



## Analysis of accessibility to anti-tuberculosis drugs in the Asia-Pacific region between 2019 and 2022



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### A B S T R A C T

**Objective:** Equitable access to anti-tuberculosis drugs remains a pressing global health challenge. We aim to investigate consumption trends across nine Asia-Pacific countries between 2019 and 2022.

**Methods:** We used pharmaceutical sales data from three databases to analyze 17 anti-tuberculosis drugs across nine countries. Consumption was measured in standardized units per 1000 tuberculosis cases. Compound annual growth rate assessed trends, and Spearman correlation examined associations with six health and economic indicators.

**Results:** Consumption growth rates ranged from  $-39.2\%$  to  $+58.2\%$  across countries. Lower-middle-income economies had substantially lower median consumption (2157 units per 1000 cases) than upper-middle-income economies (14,417 units per 1000 cases). First-line drugs accounted for over 90% of total sales, while next-generation drugs for drug-resistant tuberculosis showed limited availability. Consumption correlated strongly with GDP per capita, life expectancy, Human Development Index, and Universal Health Coverage index.

**Conclusions:** Significant disparities in drug accessibility persist across the Asia-Pacific region. Achieving the WHO End Tuberculosis Strategy goals requires accelerating drug regulatory approvals, strengthening public-private collaboration, and sustained international support for resource-limited settings.

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### Introduction

Tuberculosis (TB) remains the most lethal infectious disease worldwide. According to the World Health Organization (WHO)'s Tuberculosis Report 2024, the annual number of new TB cases per 100,000 population globally increased by 4.6% from 129 in 2020 to

134 in 2023 [1]. Beyond its clinical severity, TB imposes a massive economic burden on patients and health systems worldwide. The disease disproportionately affects the economically active population, leading to substantial productivity losses, and approximately half of all TB-affected households face catastrophic total costs that push vulnerable populations into deeper poverty [2,3]. Of these, the Asia-Pacific region has the highest burden of TB globally, with China, India, Indonesia, and the Philippines leading the world in terms of incidence. Effective anti-TB treatment is the cornerstone of TB control, not only saving individual lives but also preventing TB transmission. It is one of the most critical ways to achieve the ambitious goals of the WHO's End TB Strategy, which aims to reduce TB incidence and mortality by 90% and 95%, respectively, by 2035 [4]. This therapeutic evolution includes established first-line drugs (isoniazid, rifampicin, ethambutol, and pyrazinamide) that

**Abbreviations:** CAGR, Compound annual growth rate; MDR, Multidrug-resistant; NGO, Non-governmental organization; NTP, National TB Programmes; GDF, Global Drug Facility; GDP, Gross domestic product; HDI, Human Development Index; SU, Standard units; TB, Tuberculosis; UHC, Universal Health Coverage; WHO, World Health Organization.

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remain effective in drug-sensitive TB, supplemented by second-line and repositioned drugs, such as linezolid, clofazimine, and fluoroquinolones, for complicated cases. The introduction of next-generation anti-multidrug-resistant-TB (MDR-TB) drugs, including bedaquiline, delamanid, and pretomanid, has further revolutionized the expansion of treatment options [5]. These anti-TB drugs with highly selective antimicrobial mechanisms, significant therapeutic efficacy, and improved safety have been developed and rapidly adopted into clinical practice over the past decade [6]. These drugs have been used in diverse patient populations, including children, adolescents, and adults. However, research and development (R&D) and production of anti-TB drugs require significant financial investment due to complex regulatory pathways and manufacturing requirements [7]. This complexity may be reflected in access challenges, particularly regarding equitable access to medicines for patients in resource-limited settings.

The large populations and high TB burden in the Asia-Pacific region create a considerable demand for anti-TB treatment [1,8]. While international organizations, such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, and the Stop TB Partnership's Global Drug Facility (GDF), have historically provided essential support for TB treatment in resource-limited settings [9,10], there are limited studies on consumption patterns of anti-TB drugs between countries and regions at different income levels within the Asia-Pacific region. Additionally, rapid economic growth in the region has significantly reduced extreme poverty in recent decades, yet uneven development may also lead to disparities in access to anti-TB drugs [11,12].

This study used data from pharmaceutical databases to investigate consumption patterns of anti-TB drugs in the Asia-Pacific region and compare accessibility trends across the region. We also examined the impact of health system performance indicators and economic factors on anti-TB drug consumption to inform global health policy on equitable access to TB treatment.

## Methods

### Study setting and data sources

This cross-sectional study used data on sales of anti-TB drugs from the Asia-Pacific countries obtained from three pharmaceutical databases. For countries other than China, data were obtained from the IQVIA-MIDAS database. This database contains information on drugs sold by pharmaceutical companies to retail and hospital pharmacies across various countries, in a standardized format for global analyses. This dataset has been used in several high-impact drug utilization studies. The IQVIA-MIDAS database audits 14 Asia-Pacific countries, and we included eight Asia-Pacific countries for which data were available: Bangladesh, India, Indonesia, Malaysia, Pakistan, the Philippines, Thailand, and Vietnam. For China, data on anti-TB drug sales in the hospital sector were obtained from the Pharmaceutical Database (PDB), and data in the retail pharmacy sector were obtained from the Retail Pharmacy Database (RPDB), both developed by the China National Pharmaceutical Industry Information Center [11–13].

Due to database limitations, we only extracted quarterly sales of all anti-TB drugs in standard units (SU) for the selected countries from quarter 1,2019, to quarter 4,2022. All the datasets included country, setting (retail or hospital), generic name, quarter, year, strength, dosage form, manufacturer's name, and sales volume expressed in SU [14–17]. It should be noted that the data did not include medicines distributed through international aid programmes or public health channels outside of procurement systems. The accuracy and representativeness of the data have been checked and ensured by a specially developed algorithm [18]. The SU is defined as the smallest commonly used dose of the prod-

uct dosage form, facilitating comparisons of different anti-TB drug dosage forms across countries.

### Availability of anti-TB drugs

We first generated a complete list of TB antimicrobials based on the "J4A antitubercular products" section using the three-level Anatomical Therapeutic Chemical (ATC) classification system. All anti-TB drugs were further screened by excluding vitamins, minerals/trace elements, and natural plant extracts, based on the drugs' clinical usage era, the historical therapeutic context published by the WHO [19,20], and the global introduction process between 2019 and 2022. This study categorises the anti-TB drugs included in the databases into four groups: (1) First-line drugs, as the basic regimen for treating drug-sensitive TB; (2) Second-line traditional drugs, including traditional drugs widely used in MDR-TB; (3) Next-generation anti-MDR-TB drugs, which refer to innovative MDR-TB medications introduced in the past decade; and (4) Other special drugs, intended for specific clinical scenarios or exhibiting significant variations in procurement across countries. This classification serves to examine disparities in drug availability and is not equivalent to the WHO's therapeutic grouping system. The detailed descriptions of the selected anti-TB drugs are shown in Supplementary Figure 1 and Supplementary Table 1.

### Accessibility of anti-TB drugs

We assumed that the sales volumes obtained from the IQVIA-MIDAS, PDB, and RPDB databases were approximately equivalent to the actual annual consumption of anti-TB drugs in the included countries [21,18,22]. We aggregated the quarterly data to the annual level and further calculated the number of SUs sold per 1000 incident cases in the population to show the anti-TB drug use rate per case. We have also included TB incidence rates by country to compare trends with corresponding SU per 1000 cases, thereby reflecting drug accessibility to some extent. Data on TB incidence in countries from 2019 to 2022 were obtained from the WHO's Tuberculosis Report 2024 [1].

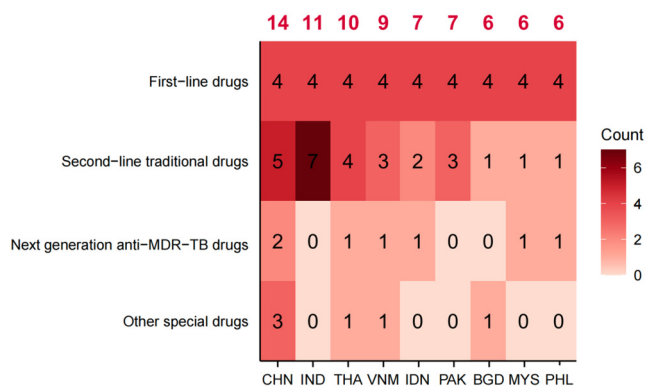
### Health, economic, and system factors

Drawing on previous literature [22,23], we selected six health, economic, and systems-related indicators to explore the determinants of anti-TB drug accessibility. These indicators were chosen because they comprehensively capture a country's financial capacity, health system investment and infrastructure, population health outcomes, and overall development and health system performance, all of which have proved to be key factors affecting drug accessibility.

The six indicators included (1) Gross domestic product (GDP) per capita; (2) Percentage of health expenditure from governmental total expenditure; (3) Doctors density (number of doctors per 1000 population); (4) Life expectancy at birth; (5) Human Development Index (HDI); and (6) Universal Health Coverage index (UHCI). Data on GDP per capita were taken from the International Monetary Fund (IMF). The remaining five indicators were from the WHO and the Organization for Economic Cooperation and Development, using the latest available year. A detailed description of the sources of the indicators is shown in Supplementary Table 3.

### Data analysis

We summarized the consumption of anti-TB drugs across countries between 2019 and 2022. The consumption trend of each country was assessed by calculating the compound annual growth



**Figure 1.** Number of available anti-TB drugs by country between 2019 and 2022. Abbreviations: BGD: Bangladesh, CHN: China, IDN: Indonesia, IND: India, MYS: Malaysia, PAK: Pakistan, PHL: Philippines, THA: Thailand, VNM: Vietnam.

rate (CAGR). The formula is as follows:

$$CAGR_{consumption} = \left[ \left( \frac{SU \text{ per year per } 1000 \text{ cases in } 2022}{SU \text{ per year per } 1000 \text{ cases in } 2019} \right)^{\frac{1}{N}} - 1 \right] \times 100\%$$

N is the number of years of data available.

We showed consumption results according to the World Bank’s 2022 classification criteria based on the country’s income level: “lower-middle-income economies (LMIE) and upper-middle-income economies (UMIE).” We used the mean and standard deviation to summarize yearly consumption for symmetrically distributed data, and the median and interquartile range (IQR) to summarize skewed/asymmetrically distributed data.

We used Spearman’s rank correlation analysis to examine the association between anti-TB drug consumption and six health-economic-social indicators across nine countries, and coefficients were considered statistically significant when  $P < 0.05$ . All data analysis and visualization were performed using R Studio Version 4.3.2.

**Results**

The nine countries in the Asia-Pacific region included in this study exhibited an overall trend of declining tuberculosis incidence rates between 2019 and 2022, followed by an increase. However,

they remain considerably distant from achieving the WHO End TB Strategy’s 2025 milestone— a 50% reduction in tuberculosis incidence compared to their respective 2015 baseline levels (Supplementary Figure 1).

This study screened and included 17 anti-TB drugs from 25 anti-TB products (Supplementary Figure 2). Among these, First-line drugs included four agents: ethambutol, isoniazid, pyrazinamide, and rifampicin; Second-line traditional drugs included eight agents: aminosalicylic acid, capreomycin, protionamide, cycloserine, ethionamide, streptomycin, terizidone, and pasiniazid. Next-generation anti-MDR-TB drugs included two agents: bedaquiline and delamanid; Other specialized drugs included three agents: rifabutin, rifapentine, and rifamycin sodium (injectable) (Supplementary Table 1).

*Availability of anti-TB drugs during 2019-2022*

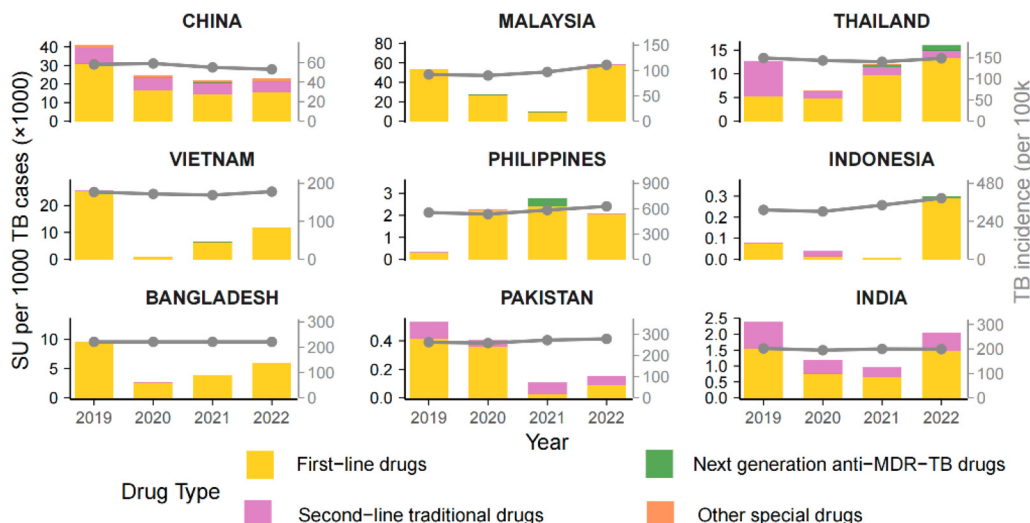
As shown in Figure 1, the number of available anti-TB drugs ranged from six in Bangladesh, Malaysia, and the Philippines to 14 in China. First-line anti-TB drugs were available in all nine countries. Among all available drug products, India had the highest number of second-line traditional anti-TB drugs, followed by China and Thailand. In addition, only China, Indonesia, Malaysia, the Philippines, Thailand, and Vietnam had next-generation anti-MDR-TB drugs available between 2019 and 2022.

*Accessibility of anti-TB drugs during 2019-2022*

In all nine countries, the total consumption of first-line anti-TB drugs was the highest, all exceeding 90% of total sales of anti-TB medications from 2019 to 2022 (Supplementary Table 2). Consumption of anti-TB drugs per 1000 TB cases was uneven among the selected Asia-Pacific countries. Malaysia had the highest average consumption per 1000 cases (30,855.2 SU per 1000 cases). The country with the lowest availability was Indonesia (78.7 SU per 1000 cases) (Supplementary Table 2).

There was a significant imbalance in SU consumption of anti-TB drugs per 1000 cases across countries in the study (Figure 2). Between 2019 and 2022, the median consumption of anti-TB drugs in LMIEs was 2156.8 (IQR:3529.6), which was lower than that in UMIEs (median: 14,416.6; IQR: 20,407.2).

Table 1 shows anti-TB drug consumption per 1000 cases in 2022 by country, along with the corresponding compound an-



**Figure 2.** Yearly anti-TB drug consumption (SU/1000 cases) in nine Asia-Pacific countries.

Abbreviations: SU: standard units, defined as the smallest common dose of a product form, which enables the comparison among anti-TB drugs in different forms.

**Table 1**  
Anti-TB drug consumption in 2022 by country and income level in nine Asia-Pacific countries.

Income level	Countries/regions	GDP per capita	Consumption	
			CAGR (%)	SU per 1000 TB cases ( $\times 1000$ )
LMIEs	Bangladesh	2716.5	-16.9	6.0
	India	2347.4	-4.85	2.0
	Pakistan	1538.3	-39.2	0.2
	Philippines	3548.1	58.2	2.1
	Vietnam	4147.7	-26.4	11.9
UMIEs	China	12,970.6	-17.8	22.7
	Indonesia	4730.8	39.9	0.3
	Malaysia	11,748.1	3.49	58.5
	Thailand	6909.4	9.67	16.1

Abbreviations: CAGR: compound annual growth rate of all anti-TB drugs, GDP: gross domestic product, SU: standard units, defined as the smallest common dose of a product form, which enables the comparison among anti-TB drugs in different forms, LMIEs: lower-middle income economies, UMIEs: upper-middle income economies.

nual growth rate (CAGR). The CAGR of consumption across the nine Asia-Pacific countries ranged from -39.2% to 58.2%. Pakistan (-39.2%), Vietnam (-26.4%), China (-17.8%), Bangladesh (-16.9%), and India (-4.85%) showed a decreasing trend in consumption per 1000 cases. The Philippines (58.2%), Indonesia (39.9%), and Thailand (9.67%) showed a clear upward trend in consumption per 1000 cases, while Malaysia (3.49%) showed a smaller upward trend. Overall, consumption in LMIEs grew at a significantly faster rate than in UMIEs. However, in 2022, access to anti-TB drugs in Indonesia and the Philippines was still much lower than in other Asia-Pacific countries in the study. Indonesia's consumption (300 SU per 1000 cases) represented a fraction of that in the country with the highest consumption (Malaysia, 58,500 SU per 1000 cases).

#### *Economic and health system factors related to anti-TB drug consumption*

In two-by-two comparative analyses, we found that anti-TB drug consumption showed significantly stronger correlations with GDP across all countries in the study ( $r = 0.8$ ,  $P = 0.0138$ ). However, neither the percentage of health expenditure from government total expenditure ( $r = 0.367$ ,  $P = 0.34$ ) nor doctor density ( $r = 0.633$ ,  $P = 0.08$ ) showed a significant correlation with anti-TB drug consumption. The study found strong correlations between anti-TB drug accessibility and life expectancy ( $r = 0.933$ ,  $P < 0.001$ ), HDI ( $r = 0.883$ ,  $P = 0.0031$ ), and UHC index ( $r = 0.833$ ,  $P = 0.0083$ ). Details can be seen in [Figure 3](#).

#### **Discussion**

The global burden of TB is particularly pronounced in the Asia-Pacific region. Despite ongoing advances in anti-TB treatment, antimicrobial resistance remains a persistent challenge. [1] The high costs associated with developing anti-TB drugs and navigating complex regulatory pathways hinder equitable access to treatment for populations at different stages of economic development.

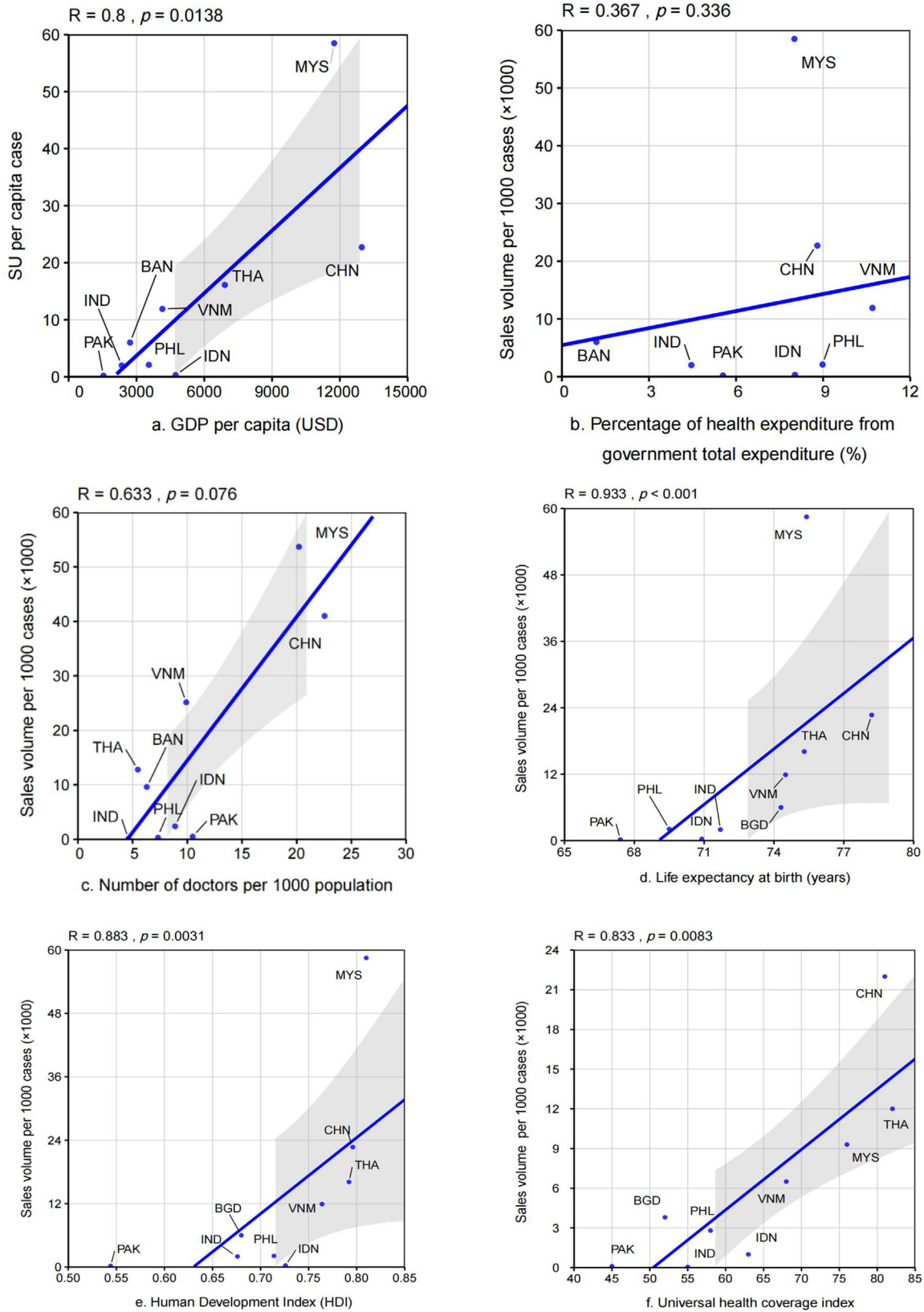
We observed divergent trends in anti-TB drug consumption between 2019 and 2022, with compound annual growth rates ranging from -39.2% to 58.2%. In 2022, consumption of anti-TB drugs per 1000 TB cases in LMIEs with high TB burden in terms of the incidence rate was only a small fraction of that in UMIEs, revealing significant inequalities in accessibility. Anti-TB drug consumption patterns in the Asia-Pacific countries in the study were highly correlated with economic development and the health system, including GDP, life expectancy, HDI, and UHC index.

In this study, first-line drugs accounted for the majority (90%) of anti-TB drug sales across all countries. Only six countries showed

availability of next-generation anti-MDR-TB drugs. This finding suggests that, despite the introduction of next-generation anti-MDR-TB regimens such as bedaquiline, delamanid, and pretomanid, which have demonstrated treatment success rates exceeding 89–93% in clinical trials and represent a landmark breakthrough after decades of stagnation in TB drug development [24,25], access to these newer therapies remains extremely limited, especially in LMIEs where significant unmet demand persists for advanced regimens. This limited access can be attributed to several factors, including 1) the high cost of new anti-TB drugs, which limits market penetration in resource-limited settings [26], 2) the complexity of the regulatory approval process for new drugs in different countries [27], 3) the limited healthcare infrastructures required to implement advanced TB treatment, [28] and 4) differences in need as well as guidelines used and financial sources of in the national TB programmes (NTPs).

In addition, we observed mixed consumption trends among countries. While some high TB burden countries showed rapid growth in consumption of anti-TB drugs, notably the Philippines (58.2%) and Indonesia (39.9%), the interpretation of these growth rates requires careful consideration of baseline levels and funding structures. Despite Indonesia being classified as an UMIEs and exhibiting the second-fastest market growth rate (CAGR: 39.9%) in this study, its absolute consumption remained extremely low (approximately 300 SU per 1000 cases in 2022), representing less than one two-hundredth of Malaysia's consumption level. These can be attributed to two principal factors. First, the high growth rate largely reflects a post-COVID-19 rebound from a severely depressed baseline. TB case notifications plummeted by 31% from 559,847 in 2019 to 384,025 in 2020, followed by a strong rebound to 708,658 in 2022—representing an 85% surge from 2020 [1]. Second, the persistently low absolute consumption in 2022 stems from substantial underreporting and health system fragmentation. The 2022 TB Joint External Monitoring Mission identified striking under-notification from private health providers, particularly general practitioners [29]. Furthermore, policy misalignment persists: while TB treatment guidelines encourage outpatient care, the national health insurance primarily covers inpatient services, leaving private sector TB cases largely unreported [30].

Meanwhile, several countries showed a declining trend: Pakistan (-39.2%), Vietnam (-26.4%), China (-17.8%), Bangladesh (-16.9%), and India (-4.85%). In countries with a high TB incidence, including Bangladesh, India, Pakistan, and Vietnam, the downward trend in consumption from 2019 to 2022 may be due to: 1) decreased case detection during the COVID-19 pandemic [31], 2) a transition to shorter treatment regimens, which reduces total drug demand, [32] and 3) changes in drug procurement and distribution systems. The particularly steep decline in anti-TB drug



**Figure 3.** Correlation between anti-TB drug consumption and health system indicators in nine Asia-Pacific countries. Abbreviations: BGD: Bangladesh, CHN: China, IDN: Indonesia, IND: India, MYS: Malaysia, PAK: Pakistan, PHL: Philippines, THA: Thailand, VNM: Vietnam.

consumption in Pakistan (CAGR:  $-39.2\%$ ) warrants specific attention. First, Pakistan has a massive private healthcare sector where approximately 85% of TB initial care-seeking occurs. However, this system accounts for only 15% of healthcare facilities with tuberculosis diagnosis and treatment capabilities, and a significant proportion of tuberculosis cases remain unreported to the NTP. The 2022 TB Programme Review identified a 60% funding gap (2021–2023) and fragmented electronic systems for data collection, which severely limited case detection and drug procurement through official channels [33]. In addition, private sector TB treatment often deviates from NTP guidelines, with high treatment attrition rates and intermittent case management practices, meaning drug consumption may not align with standardized regimens [34]. A similar phenomenon also exists in India. Their National Tuberculosis Elimination Programme (NTEP) implements the Directly Observed Treatment, Short-course (DOTS) strategy to ensure standardized first-line treatment and improve patient adherence. Under DOTS, patients receive supervised, quality-assured medications tailored to their disease categorization. However, India's healthcare landscape is characterized by a massive and fragmented private sector, where over half of all TB patients seek initial care. Integrating this sector remains a formidable challenge; private providers often deviate from standard DOTS regimens, leading to unstandardized prescriptions, significant underreporting to the national surveillance system, and incomplete reflections of actual anti-TB drug consumption in formal pharmaceutical sales databases [35,36].

The lower anti-TB drug consumption in LMIEs compared to UMIEs may primarily reflect substantial gaps in TB case detection and treatment coverage rather than individual affordability. Four high-burden countries—India, Indonesia, the Philippines, and Pakistan—accounted for over half of the global gap between case notifications and estimated TB incidence in 2022, indicating that a large proportion of TB cases remain undiagnosed and untreated. Furthermore, treatment coverage in the least efficient countries can be as low as 38.7% compared to 87.3% in the most efficient countries [37]. Furthermore, while TB treatment is often provided free through donor-supported NTP in both income groups, limited healthcare infrastructures, inadequate diagnostic capacity, and high rates of underdiagnosis in lower-income settings result in fewer patients accessing treatment and consequently lower recorded drug consumption. Additionally, private sector TB drug sales represent more than half of all TB drugs distributed in India and Indonesia, and between one-third and one-half in the Philippines and Pakistan. However, quality of care in the private sector often falls short of international standards, with over 35% of dosages falling outside WHO treatment recommendations [38,39].

Our correlation analysis suggested that country-specific economic and healthcare system indicators partially explain variations in anti-TB drug usage. We found a strong correlation between GDP per capita and anti-TB drug accessibility, with access to anti-TB drugs in LMIEs being a fraction of that in UMIEs such as Malaysia and China. As other studies of drug consumption have shown, the level of national income, as measured by GDP per capita, is the most critical factor influencing the accessibility of new therapeutic drugs [40,41].

Moreover, the life expectancy, HDI, and the UHCI also constitute a comprehensive set of indicators reflecting a country's level of development. Studies have shown that inequality in access to anti-TB drugs is more likely to be influenced by life expectancy in LMIEs. However, moderate correlations were also observed between the HDI and the UHCI, possibly because life expectancy, as a single, direct indicator of health outcomes, is sensitive to access to anti-TB drugs. In contrast, TB predominantly affects the productive-age population, and the significant mortality impact of TB in LMIEs makes its association with life expectancy more direct than the composite development indicator [42].

This study has several limitations. First, from a national and supranational perspective, our analyses relied on the IQVIA-MIDAS, PDB, and RPDB, which captured pharmaceutical sales from public hospitals and retail pharmacy channels. While these databases provide highly standardized metrics for cross-country comparisons, they cannot be considered exhaustively representative of the entire market. Also their coverage was limited to nine Asia-Pacific countries, excluding several high-TB-burden nations such as Cambodia and Myanmar due to data unavailability. These databases do not capture anti-TB drugs directly distributed through non-governmental organizations (NGO). Future research should aim to identify and integrate more comprehensive, multi-source databases to fully capture the entire spectrum of anti-TB drug distribution. Second, although these data sources represent the most comprehensive pharmaceutical market intelligence, sales volumes may still underestimate actual drug utilization, as the databases did not capture informal or unreported sales channels. In addition, sales data may not fully reflect actual consumption due to factors such as drug wastage, stockpiling, or inefficiencies in the distribution systems. Third, our drug selection was based on the ATC third-level classification of antimycobacterials (J04A), which excluded fluoroquinolones and oxazolidinones, which are essential for MDR-TB treatment. These agents were classified under broader antibacterial categories (J01), and their specific use for TB treatment cannot be distinguished from sales data alone, potentially leading to an underestimation of access to treatment for drug-resistant TB. Fourth, the cross-sectional nature of the association analyses precluded causal inference and limited the ability to control for confounding factors, disease severity, or treatment outcomes. Further research is required to better understand the underlying mechanisms of disparities in drug accessibility.

## Conclusion

This study provides a systematic analysis of the dynamics of anti-TB drug consumption, revealing substantial disparities in drug accessibility across nine Asia-Pacific countries. Between 2019 and 2022, first-line drugs dominated the market ( $>90\%$ ), while next-generation MDR-TB drugs showed extremely limited penetration, particularly in lower-middle-income economies where drug consumption volumes correlated strongly with economic indicators such as GDP, HDI, and UHCI.

Moving forward, achieving the WHO's End TB Strategy requires multifaceted interventions. Countries with substantial gaps in case detection must prioritize strengthening public-private partnerships to standardize treatment protocols across sectors. Additionally, regulatory approval mechanisms must be optimized to ensure timely access to next-generation MDR-TB drugs in resource-limited settings. Sustained international donor commitments and addressing policy misalignments in health insurance coverage are also crucial. Finally, the healthcare disruptions experienced during the COVID-19 pandemic underscore the critical importance of integrating TB services into primary healthcare systems to enhance overall service resilience against future crises.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Author contributions

Conceptualization: **ZP, MX**; Data curation: **ZP**; Formal analysis: **ZP**; Methodology: **ZP**; Project administration: **ZP, MX**; Resources: **MX, SKO, SY**; Supervision: **MX**; Visualization: **ZP**; Writing – original draft: **ZP**; Writing – review & editing: **ZP, SKO, SY, CH, MX**.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108586.

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