage 4 strains (χ² = 0.232, P = 0.630). Our findings indicate that the

variants classified as "uncertain significance" may be the main genetic

determinants causing discordant results, highlighting their associations with

INH resistance that need to be further investigated.

**IMPORTANCE:** This study addresses a critical challenge in drug susceptibility

testing (DST): the discrepancies in DST results for isoniazid (INH) between the

Bactec MGIT 960 system and the GenoType MTBDRplus assay. These discordant

results significantly complicate treatment decisions, potentially leading to

suboptimal patient outcomes. Using MIC assays and WGS on 53 clinical

Mycobacterium tuberculosis strains, we provide valuable insights into the

genetic basis of INH resistance. Our findings showed that only a small fraction

of strains carried variants definitively linked to INH resistance, while a

larger number harbored variants of uncertain significance across multiple genes,

underscoring the complexity of INH resistance mechanisms. This study highlights

the urgent need to refine our understanding of these "Group 3: uncertain

significance" variants, as they appear to be a primary driver of the

discrepancies. Additionally, this study emphasizes the importance of integrating

advanced sequencing tools into DST to improve the accuracy of INH resistance

detection.

DOI: 10.1128/spectrum.01101-25

PMID: 41031815

**16. Global Health. 2025 Sep 29;21(1):53. doi: 10.1186/s12992-025-01150-3.**

Evaluation of integration in WHO's tuberculosis, HIV, and antimicrobial

resistance policies through the social-ecological lens.

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**BACKGROUND:** TB, HIV, and AMR are closely related global health challenges. In

the context of limited global health funds and insufficient resources, an

integrated tuberculosis, HIV and antimicrobial resistance prevention and control

method will play an important role in the optimization of resources and

cost-effectiveness.

**OBJECTIVE:** This study aims to analyze the degree of policy integration for

issues of tuberculosis, HIV and antimicrobial resistance in global health

strategies and make recommendations for improving global health governance on

related issues.

**METHODS:** We conducted a thorough analysis of global health policy documents from

January 2015 to February 2024, using both quantitative and qualitative

approaches. Our focus was on assessing the integration effectiveness of current

global health governance mechanisms in addressing tuberculosis, HIV, and

antimicrobial resistance from the global governance view based on the content

analysis through word frequency analysis and thematic framework analysis.

Besides, we conduct a thematic framework analysis of the action plans and policy

recommendations outlined in the most recent reports from UNAIDS, Stop TB, and

UNEP on HIV, TB and AMR.

**RESULTS:** The analysis revealed that most documents address TB, HIV, and AMR in

isolation, with limited integration and intersectionality. TB and HIV are more

frequently linked, while AMR is less associated with the other two. The proposed

action lacks specific provisions for joint implementation or monitoring of the

evaluation. Additionally, no documented comprehensive overview includes the

overall framework of three health priorities.

**CONCLUSIONS:** The study found that the current global health governance mechanism

is significantly inadequate in dealing with integration solutions among

tuberculosis, HIV and antimicrobial resistance. So we propose establishing

integrated governance and coordination mechanisms for the same population at

both horizontal and vertical levels, including individual, interpersonal,

community, institutional, and societal levels, and developing an integrated

policy framework to facilitate better resolution to address the association

between TB, HIV infection and antimicrobial resistance in a resource-limited

context.

CLINICAL TRIAL NUMBER: Not applicable.

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PMID: 41024081 [Indexed for MEDLINE]

**17. BMC Infect Dis. 2025 Sep 29;25(1):1187. doi: 10.1186/s12879-025-11623-w.**

CCR4⁺ memory Tregs and PD-1⁺ T cells as novel immunodiagnostic biomarkers for

active tuberculosis.

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**BACKGROUND:** Tuberculosis (TB), caused by Mycobacterium tuberculosis(M.tb),

remains a major global infectious disease. T cell-mediated immune responses play

a crucial role in host defense against TB. Investigating the differentiation and

functional status of T cell subsets may help identify novel biomarkers for the

diagnosis and prediction of active tuberculosis (ATB).

**METHODS:** This study enrolled 140 ATB patients and 140 healthy controls (HC) to

investigate the immunophenotypic differences in T cell subsets within peripheral

blood mononuclear cells (PBMC). Univariate and multivariate analyses were

conducted to evaluate the association between T cell subsets and TB infection,

as well as their potential value in predicting ATB. Propensity score matching

was used to analyze the immunophenotypic differences in PBMC between mild and

severe ATB patients.

**RESULTS:** Compared with HC, ATB patients exhibited higher frequencies of CD3⁺ T

cells (P < 0.0001), lower frequencies of CD4⁺ central memory T cells (CM)

(P < 0.01) and CD8⁺ Effector T cells (P < 0.05), and increased frequencies of

CD8⁺ CM (P < 0.01). Expression of programmed cell death protein 1 (PD-1) on CD4⁺

and CD8⁺ T cells was downregulated, while Human Leukocyte Antigen - DR (HLA-DR)

expression was upregulated. CCR4⁺ memory regulatory T cells (Tregs), CD8+PD-1+ T

cells, and CD4+PD-1+ T cells were closely associated with TB infection and

showed potential value in predicting ATB. Severe ATB patients had more CD8⁺

HLA-DR+ T cells (P < 0.05) and fewer CD4⁺ Effector T cells (P < 0.05).

**CONCLUSION:** Differentiation and function of T cell subset are associated with TB

infection. CCR4⁺ memory Tregs, CD4+PD-1+ T cells, and CD8+PD-1+ T cells show

potential predictive value for ATB.

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PMID: 41023888 [Indexed for MEDLINE]

**18. BMC Infect Dis. 2025 Sep 29;25(1):1184. doi: 10.1186/s12879-025-11320-8.**

Predicting treatment outcomes in drug-sensitive pulmonary tuberculosis patients

in rural eastern China.

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Chen ZH(5), Zhang B(2), Zhang RR(6), Zhuang X(7), Zhu GB(8), Qin G(9).

**Tian Tian, Jia-Wang Lu, Ting Jiang, Cheng-Yu Li, Zhi-Ao Tian, Qun Xie, Zhong-Hui Chen, Bin Zhang, Rong-Rong Zhang, Xun Zhuang, Guo-Bing Zhu\*, Gang Qin\***

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**BACKGROUND:** This study aimed to identify risk factors associated with

unsuccessful treatment outcomes among newly diagnosed drug-sensitive pulmonary

tuberculosis (PTB) patients in rural eastern China and to develop a prediction

model for treatment outcomes.

**METHODS:** This study analyzed 838 newly diagnosed drug-sensitive PTB patients in

rural eastern China (2021-2023). Treatment outcomes (unsuccessful treatment)

were assessed using WHO guidelines. The cohort was randomly divided into a

training set (70%) and a validation set (30%) for internal validation.

Multivariate logistic regression identified predictors, including age,

malnutrition, comorbidities, hemoglobin levels, and sputum smear grades.

Decision curve analysis (DCA) was performed to evaluate the clinical utility of

the prediction model by quantifying the net benefit across a range of threshold

probabilities.

**RESULTS:** The prediction model identified six independent predictors of

unsuccessful treatment outcomes: diabetes, chronic lung disease, alcohol use,

hypoalbuminemia, anemia, and sputum smear grades. The area under the receiver

operating characteristic curve (AUC) was 0.754 (95% CI: 0.676-0.833), indicating

good discriminative ability. The model demonstrated moderate accuracy across

three risk categories. A nomogram was developed to visually represent the model,

enabling clinicians to estimate individual patient risk based on these six

predictors. Additionally, an online calculator was created to facilitate easy

and practical application of the model in clinical settings. Decision curve

analysis (DCA) further validated the clinical utility of the model, showing a

significant net benefit across a wide range of threshold probabilities (2-54%),

supporting its applicability for guiding clinical decision-making.

**CONCLUSIONS:** The prediction model serves as a valuable tool for clinicians to

identify high-risk PTB patients and tailor interventions effectively. This

approach can enhance treatment strategies and contribute to better TB control in

rural eastern China.

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**19. Commun Biol. 2025 Sep 29;8(1):1379. doi: 10.1038/s42003-025-08841-y.**

Isoleucyl-tRNA synthetase depletion reveals vulnerabilities in Mycobacterium

abscessus and Mycobacterium marinum.

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Mycobacterium abscessus and Mycobacterium marinum are nontuberculous

mycobacteria that pose significant challenges due to their high drug resistance

and persistence in hostile host environments. Aminoacyl-tRNA synthetases, such

as isoleucyl-tRNA synthetase (IleRS), are crucial for protein synthesis and

represent promising targets for antimicrobial development. This study

investigates the role of IleRS in mycobacterial growth, metabolism, and

pathogenesis using conditional gene silencing combined with microbiological,

metabolomic, and transcriptomic analyses. Our findings indicate that IleRS is

essential for mycobacterial growth and survival during infection. Depletion of

IleRS disrupts branched-chain amino acid and pantothenate biosynthesis, leading

to metabolic vulnerabilities and impaired persistence in macrophages and in

mouse infection models. Based on our metabolic findings, we tested drug

susceptibility and found that depletion of IleRS enhances sensitivity to

pyrazinamide, highlighting a synergistic effect that could improve tuberculosis

treatment. Furthermore, global gene set enrichment analysis reveals that IleRS

knockdown might promote bacterial clearance by upregulating cholesterol

metabolism and lysosome organization processes in macrophages. These results

establish IleRS as a potential therapeutic target, offering new insights into

reducing drug resistance and enhancing current treatment regimens for

mycobacterial infections, including tuberculosis.

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Mapping Nutrition and Tuberculosis Research: Insights From Bibliometric

Perspective.

Li C(1)(2), Gao B(3), Xiao H(4), Shi W(1), Lu H(1), Miao G(1), Tu X(5), Tang

Y(1), Shen H(1)(6)(7).

**Chenqi Li, Biao Gao, Hongmei Xiao, Wenjing Shi, Hongtao Lu, Gen Miao, Xiaohua Tu\*, Yuxiao Tang\*, Hui Shen\***

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**BACKGROUND:** Malnutrition and tuberculosis form a mutually reinforcing vicious

cycle. While nutritional interventions are crucial for TB management, the

knowledge structure and research frontiers remain insufficiently characterised.

**OBJECTIVE:** To systematically analyse the structure, trajectory and frontiers of

research in the nutrition-tuberculosis field using bibliometric methods.

**METHODS:** Relevant literature published since 2007 was retrieved from the Web of

Science Core Collection database. CiteSpace was employed to perform

multidimensional analyses, including co-occurrence, cluster timeline

visualisation and burst detection for keywords, citations and authors, thereby

constructing knowledge maps and identifying key nodes through network centrality

metrics.

**RESULTS:** A total of 4502 bibliographic records were analysed. Key findings

include: (1) Vitamin D occupies a central position (frequency 326, centrality

70), bridging basic immune mechanisms and clinical applications; (2) research

paradigms evolved from molecular mechanism exploration (2007-2012), through

clinical translation validation (2011-2019), to systems biology integration

(2019-2025); (3) gut microbiota (burst strength 11.73) and (fatty) acids emerged

as frontiers; (4) diabetes-tuberculosis comorbidity revealed the complexity of

metabolic-immune interaction networks and (5) high citation frequency of WHO

reports indicates a pressing need for translating research into policy.

**CONCLUSIONS:** Nutrition-tuberculosis research is shifting from single-nutrient

studies towards integrated 'nutrition-microbiome-metabolism-immunity' networks.

Vitamin D remains central, but future priorities should focus on precision

interventions, multi-omics integration and translation from mechanism to

practice, especially for high-risk groups.

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**21. Infect Dis Model. 2025 Sep 12;11(1):121-142. doi: 10.1016/j.idm.2025.09.002.**

**eCollection 2026 Mar.**

Dynamics and optimal control for tuberculosis transmission via a data-validated

periodic model.

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China is the third-largest contributor to the global incidence of tuberculosis

(TB), and there are significant differences in the prevalence of TB among

different age groups. Therefore, it is necessary to study the contribution of

adolescents to the transmission of tuberculosis. Given that tuberculosis in

mainland China exhibits periodic transmission characteristics, a non-autonomous

differential equation model that considers age stage and periodic transmission

has been proposed. We derived the basic reproduction number R 0 of this model

and proved the global asymptotic stability of the disease-free equilibrium when

R 0 < 1, as well as the persistence of the disease when R 0 > 1. We estimated

the basic reproduction number R 0 = 1.18, which indicates that tuberculosis in

mainland China is of low endemicity. Sensitivity analysis tells us that the

adolescent group has a significant impact on the transmission of tuberculosis

and is an indispensable force. Furthermore, we constructed a tuberculosis

transmission control model and proposed four optimal control strategies,

calculated the strategy-related benefits (ACER) and the incremental benefits

between strategies (ICER), and further provided targeted recommendations for

controlling tuberculosis transmission among different groups.

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**22. Comput Struct Biotechnol J. 2025 Sep 12;27:4065-4077. doi:**

**10.1016/j.csbj.2025.09.015. eCollection 2025.**

Computational epitope profiling and AI-driven protein engineering enable

rational design of multi-epitope vaccines against Mycobacterium tuberculosis.

Li X(1), Tao X(1), Zhong M(1), Wang Y(1), Xue H(1), Andongma BT(2), Chou SH(2),

Wei H(1), He J(2), Yang H(1)(3).

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a major

global health threat, accounting for approximately 1.5 million deaths annually.

The rise of antibiotic-resistant strains further complicates treatment efforts.

While vaccination is a cornerstone of disease control, the only licensed TB

vaccine, Bacille Calmette-Guérin (BCG), shows limited efficacy in adults. There

is thus a critical need for more effective vaccines. Multi-epitope vaccines,

which incorporate key epitopes from multiple antigens, offer a promising

strategy by eliciting both humoral and cellular immunity. Here, we employed a

comparative epitopomics approach to identify immunodominant epitopes from eight

major Mtb antigens and selected 17 potent epitopes for the design of a

multi-epitope antigen. Using AI-driven protein design, we systematically

optimized epitope arrangement and flanking sequences to generate a stable,

structurally integrated antigen-MtbEpi-17. Computational analyses suggest that

MtbEpi-17 can effectively interact with TLR2 and TLR4, potentially stimulating

robust innate and adaptive immune responses. Our study provides a rational

design framework for multi-epitope vaccines, and proposes MtbEpi-17 as a strong

candidate for further preclinical and clinical evaluation.

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**eCollection 2025.**

Establishment and application of a TaqMan-based quantitative PCR assay for

simultaneous detection of bovine Brucella spp. and Mycobacterium spp.

Zhang S(1)(2)(3), Zhao H(1)(2)(4), Guo Q(1)(2)(4), Xue R(2)(4), Jiang Z(2)(4),

Jiang W(2)(4), Xing L(2)(4), Wei X(1), Diao Y(1), Tang Y(5), Lan Z(2)(4), Zhang

Y(2)(4).

**Shuai Zhang, Hui Zhao, Qiuju Guo, Ruixue Xue, Zixin Jiang, Wenduo Jiang, Linlin Xing, Xinhui Wei, Youxiang Diao, Yi Tang\*, Zouran Lan\*, Yue Zhang\***

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Brucellosis and tuberculosis are two zoonotic, chronic infectious diseases

caused by bacteria of the genus Brucella and Mycobacterium, respectively, which

pose significant hazards to both animal husbandry and human health. Currently,

mixed infections of these two pathogens are prevalent in livestock production;

thus, establishing a molecular diagnostic method for the simultaneous detection

and analysis of brucellosis and tuberculosis is crucial for the prevention and

control of these diseases. By utilizing conserved regions within the genomes of

Brucella and Mycobacterium, we designed specific primers and probes. After

optimizing the developed qPCR assay conditions, we determined the lower limit of

detection to be ten copies/ μL. Cross-testing with other bovine-derived

pathogens demonstrated no cross-reactivity. Repeatability tests indicated that

the coefficient of variation for the developed qPCR assay was less than 4.10%

both within and between batches. We employed both the developed qPCR assay and a

commercial qPCR assay to analyze sixty mixed infection samples of Brucella and

Mycobacterium from various regions. The results revealed positivity rates of

100% and 96.67% for Brucella, and 100% and 95.00% for Mycobacterium,

respectively. These findings indicate that a highly sensitive, specific,

reproducible, and versatile qPCR method has been developed for the simultaneous

quantitative detection of Brucella and Mycobacterium, which can be applied in

studying the pathogenesis and epidemiology of these pathogens.

Copyright © 2025 Zhang, Zhao, Guo, Xue, Jiang, Jiang, Xing, Wei, Diao, Tang, Lan

and Zhang.

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**24. J Clin Tuberc Other Mycobact Dis. 2025 Sep 12;41:100561. doi:**

**10.1016/j.jctube.2025.100561. eCollection 2025 Dec.**

Mycobacterium tuberculosis infection status and associated factors among

household close contacts of rifampicin-resistant pulmonary tuberculosis

patients: A single-center cross-sectional study.

Shi Z(1), Peng J(2), Li X(1), Fu X(1), Zou L(1), Chen Q(1), Huang T(1), Zhou

Y(1), Zhu H(1), Wang Y(1), Tang S(3), Wu G(1).

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**BACKGROUND:** Rifampicin-resistant tuberculosis (RR-TB) is a major global public

health challenge. Household close contacts (HHCs) of RR-TB patients face a high

risk of Mycobacterium tuberculosis infection. Southwestern China carries a heavy

RR-TB burden, yet research data on the infection status of this population

remain scarce. This study aimed to evaluate the incidence of latent tuberculosis

infection (LTBI) and active tuberculosis disease (TBD) and their associated

factors among HHCs of RR-TB patients in this region through active screening,

providing data support for optimizing regional RR-TB prevention and control

strategies.

**METHODS:** Using a cross-sectional design, HHCs of RR-TB patients diagnosed at

Chengdu Public Health Clinical Medical Center from October 1, 2023, to March 30,

2025, were enrolled. Clinical data were collected via a self-designed

questionnaire including gender, age, body mass index (BMI), relationship to

index case, living environment, chronic comorbidities, medication history, and

TBD-suspicious symptom screening. TBD screening used chest digital radiography

(DR) or computed tomography (CT). Clinical data of index cases were extracted

from the hospital information system (HIS), covering sputum acid-fast bacillus

smear, sputum mycobacterial culture, sputum molecular testing for M.

tuberculosis, fluoroquinolone resistance, extent of pulmonary lesions, and

cavitation status. TB infection screening employed tuberculin skin test (TST),

ESAT6-CFP10 fusion protein skin test (EC), or interferon-γ release assays

(IGRA). Infection status was categorized as uninfected, LTBI, or TBD based on

screening results, clinical symptoms, and imaging findings. Incidence rates of

LTBI and TBD were calculated. Chi-square tests compared clinical characteristics

across infection states. Multivariable logistic regression analyzed factors

associated with LTBI and TBD (versus uninfected).

**RESULTS:** 264 HHCs from 197 RR-TB index cases were included: 113 males (42.8 %),

151 females (57.2 %), aged 3-78 years (mean 42.4 ± 15.1). Among 209 participants

tested with TST: 117 (44.3 %) had induration diameter [0, 5) mm, 17 (6.4 %) [5,

10) mm, 30 (11.4 %) [10, 15) mm, 45 (17.1 %) ≥ 15 mm. Among 46 EC-tested: 29 (11.0 %) had [0, 5) mm, 17 (6.4 %) ≥ 5 mm. Among 9 IGRA-tested: 1 (0.4 %)

negative, 8 (3.0 %) positive. After cluster-effect adjustment, LTBI incidence

was 31.2 % (95 % confidence interval [CI]: 25.8-38.3), TBD incidence 9.9 % (95 % CI: 6.4-13.6). The proportion of spousal relationships to index cases was higher in LTBI/TBD groups than uninfected (P < 0.05). BMI < 18.5 kg/m2 and positive TBD symptom screening were more frequent in TBD than uninfected/LTBI groups (P < 0.05). Pulmonary cavitation in index cases was more common in TBD contacts (P < 0.05). Multivariable analysis showed spousal relationship was an

independent associated factor for LTBI (adjusted odds ratio [aOR] = 2.102, 95 %

CI = 1.201-3.677; P = 0.009). Factors associated with TBD included: spousal

relationship (aOR = 3.949, 95 % CI = 1.553-10.042; P = 0.004), positive TBD symptoms (aOR = 41.988, 95 % CI = 4.270-412.886; P = 0.001), and pulmonary cavitation in index case (aOR = 2.881, 95 % CI = 1.103-7.523; P = 0.031).

**CONCLUSION:** High LTBI and TBD rates exist among RR-TB HHCs in this region.

Spousal relationship is a risk factor for both LTBI and TBD; positive TBD

symptoms and pulmonary cavitation in index cases correlate with TBD. Active

screening for RR-TB HHCs and risk-stratified control strategies are recommended

to block transmission chains.

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**2025.**

Contrast-induced encephalopathy following bronchial artery embolization: A case

report and literature review in a patient with pulmonary tuberculosis and

aspergillosis.

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The current study analyzed a case of contrast-induced encephalopathy (CIE)

following bronchial artery embolization (BAE) in a patient with hemoptysis due

to pulmonary tuberculosis complicated by pulmonary aspergillosis. A 56-year-old

male patient developed CIE after BAE was retrospectively analyzed. An ectopic

bronchial artery originates from the proximal segment of the right vertebral

artery. The patient developed CIE postoperatively, which resolved after

treatment with corticosteroids and intracranial pressure reduction. A follow-up

cranial MRI after 6 months showed complete resolution of previous edema. A

literature review identified three cases of CIE after BAE, all presenting with

hemoptysis, and symptom resolution within 3 days.

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**26. EBioMedicine. 2025 Sep 27;120:105945. doi: 10.1016/j.ebiom.2025.105945. Online ahead of print.**

Peripheral blood neutrophil proteomic profiling with transcriptomic data

integration reveals biomarkers for tuberculosis infection diagnosis.

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**Jiarong Yang, Zizheng Lv, Liguo Liu, Han Zhang, Jie Hu, Xingzhu Geng, Henan Xin, Zisen Liu, Lei Gao, Xiaobing Zhang, Yanli Xu\*, Rongmei Liu\*, Qi Jin\*, Jianhua Zheng\***

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**BACKGROUND:** Tuberculosis (TB) is one of the deadliest infectious diseases

worldwide, causing millions of new cases and deaths annually. Rapid and accurate

TB diagnostics are essential for TB control, yet current methods do not fully

meet global needs. Peripheral blood neutrophils play a critical role in TB

infection and represent a promising source of diagnostic markers.

**METHODS:** We conducted a cross-sectional proteomic analysis to characterise

neutrophil protein profiles in individuals with active TB (ATB), latent TB

infection (LTBI), and healthy controls (HC). Stringent criteria were applied to

identify differentially expressed proteins (DEPs) among these groups.

Transcriptomic data were integrated to perform pathway enrichment analysis of

DEPs. Three DEPs (B2M, TXN, and PRDX5) were further validated as candidate

diagnostic biomarkers for Mycobacterium tuberculosis (MTB) infection using

automated western blotting in a cohort of 319 individuals, including 71 ATB, 142

LTBI, and 106 HC.

**FINDINGS:** Hundreds of DEPs were identified across the three groups. Integrated

transcriptomic analysis revealed significant enrichment of DEPs in the NOD-like

receptor signalling pathway. Receiver operating characteristic analysis of the

three-protein combination (B2M, TXN, and PRDX5) yielded an area under the curve

of 0.9847, with a sensitivity of 95.11% and a specificity of 96.23% for

detecting MTB infection.

**INTERPRETATION:** This study presents a comprehensive proteomic profile of

neutrophils under different MTB infection states, and this three-protein

combination may assist in the diagnosis of MTB infection.

**FUNDING:** This work was supported by the Chinese Academy of Medical Sciences

(CAMS) Innovation Fund for Medical Sciences (2021-I2M-1-037) and the National

Science and Technology Major Project of China (20212017ZX10201301-002-003).

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