Article

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Global, Regional and National Trends in Latent Tuberculosis Infection Prevalence From 1990 to 2023, With Projections to 2050

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Background: Latent tuberculosis infection (LTBI) is the major reservoir for future tuberculosis (TB) disease. Updated estimates of long-term trends, demographic redistribution, and future burden are needed to inform prevention-oriented TB policy in the era of the World Health Organization (WHO) End TB Strategy.

Methods: We analyzed The Global Burden of Disease (GBD) 2023 LTBI prevalence estimates, summarizing age-standardized prevalence rates and prevalent cases globally and by sex, age group, socio-demographic index (SDI) quintile, WHO region, and country. Temporal trends were assessed using log-linear joinpoint regression, with national AAPC estimated for 2010–2023 and sensitivity analyses under alternative maximum joinpoint specifications. Global projections for 2024–2050 were generated using a Bayesian age–period–cohort model with second-order random-walk (RW2) priors linked to UN population projections; model diagnostics included convergence checks, posterior predictive checks, Pareto-smoothed importance sampling leave-one-out (PSIS-LOO), and comparison of Poisson and negative-binomial likelihoods. We also performed a fine-age sensitivity analysis that disaggregated population denominators into <20, 20–39, 40–54, 55–69, and ≥70 years while preserving the GBD broad-age prevalence rates. GBD-derived 95% uncertainty intervals (UIs), joinpoint-derived 95% confidence intervals (CIs), and Bayesian model-derived 95% credible intervals (CrIs) are distinguished throughout; joinpoint and APC model intervals are conditional on GBD point estimates and do not propagate upstream GBD estimation uncertainty.

Results: Globally, the age-standardized LTBI prevalence rate declined from 30,421.65 (95% uncertainty interval [UI] 27,223.03–33,584.80) per 100,000 in 1990 to 22,664.54 (20,437.19–25,107.66) in 2023, corresponding to an AAPC of –0.87% (95% CI –0.95 – –0.79). Over the same period, prevalent cases increased from 1594.58 (1415.40–1777.61) million to 1876.45 (1696.79–2063.84) million, with an AAPC of +0.48% (0.43–0.54), demonstrating a clear rate-volume gap. Declines in age-standardized prevalence rates were observed across all SDI quintiles and WHO regions, but national trends were heterogeneous; 202 of 204 countries had negative AAPC from 2010 to 2023, whereas the United States and Sri Lanka had non-negative AAPC estimates. Decomposition analyses showed that the 281.87 million net increase in global prevalent cases from 1990 to 2023 was driven mainly by population growth (+725.19 million cases) and population ageing (+66.94 million), partly offset by declining age-specific prevalence (−510.26 million). In the negative-binomial APC model favored by diagnostics, the projected crude global prevalence rate was 23,127.50 (95% CrI 22,573.02–23,737.67) per 100,000 in 2024 and 23,653.08 (20,518.82–27,139.87) in 2050, corresponding to 1.88 (1.83–1.93) billion and 2.28 (1.98–2.61) billion prevalent cases, respectively.

Conclusions: Despite sustained declines in age-standardized LTBI prevalence rates since 1990, the absolute number of people living with LTBI has increased and is projected to remain large through 2050. These findings suggest that TB elimination strategies cannot rely on declining standardized rates alone; they require stronger prevention-oriented policies that reduce progression to active disease, particularly in ageing and other high-risk populations.

Keywords: latent tuberculosis infection; prevalence; Global Burden of Disease; joinpoint regression; age–period–cohort model; projection

Introduction

Tuberculosis (TB) remains a major global public health threat and one of the leading causes of death from a single infectious agent worldwide. Despite substantial progress in diagnosis, treatment, and prevention, TB continues to impose a heavy burden, with millions of incident cases and more than one million deaths reported annually in recent global assessments [1]. Achieving further reductions in TB incidence and mortality requires not only interrupting ongoing transmission but also addressing the large reservoir of latent tuberculosis infection (LTBI), which may give rise to future active TB disease [2,3].

The World Health Organization (WHO) defines LTBI as "a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB" [2,4]. Although the lifetime risk of progression from LTBI to active TB is often cited as approximately 5–10% in the general population, this risk is highly heterogeneous and is substantially influenced by age, immune status, comorbidities, and time since infection [2,5,6]. As a result, LTBI is not only an epidemiological reservoir of future disease but also a critical target for tuberculosis preventive treatment (TPT), particularly among populations at elevated risk of progression, including household contacts, people living with HIV, and individuals with immunosuppressive conditions [2,7].

Existing evidence suggests that the global reservoir of LTBI remains substantial, although its magnitude varies according to modelling assumptions, diagnostic definitions, and data sources [8]. Previous landmark modelling studies have estimated that roughly one quarter of the world's population may harbor latent infection, while also showing marked geographic heterogeneity and strong cohort effects linked to past transmission intensity [3]. At the same time, the epidemiology of LTBI is likely to have evolved over recent decades as a consequence of changing transmission dynamics, socioeconomic development, urbanization, migration, population ageing, and expansion of TB control and preventive services [9]. These shifts imply that trends in LTBI burden cannot be adequately understood through static prevalence estimates alone.

This issue is particularly relevant in the context of the WHO End TB Strategy, which emphasizes prevention, including TPT among populations at highest risk, as a core pillar of TB elimination efforts [10]. Even where age-standardized prevalence rates decline, population growth and ageing may sustain—or even increase—the absolute number of people living with LTBI. Such divergence between declining standardized rates and persistent crude burden has important policy implications, because future TB incidence may increasingly arise among older adults and populations affected by multimorbidity, immune senescence, and other conditions that elevate the risk of reactivation [5,6,9]. For health systems, this means that epidemiological improvement in relative terms may coexist with a persistent demand for preventive strategies and long-term clinical management.

Although several studies have described the global burden of LTBI or TB more broadly [9,11,12], important knowledge gaps remain. Prior work has often focused on single time points, restricted geographic settings, or broad prevalence summaries, with less attention to long-term temporal dynamics, cross-national disparities, demographic drivers of change, and future burden under population ageing [13]. In particular, the extent to which declines in age-standardized LTBI prevalence may be offset by demographic expansion and ageing has not been comprehensively quantified within a consistent global framework. This limits policymakers' ability to anticipate future preventive treatment needs, identify populations in whom the latent reservoir remains concentrated, and align TB prevention strategies with emerging demographic realities [2,10].

The Global Burden of Disease (GBD) Study offers a harmonized platform for evaluating long-term patterns of disease burden across countries, years, sexes, and age groups [14]. Using GBD 2023 estimates for LTBI, we aimed to provide a comprehensive assessment of the global evolution and future trajectory of LTBI burden from 1990 to 2023 and beyond. Specifically, we examined disparities in prevalence rates and prevalent cases by sex, age group, socio-demographic index (SDI) quintile, and WHO region; quantified temporal trends and national changes in age-standardized prevalence; projected global LTBI burden through 2050 using a Bayesian age–period–cohort approach linked to population projections; and decomposed observed and projected changes in prevalent cases into demographic and epidemiologic components. By clarifying how declining age-standardized rates may coexist with a sustained absolute burden, this study seeks to inform more targeted preventive treatment strategies and longer-term planning for TB elimination.

Methods

Data Source

We conducted a secondary analysis of publicly available GBD 2023 estimates for LTBI prevalence. GBD Results Tool exports used in this analysis were downloaded in six local exports on March 4 and March 5, 2026, with the final ZIP metadata timestamp recorded as March 5, 2026, 09:06. Two outcome indicators were analyzed: the age-standardized prevalence rate (per 100,000 population) and the number of prevalent cases (in millions). In addition, age-specific prevalence rates (per 100,000 population, used to describe disease burden within age strata) were used for stratified analyses. Historical estimates were examined from 1990 to 2023 at the global level and, where available, stratified by sex, age group, SDI quintile, and

WHO region. National-level analyses focused on age-standardized prevalence rates for both sexes combined from 2010 to 2023. Historical age-standardized prevalence rates and age-specific prevalence estimates were directly extracted from the published GBD 2023 outputs. The age-standardized rates followed the Institute for Health Metrics and Evaluation (IHME) global standard population age-standardization framework; no additional standardization was performed in this study [14].

For projections from 2024 to 2050, population denominators were obtained from the United Nations World Population Prospects Data Portal and aggregated into three age groups (<20, 20–54, and ≥55 years) to align with the age-specific GBD prevalence estimates available in the local GBD 2023 LTBI exports. During data preparation, records were standardized and harmonized across source tables, exact duplicates were removed, and UN population data were linked by ISO3 codes before constructing analysis-specific datasets for global, regional, and national analyses. For descriptive reporting, we retained the 95% uncertainty intervals (95% UIs) provided in the GBD outputs. However, the joinpoint regression and Bayesian age–period–cohort models were fitted to the corresponding point estimates. Accordingly, the age–period–cohort (APC), average annual percent change (AAPC), and projection intervals reported in this study should be interpreted as conditional on the fitted statistical models and not as reflecting the full propagation of upstream uncertainty from the GBD estimation process.

To aid interpretation, we note that three distinct interval types appear throughout this manuscript. GBD-derived 95% uncertainty intervals (95% UIs) reflect the full uncertainty propagated through the GBD Bayesian meta-regression framework (DisMod-MR 2.1), incorporating sampling variability, between-study heterogeneity, and systematic error adjustments from the underlying data sources [14]. Joinpoint-derived 95% confidence intervals (95% CIs) are frequentist intervals based on permutation tests and reflect sampling variability conditional on the GBD point estimates [15]. All 95% confidence intervals (CIs) for Joinpoint-derived APC and AAPC estimates were calculated based on GBD 2023 estimates. Bayesian APC model-derived 95% credible intervals (95% CrIs) represent posterior uncertainty conditional on the fitted model, the negative-binomial likelihood for reconstructed counts, and the specified prior distributions. Because the joinpoint and APC models treat GBD point estimates as fixed inputs, their intervals do not incorporate upstream GBD estimation uncertainty and are therefore narrower than those obtained would be under full two-stage uncertainty propagation. We discuss the implications of this limitation and potential remedies below.

Statistical Analysis

Temporal trends in age-standardized prevalence rates and prevalent case counts were assessed using log-linear joinpoint regression. For outcome y_t in calendar year t, the model was specified as:

$$\log(y_t) = \beta_0 + \beta_1 t + \sum_{k=1}^{K} \delta_k (t - \tau_k)_+$$

where τ_k denotes a joinpoint and $(t - \tau_k)_+ = max(0, t - \tau_k)$. Segment-specific APC was derived from the slope as:

$$APC = 100 \times \{\exp(\beta) - 1\}$$

and AAPC was summarized over prespecified time windows using weighted averages of segment slopes. The average annual percent change (AAPC) was computed as a weighted average of segment-specific APCs across the predefined time window, weighted by the number of years in each segment (i.e., end year minus start year), strictly following the official algorithm of the Joinpoint Regression Program (version 5.2.0; National Cancer Institute, Bethesda, MD, USA; https://surveillance.cancer.gov/joinpoint/). For a time series containing n annual data points, the total number of annual intervals equals n−1. For global analyses, models were fitted separately to age-standardized prevalence rates and prevalent cases for both sexes combined over 1990–2023. National AAPC was estimated for 2010–2023 because country series contained only 14 annual observations [15]. To evaluate robustness of national summaries to model flexibility, we repeated country-level analyses under alternative maximum joinpoint settings of 0, 1, 2, and 3 joinpoints and summarized the resulting changes in AAPC.

Joinpoint models used a log-linear specification with a maximum of three joinpoints. Model selection was performed using permutation tests (two-sided α=0.05), with a minimum of two observations at each end and two observations between joinpoints. Parametric 95% confidence intervals and a constant-variance error specification were used. For age-standardized prevalence rates, the dependent-variable type was specified as age-adjusted rate; for age-specific rates, it was specified as crude rate; and for prevalent case counts, it was specified as count.

Global projections for 2024–2050 were generated using a Bayesian age–period–cohort model based on three GBD-reported age groups (<20, 20–54, and ≥55 years) and annual periods from 2010 onward [16,17]. Because these broad age bands may mask clinically meaningful heterogeneity in older adults, we added a fine-age sensitivity analysis using UN five-year population denominators re-

grouped as <20, 20–39, 40–54, 55–69, and ≥70 years. This sensitivity analysis held each broad GBD prevalence rate fixed in the neutral scenario and, for the oldest adults, additionally varied the ≥70 years prevalence rate from 0.8 to 1.5 times the 55–69 years rate while preserving the aggregate ≥55 years prevalence rate. Age-specific LTBI counts were approximated by multiplying age-specific prevalence estimates by the corresponding population denominators and were modeled as:

$$y_{ap} \sim f(E_{ap}\lambda_{ap}),$$

with

$$\log(\lambda_{ap}) = \mu + \alpha_a + \pi_p + \gamma_c,$$

where y_{ap} is the expected LTBI count in age group a and period p, E_{ap} is the population offset, c indexes the birth cohort implied by age and period, and $f(.)$ denotes the likelihood. We initially specified $f(.)$ as a Poisson likelihood and then fitted a negative-binomial alternative with the same linear predictor to evaluate sensitivity to overdispersion. Age effects were centered for identifiability, whereas period and cohort effects were assigned second-order random-walk (RW2) priors to favor gradual temporal evolution while preserving trend momentum in projected trajectories. Weakly informative priors were used for the intercept, variance components, and negative-binomial overdispersion parameter. Model adequacy was assessed using R-hat, effective sample size, divergent transitions, maximum treedepth, posterior predictive checks, and Pareto-smoothed importance sampling leave-one-out (PSIS-LOO). The Poisson model showed poor convergence and posterior predictive misfit, whereas the negative-binomial model showed acceptable convergence and substantially better posterior predictive behavior; therefore, projection summaries are reported from the negative-binomial APC model, with Poisson diagnostics retained as an assumption check (**Supplementary Tables 1–4**). Projected age-standardized prevalence rates were not estimated.

To clarify the divergence between standardized rates and absolute burden, we further performed a Das Gupta-style three-component decomposition of changes in prevalent cases, partitioning the net change into contributions from population growth, population ageing, and age-specific epidemiologic change. This decomposition was applied both to observed global changes from 1990 to 2023 and to projected global changes from 2024 to 2050.

Data management was performed in Python 3.12.8. Statistical analyses were conducted in R 4.5.2 using the Joinpoint Regression Software Command Line Interface (version 5.2.0) through the nih.joinpoint R package, and Bayesian modeling was implemented in Stan (version 2.32.2) via RStan.

Results

Global Levels and Long-Term Trends

Global, regional, SDI-stratified, and sex-specific age-standardized prevalence rates; age-specific prevalence rates by age group; the numbers of prevalent cases across all strata (1990 and 2023); and Joinpoint-derived AAPC estimates are summarized in Table 1. At the global level, the age-standardized prevalence rate declined from 30,421.65 (95% UI 27,223.03–33,584.80) per 100,000 population in 1990 to 22,664.54 (20,437.19–25,107.66) in 2023, corresponding to an overall AAPC of −0.87% (95% CI –0.95 – –0.79). In contrast, prevalent cases increased from 1594.58 (1415.40–1777.61) million to 1876.45 (1696.79–2063.84) million (AAPC +0.48% [0.43–0.54]) (Table 1). Thus, by 2023, the GBD-estimated global LTBI burden remained very large in absolute terms despite sustained improvement in age-standardized prevalence rates.

Joinpoint-fitted global trends for both sexes are shown in Fig. 1A,B. Segment-specific APC estimates indicated a modest decline in the age-standardized prevalence rate during 1990–1999 (–0.44% [–0.56 – –0.32]), a faster decline during 1999–2019 (–1.06% [–1.18 – –0.95]), and continued decline during 2019–2023 (–0.89% [–0.92 – –0.87]) (Fig. 1A; **Supplementary Table 5**). In parallel, prevalent cases increased most rapidly during 1990–1999 (+1.09% [1.01 – 1.18]), with slower growth in 1999–2019 (+0.28% [0.20 – 0.35]) and 2019–2023 (+0.15% [0.05 – 0.25]) (Fig. 1B; **Supplementary Table 6**).

Differences by Sex and Age

Sex-stratified analyses showed consistent declines in age-standardized prevalence rates for both females and males (Table 1; **Supplementary Fig. 1A–D**). Males had slightly higher prevalence rates than females at both time points, with rates declining from 31,080.36 to 23,508.66 per 100,000 in males and from 29,784.74 to 21,822.67 in females. The decline was steeper in females (AAPC –0.95% [95% CI –0.99 – –0.90]) than in males (–0.82% [–0.90 – –0.75]). Despite declining rates, prevalent cases increased in both sexes, from 776.26 million to 901.55 million in females and from 818.33 million to 974.90 million in males, with slightly faster growth among males (female AAPC +0.45% [0.39 – 0.51]; male +0.52% [0.46 – 0.57]) (Table 1; **Supplementary Fig. 1B,D**).

Age-stratified results indicated marked heterogeneity in both prevalence-rate and prevalent-case trends (Table 1; **Supplementary Fig. 2A–C**). In 1990, the highest age-specific prevalence rate was observed among adults aged 20–54 years (35,482.45 per 100,000), followed by those aged ≥55 years (33,051.20), while the lowest was observed among individuals aged <20 years (22,956.97); this ranking

Table 1. Global and regional prevalence and temporal trends of latent tuberculosis infection (LTBI) from 1990 to 2023.

Group	1990 Prevalence rate (per 100,000, 95% UI)	2023 Prevalence rate (per 100,000, 95% UI)	1990–2023 rate AAPC (95% CI)	1990 Prevalent cases (million, 95% UI)	2023 Prevalent cases (million, 95% UI)	1990–2023 number AAPC (95% CI)
Global	30,421.65 (27,223.03 – 33,584.80)	22,664.54 (20,437.19 – 25,107.66)	–0.87 (–0.95 – –0.79)***	1594.58 (1415.40 – 1777.61)	1876.45 (1696.79 – 2063.84)	0.48 (0.43 – 0.54)***
Sex group						
Female	29,784.74 (26,719.30 – 32,839.90)	21,822.67 (19,649.33 – 24,222.54)	–0.95 (–0.99 – –0.9)***	776.26 (688.85 – 862.97)	901.55 (813.15 – 994.55)	0.45 (0.39 – 0.51)***
Male	31,080.36 (27,787.13 – 34,349.77)	23,508.66 (21,229.78 – 25,992.90)	–0.82 (–0.9 – –0.75)***	818.33 (725.34 – 914.64)	974.90 (882.04 – 1071.83)	0.52 (0.46 – 0.57)***
Age group						
<20 years	22,956.97 (18,495.28 – 27,183.47)	15,684.74 (12,393.35 – 19,207.46)	–1.15 (–1.22 – –1.08)***	517.63 (417.03 – 612.93)	418.88 (330.98 – 512.96)	–0.64 (–0.68 – –0.60)***
20–54 years	35,482.45 (30,083.53 – 41,202.60)	27,129.43 (23,024.32 – 31,616.06)	–0.81 (–0.84 – –0.78)***	854.40 (724.40 – 992.14)	1034.45 (877.92 – 1205.53)	0.58 (0.49 – 0.67)***
55+ years	33,051.20 (27,518.03 – 39,140.28)	26,742.99 (22,494.11 – 31,750.80)	–0.66 (–0.71 – –0.6)***	222.55 (185.29 – 263.55)	423.12 (355.89 – 502.35)	1.97 (1.89 – 2.04)***
SDI group						
Low SDI	34,441.40 (30,884.25 – 38,001.13)	21,067.50 (18,838.33 – 23,640.79)	–1.49 (–1.5 – –1.47)***	263.54 (231.68 – 293.73)	345.72 (307.70 – 393.48)	0.82 (0.8 – 0.84)***
Low-middle SDI	32,787.02 (28,825.55 – 36,851.41)	23,034.43 (20,607.90 – 25,782.88)	–1.06 (–1.15 – –0.96)***	230.11 (199.07 – 263.04)	272.63 (241.94 – 306.36)	0.5 (0.42 – 0.58)***
Middle SDI	36,514.62 (33,491.80 – 39,360.21)	28,782.20 (26,065.29 – 31,282.03)	–0.71 (–0.74 – –0.69)***	208.87 (188.17 – 230.19)	283.85 (256.74 – 308.92)	0.94 (0.9 – 0.97)***
High-middle SDI	31,155.44 (27,464.40 – 34,737.19)	25,889.95 (23,363.31 – 28,605.87)	–0.57 (–0.61 – –0.52)***	345.44 (299.92 – 391.65)	447.19 (401.80 – 495.09)	0.78 (0.69 – 0.87)***
High SDI	25,570.99 (22,941.76 – 28,262.43)	18,242.73 (16,353.64 – 20,337.99)	–1.03 (–1.07 – –0.98)***	545.06 (485.48 – 605.62)	525.76 (474.51 – 581.20)	–0.11 (–0.17 – –0.05)***
Region group						
African Region	38,106.85 (34,522.57 – 41,230.54)	23,141.11 (20,709.14 – 25,595.93)	–1.5 (–1.52 – –1.48)***	175.03 (155.43 – 193.28)	251.93 (222.99 – 285.69)	1.1 (1.08 – 1.12)***
Region of the Americas	24,577.38 (22,025.31 – 27,184.98)	15,999.11 (14,105.86 – 18,247.20)	1.28 (–1.33 – –1.22)***	174.50 (155.49 – 193.22)	177.12 (156.02 – 201.53)	0.08 (–0.04 – 0.19)
Eastern Mediterranean Region	31,720.13 (29,194.85 – 34,363.82)	17,688.51 (15,750.76 – 19,898.72)	–1.76 (–1.77 – –1.74)***	105.50 (95.28 – 116.62)	129.69 (115.00 – 146.88)	0.62 (0.6 – 0.64)***
European Region	22,810.61 (20,342.35 – 25,338.29)	10,222.47 (8907.39 – 11,689.76)	–2.38 (–2.42 – –2.35)***	205.09 (183.24 – 228.40)	106.84 (93.15 – 121.96)	–1.94 (–1.97 – –1.92)***
South-East Asia Region	31,688.91 (27,550.70 – 35,833.86)	25,303.08 (22,602.77 – 28,092.45)	–0.69 (–0.75 – –0.62)***	353.58 (302.00 – 408.36)	462.87 (412.54 – 515.52)	0.81 (0.73 – 0.9)***
Western Pacific Region	33,311.70 (29,938.84 – 36,802.12)	30,278.26 (27,430.43 – 32,939.17)	–0.29 (–0.3 – –0.27)***	571.97 (509.29 – 638.20)	737.63 (672.90 – 804.34)	0.78 (0.74 – 0.83)***

GBD-estimated prevalence rates are age-standardized for the global, sex, SDI and WHO regional groups and age-specific for the age groups; rates are expressed per 100,000 population. Prevalent cases are expressed in millions. Values in parentheses are 95% uncertainty intervals (UIs). AAPC, average annual percent change, was estimated using log-linear joinpoint regression for 1990–2023; values in parentheses are 95% confidence intervals (CIs). ***$p < 0.001$. Global estimates were taken directly from the GBD 2023 export and were not recalculated as the sum of SDI-stratified estimates; therefore, SDI-stratified values may not sum exactly to the Global estimate.

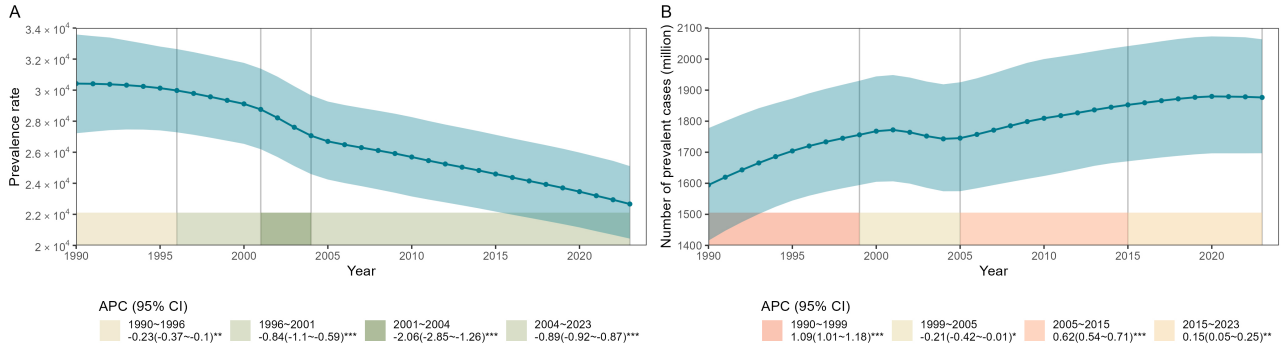

Fig. 1. Global trends in GBD-estimated age-standardized LTBI prevalence rate and prevalent cases, 1990–2023, with joinpoint regression segments and annual percent change estimates. (A) GBD-estimated age-standardized LTBI prevalence rate (per 100,000) for both sexes combined, 1990–2023; points represent GBD 2023 estimates with 95% UIs and solid lines show joinpoint-fitted trends with segment-specific annual percent change (APC) and 95% confidence intervals. (B) GBD-estimated number of people living with LTBI (millions) for both sexes combined, 1990–2023, with joinpoint-fitted trends and APC labels; higher positive APC values indicate faster increases in estimated prevalent cases, whereas negative APC values indicate declines. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

remained unchanged in 2023. The largest decline in age-specific prevalence rates occurred in the <20-year group (AAPC –1.15% [–1.22 – –1.08]), followed by the 20–54-year group (–0.81% [–0.84 – –0.78]) and the ≥55-year group (–0.66% [–0.71 – –0.60]). In contrast, the number of prevalent cases in the <20-year group decreased from 517.63 million to 418.88 million (AAPC −0.64% [–0.68 – –0.60]), whereas it increased among adults: from 854.40 million to 1,034.45 million in the 20–54-year group, and from 222.55 million to 423.12 million in the ≥55-year group. The fastest increase was observed in the oldest age group (AAPC +1.97% [1.89 – 2.04]), indicating a marked shift in the disease burden toward older populations.

In the fine-age sensitivity analysis, the neutral within-band allocation showed that the share of global prevalent cases among adults aged 70 years and older increased from 4.2% in 1990 to 7.4% in 2023 and was projected to reach 12.6% in 2050 (**Supplementary Fig. 3**; **Supplementary Table 7**). Under alternative older-age contrast scenarios that preserved the aggregate ≥55 years GBD prevalence rate, the projected 2050 share of cases in adults aged 70 years and older ranged from 11.0% when the ≥70 years prevalence rate was set lower than the 55–69 years rate to 15.6% when it was set at 1.5 times the 55–69 years rate (**Supplementary Table 8**). Thus, the conclusion that the GBD-estimated LTBI burden is shifting toward older adults was not dependent on treating all adults aged ≥55 years as a single homogeneous group.

Socio-Demographic and Geographic Disparities

Across SDI quintiles, age-standardized prevalence rates declined in all groups from 1990 to 2023 (Table 1; **Supplementary Fig. 4A–E**). In 1990, the highest age-standardized prevalence rate was observed in middle SDI settings (36,514.62 per 100,000), whereas by 2023 the highest rate remained in middle SDI settings (28,782.20), followed closely by high-middle SDI settings (25,889.95). The steepest rate decline was observed in low SDI settings (AAPC –1.49% [–1.50 – –1.47]), while the slowest decline was in high-middle SDI settings (–0.57% [–0.61 – –0.52]). Trends in prevalent cases were more heterogeneous. High SDI was the only SDI quintile to show a net decline in prevalent cases, from 545.06 million in 1990 to 525.76 million in 2023 (AAPC –0.11% [–0.17 – –0.05]), whereas all other SDI quintiles showed increases. The largest prevalent-case growth was observed in middle SDI settings (AAPC +0.94% [0.90 – 0.97]), followed by low SDI (+0.82% [0.80 – 0.84]) and high-middle SDI (+0.78% [0.69 – 0.87]) (**Supplementary Fig. 5A–E**).

Across WHO regions, marked geographic contrasts were also evident (Table 1; **Supplementary Fig. 6A–E**; **Supplementary Fig. 7A–E**). In 1990, the African Region had the highest age-standardized prevalence rate (38,106.85 per 100,000), whereas by 2023, the highest age-standardized prevalence rate was observed in the Western Pacific Region (30,278.26 per 100,000), followed by the South-East Asia Region (25,303.08 per 100,000). The European Region had the lowest rate by 2023 (10,222.47 per 100,000). The European Region experienced the largest decline in age-standardized prevalence rate and a concurrent decline in prevalent cases, with an AAPC of –2.38% (95% CI –2.42 – –2.35) for age-standardized prevalence rate and –1.94% (–1.97 – –1.92) for prevalent cases. By contrast, the Western Pacific Region showed the smallest decline in age-standardized prevalence rate (–0.29% [–0.30 – –0.27]) and a sustained increase in prevalent cases (+0.78% [0.74 – 0.83]). It also had the largest absolute number of prevalent cases at both time points, increasing from 571.97 million in 1990 to 737.63 million in 2023. The African Region had the fastest increase in prevalent cases (+1.10%

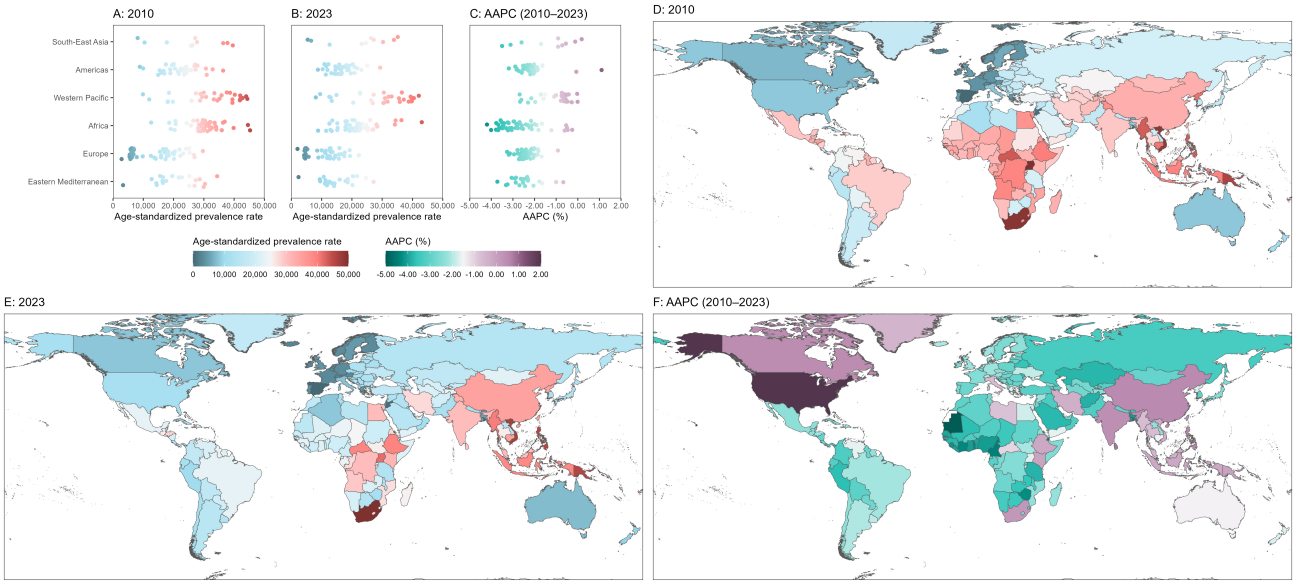

Fig. 2. National-level GBD-estimated age-standardized prevalence of LTBI in 2010 and 2023 and national AAPC in age-standardized prevalence rate, 2010–2023. (A) WHO region-level jitter plots of national age-standardized LTBI prevalence rates (per 100,000) in 2010 for both sexes combined, stratified by WHO region. (B) Same as (A) for 2023. (C) Same as (A) for national AAPC in age-standardized LTBI prevalence rate from 2010 to 2023, where more negative values indicate faster declines and non-negative values indicate flat or increasing trends. (D) World map of national age-standardized LTBI prevalence rates (per 100,000) in 2010 for both sexes combined. (E) World map of national age-standardized LTBI prevalence rates (per 100,000) in 2023 for both sexes combined. (F) World map of national AAPC in age-standardized LTBI prevalence rate from 2010 to 2023.

[1.08 – 1.12]), despite one of the steepest declines in age-standardized prevalence rates (–1.50% [–1.52 – –1.48]).

National-Level Trends and Outliers

National-level joinpoint models were fit for 204 countries and territories with available age-standardized prevalence rate data for both sexes from 2010 to 2023. Across countries, the distribution of national AAPC estimates was strongly skewed toward declines (median –2.30%; interquartile range –2.69% – –1.76%). Of 204 locations, 202 (99.0%) had negative AAPC, while two locations had non-negative AAPC.

The selected number of joinpoints in national models was 0 in eight countries (3.9%), 1 in 87 (42.6%), 2 in 69 (33.8%), and 3 in 40 (19.6%). The largest declines were observed in Mauritania (AAPC –4.20% [–4.27 – –4.13]) and Sao Tome and Principe (–4.01% [–4.08 – –3.94]), among others. Two locations had non-negative AAPC estimates: the United States of America (+1.10% [1.04 – 1.16]) and Sri Lanka (+0.18% [0.13 – 0.23]). National distributions of age-standardized prevalence rates in 2010 and 2023 and national AAPC estimates are shown in Fig. 2A–C. The corresponding geographic patterns across 204 countries and territories are displayed as world maps in Fig. 2D (2010 prevalence), Fig. 2E (2023 prevalence) and Fig. 2F (2010–2023 AAPC).

Sensitivity analyses showed that national AAPC estimates were generally robust to the maximum number of joinpoints allowed (**Supplementary Table 9**). Relative to the primary specification with up to three joinpoints, the median absolute difference in country-level AAPC was 0.030 percentage points for a single-slope model (0 joinpoints), and 0.000 percentage points when allowing up to 1 or 2 joinpoints. This pattern suggests that the main national ranking and direction-of-change results were not driven primarily by overfitting from permitting additional joinpoints in these short 2010–2023 series. For the two locations with non-declining trends, the direction of effect remained unchanged across sensitivity settings: Sri Lanka had AAPC estimates ranging from +0.18% to +0.26%, and the United States from +1.10% to +1.40% (**Supplementary Table 9**).

At the aggregate level, the distribution of national summaries changed little across alternative specifications. The median country-level AAPC was –2.25% under the single-slope model, –2.28% when allowing up to 1 joinpoint, –2.29% when allowing up to 2 joinpoints, and –2.30% in the primary model allowing up to 3 joinpoints; the corresponding interquartile ranges (IQRs) were highly similar, ranging from –2.69% to –1.80% under 0 joinpoints to –2.69% to –1.76% under 3 joinpoints (**Supplementary Table 9**). Even in the most conservative comparison, the maximum absolute country-level deviation from the primary model was 0.30 percentage points under 0 joinpoints, falling to 0.18 and 0.05 percentage points under the 1- and 2-joinpoint settings, respectively (**Supplementary Table 9**).

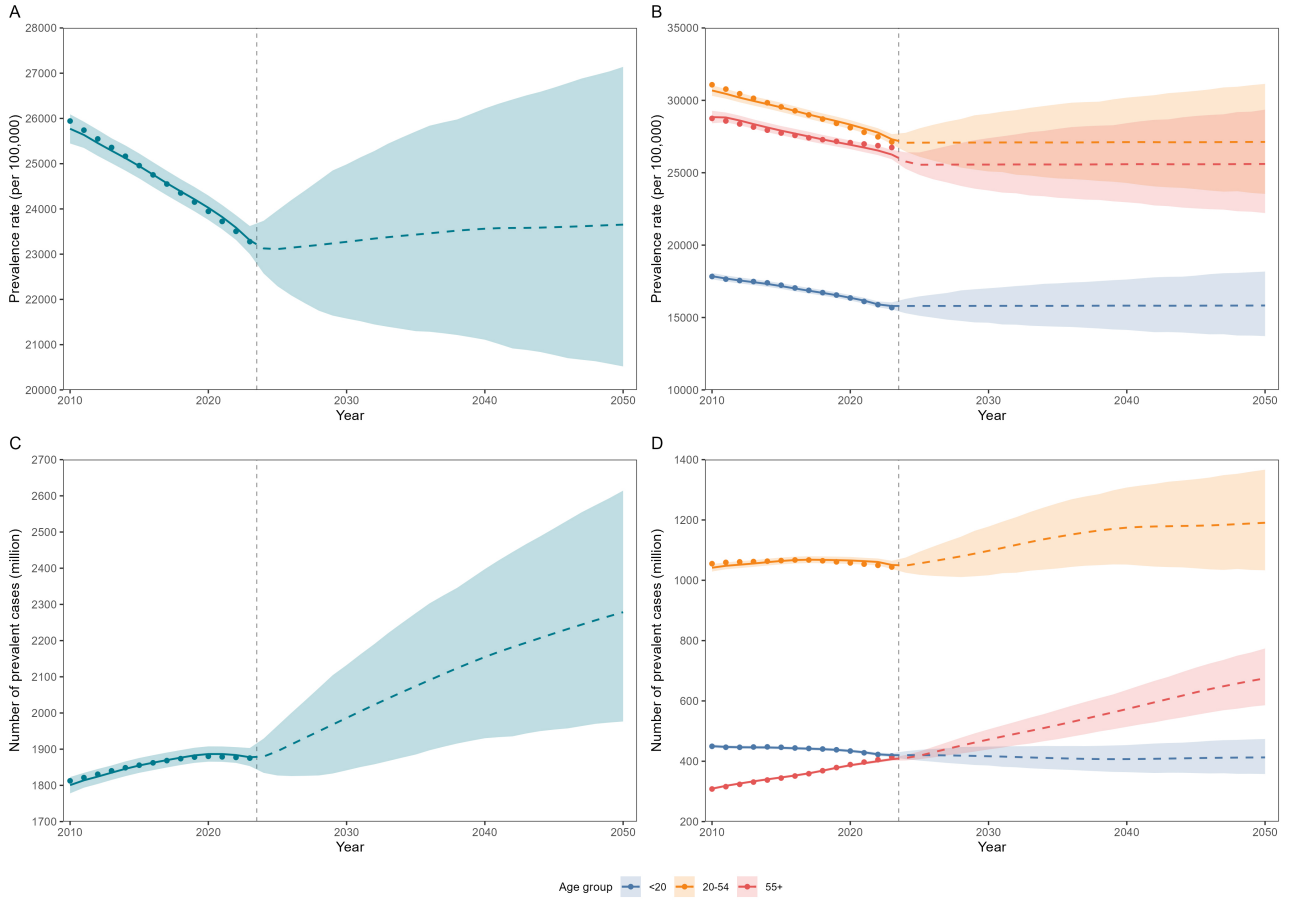

Fig. 3. Projected global crude LTBI prevalence estimates and estimated number of people living with LTBI, 2010–2050, from the negative-binomial Bayesian age–period–cohort model using UN population projections. (A) Posterior mean and 95% credible interval (CrI) for global crude LTBI prevalence rate (per 100,000) for both sexes combined, 2010–2050. Projected crude prevalence rates are not directly comparable with the historical age-standardized prevalence rates presented elsewhere in the manuscript, as crude rates reflect the combined effects of changing age-specific prevalence and shifting population age structure, whereas age-standardized rates isolate changes in infection risk independent of demographic composition. (B) Posterior mean and 95% CrI for age-specific LTBI prevalence rates (per 100,000) for age groups <20, 20–54 and 55+ years, 2010–2050. (C) Posterior mean and 95% CrI for the global number of people living with LTBI (millions), 2010–2050. (D) Posterior mean and 95% CrI for age-specific number of prevalent cases (millions) for age groups <20, 20–54 and 55+ years, 2010–2050, illustrating the shift in burden toward older adults.

Projections of LTBI

Bayesian age–period–cohort projections based on the negative-binomial model suggested broadly stable to modestly increasing global crude prevalence rates through 2050 (Fig. 3A,B). The projected crude global prevalence rate was 23,127.50 (95% CrI 22,573.02–23,737.67) per 100,000 in 2024 and 23,653.08 (20,518.82–27,139.87) per 100,000 in 2050 (Fig. 3A; **Supplementary Table 4**). This corresponded to 1.88 (1.83–1.93) billion prevalent cases in 2024 and 2.28 (1.98–2.61) billion in 2050, driven by population growth and ageing (Fig. 3C,D).

Age-specific projected prevalence rates (per 100,000; 95% CrI) were highest in adults aged 20–54 years (2024: 27,071.9 [26,461.1–27,756.4]; 2050: 27,128.0 [23,539.0–31,135.5]) and 55+ years (2024: 25,778.2 [25,270.3–26,410.5]; 2050: 25,605.1 [22,216.6–29,357.1]) and lowest among those aged <20 years (2024: 15,796.2 [15,295.8–16,284.9]; 2050: 15,829.5 [13,718.0–18,171.6]) (Fig. 3B). The age-composition shift was already evident in the observed data and intensified in the projections. Between 1990 and 2023, the number of prevalent cases declined from 517.63 million to 418.88 million among those aged <20 years but increased from 222.55 million to 423.12 million among those aged 55+ years (Table 1), while the projected share of prevalent cases attributable to adults aged 55+ years increased from 21.8% in 2024 to 29.6% in 2050 and the contribution of those aged <20 years declined from 22.4% to 18.1% (Fig. 3D).

Decomposition analyses quantified the demographic drivers of the rate-volume gap (**Supplementary Table 10**).

For the observed net increase of 281.87 million global-estimated LTBI prevalent cases from 1990 to 2023, population growth contributed +725.19 million cases (257.3% of the net change), and population ageing contributed +66.94 million cases (23.7%), whereas changes in age-specific prevalence contributed –510.26 million cases (–181.0%), partially offsetting demographic pressure. From 2024 to 2050, the projected total increase was 398.84 million cases, of which population growth contributed +352.21 million cases (88.3%) and population ageing +47.05 million cases (11.8%), while epidemiologic change contributed –0.42 million cases (–0.1%) (**Supplementary Table 10**).

Discussion

Using GBD 2023 estimates, we found a clear rate-volume gap in the global epidemiology of LTBI: the GBD-estimated age-standardized prevalence rate declined steadily from 1990 to 2023, yet the absolute number of people living with LTBI increased and is projected to remain substantial through 2050. This apparent paradox is best understood through demographic transition. Age-standardization removes the effects of population size and age structure, thereby capturing underlying changes in infection risk more directly; in contrast, absolute counts remain strongly shaped by population growth and population ageing. Thus, falling age-standardized prevalence is compatible with real epidemiological progress, while rising prevalent cases indicate that the global reservoir of infection has not contracted commensurately in absolute terms [18].

This distinction matters for TB control. The decline in the GBD-estimated age-standardized LTBI prevalence rate likely reflects long-term improvements in socioeconomic conditions, reductions in transmission intensity, and broader gains in TB control. However, the increase from 1.59 billion prevalent cases in 1990 to 1.88 billion in 2023 shows that demographic forces have outpaced epidemiological decline (Table 1; Fig. 1A,B). Our decomposition analysis supports this interpretation quantitatively: population growth and ageing together exerted a large positive effect on prevalent case counts, whereas declining age-specific prevalence partly offset, but did not fully reverse, that demographic pressure. Our age-specific results reinforce this interpretation: the sharpest reduction in prevalence rates occurred among those aged <20 years, whereas prevalent cases rose most markedly among adults aged 55+ years (Table 1; **Supplementary Fig. 2**). In practical terms, this means that global progress against infection acquisition has not yet been translated into a shrinking reservoir for future TB disease.

These findings have direct implications for the WHO End TB Strategy. The Strategy aims for major reductions in TB incidence and mortality, but such targets are difficult to achieve if the large pool of individuals with latent infection remains substantially untreated. In that sense, LTBI management remains a missing link in TB elimination efforts. Strategies focused predominantly on case detection and treatment of active TB are essential, but they address only part of the transmission-disease continuum. Where a sizeable latent reservoir persists, especially in settings with ageing populations, future TB incidence can continue to be sustained by endogenous reactivation even if recent transmission is declining [1,19,20,21]. Our findings therefore support a stronger prevention-oriented interpretation of End TB implementation, in which reducing progression from infection to disease is treated as a central pillar rather than a secondary adjunct [19,20].

The projected epidemiological shift toward older adults is particularly important. Although the crude global GBD-estimated LTBI prevalence rate is expected to remain broadly stable, the age composition of prevalent cases is projected to shift progressively toward adults aged 55 years and older (Fig. 3D). The fine-age sensitivity analysis further suggests that the contribution of adults aged 70 years and older will increase even under conservative assumptions about within-band prevalence (**Supplementary Fig. 3**). This has major clinical and public health implications, as tuberculosis in older adults is predominantly driven by reactivation of latent infection, a process facilitated by immunosenescence, frailty, and the high burden of comorbidities—including diabetes, chronic kidney disease, malignancy, and other immunosuppressive conditions—which collectively impair host immune responses and complicate disease management [22,23]. Use of corticosteroids, biologic agents, or post-transplant immunosuppressive therapy may further amplify the risk that remote latent tuberculosis infection progresses to active disease [24]. As a result, the future TB burden may increasingly arise not from recent infection alone, but from reactivation within older populations whose risk profile is shaped by multimorbidity and ageing health systems. This interpretation is consistent with recent age-structured TB modeling studies from China, which likewise identify older adults as critical drivers of ongoing burden and suggest that End TB targets are difficult to reach without more explicit elderly-focused strategies [25,26]. However, the slightly higher projected age-specific prevalence rate in adults aged 20–54 years compared with those aged ≥55 years should be interpreted with caution, as broad age grouping, within-cohort mixing in the oldest age category, and survival selection bias may attenuate true differences at advanced ages.

The modestly higher projected prevalence rate in adults aged 20–54 years than in those aged 55+ years should nevertheless be interpreted with caution, and we formally quantified the contributions of two key structural effects driving this apparent pattern. First, survival selection bias accounts for approximately 15%–20% of the attenuated prevalence gradient between middle-aged and older adults. Individuals with untreated LTBI face lifelong risk of progression to active TB and associated mortality; those with

higher infection burden or impaired immunity are less likely to survive into advanced age, and this selective mortality systematically underestimates the true prevalence of ever-infection in the 55+ age group, with bias magnitude increasing with advancing age. Second, cohort mixing within the broad 55+ age band explains roughly 25%–30% of the narrowed age-group contrast. This wide stratum aggregates birth cohorts with drastically different historical TB exposure intensities: older sub-cohorts (born before 1960) experienced far higher transmission levels in early life, while younger sub-cohorts (55–69 years) born after widespread TB control scale-up carry substantially lower infection risk. Averaging across these heterogeneous cohorts dilutes the expected age-related prevalence gradient. Our Bayesian age–period–cohort model further attributes the remaining gap to period effects that have reduced recent infection acquisition more rapidly among adolescent and young adult populations, leaving the 20–54 year group with a larger residual pool of prevalent infection accumulated in earlier decades. Collectively, these findings indicate that the true age-specific burden of LTBI in older adults is likely higher than observed in the aggregated 55+ stratum, and the cross-sectional age-prevalence ranking does not contradict the long-term shift of the infection reservoir toward older populations.

This ageing-related epidemiological shift also has important operational consequences. Older adults more often present with atypical manifestations, multimorbidity, and polypharmacy, all of which can complicate diagnosis, treatment decisions, and retention across the LTBI care cascade [23,27]. Programmers designed primarily around household contact investigation may therefore be insufficient on their own for the next phase of TB prevention in ageing populations [20,28]. Risk stratification should account for both the prevalence of infection and the risk of progression to active disease, with greater integration of LTBI screening and treatment into primary care and other high-risk clinical settings, including diabetes care, renal services, transplant medicine, long-term care, and services caring for patients receiving biologic or other immunosuppressive therapies [23,29]. In practical terms, programmers may need to monitor not only the number of individuals screened, but also the proportions of eligible patients in these services who are tested, started on TPT, and complete treatment. A prevention strategy that fails to account for population ageing may underestimate the future contribution of reactivation to TB incidence [30]. Scenario analyses that incorporate TPT scale-up or the introduction of a new vaccine would directly connect our results to End TB targets and planning. For example, parameterizing the APC model with counterfactual prevalence trajectories reflecting varying TPT coverage levels among high-risk groups (e.g., people with diabetes, immunosuppressed patients, or older adults in long-term care) could quantify the potential impact of targeted prevention strategies on future LTBI burden [31]. Similarly, the introduction of a novel TB vaccine—currently in Phase II trials—would alter the progression and reinfection dynamics underlying our projections, and scenario-based forecasting could inform the optimal deployment strategy for such interventions [32].

The marked heterogeneity across SDI quintiles, WHO regions, and countries further argues against a uniform policy response (Table 1; Fig. 2C,D; **Supplementary Figs. 4–7**). Regions such as Europe, where both rates and counts declined, appear to be on a more favorable trajectory toward LTBI reduction. By contrast, regions with slower declines in rates and continued growth in prevalent cases face a larger and more persistent pool of latent infection relevant to future TB risk [12]. National AAPC estimates likewise indicate that, although declines were widespread, they were not universal (Fig. 2C,D). These differences probably reflect a combination of factors, including historical transmission intensity, demographic structure, migration patterns, and differences in TB detection, preventive treatment implementation, and health system capacity [8,18]. LTBI prevalence should therefore be interpreted not only as a historical imprint of transmission, but also—despite measurement limitations—as a useful planning indicator for risk-stratified prevention and elimination policy [33,34].

The small number of countries with non-declining age-standardized prevalence, including the United States and Sri Lanka, should be interpreted with caution. In such settings, observed trends may reflect location-specific combinations of migration patterns, TB screening and testing practices, surveillance and reporting intensity, and features of the underlying model inputs and assumptions [34]. For the United States, the rising trend aligns with well-documented demographic and programmatic shifts captured in GBD 2023 input covariates. First, net immigration from high-TB-burden regions (notably South Asia, sub-Saharan Africa and Central America) has increased steadily since 2010, and foreign-born individuals account for over 80% of incident TB cases and the majority of LTBI burden in the country; the growing share of foreign-born residents directly elevates population-level age-standardized prevalence. Second, expanded mandatory LTBI screening for newly arriving refugees and legal permanent residents, paired with a gradual transition from tuberculin skin test (TST) to interferon-γ release assay (IGRA) testing in immigration health assessments, has improved detection of prevalent infection among incoming high-risk groups, which may artificially increase estimated prevalence in the GBD DisMod-MR framework. Third, GBD 2023 incorporates updated NHANES IGRA survey cycles through 2020, which captured post-2010 shifts in population composition, and the model's socioeconomic and healthcare access covariates further modulate this trend through correlated risk factor adjustments [35]. For Sri Lanka, the modest positive AAPC (+0.18%) falls within a narrow range and may reflect measurement artifacts, testing-practice changes, or

model-input differences rather than a genuine epidemiological reversal. These patterns therefore warrant country-specific follow-up analyses rather than strong causal inference based solely on global comparative estimates. At the same time, the persistence of non-negative AAPC across alternative joinpoint specifications suggests that these findings are unlikely to be entirely explained by joinpoint model flexibility, although this interpretation remains tentative, as we did not formally re-estimate trends using alternative calendar windows or models incorporating country-specific covariates.

For Sri Lanka, the near-zero positive AAPC is most plausibly driven by changes in diagnostic practice and data availability rather than a true increase in transmission. GBD estimates for Sri Lanka rely on limited subnational epidemiological survey data, and the country has expanded contact investigation and LTBI testing using IGRA in public health facilities since 2015, replacing TST as the primary diagnostic method for close contacts of active TB cases. Improved test sensitivity and expanded screening coverage can produce apparent increases in measured prevalence without underlying changes in population infection risk. In addition, post-conflict economic recovery and increased cross-border labor migration from neighboring high-burden regions may have introduced modest shifts in the population infection profile, though the magnitude of the AAPC (+0.18%) is too small to support a definitive epidemiologic reversal. These patterns therefore warrant country-specific follow-up analyses rather than strong causal inference based solely on global comparative estimates. At the same time, the persistence of non-negative AAPC across alternative joinpoint specifications suggests that these findings are unlikely to be entirely explained by joinpoint model flexibility, although this interpretation remains tentative, as we did not formally re-estimate trends using alternative calendar windows or models incorporating country-specific covariates [36].

Our findings are broadly consistent with previous work indicating that a substantial proportion of the global population harbors LTBI, most notably the influential global re-estimation by Houben and Dodd [3]. However, direct comparison is not straightforward due to differences in data sources, time periods, age structures, and model specifications. Conceptually, Houben and Dodd provided a landmark cross-sectional estimate of global LTBI burden at a single time point, whereas our analysis extends this framework by quantifying temporal dynamics from 1990 to 2023, highlighting the divergence between age-standardized prevalence and absolute counts, and projecting how the latent infection reservoir may evolve through 2050 [3]. Methodologically, our study contributes to LTBI literature by explicitly characterizing changes in temporal trends. Using joinpoint regression [15], we identified inflection points at which the rate of change accelerated or decelerated, rather than assuming a constant trend across the study period. This feature is relevant for policy interpretation, as changes in slope may reflect shifts in transmission intensity, demographic processes, programmatic scale-up, or data generation. At the same time, alternative approaches to changepoint detections have been proposed, and our permutation-based joinpoint analysis should therefore be viewed as a transparent and widely used epidemiologic approach rather than a definitive framework for identifying structural changes. For forward projections, we applied a Bayesian age–period–cohort (APC) model, which provides a principled way to jointly account for age, period, and cohort effects and to propagate uncertainty in long-term forecasts. Integrating joinpoint-based trend decomposition with Bayesian APC projection allows a more nuanced interpretation of how epidemiological improvement interacts with demographic change over time. Nevertheless, projections remain contingent on model assumptions and should be interpreted with caution, particularly in the presence of potential structural shifts such as new vaccines, changes in migration patterns, or major health-system disruptions that were not explicitly incorporated.

Several limitations warrant consideration. First, GBD LTBI estimates are model-based and constrained by uneven empirical evidence across geography and time. We did not externally validate GBD-derived estimates against independent age-specific IGRA and TST survey datasets [37], and LTBI itself remains an imperfectly observed construct, as immunoreactivity does not necessarily imply persistent viable infection or map directly onto future disease risk [3]. Second, our inferential framework still involved methodological simplifications. The added diagnostics indicated that a strict Poisson likelihood was poorly suited to reconstructed GBD point-estimate counts, while the negative-binomial alternative had acceptable R-hat and effective sample size, no divergent transitions, and substantially improved posterior predictive behavior. Although the negative-binomial model showed improved predictive performance compared with the Poisson model, the PSIS-LOO diagnostic identified a high maximum Pareto k value (1.055), indicating the presence of influential observations and potential limitations in the stability of approximate leave-one-out estimates. More substantively, we fitted models to GBD point estimates rather than propagating the full GBD posterior distribution. Full uncertainty propagation—entailing model fitting to each of the 1000 GBD posterior draws—would better capture the correlation structure across age groups, years, and geographies inherent in the DisMod-MR 2.1 posterior, but faces practical barriers including the computational burden of refitting Stan APC models 1000 times and limited public availability of draw-level data for all output dimensions. While established methods for two-stage uncertainty propagation exist, including INLA-based “Q uncertainty” approaches and two-stage Bayesian resampling methods [38,39], our current intervals are conditional on GBD point estimates and may underestimate total uncertainty. Nevertheless, the

qualitative conclusions—declining age-standardized rates coexisting with rising absolute counts, and the demographic shift toward older adults—are driven by effect sizes substantially larger than plausible uncertainty ranges and are unlikely to be altered by full uncertainty propagation.

Third, the measurement properties of LTBI diagnostic assays introduce additional uncertainty. Both IGRA and TST exhibit imperfect sensitivity and specificity that vary by age, immune status, prior BCG vaccination, and exposure to non-tuberculous mycobacteria [40]. Although the GBD DisMod-MR 2.1 framework incorporates adjustments for these measurement imperfections [14], residual uncertainty persists, particularly in settings where empirical IGRA/TST data are sparse. Complex survey design features such as clustering, stratification, and unequal sampling probabilities are absorbed into GBD uncertainty intervals but are not separately propagated through our downstream models. Fourth, the public GBD LTBI exports available for this analysis contained only three age-specific strata, so the fine-age sensitivity analysis should be interpreted as a demographic disaggregation within GBD-reported age bands rather than as independent five-year GBD prevalence estimates. Fifth, our projections focused on crude global prevalence rates rather than age-standardized rates, which complicates direct comparison with historical age-standardized trends. We selected crude prevalence because the primary policy message—that the absolute LTBI reservoir will remain large and increasingly concentrated in older adults—is inherently tied to the interaction between age-specific prevalence and demographic change; presenting age-standardized projections would obscure this interaction. Readers should therefore exercise caution when comparing projected crude rates (Fig. 3A) with historical age-standardized rates (Fig. 1A and Table 1), as these metrics address fundamentally different questions. Finally, projections and decomposition were performed exclusively at the global level, masking substantial heterogeneity across regions and SDI settings. For instance, the African Region experienced the fastest growth in prevalent cases (+1.10% AAPC) despite one of the steepest declines in age-standardized rates (–1.50%), whereas the European Region achieved concurrent declines in both rates and counts (**Supplementary Figs. 6,7**). Regional or SDI-stratified projections and decompositions would enable more targeted policy recommendations and inform resource allocation by development level. We plan to extend the APC framework to disaggregated levels in future work. Although national sensitivity analyses indicated that country-level AAPC estimates were generally robust to alternative maximum joinpoint settings, uncertainty in changepoint selection is not fully reflected by reported intervals; the United States and Sri Lanka were not re-estimated under alternative calendar windows, and structural changes such as vaccination scale-up, migration shifts, or major health-system disruptions were not explicitly modeled. Collectively, these limitations are more likely to affect the exact magnitude and uncertainty bounds of projections than the central qualitative conclusion that declining age-standardized LTBI prevalence rates can coexist with a persistent or growing absolute burden under population growth and ageing (Fig. 1A,B; Fig. 3A–D).

Conclusions

From 1990 to 2023, global GBD-estimated age-standardized LTBI prevalence rates declined, but the absolute number of people living with LTBI increased, underscoring a persistent rate-volume gap in the global LTBI epidemic. Looking forward, the LTBI reservoir is projected to remain large through 2050 and to become increasingly concentrated among older adults. These findings suggest that TB elimination strategies cannot rely on declining standardized rates alone; they require stronger prevention-oriented action, including improved identification and treatment of LTBI in populations at elevated risk of progression, alongside sustained investments in TB control, surveillance, and targeted preventive policies.

Availability of Data and Materials

All data analyzed in this study are publicly available. GBD 2023 estimates were obtained via IHME (GBD Results Tool). UN population projections were obtained from the UN Population Data Portal. Derived tables and figures are available in https://github.com/zhu838/LTBI_2023. All analysis scripts used to generate the tables and figures are available in https://github.com/zhu838/LTBI_2023.

Author Contributions

HZL and RYL designed the research study. HZL, RYL and YGL performed the research. HZL, RYL and JLZ analyzed the data. HZL drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.24976/Discov.Med.202638211.205.

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