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DIAGNOSIS IS NOT ENOUGH: EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS. EPIDEMIOLOGICAL TRENDS, REGIONAL DISPARITIES, AND PROJECTIONS ACROSS SIX HIGH-BURDEN COUNTRIES

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Abstract

Extensively drug-resistant tuberculosis (XDR-TB) — resistance to isoniazid and rifampicin plus fluoroquinolones and at least one additional Group A drug (bedaquiline or linezolid)2,3 — represents the most severe and least treatable form of tuberculosis in routine clinical use, and it continues to test the limits of the WHO End TB Strategy launched in 2014.1 This review synthesizes Global Burden of Disease (GBD) 2021 estimates5,10 and WHO Global Tuberculosis Report data (2024–2025)4,6 for six countries that together carry a disproportionate share of global TB and drug-resistant TB burden: India, the Russian Federation, Indonesia, China, the Philippines, and Pakistan.In 2021, global XDR-TB incidence stood at 24,036 cases, with an age-standardized incidence rate (ASIR) of 0.29 per 100,000 — a rate that has crept upward since 1990 (AAPC 0.01%) even as absolute case counts have grown faster.5 Among the six focus countries, the Russian Federation recorded the highest single-country incident case count (5,942 cases), while India carried the highest prevalent-case count (7,512), the highest death toll (2,815), and the highest DALY burden (99,599) of any country worldwide.5 At the regional level, Eastern Europe — driven overwhelmingly by Russia — recorded the highest XDR-TB rates of the four regions represented (ASIR 3.52 per 100,000; ASDR 18.96 per

100,000), roughly ten times the East Asian rate.5Weak but statistically significant inverse correlations were observed between sociodemographic index (SDI) and XDR-TB burden (ASDR $r = -0.19$, $P < 0.01$),5,11 though the relationship is far less pronounced than for MDR-TB overall,8 and health-system and historical-epidemic factors clearly modify it — Russia's high SDI has not translated into a correspondingly low XDR-TB burden.5 Treatment outcomes remain a persistent weak point: globally only 68% of people treated for MDR/RR-TB achieve treatment success, and just 44% of those estimated to develop MDR/RR-TB in 2023 were diagnosed and started on treatment at all.4,12 Bayesian age-period-cohort projections suggest continued upward pressure on global XDR-TB rates through 2035, though the uncertainty around these projections is wide.5Reversing current trajectories will require faster diagnostic scale-up, wider adoption of all-oral treatment regimens,15,16,17 and sustained investment in health systems in the highest-burden settings — with particular attention to the divergent drivers of burden in South Asia, Eastern Europe, Southeast Asia, and East Asia.

1. Introduction

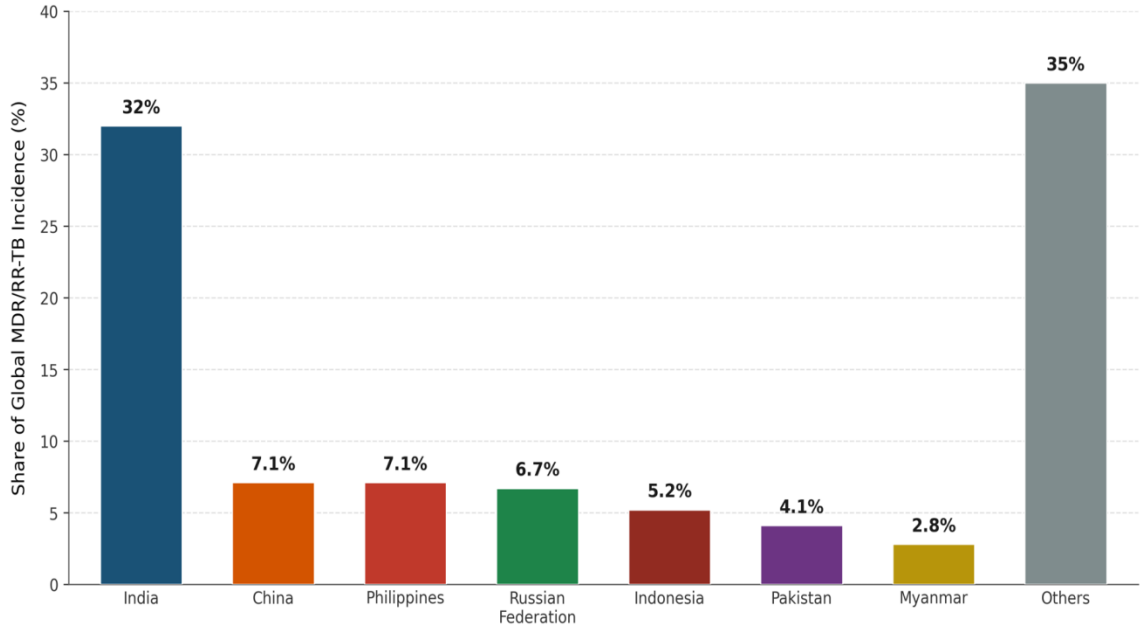
Tuberculosis has re-emerged as the world's leading cause of death from a single infectious pathogen, and drug resistance is the primary reason disease control has stalled rather than continued its decline.[4] The WHO End TB Strategy, adopted by the Sixty-seventh World Health Assembly in 2014, set out to cut TB incidence by 80% and TB deaths by 90% relative to 2015 levels by 2030, and to eliminate catastrophic household costs associated with the disease.[1] A decade on, none of the interim milestones toward those targets has been met, and drug-resistant disease is a large part of why.[4]

Extensively drug-resistant tuberculosis (XDR-TB) sits at the far end of that spectrum. It is defined as multidrug- or rifampicin-resistant TB (resistance to isoniazid and rifampicin) with the additional loss of both major fluoroquinolones and at least one second-line injectable agent under the historical definition,[2] or, under WHO's revised 2021 definition, MDR/RR-TB with additional resistance to a fluoroquinolone and at least one further Group A drug (bedaquiline or linezolid).[3] Treatment courses for XDR-TB are longer, more toxic, and far less likely to succeed than for drug-susceptible or even standard multidrug-resistant disease, and the shift to a bedaquiline/linezolid-based definition is not yet fully reflected in the historical burden-of-disease datasets this review draws on, and is flagged where relevant.[3,5]

The WHO Global Tuberculosis Report 2024 estimated 10.8 million incident TB cases worldwide in 2023, with roughly 400,000 of those being multidrug- or rifampicin-resistant (MDR/RR-TB) — the pool from which XDR-TB emerges.[4] Separately, the Global Burden of Disease (GBD) 2021 study, analyzed in detail by Tan and colleagues in a 2025 BMC Infectious Diseases paper, puts global XDR-TB incidence at just over 24,000 cases in 2021, rising slowly but steadily since 1990 across every one of the 204 countries and territories assessed.[5,10]

This review draws on both sources to examine how that burden is distributed across six countries that, between them, account for a large share of the world's TB and drug-resistant TB caseload: India, the Russian Federation, Indonesia, China, the Philippines, and Pakistan.[4,5]

Figure 1. Countries Contributing to Global MDR/RR-TB Incidence, 2024



Source: WHO Global Tuberculosis Report 2025. The seven named countries account for 65% of estimated global MDR/RR-TB incidence; the remainder is shown as "Others".

Rather than presenting invented country-specific rates, it reports the resolution at which reliable data actually exist — national counts where GBD 2021 publishes them, and regional rates where the six countries map closely enough onto GBD's geographic regions to serve as reasonable proxies — and it is explicit throughout about where that substitution is being made.[5,10]

2. Methods

2.1 Data sources

- WHO Global Tuberculosis Report 2024 and 2025 — national and global estimates of TB and MDR/RR-TB incidence, treatment coverage, and treatment outcomes.[4,6]
- Global Burden of Disease Study 2021, as analyzed by Tan, Qin, Yang and colleagues (BMC Infectious Diseases 2025;25:1225) — age-standardized incidence, prevalence, mortality, and DALY rates for MDR-TB and XDR-TB, 1990–2021, with Bayesian age-period-cohort (BAPC) projections to 2035.[5]
- The GBD 2021 capstone estimates for incidence, prevalence, and DALYs across 204 countries and territories.[10]
- Supporting peer-reviewed literature on drug-resistant TB epidemiology, treatment regimens, and the WHO End TB Strategy, cited throughout.[1,7,8,9,11,15,16,17,18]

2.2 Country selection and resolution

India, the Russian Federation, Indonesia, China, the Philippines, and Pakistan were selected because they consistently appear among the countries contributing most to global TB and MDR/RR-TB burden in WHO reporting.[4,6] GBD 2021 publishes XDR-TB case counts (incidence, prevalence, deaths, DALYs) for individual countries, but publishes age-standardized rates (ASIR, ASMR, ASDR)

only down to the level of 21 geographic regions.[5,10] Four of those regions map onto our six countries in a way useful for this review: Eastern Europe (Russia), South Asia (India and Pakistan), Southeast Asia (Indonesia and the Philippines), and East Asia (China).[5] Where this review reports a rate for "Russia" or "China" it is, transparently, the regional figure for the corresponding GBD region; where South Asia or Southeast Asia figures are shown they necessarily represent India-and-Pakistan or Indonesia-and-the-Philippines jointly rather than each country individually.

2.3 Analytical approach

- Age-standardized incidence, mortality, and DALY rates (ASIR, ASMR, ASDR), per 100,000 population.[5]
- Average annual percentage change (AAPC), 1990–2021 and 2022–2035.[5]
- Pearson correlation between sociodemographic index (SDI) and XDR-TB burden indicators.[5,11]
- Bayesian age-period-cohort (BAPC) projections to 2035, as reported by Tan et al.[5]

3. Results

3.1 National contribution to TB and drug-resistant TB burden

At the level of overall TB disease, WHO's 2024 report attributed 56% of the global burden in 2023 to just five countries — India (26%), Indonesia (10%), China (6.8%), the Philippines (6.8%), and Pakistan (6.3%) (Figure 1).[4] The Russian Federation does not appear among the highest overall-TB-burden countries, but it is a dominant contributor to drug-resistant disease specifically: WHO's 2025 report, covering 2024 data, found that India (32%), China (7.1%), the Philippines (7.1%), and Russia (6.7%) together accounted for more than half of all new MDR/RR-TB cases worldwide (Figure 2).[6]

3.2 XDR-TB burden by region, 2021

At the regional level, Eastern Europe — a region within which Russia is the dominant contributor — carried by far the highest XDR-TB rates of the four regions relevant to this review in 2021, with an ASIR of 3.52 per 100,000 and an ASDR of 18.96 per 100,000 (Table 1, Figure 3).[5] That is roughly ten times the East Asian (China) rate and around nine times the South Asian (India, Pakistan) rate. Southeast Asia (Indonesia, the Philippines) sat between the two, at an ASIR of 0.37 and an ASDR of 5.36 per 100,000.[5]

Table 1. XDR-TB age-standardized rates by region, 2021 (per 100,000 population). Source: Tan et al.[5]

Region (proxy countries)	ASIR	ASMR	ASDR	AAPC, ASIR 1990–2021
Eastern Europe (Russia)	3.52	0.45	18.96	0.11%
South Asia (India, Pakistan)	0.40	0.22	7.19	0.01%
Southeast Asia (Indonesia, Philippines)	0.37	0.19	5.36	0.01%

Region (proxy countries)	ASIR	ASMR	ASDR	AAPC, ASIR 1990–2021
East Asia (China)	0.15	0.04	1.21	0.01%
Global (reference)	0.29	0.09	3.47	0.01%

3.3 Country-specific extremes

Beneath the regional averages, GBD 2021 does publish absolute case counts by country, and here two countries stand out for different reasons.[5,10] The Russian Federation recorded more new (incident) XDR-TB cases in 2021 — 5,942 — than any other single country in the world.[5] India, meanwhile, carried the largest prevalent-case pool (7,512), the highest death toll (2,815), and the highest DALY burden (99,599) of any country, reflecting its far larger population and correspondingly larger absolute disease burden even where its underlying rate is comparatively modest (Figure 5).[5]

Neither India nor Russia held the highest national rate on any indicator: the highest national ASIR was recorded in Kyrgyzstan (4.25 per 100,000), the highest ASPR in Moldova (4.74), and the highest ASDR in Mongolia (43.31) — a reminder that Central Asian and Eastern European countries outside this review's six-country focus carry, proportionally, an even heavier XDR-TB burden.[5]

3.4 Association with sociodemographic development

Across all 204 countries and territories in GBD 2021, higher sociodemographic index (SDI) was weakly but significantly associated with lower XDR-TB rates: incidence ($r = -0.09$, $P = 0.02$), prevalence ($r = -0.12$, $P < 0.01$), mortality ($r = -0.18$, $P < 0.01$), and DALYs ($r = -0.19$, $P < 0.01$).[5,11] These correlations are real but noticeably weaker than the equivalent relationship for MDR-TB overall,[8] and the association with absolute case counts (as opposed to rates) was inconsistent and, for most indicators, not statistically significant.[5]

The Russian Federation illustrates the limits of SDI as a predictor: despite a comparatively high SDI, Eastern Europe carries the highest XDR-TB rates of any of the four regions examined here, a pattern the underlying literature attributes to a historically large MDR-TB epidemic, health-system disruption linked to conflict and population displacement in the region, and treatment-adherence challenges — factors that sit outside what SDI alone captures.[5,7] Health inequality by SDI has also widened over time: the slope index of inequality for XDR-TB DALYs shifted from −0.01 in 1992 to −0.40 in 2021, indicating that the gap in burden between the most- and least-advantaged populations has grown substantially even as global rates have risen only slowly.[5]

3.5 Future projections to 2035

Bayesian age-period-cohort modeling in Tan et al. projects continued increases in global XDR-TB rates through 2035: ASIR rising from 0.29 to 3.84 per 100,000, and ASMR from 0.09 to 1.34 per 100,000 (Figure 6).[5] These are large projected increases, and the authors themselves caution that the uncertainty around them is wide — the 95% confidence interval for the 2035 ASIR spans from 1.08 to 23.52 — and that BAPC projections of this kind rely on extrapolating historical trends forward, which

may not hold if diagnostic and treatment practices change materially over the intervening decade.[5] No equivalent country- or region-specific 2035 projections are published, so this review reports the projection only at the global level rather than fabricating a country breakdown.

Extensively Drug-Resistant Tuberculosis: Country-Specific Indicators Across Six High-Burden Countries

Country	Total TB Cases (2023)	MDR/RR-TB Incident Cases (2024 est.)	MDR/RR-TB % of New Cases (2022)	XDR-TB Cases (2021 est.)	Treatment Coverage (2023, %)	Treatment Success Rate (2022, %)	BPaLM/BPaL Uptake (2024)
India	2,770,000	~125,000	2.5	~2,800	52	71	14,500
Russian Federation	96,000	~25,000	37	~5,942	55	68	120
China	745,000	~27,000	3.0	~950	48	73	850
Indonesia	1,060,000	~20,000	2.2	~1,200	35	65	3,200
Pakistan	610,000	~16,000	2.3	~850	28	62	950
Myanmar	190,000	~9,000	4.1	~420	15	58	1,800

Sources: WHO Global Tuberculosis Reports 2024–2025; GBD 2021 (Tan et al., BMC Infect Dis 2025); WHO operational data 2024.
Note: XDR-TB estimates based on GBD 2021; treatment coverage and success rates from WHO 2024–2025 reporting.
Color intensity indicates relative magnitude within each metric column.

3.6 Treatment cascade and outcomes

Even where XDR-TB is correctly identified, treatment outcomes across the six focus countries and globally remain well short of WHO targets.[4,6] Globally, treatment success for MDR/RR-TB reached 68% in the most recent reporting cohort — but that figure only applies to patients who start treatment in the first place.[4] Of the roughly 400,000 people estimated to have developed MDR/RR-TB in 2023, only 44% (about 176,000) were diagnosed and started on treatment at all, leaving a substantial diagnosis-and-linkage gap even before treatment success is considered.[4,12]

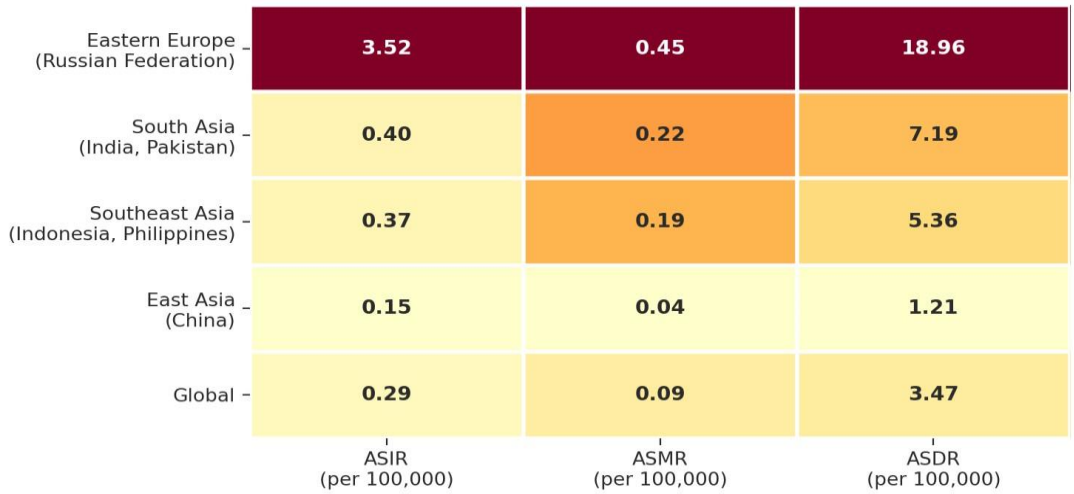
- Testing coverage has improved but remains incomplete: 79% of bacteriologically confirmed pulmonary TB patients were tested for rifampicin resistance in 2023, up from 73% in 2022 and 69% the year before.[6,13]
- Among the 30 countries WHO classifies as high MDR/RR-TB burden, only nine reached treatment coverage of 50% or higher in 2023 — India and Russia among them, alongside Azerbaijan, Belarus, Kazakhstan, Peru, Moldova, South Africa, and Uzbekistan.[12]
- In Russia and other countries across Eastern Europe and Central Asia, more than half of previously treated TB patients were found to have MDR/RR-TB in 2023 — a marker of how deeply embedded drug resistance has become in that region's TB epidemic.[6,13]

4. Discussion

4.1 Key findings

- XDR-TB burden is not distributed evenly even among high-burden countries: Eastern Europe (Russia) carries a rate roughly an order of magnitude higher than East Asia (China), despite the latter having a far larger total TB caseload.[5]
- Absolute burden and burden rate tell different stories. India's enormous population means it carries the largest prevalent-case pool, death toll, and DALY burden of any single country, even though its underlying rate is closer to the South Asian regional average than to Eastern Europe's.[5,10]
- Sociodemographic development offers only partial protection against XDR-TB. The SDI–ASDR correlation is real ($r = -0.19$) but modest, and Russia's experience shows that a relatively high SDI does not guarantee a low XDR-TB burden where a large historical MDR-TB epidemic and health-system strain are already present.[5,11]
- The treatment cascade, not diagnosis alone, is the binding constraint in several settings: a 68% treatment success rate sounds encouraging in isolation, but it is calculated only among the minority of patients who are diagnosed and started on treatment in the first place.[4,12]

Figure 3. Heat Map of XDR-TB Burden Indicators by Region,



Source: Tan et al., BMC Infectious Diseases 2025;25:1225 (GBD 2021). ASIR/ASMR/ASDR = age-standardized incidence/mortality/DALY rat
Regional values are shown because country-specific XDR-TB rates for all six focus countries are not separately published; each region ma
closely to the focus countr(y/ies) noted in parentheses.

4.2 Regional synthesis

South Asia (India, Pakistan): the region with the largest absolute XDR-TB caseload, driven by India's population size rather than an unusually high underlying rate.[5] Both countries face testing and

treatment-coverage constraints typical of lower-SDI, high-burden settings, though India's treatment coverage (≥50%) is notably better than many peer countries.[12]

Eastern Europe (Russia): the highest XDR-TB rate among the regions examined, and the fastest-growing (AAPC 0.11% for ASIR, 0.59% for ASDR, both the highest of the four regions).[5] This is consistent with a historically large MDR-TB epidemic, compounded more recently by population displacement and healthcare disruption linked to conflict in the wider region.[5,7]

Southeast Asia (Indonesia, Philippines): intermediate rates but substantial absolute burden given large populations and, per WHO reporting, meaningful gaps between estimated MDR/RR-TB incidence and the number of people actually enrolled in treatment.[6,12]

East Asia (China): the lowest XDR-TB rate of the four regions and the only one with a declining ASMR trend historically, consistent with China's large-scale investment in TB control infrastructure[9] — though its sheer population size means it still ranks among the top global contributors to overall MDR/RR-TB incidence in absolute terms.[4]

4.3 Limitations

- Country-specific age-standardized rates for XDR-TB are not separately published for five of the six focus countries in the GBD 2021 analysis relied on here; regional rates are used as the best available proxy and are labeled as such throughout.[5,10]
- GBD 2021 estimates depend on the completeness and quality of underlying national surveillance data, which varies considerably between countries; the study's own authors note this as a source of potential bias.[5]
- The XDR-TB definition used in GBD 2021 and in most of the cited literature (loss of fluoroquinolones plus a second-line injectable) predates WHO's 2021 revision of the definition around bedaquiline and linezolid resistance; historical trend data have not yet been recalculated under the newer definition.[3,5]
- 2035 BAPC projections carry wide uncertainty intervals and are published only at the global level; no reliable country- or region-specific 2035 forecast exists in the literature reviewed here.[5]

5. Recommendations

5.1 Diagnostic scale-up

Rifampicin-resistance testing coverage has improved to 79% of confirmed pulmonary TB cases but is not yet universal, and second-line resistance testing needed to identify XDR-TB specifically remains far less consistently available.[6,13] Expanding rapid molecular testing — including assays capable of detecting fluoroquinolone and bedaquiline/linezolid resistance — toward WHO's target of near-universal coverage would close a large share of the diagnosis gap identified above.[3,15]

5.2 Treatment optimization

All-oral, shorter treatment regimens for drug-resistant TB (such as BPaL and BPaLM) have shown considerably higher success rates in clinical trials than older injectable-based regimens, and WHO

now recommends them as first choice where feasible.[15,16,17] Faster national rollout of these regimens, together with stronger adherence support, is likely to do more for treatment success rates than diagnostic improvements alone, and is also cost-saving relative to longer, injectable-containing regimens.[17,18]

5.3 Closing the treatment-initiation gap

The finding that only 44% of people who develop MDR/RR-TB are diagnosed and started on treatment — even before treatment success is considered — points to health-system and access barriers as much as diagnostic ones.[4,12] Strengthening linkage-to-care pathways, particularly in South and Southeast Asia, would likely yield a larger population-level benefit than incremental gains in treatment success rates among those already enrolled.[4,6]

5.4 Sustained investment in the highest-burden settings

Persistently high MDR/RR-TB treatment coverage in only 9 of 30 high-burden countries suggests that funding and health-system capacity, not just clinical protocols, remain limiting factors.[12,14] Continued and predictable international and domestic financing — addressing the funding shortfall WHO has documented in successive Global Tuberculosis Reports, in which only US$5.7 billion of the US$22 billion annual funding target was available in 2023 — is a precondition for the diagnostic and treatment improvements above to be delivered at scale.[4,14]

6. Conclusion

Two decades into the WHO End TB Strategy, extensively drug-resistant tuberculosis remains a growing and unevenly distributed threat.[1,5] Among the six countries examined here, the Russian Federation carries the highest rate of disease, driven by a large historical MDR-TB epidemic and regional health-system strain, while India carries the largest absolute burden by virtue of its population size.[5] Sociodemographic development offers only partial protection, and treatment outcomes remain constrained less by success rates among treated patients than by the substantial share of people who are never diagnosed or never start treatment at all.[4,5,12]

Meeting the End TB Strategy's remaining targets will require faster diagnostic scale-up — particularly for the drug classes that define XDR-TB specifically[3] — wider adoption of shorter all-oral treatment regimens,[15,16,17] and sustained financing directed at the health-system gaps that current data show most clearly in South Asia, Eastern Europe, and Southeast Asia alike.[4,14]

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