6th KATRD TB and NTM International Symposium

Drug Resistance and Diagnostic Approaches of *Mycobacterium tuberculosis* in South Korea

- *Resistance Patterns, Diagnostic Challenges, and Emerging Molecular Approaches*

Gyeong In Lee

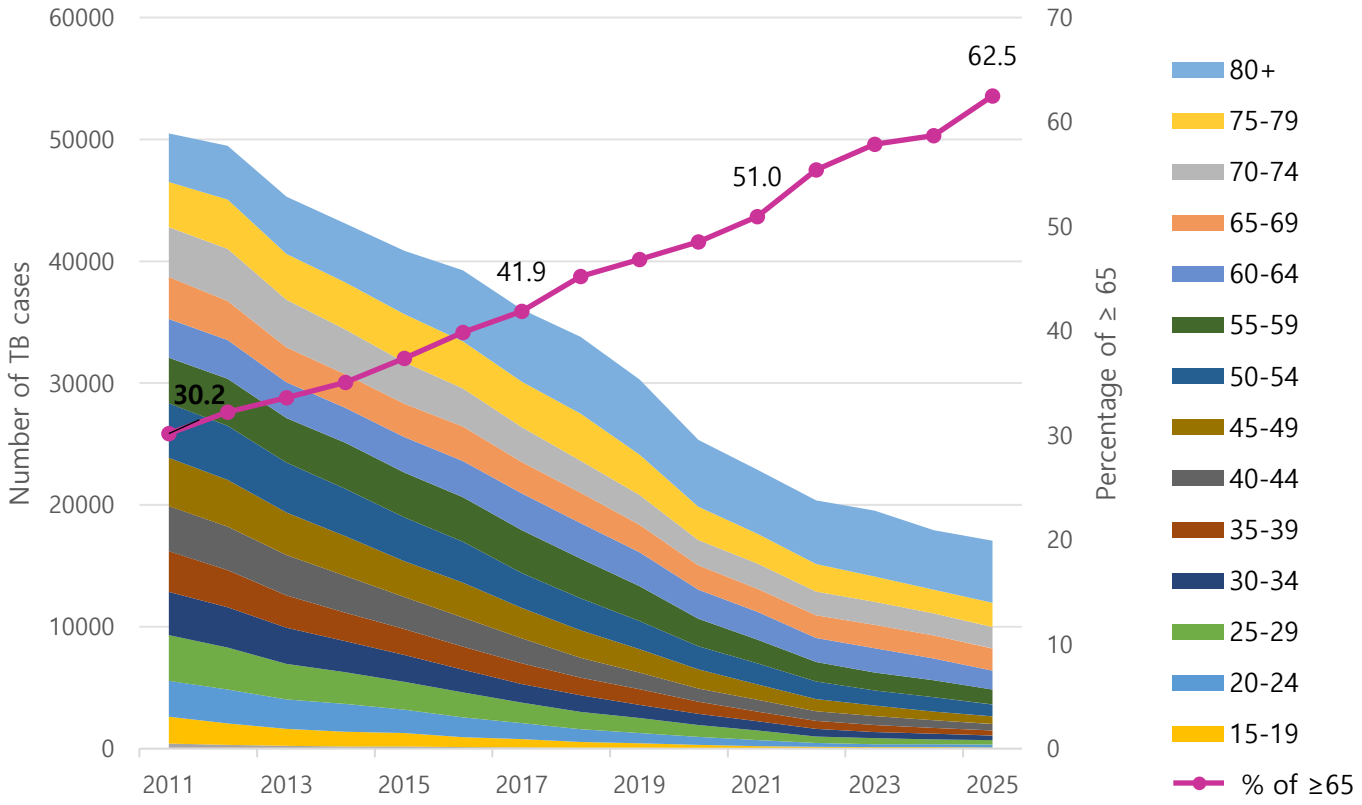
2026. 10. 24

CONTENTS

- Korean TB context
- Drug resistance landscape in Korea
- Diagnostic approaches & challenges
- Emerging molecular approaches
- Take-home messages

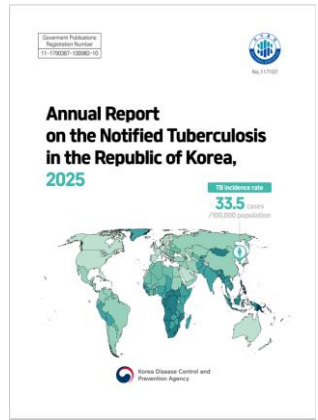
TB in South Korea: Declining Notifications, an Aging Patient Population

TB cases by Age group and proportion of TB cases aged 65 years and older, 2011–2025



TB Case Incidence in 2025

- **Number of notified TB cases 17,070** (33.5/10^5)
  New TB cases 13,713 (26.9/10^5)
- **Number of TB deaths 1,347** (2.6/10^5) (2024)
  Second highest mortality rate among infectious diseases

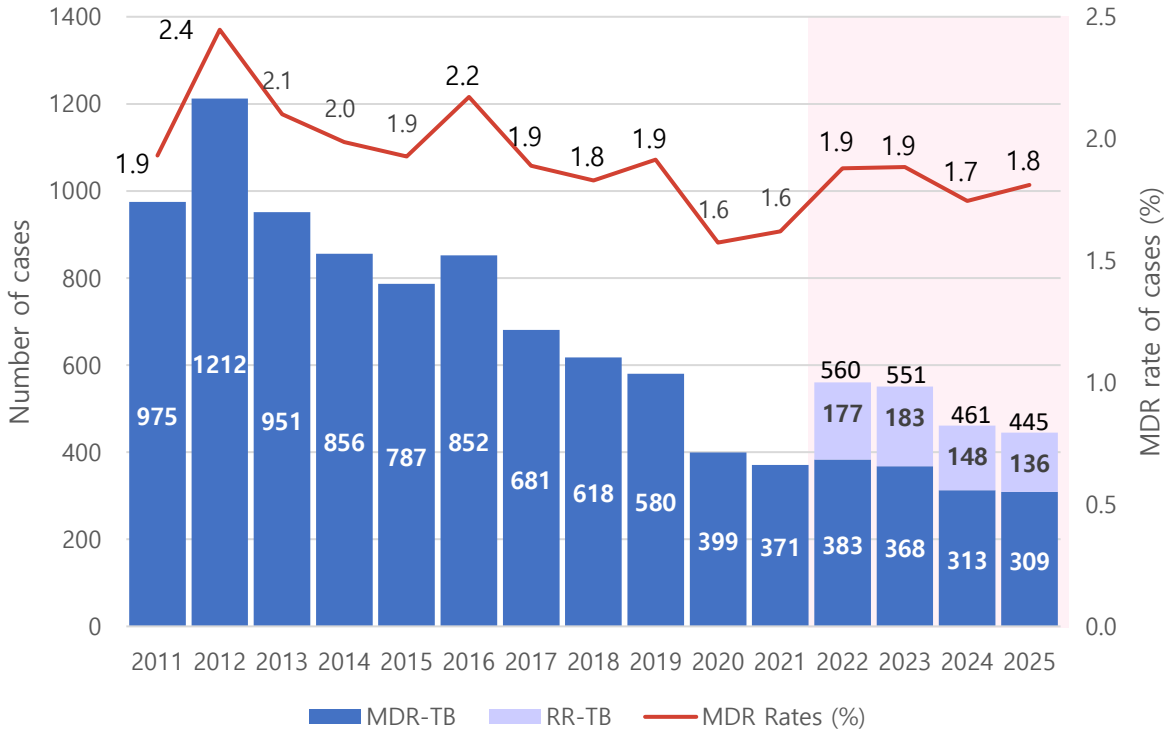


Source: KDCA, Annual Reports on the Notified Tuberculosis in the Republic of Korea, 2011–2025.

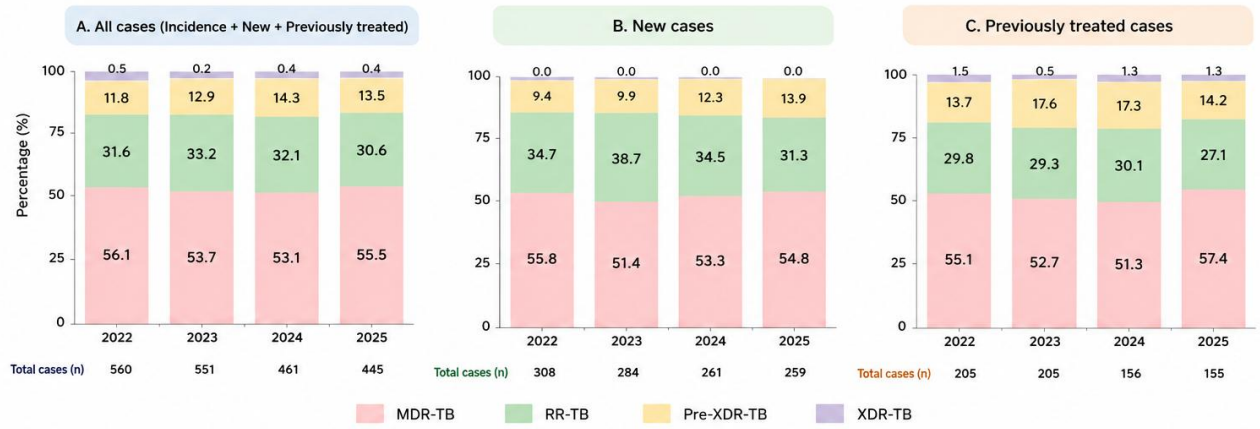
Drug-Resistant TB in South Korea

The total number of notified MDR TB cases decreased from **975** in 2011 to **309** in 2025

MDR-TB and MDR/RR-TB notification, 2011-2025



Resistant pattern composition among MDR/RR-TB cases in Korea, 2022-2025



No XDR-TB cases were notified among new cases, 2022–2025.

The burden of MDR/RR-TB has declined substantially in Korea, but drug-resistant TB remains clinically important.

Source: KDCA, Annual Reports on the Notified Tuberculosis in the Republic of Korea, 2011–2025.

KIT DST Data: Study Population and Analysis

	LJ DST	BMD DST
Study period	2020–2025	2021–2025
Study population	50,131 tested isolates	2,336 MDR/RR-TB isolates
Analysis	Annual drug resistance rates and resistance patterns	BDQ, DLM, LZD, and CFZ resistance

Confirmed repeat submissions were removed within each calendar year, retaining the first isolate.
Resistance rates were calculated using valid results for each drug.

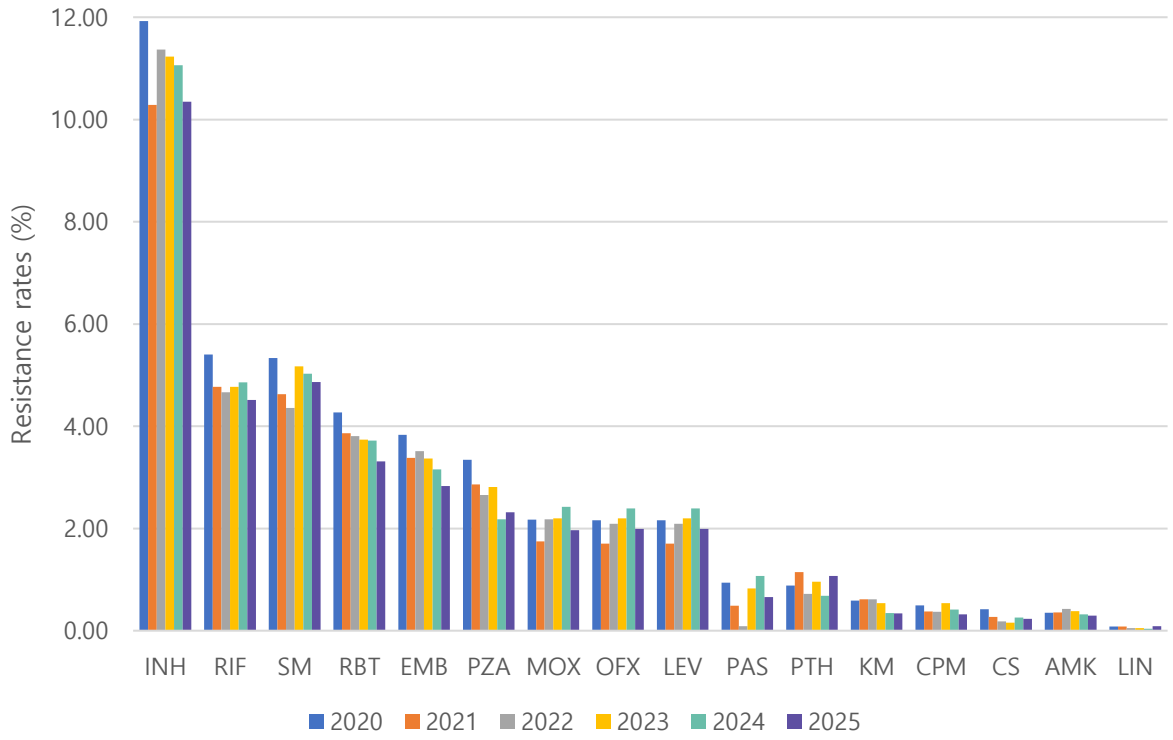
Referral laboratory data; findings describe tested isolates and do not represent population-based national resistance estimates.

Drug Resistance Profiles in Korean MTB Isolates

Annual drug resistance rate (%) by drug (2020-2025)

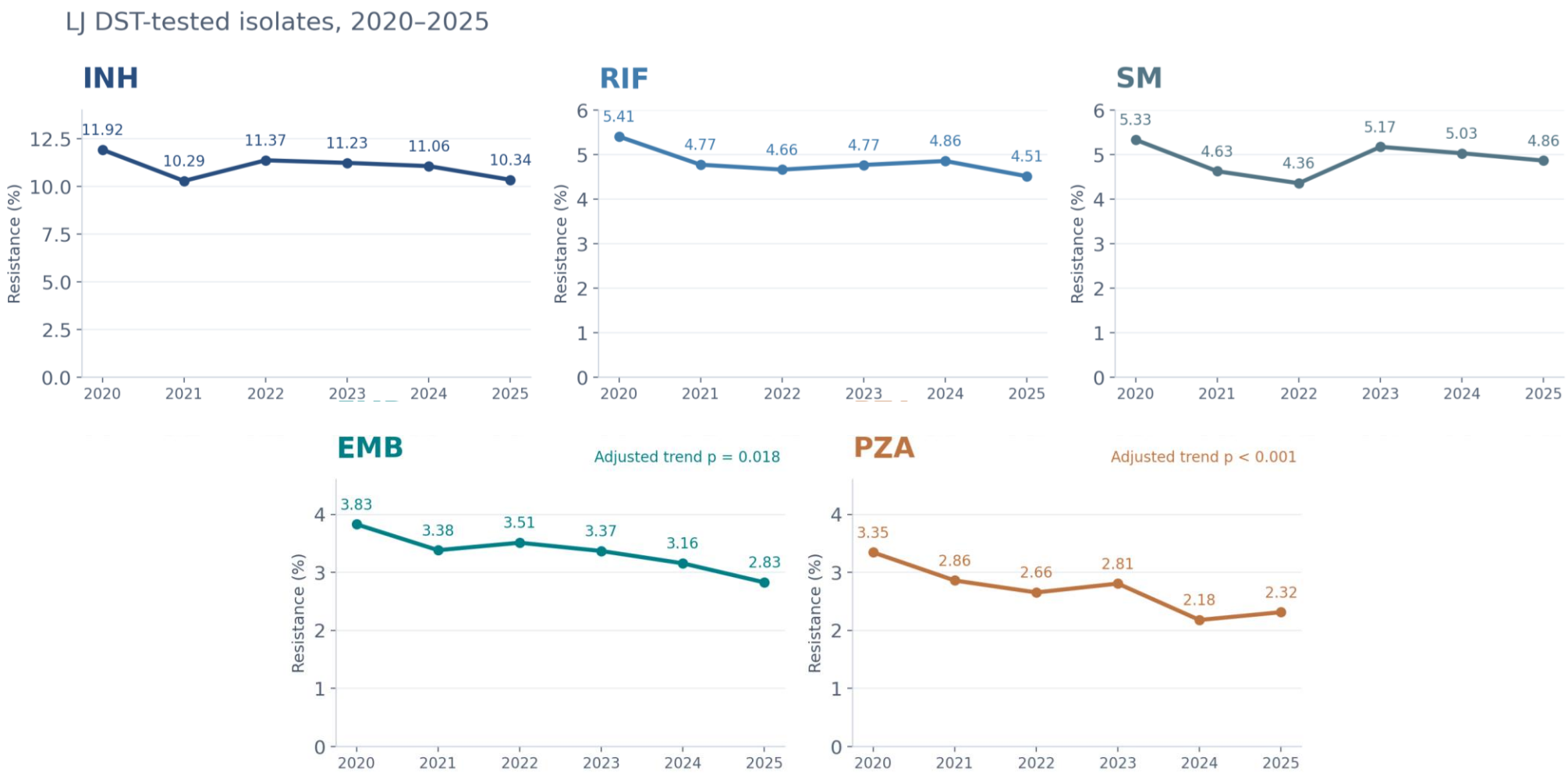
Drug	2020	2021	2022	2023	2024	2025
INH	11.92	10.29	11.37	11.23	11.06	10.34
RIF	5.41	4.77	4.66	4.77	4.86	4.51
SM	5.33	4.63	4.36	5.17	5.03	4.86
RBT	4.27	3.86	3.81	3.74	3.72	3.31
EMB	3.83	3.38	3.51	3.37	3.16	2.83
PZA	3.35	2.86	2.66	2.81	2.18	2.32
MOX	2.17	1.74	2.18	2.20	2.42	1.96
OFX	2.16	1.70	2.09	2.20	2.39	1.99
LEV	2.16	1.70	2.09	2.20	2.39	1.99
PAS	0.94	0.49	0.09	0.82	1.07	0.66
PTH	0.89	1.15	0.72	0.96	0.68	1.07
KM	0.59	0.62	0.61	0.54	0.35	0.34
CPM	0.49	0.38	0.37	0.54	0.41	0.32
CS	0.42	0.27	0.18	0.16	0.25	0.23
AMK	0.35	0.36	0.43	0.38	0.32	0.29
LIN	0.08	0.08	0.05	0.05	0.04	0.09

% = resistant isolates/tested isolates in each year



Isolates tested at the Korean Institute of Tuberculosis, 2020–2025

Key Findings from LJ Resistance Analysis



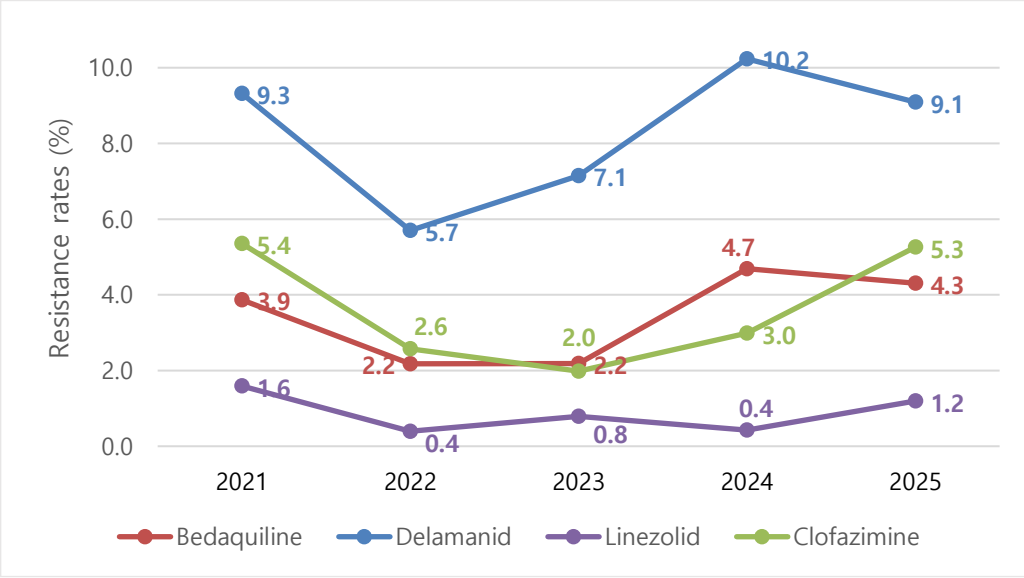
Isolates tested at the Korean Institute of Tuberculosis, 2020–2025

BDQ, DLM, LZD, and CFZ Resistance among MDR/RR Isolates, 2021–2025

Resistance to BDQ, DLM, LZD, and CFZ among BMD-Tested MDR/RR Isolates in Korea, 2021–2025

	2021	2022	2023	2024	2025
	(n=440/ 392*)	(n=505)	(n=504)	(n=469)	(n=418)
Bedaquiline	17 (3.9)	11 (2.2)	11 (2.2)	22 (4.7)	18 (4.3)
Delamanid	41 (9.3)	29 (5.7)	36 (7.1)	48 (10.2)	38 (9.1)
Linezolid	7 (1.6)	2 (0.4)	4 (0.8)	2 (0.4)	5 (1.2)
Clofazimine*	21 (5.4)	13 (2.6)	10 (2.0)	14 (3.0)	22 (5.3)

Values are n (%). In 2021, the denominator for CFZ was 392*; for the other three drugs, it was 440.



No significant between-year differences or linear trends were detected after Holm adjustment.

Temporal Changes in Selected Resistance Patterns among Drug-Resistant Isolates, 2020–2025

	2020	2021	2022	2023	2024	2025
INH mono-resistance	27.52	28.39	32.72	29.47	28.98	26.73
SM mono-resistance	9.84	10.62	9.53	13.15	10.66	13.17
INH+SM	6.46	6.64	6.27	5.39	5.42	6.93
OFX+MOX+LEV	5.52	4.06	6.43	5.76	7.48	6.33
INH+RIF+RBT	3.39	2.36	3.02	2.29	3.44	4.12
INH+PTH	1.32	2.80	1.91	2.07	1.46	3.32
INH+RIF	1.13	0.96	0.71	0.59	1.81	2.51
RIF+RBT	2.70	4.20	3.26	2.88	3.53	2.41
INH+EMB	2.32	1.92	2.86	2.73	3.10	2.31
INH+RIF+RBT+SM+EMB+PZA	2.88	1.77	2.38	1.11	0.86	1.71
CS+PZA	1.88	1.03	0.56	0.59	1.03	1.51
RIF mono-resistance	0.88	0.66	0.48	0.59	0.77	1.51
INH+RIF+RBT+PZA	1.32	1.25	0.64	1.03	0.69	1.41
INH+RIF+RBT+SM	1.07	1.62	1.35	1.70	1.20	1.31
INH+RIF+RBT+EMB+PZA	1.57	1.62	1.91	1.18	0.69	1.21
INH+RIF+RBT+EMB	2.13	1.99	3.26	2.07	1.55	1.01
PZA mono-resistance	1.94	3.02	0.95	1.92	0.34	1.01
INH+RIF+RBT+SM+EMB+OFX+MOX+LEV+PZA	0.94	0.52	0.87	0.81	2.15	1.01
INH+PZA	0.56	0.37	1.27			0.70
INH+RIF+EMB+PZA		0.52	0.64			0.60
EMB mono-resistance	0.94	0.74	0.87	1.18	1.55	0.50
INH+SM+PAS	0.94	0.37		0.81	2.24	0.50
INH+SM+PTH	0.69	0.59				0.50
INH+RIF+RBT+SM+PZA	0.75	0.59	0.48	1.11	0.69	0.40
KM+CPM+AMK			0.64	0.52		0.40
INH+PAS	1.00	0.81		1.40	1.12	0.40
KM mono-resistance	0.69			0.81	0.43	
CPM mono-resistance	0.69			0.81	0.43	
INH+RIF+RBT+EMB+OFX+MOX+LEV				0.44	0.43	
INH+RIF+RBT+SM+EMB+OFX+MOX+LEV					0.43	
INH+EMB+PZA		0.37	0.48			
MOX mono-resistance			0.32			
INH+RIF+RBT+OFX+MOX+LEV			0.24			

Resistance pattern	2020 (%)	2025 (%)	Between-year heterogeneity, adjusted p^1	Linear trend, adjusted p^2
INH mono-resistance	27.52	26.73	0.597	1.000
SM mono-resistance	9.84	13.17	0.185	0.196
OFX+MOX+LEV	5.52	6.33	0.282	0.373
INH+RIF	1.13	2.51	**0.005**	0.071
INH+RIF+RBT+SM+EMB +PZA	2.88	1.71	**0.019**	**0.020**
PZA mono-resistance	1.94	1.01	**<0.001**	**0.004**

[1] Pearson's chi-square test across all six years (2020–2025).
[2] Two-sided Cochran–Armitage test for linear trend.
Holm adjustment was applied across 40 tests involving 20 patterns with counts available in all six years. Percentages represent the proportion of each pattern among isolates resistant to ≥1 drug.

Annual Rankings and Frequencies of Selected Resistance Patterns, 2020–2025 Patterns ordered by their 2025 frequency

Resistance pattern	2020	2021	2022	2023	2024	2025
	Rank (%)	Rank (%)	Rank (%)	Rank (%)	Rank (%)	Rank (%)
INH mono-resistance	**1 (27.52%)**	**1 (28.39%)**	**1 (32.72%)**	**1 (29.47%)**	**1 (28.98%)**	**1 (26.73%)**
SM mono-resistance	**2 (9.84%)**	**2 (10.62%)**	**2 (9.53%)**	**2 (13.15%)**	**2 (10.66%)**	**2 (13.17%)**
INH+SM	**3 (6.46%)**	**3 (6.64%)**	**4 (6.27%)**	**4 (5.39%)**	**4 (5.42%)**	**3 (6.93%)**
OFX+MOX+LEV	**4 (5.52%)**	**5 (4.06%)**	**3 (6.43%)**	**3 (5.76%)**	**3 (7.48%)**	**4 (6.33%)**
INH+RIF+RBT	**5 (3.39%)**	8 (2.36%)	7 (3.02%)	7 (2.29%)	6 (3.44%)	**5 (4.12%)**
INH+PTH	13 (1.32%)	7 (2.80%)	11 (1.91%)	9 (2.07%)	13 (1.46%)	6 (3.32%)
INH+RIF	15 (1.13%)	16 (0.96%)	17 (0.71%)	23 (0.59%)	10 (1.81%)	7 (2.51%)
RIF+RBT	7 (2.70%)	**4 (4.20%)**	**5 (3.26%)**	**5 (2.88%)**	**5 (3.53%)**	8 (2.41%)
INH+EMB	8 (2.32%)	10 (1.92%)	8 (2.86%)	6 (2.73%)	7 (3.10%)	9 (2.31%)
INH+RIF+RBT+SM+EMB+PZA	6 (2.88%)	11 (1.77%)	9 (2.38%)	15 (1.11%)	17 (0.86%)	10 (1.71%)
CS+PZA	11 (1.88%)	15 (1.03%)	21 (0.56%)	22 (0.59%)	16 (1.03%)	11 (1.51%)
RIF mono-resistance	21 (0.88%)	19 (0.66%)	22 (0.48%)	24 (0.59%)	18 (0.77%)	12 (1.51%)
INH+RIF+RBT+PZA	14 (1.32%)	14 (1.25%)	18 (0.64%)	17 (1.03%)	20 (0.69%)	13 (1.41%)
INH+RIF+RBT+SM	16 (1.07%)	13 (1.62%)	12 (1.35%)	11 (1.70%)	14 (1.20%)	14 (1.31%)
INH+RIF+RBT+EMB+PZA	12 (1.57%)	12 (1.62%)	10 (1.91%)	13 (1.18%)	19 (0.69%)	15 (1.21%)
INH+RIF+RBT+EMB	9 (2.13%)	9 (1.99%)	6 (3.26%)	8 (2.07%)	11 (1.55%)	16 (1.01%)

Cells show listing order (frequency %). Equal-frequency patterns may have different listing positions.
Percentages are calculated among isolates resistant to ≥1 drug in each year.

INH and SM mono-resistance consistently occupied the first two positions.

Annual Rankings and Frequencies of Selected Resistance Patterns, 2020–2025 Patterns ordered by their 2025 frequency (continued)

Resistance pattern	2020	2021	2022	2023	2024	2025
	Rank (%)	Rank (%)	Rank (%)	Rank (%)	Rank (%)	Rank (%)
PZA mono-resistance	10 (1.94%)	6 (3.02%)	14 (0.95%)	10 (1.92%)	26 (0.34%)	17 (1.01%)
INH+RIF+RBT+SM+EMB+OFX+MOX+LEV+PZA	19 (0.94%)	22 (0.52%)	16 (0.87%)	18 (0.81%)	9 (2.15%)	18 (1.01%)
INH+PZA	26 (0.56%)	24 (0.37%)	13 (1.27%)	-	-	19 (0.70%)
INH+RIF+EMB+PZA	-	23 (0.52%)	20 (0.64%)	-	-	20 (0.60%)
EMB mono-resistance	18 (0.94%)	18 (0.74%)	15 (0.87%)	14 (1.18%)	12 (1.55%)	21 (0.50%)
INH+SM+PAS	20 (0.94%)	26 (0.37%)	-	20 (0.81%)	8 (2.24%)	22 (0.50%)
INH+SM+PTH	24 (0.69%)	21 (0.59%)	-	-	-	23 (0.50%)
INH+RIF+RBT+SM+PZA	22 (0.75%)	20 (0.59%)	23 (0.48%)	16 (1.11%)	21 (0.69%)	24 (0.40%)
KM+CPM+AMK	-	-	19 (0.64%)	25 (0.52%)	-	25 (0.40%)
INH+PAS	17 (1.00%)	17 (0.81%)	-	12 (1.40%)	15 (1.12%)	26 (0.40%)
Additional patterns listed in earlier years						
KM mono-resistance	23 (0.69%)	-	-	19 (0.81%)	22 (0.43%)	-
CPM mono-resistance	25 (0.69%)	-	-	21 (0.81%)	25 (0.43%)	-
INH+RIF+RBT+EMB+OFX+MOX+LEV	-	-	-	26 (0.44%)	23 (0.43%)	-
INH+RIF+RBT+SM+EMB+OFX+MOX+LEV	-	-	-	-	24 (0.43%)	-
INH+EMB+PZA	-	25 (0.37%)	24 (0.48%)	-	-	-
MOX mono-resistance	-	-	25 (0.32%)	-	-	-
INH+RIF+RBT+OFX+MOX+LEV	-	-	26 (0.24%)	-	-	-

—: Not listed in the available annual top-26 table; does not indicate zero cases.

Pairwise Co-resistance among LJ DST-Tested Isolates, 2020–2025

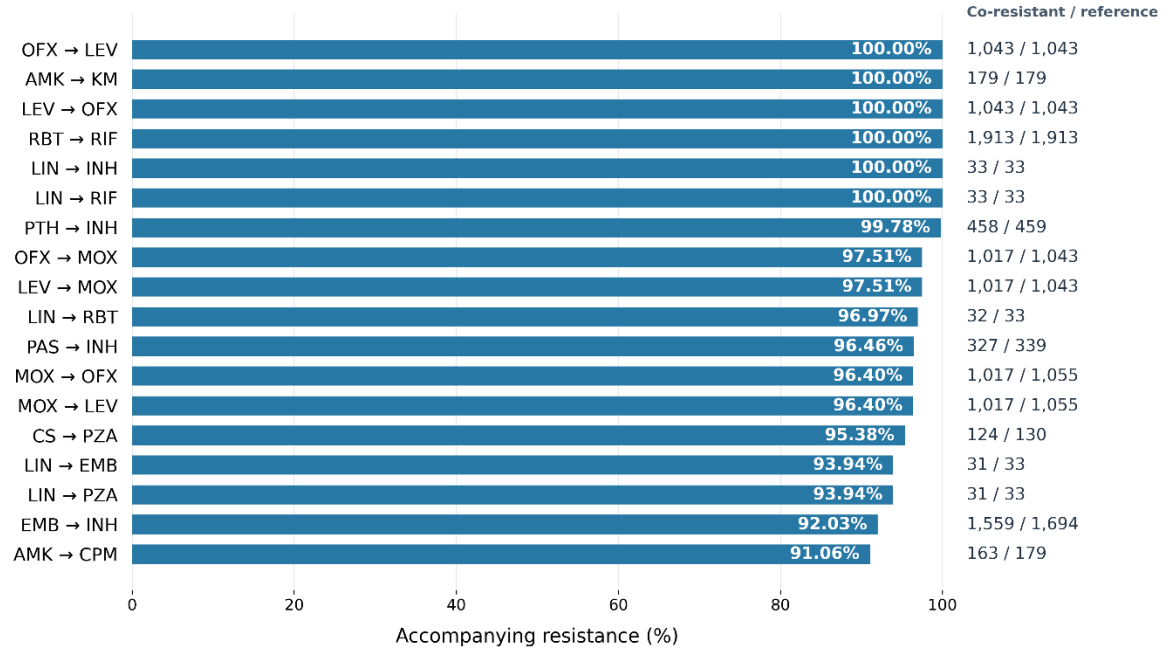
Pairwise Co-resistance among *M. tuberculosis* Isolates by LJ DST, 2020–2025

	INH	PTH	RIF	RBT	EMB	PAS	MOX	OFX	LEV	LIN	PZA	CS	KM	AMK	SM	CPM
INH (n=5,545)	-	8.3	36.1	28.2	28.1	5.9	9.6	9.4	9.4	0.6	19.4	0.8	3.4	2.4	27.7	2.5
PTH (n=459)	99.8	-	47.5	38.1	42.9	14.4	30.1	29.8	29.8	1.5	39.4	5.4	13.1	9.2	28.8	9.6
RIF (n=2,433)	82.2	9.0	-	78.6	52.0	6.1	20.1	19.7	19.7	1.4	42.3	1.6	7.1	5.3	35.2	5.2
RBT (n=1,913)	81.9	9.1	100.0	-	53.4	5.8	20.9	20.5	20.5	1.7	43.8	1.5	7.4	5.3	38.2	5.3
EMB (n=1,694)	92.0	11.6	74.7	60.3	-	8.21	24.6	23.6	23.6	1.8	47.0	2.1	8.9	6.6	40.6	6.5
PAS (n=339)	96.5	19.5	43.7	32.7	41.0	-	18.6	18.3	18.3	1.2	32.4	5.3	9.7	8.0	44.0	8.3
MOX (n=1,055)	50.2	13.1	46.4	37.9	39.4	6.0	-	96.4	96.4	2.6	37.3	3.1	9.1	6.5	24.5	6.5
OFX (n=1,043)	50.0	13.1	45.9	37.6	38.4	5.9	97.5	-	100.0	2.6	36.8	3.2	8.8	6.1	24.8	6.1
LEV (n=1,043)	50.0	13.1	45.9	37.6	38.4	5.9	97.5	100.0	-	2.59	36.8	3.16	8.82	6.1	24.8	6.1
LIN (n=33)	100.0	21.2	100.0	97.0	93.9	12.1	81.8	81.8	81.8	-	93.9	9.09	42.4	12.1	84.8	9.1
PZA (n=1,372)	78.6	13.2	75.0	61.0	58.1	8.0	28.7	28.0	28.0	2.3	-	9.04	9.69	6.8	36.6	6.5
CS (n=130)	32.3	19.2	30.8	21.5	26.9	13.8	25.4	25.4	25.4	2.3	95.4	-	11.5	6.9	10.0	7.7
KM (n=260)	71.5	23.1	66.2	54.6	58.1	12.7	36.9	35.4	35.4	5.4	51.2	5.8	-	68.8	42.7	63.8
AMK (n=179)	73.7	23.5	71.5	56.4	62.6	15.1	38.5	35.8	35.8	2.2	52.0	5.0	100.0	-	41.3	91.1
SM (n=2,458)	62.6	5.4	34.8	29.7	28.0	6.1	10.5	10.5	10.5	1.1	20.4	0.5	4.5	3.0	-	3.2
CPM (n=212)	64.6	20.8	59.9	47.6	51.9	13.2	32.5	30.2	30.2	1.4	42.0	4.7	78.3	76.9	37.3	-

Drug pairs with high accompanying resistance

Selected directions with accompanying resistance ≥90%

Reference drug resistance → accompanying drug resistance



7,722 isolates resistant to at least one drug; all drug results available.
The 90% cutoff is a display criterion, not a test of statistical significance or cross-resistance.

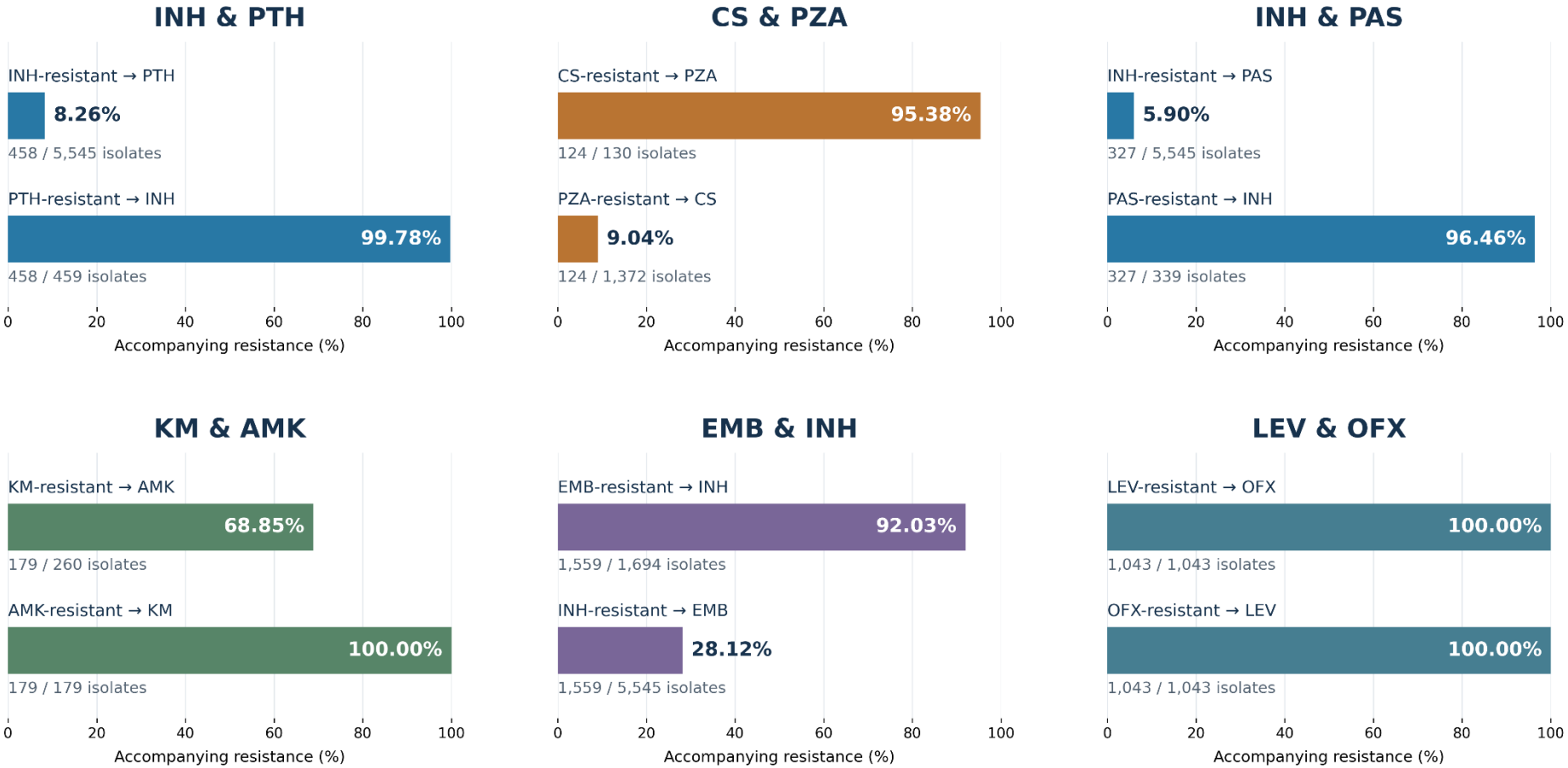
Each cell shows resistance to the column drug among isolates resistant to the row drug (%); percentages do not sum to 100%.

Selected Co-resistance Relationships by LJ DST, 2020–2025

Accompanying resistance in selected drug pairs

Reference drug resistance → accompanying drug resistance

Each pair is shown in both directions; percentages use the reference-drug-resistant group as the denominator.



7,722 M. tuberculosis isolates resistant to at least one drug; all drug results available.
Counts below each bar: isolates resistant to both drugs / isolates resistant to the reference drug.

Co-resistance among MDR/RR-TB Isolates with Valid Common-panel Results, 2021–2025

Co-resistance among BDQ-, DLM-, LZD-, and CFZ-resistant isolates

MDR/RR isolates, 2021–2025 • Valid results for the common drug panel

Co-resistant drug	BDQ-resistant n = 71	DLM-resistant n = 178	LZD-resistant n = 18	CFZ-resistant n = 80
INH	63 (88.7)	155 (87.1)	18 (100.0)	67 (83.8)
RIF	58 (81.7)	127 (71.3)	17 (94.4)	73 (91.3)
EMB	25 (35.2)	30 (16.9)	9 (50.0)	22 (27.5)
MOX	19 (26.8)	27 (15.2)	**11 (61.1)**	18 (22.5)
LEV	18 (25.4)	21 (11.8)	**12 (66.7)**	22 (27.5)
BDQ	—	11 (6.2)	4 (22.2)	**44 (55.0)**
DLM	11 (15.5)	—	7 (38.9)	9 (11.3)
LZD	4 (5.6)	7 (3.9)	—	5 (6.3)
CFZ	**44 (62.0)**	9 (5.1)	5 (27.8)	—

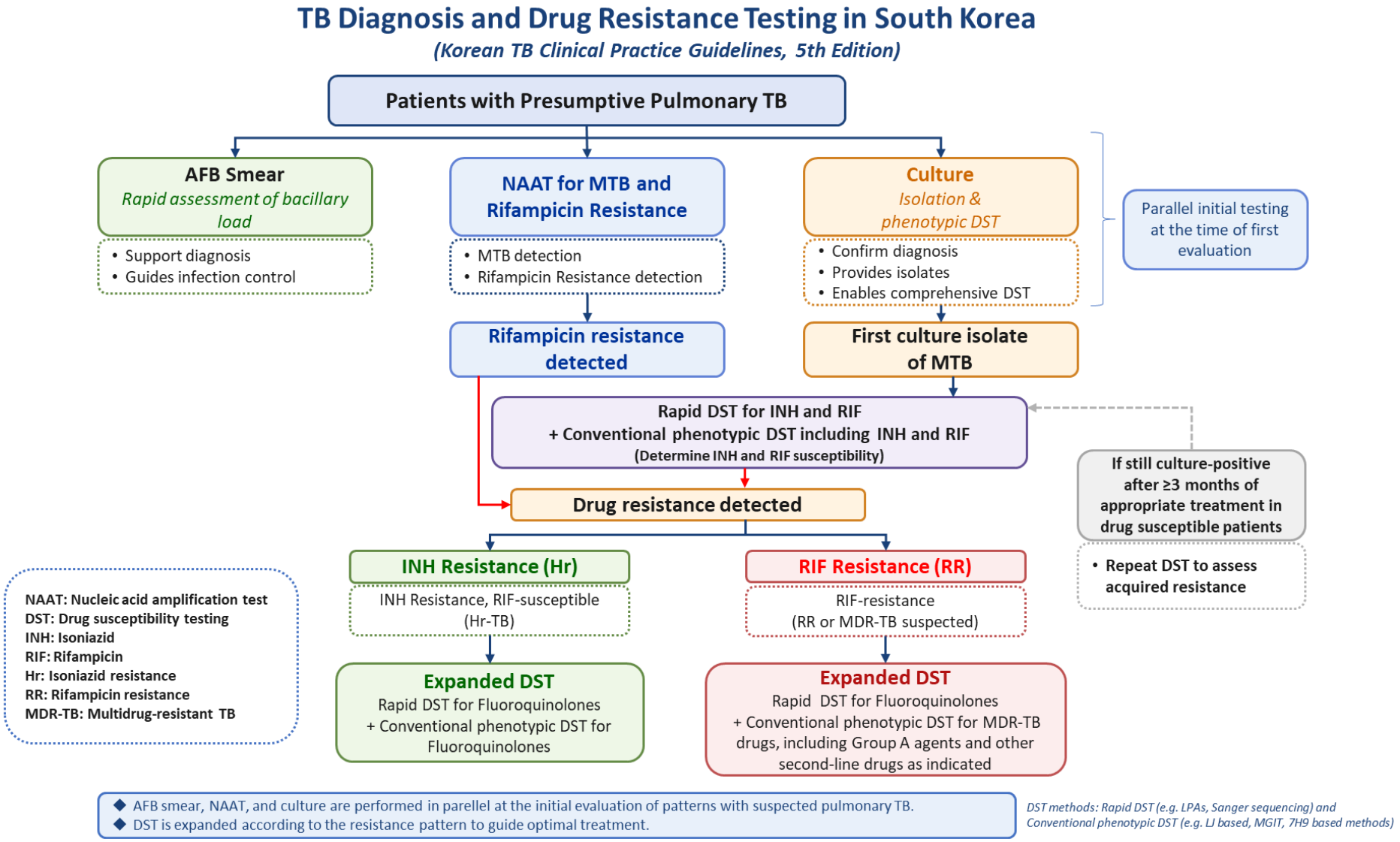
Values are n (%); each column uses its index-drug-resistant group as the denominator.

A single isolate may have resistance to multiple drugs. Co-resistance does not establish cross-resistance.

BDQ–CFZ: 44 shared isolates

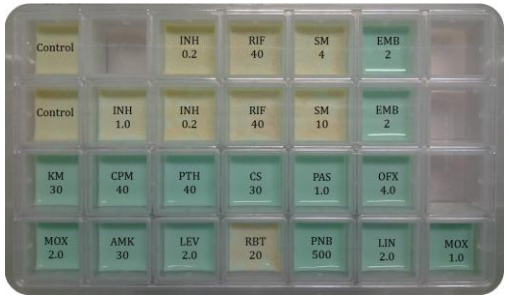
LZD group: MOX / LEV co-resistance

Current Diagnostic and DST Approaches in South Korea



Diagnostic and DST Platforms Used in South Korea

통상감수성검사 Phenotypic DST



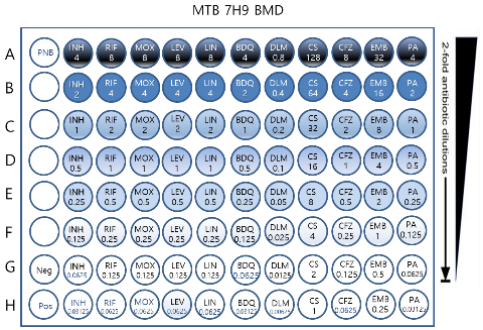
고체배지:절대농도법
(absolute concentration method, LJ)



액체배지:자동화 액체배양시스템

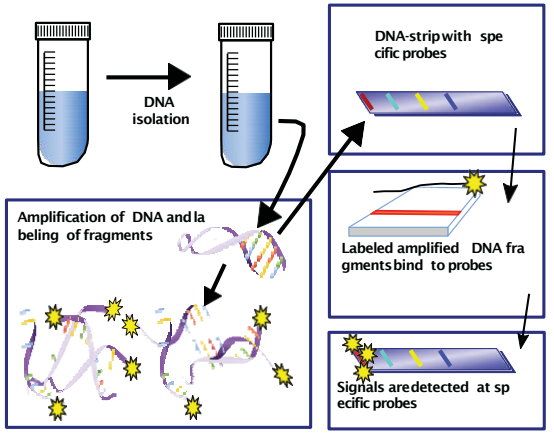


고체배지:비율법(proportion method, LJ/agar)



액체배지:최소억제농도(MIC)

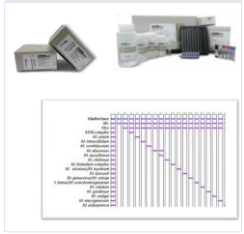
신속감수성검사 Molecular DST



Line probe assay



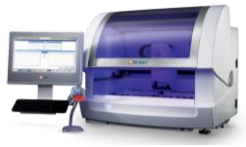
AdvanSure™ MDR-TB GenoBlot Assay



YD diagnostics MolecuTech REBA Myco-ID®



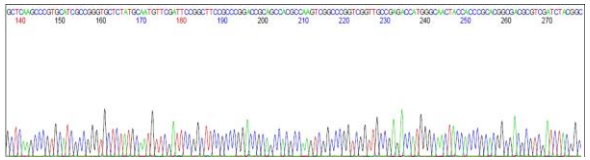
Xpert® MTB/RIF Ultra (Cepheid)



BD MAX™ MDR-TB (Becton Dickinson)



cobas® MTB and cobas MTB-RIF/INH (Roche)



Sanger sequencing; quinolones, INH, RIF

DST Methods Used in South Korea

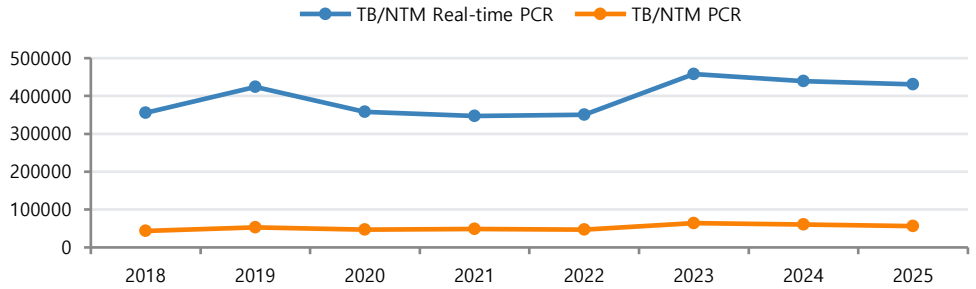
Method	Information provided	Examples
Solid-medium DST	Growth-based susceptibility at defined drug concentrations	LJ absolute concentration method Proportion method on solid media
Liquid-medium DST	Growth-based susceptibility MIC with suitable methods	Automated liquid-culture systems Broth microdilution (BMD)
Rapid molecular DST	Early detection of resistance within assay targets	Line probe assays Automated NAAT platforms
Targeted sequencing	Sequence information for selected resistance genes	Sanger sequencing e.g. *rpoB*, *katG*/*inhA*, *gyrA*/*gyrB*

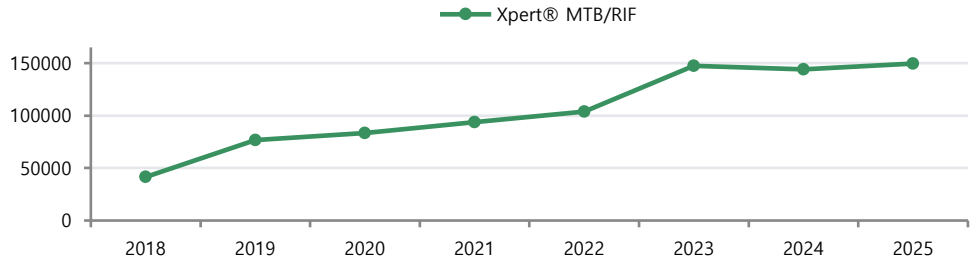
The assay and drug panel determine the information available

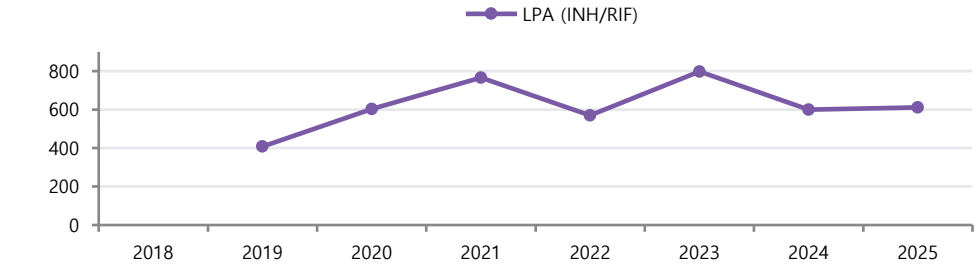
Korean TB Clinical Practice Guidelines, 5th ed. (2024); KDCA National TB Guidelines (2026)

Test Utilization in South Korea, 2018–2025

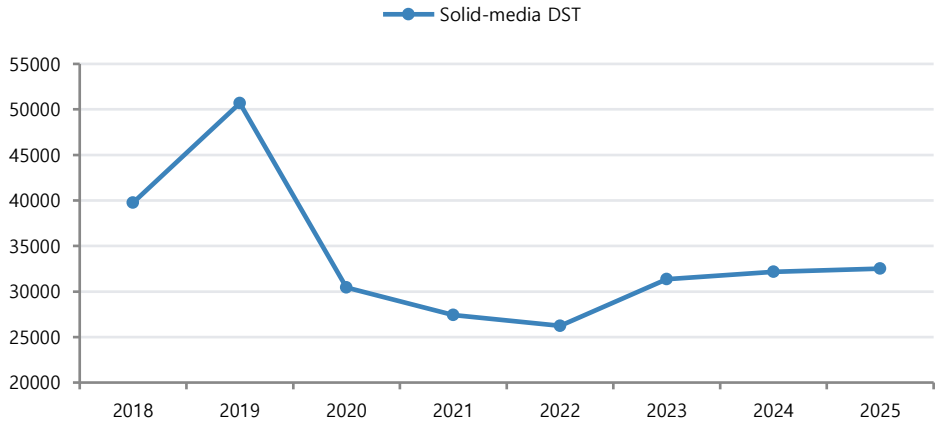
Molecular tests

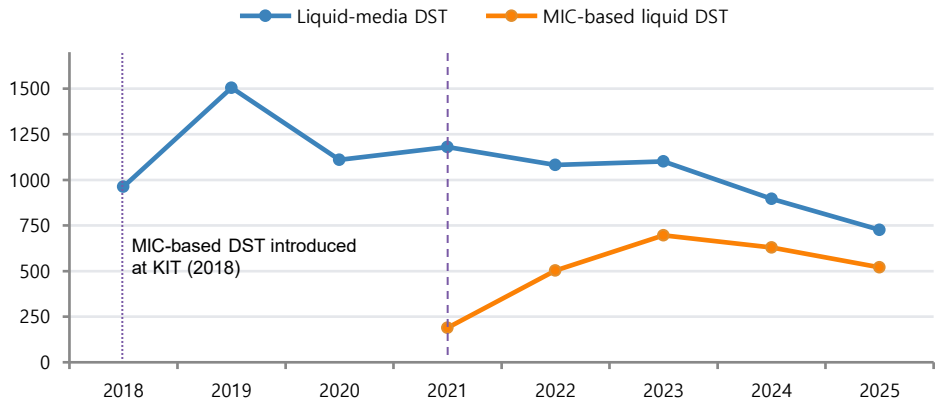






Phenotypic DST





Test volumes describe utilization and do not represent unique patient counts

Source: Health Insurance Review & Assessment Service (HIRA), publicly available statistics, 2018–2025.

Phenotypic and Molecular DST

	Phenotypic DST	Rapid molecular DST
What it measures	Growth in the presence of a drug	Resistance-associated variants within assay targets
Typical output	Susceptible / resistant MIC with suitable methods	Resistance detected / not detected Indeterminate results may occur
Main contribution	Drug-specific growth response Resistance beyond known variants	Early resistance information for drugs covered by the assay
Interpretive limits	Medium and critical concentration Reliability differs by drug	Target coverage and variant evidence Sensitivity differs by drug and assay

Joint interpretation combines measured growth with molecular evidence

WHO Operational Handbook on Tuberculosis, Module 3: Diagnosis (2025), Section 2.5

Diagnostic Challenges in Routine DST

Issue	Why interpretation can be difficult
Time to result	Culture-based DST requires growth Rapid molecular tests provide earlier resistance information
Phenotypic classification	Medium and critical concentration affect classification Some *rpoB* variants can yield susceptible phenotypic results
Molecular coverage	Assays differ in target regions and variant detection Resistance outside the target may remain undetected

Interpretation requires consideration of the test method, drug-specific criteria, and molecular target coverage.

WHO Diagnosis Handbook (2025), Algorithm 1; WHO Critical Concentrations Report (2021)

Diagnostic Challenges in South Korea

Wider mDST use	Coverage increased from 49.1% to 96.9% in 2015–2021. Testing within ±3 months does not establish availability at treatment initiation.
Results that disagree	RIF discordance: 104/459 (22.6%) in a selected MDR/RR-TB cohort. Different results can complicate regimen selection.
Results needed sooner	The 2024 policy report describes delayed FQ results and gaps in DST access for newer drugs.

Mok et al., 2025 · Shin et al., 2024 · KDCA-commissioned policy research report, 2024 (pp. 61–62)

DST Challenges Across the Testing Pathway

Incomplete early results	Low bacillary load and limited assay targets can leave important drugs untested or results indeterminate.
Uncertain interpretation	Target coverage, rare variants and phenotypic thresholds matter. Mixed populations and different specimens can contribute to discordance.
Access and reporting	Referral, transport and additional requests extend the time to a usable result. Reports from different laboratories require joint interpretation.

Shorter regimens increase the need for timely, drug-specific information.

WHO operational handbook, Module 3, DST algorithms · Domestic implementation issues: presenter’s laboratory experience

Rapid molecular DST: speed and target coverage

Detect resistance early; check what the assay covers

Drug	Key targets*	Examples of tests
RIF	*rpoB* hotspot	Xpert MTB/RIF or Ultra; first-line LPA
INH	*katG; inhA* promoter	First-line LPA; Xpert MTB/XDR
FQs	*gyrA / gyrB*	Sequencing; second-line LPA; Xpert MTB/XDR

*Target regions and mutations covered vary by assay and version.

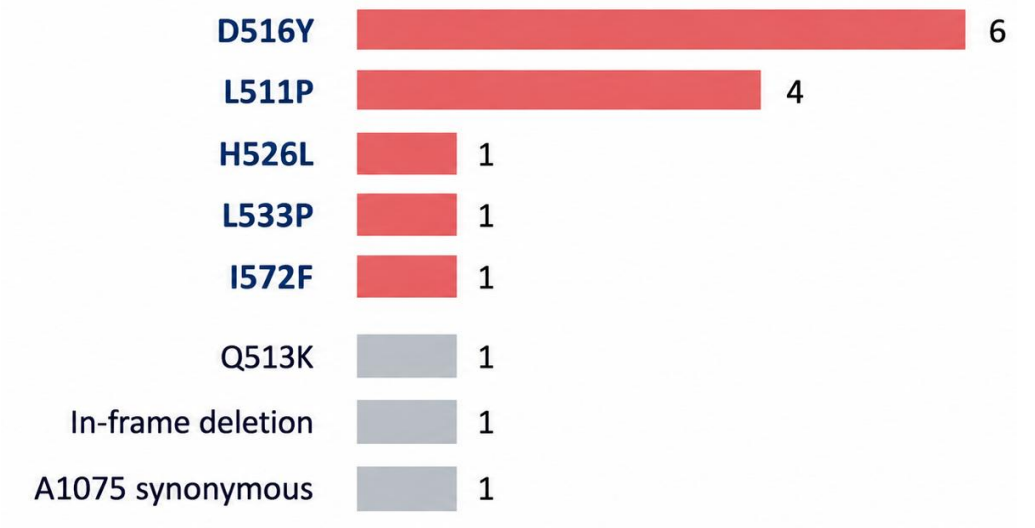
“Resistance not detected” applies to the targets tested.
It does not exclude all mechanisms of resistance.

Sources: Korean TB Guidelines, 5th ed. (2024), pp.19–20; KDCA (2026), p.118. WHO operational handbook on TB, Module 3: Diagnosis (2025), §2.4.

Molecular DST: Rapid but Target-Dependent

rpoB variant	pDST	LPA	Xpert Ultra	IRON-qPCR
I572F	**R**	S	S	S
Q513K	**R**	S	**R**	**R**
In-frame deletion	**R**	Ind.	**R**	**R**
A1075 synonymous	**R**	S	S	S

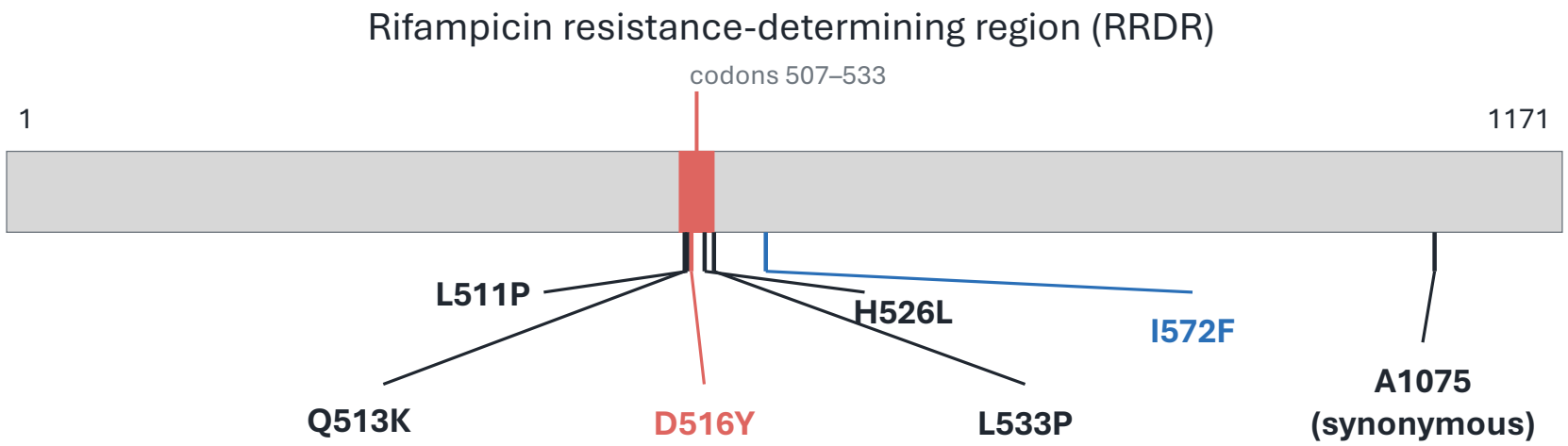
RIF Discordant pattern in KIT Data



A susceptible molecular result does not always exclude phenotypic resistance.

Illustrative KIT data: selected RIF-discordant isolates

Molecular DST: Rapid but Target-Dependent



Within RRDR: L511P, Q513K, D516Y, H526L, L533P | Outside RRDR: I572F, A1075 synonymous

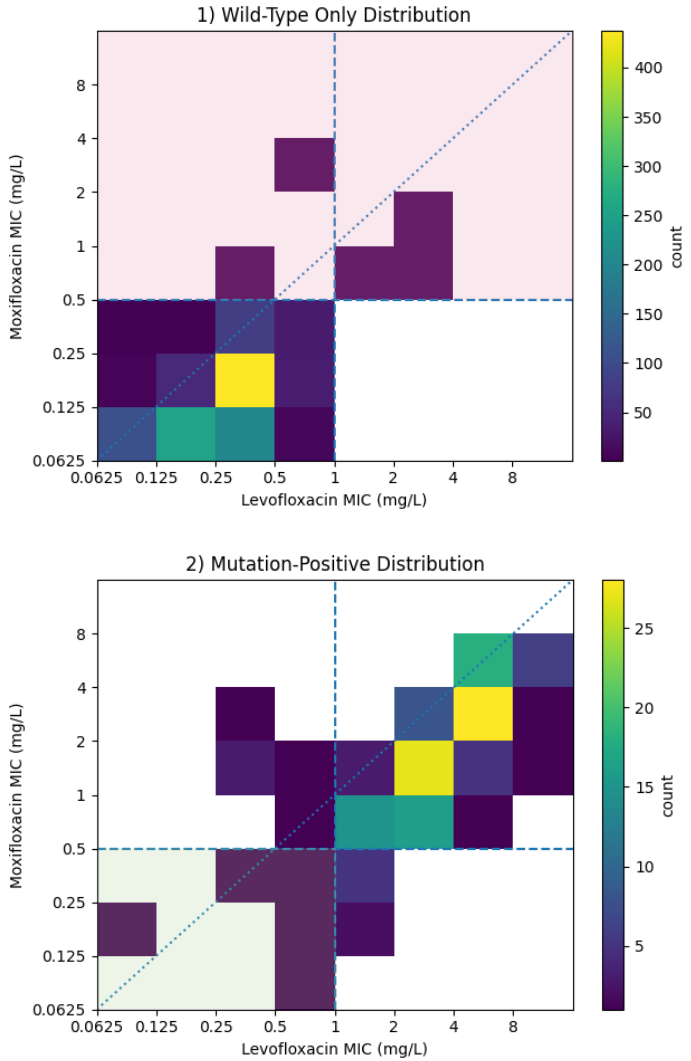
A susceptible molecular result does not always exclude phenotypic resistance.

Illustrative KIT data: selected RIF-discordant isolates

KIT Data: Sequencing Results and Phenotypic MICs

MIC categories within *gyrA*/*gyrB* sequence groups

Drug	Sequence group	S	I*	R
Levofloxacin	Wild type	1,219	1	**5**
	gyrA mutant	**3**	18	110
	gyrB mutant	**8**	7	2
Moxifloxacin	Wild type	1,216	3	**5**
	gyrA mutant	**5**	28	98
	gyrB mutant	**7**	5	5



Wild-type sequences do not exclude phenotypic resistance.

*I: inconclusive. MFX wild-type counts total 1,224 vs stated n=1,225. Rates need verification.

Source: KIT poster P0635, Table 2 · S/I/R categories follow KIT interim BMD criteria

Targeted NGS: Contribution and Remaining Gaps

Broader molecular information

Follow-on tNGS can assess multiple resistance targets after the initial TB/RIF result, with variant-level interpretation.

Drug-dependent performance

A negative result may require pDST when resistance risk is high. WHO-endorsed tNGS solutions do not cover Pa or DLM.

A workable domestic pathway

Implementation requires access, quality assurance and a clear route for additional pDST and discordance review.

Molecular results and quality-assured pDST remain complementary.

WHO operational handbook, Module 3, Algorithm 2a/2b · WHO mutation catalogue, 2nd edition, 2023

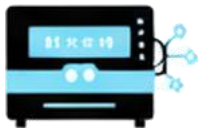
Tuberculosis drug resistant analysis based on Modified tNGS

Step 1. Sample pretreatment and Target amplification

- **Sputum preparation :** sputum pretreatment and DNA extraction
- **1st PCR** : drug resistant associated gene hotspot region PCR (e.g. INH-promoter, RIF-RRDR, FQs –QRDR etc.)
- **Clean-up :** 1st PCR product clean up (primer, dNTP, impurities removal)
- **Quantitation :** Concentration check purified PCR product

Step 2. Library construction and sequencing

- **Normalization & Pooling :** PCR product concentration based normalization and pooling
- **2nd PCR :** adapter and index attachment
- **Clean-up :** final library construction
- **Final QC and sequencing :** After library QC and NGS machine running



Step 3. Data analysis

- **Data QC :** low quality data filtering and trimming
- **Variant Calling :** Drug resistant variant calling based on reference mapping
- **Report :** sequence based variants listing and drug resistant prediction results reporting

Take-home Messages

Rapid molecular DST

Speed

- Fast answer for established targets
- Best when the clinically relevant mechanis m is
  covered

Quality-assured pDST

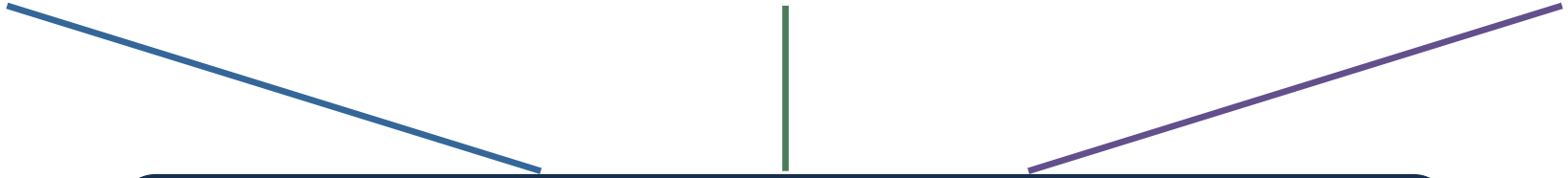
Functional resistance

- Phenotypic evidence beyond predefined targets
- Essential when sequence interpretation is incomplete or discordant

Targeted NGS

Breadth & genomic information

- Broader multi-drug profiling
- Value increases as genotype–phenotype evidence matures



Toward an Integrated Diagnostic Approach

Timely • Comprehensive • Reliable • Interpretable