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Clustering and modeling joint-trajectories of HIV/AIDS and tuberculosis mortality rates using bayesian multi-process latent growth model: A global study from 1990 to 2021

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Abstract

Background The bidirectional association of HIV/AIDS and Tuberculosis (TB) presents significant global health challenges. However, the relationship between these dual epidemics and the heterogeneity in their mortality rate patterns have not been properly addressed. Therefore, the aim of this study was to cluster and model the joint trajectories of HIV/AIDS and TB mortality rates from 1990 to 2021 worldwide.

Methods In this longitudinal study, the HIV/AIDS and TB mortality rates data for 204 countries from 1990 to 2021 were obtained from the global burden of disease database. The longitudinal k-means clustering approach was utilized to categorize countries into homogeneous subgroups based on the joint patterns of HIV/AIDS and TB mortality rates. Subsequently, the Bayesian multi-process nonlinear Latent Growth Model (LGM) was conducted to concurrently estimate the patterns of HIV/AIDS and TB mortality rates.

Results The average global TB mortality rates dropped from 30.61 to 13.34 per 100,000 between 1990 and 2021. Meanwhile, the average HIV/AIDS mortality rates rose from 10.94 to 48.42 per 100,000 by 2000 before declining to 16.90 per 100,000 in 2021. The Bayesian multi-process nonlinear LGM indicated that the intercepts for the overall HIV/AIDS and TB models were 11.168 and 30.184, and the slopes were 16.104 and − 1.040, respectively. This suggests that the initial HIV/AIDS and TB mortality rates were 11.168 and 30.184 persons per 100,000, and the rates of change were 16.104 and − 1.040 persons per 100,000 every five years. However, the strength and direction of the rate of change were dependent on the factor loading scores, as they exhibited a nonlinear trend. Finally, the 204 countries were clustered into three distinct subgroups, each with different intercepts and slopes. Cluster A demonstrated the lowest HIV/AIDS and TB mortality rates throughout the study, while Cluster C exhibited the highest mortality rates.

Conclusions Although the overall global HIV/AIDS and TB mortality rates have declined, Southern African countries continue to bear a significant burden of HIV/AIDS and TB, with no significant reduction observed in TB mortality rates from 1990 to 2021. Therefore, prioritizing these countries is crucial to achieving the Sustainable Development Goals (SDGs) of eradicating the global HIV/AIDS and TB epidemics by 2030 and 2035, respectively.

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Keywords Multi-process latent growth model, Clustering, Heterogeneity, Human immunodeficiency virus (HIV), Tuberculosis (TB)

Introduction

The bidirectional association of Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) is widely acknowledged to be close and complex, as both diseases have the ability to affect each other's natural progression [1]. These two diseases form a lethal combination that mutually accelerates the progression of each other [2]. HIV progressively weakens the immune system by targeting CD4 T-cells, rendering individuals more vulnerable to TB infection, and TB has been associated with an elevated HIV viral load, potentially expediting HIV replication and hastening the progression of HIV [3–5].

The cooperative link between the dual epidemics of TB and HIV poses significant worldwide health challenges [6]. In 2022, the World Health Organization (WHO) reported that around 39 million individuals were living with HIV. During the same year, 1.3 million people became newly infected with the virus, and there were 630,000 deaths attributed to HIV-related causes [7]. On the other hand, in 2022, there were approximately 10.6 million worldwide cases of TB. Among these cases, 6.7% were TB/HIV co-infected cases, indicating a 4.5% increase from the previous year's estimates of 10.1 million, which reversed several years of slow decline [8]. In 2022, the number of deaths attributed to TB reached 1.3 million individuals [8].

TB is a curable and preventable infectious disease. And yet, it stands as the primary cause of mortality among individuals infected with HIV, contributing to approximately one-third of AIDS-related deaths on a global scale [9]. In the absence of proper medical care, nearly half of HIV-negative individuals with TB and almost all HIV-positive individuals with TB will die [10]. Although antiretroviral treatment (ART) has contributed to a reduction in AIDS-related deaths, access to therapy is not universally available, and the outlook for curative treatments and an effective vaccine remains uncertain [11]. However, with improved access to HIV diagnosis, appropriate medical interventions, and supportive care, including the management of opportunistic infections, HIV infection has become a manageable chronic condition [7]. The intersection of HIV and TB within the framework of the Sustainable Development Goals (SDGs) highlights the urgent need for integrated health strategies [12, 13]. Achieving SDG 3.3, which aims to end epidemics of communicable diseases by 2030, necessitates a multifaceted approach to address the dual burden of HIV and TB [12, 13].

While overall mortality rates have declined, disparities persist across different regions. In a meta-analysis, it was found that 53% (95% CI: 45–61%) of excess mortality was AIDS-related, with 52% (43–60%) in Western and Central Europe and North America, and 71% (69–74%) in the Asia-Pacific region [14]. On the other hand, despite the reduction in TB notifications in Southern Africa, TB-related fatalities continue to remain high [15]. For instance, in Eswatini, TB-related deaths reduced significantly from 174 to 27 per 100,000 individuals between 2009 and 2017, largely due to improved access to treatment [15]. Nevertheless, the treatment case fatality ratio remained above 10%, highlighting persistent risks during therapy [15]. In regions like Eastern Europe, significant progress has been made, with several countries achieving a 35% reduction in TB deaths [16]. To effectively manage and control the burden of TB and HIV, it is imperative to gain a comprehensive understanding of the disparities in their patterns over time. Analyzing the historical trends and studying the mortality patterns of TB and HIV is crucial. By examining how these diseases have spread and evolved over time, public health experts can identify high-risk areas, demographic groups, and social factors contributing to their prevalence. This analytical approach enables the development of evidence-based policies and programs tailored to specific communities, ensuring that resources are allocated efficiently and effectively.

Several statistical approaches can be employed to estimate the patterns of HIV and TB mortality rates. Some studies employed the join-point regression model, age-period-cohort model, and negative binomial regression model to investigate the burdens associated with HIV and TB [17–19]. However, these statistical methods are unable to account for the interdependency among multiple outcomes and are limited in addressing the heterogeneity in longitudinal studies. Latent Growth Model (LGM) is a powerful longitudinal approach based on structural equation modeling (SEM) that utilizes two latent factors, intercept and slope, to estimate the growth trajectory of an outcome during a specific period of time [20]. The LGM is increasingly being utilized in public health research to analyze changes in health outcomes over time, providing insights into the dynamics of health interventions and their effectiveness [20]. For instance, Wang et al. explored familial factors affecting cognitive decline, using LGM to illustrate how depression mediates the relationship between family dynamics and cognitive health [21]. Kabongo and Mbonigaba employed an LGM to assess how domestic health spending impacts population health outcomes in Sub-Saharan Africa, revealing that factors like malaria and female education mediate these effects [22]. Seddig's work on

count outcomes demonstrates the versatility of LGMs in analyzing frequency data, such as healthcare utilization, which is vital for understanding public health behaviors [23]. While LGM provides a robust framework for understanding health dynamics, it is limited to estimating the trend of only a single outcome over a period of time. Nevertheless, HIV and TB are two outcome variables whose growth trajectories are correlated with each other. Multi-process LGM is an extension of the LGM designed to estimate the growth trajectories of multiple correlated outcomes simultaneously. However, this approach estimates the overall trends and cannot capture the possible heterogeneity in the patterns of multiple outcomes. Ignoring the potential variability in the growth trajectory may lead to misleading results. A common method for analyzing longitudinal data is to cluster samples into distinct subgroups with homogeneous patterns and subsequently estimate growth trajectories within each subgroup. Reducing heterogeneity in longitudinal data can help obtain more accurate and robust estimates, leading to a better understanding of the underlying trends and relationships within the data [20]. Furthermore, clustering is a valuable technique that aids in understanding the similarities within subgroups and the distinctions between different subgroups. When similar samples are clustered together, researchers can identify latent trends or relationships that might not be evident when analyzing the data comprehensively. Moreover, by identifying distinct clusters, researchers can uncover differences in behavior, attributes, or patterns between various groups within the dataset [20]. Longitudinal k-means clustering for joint trajectories is a non-parametric and non-model-based approach that can cluster samples based on their growth trajectories of multiple response variables [24]. Hence, prior to modeling, the longitudinal k-means clustering approach can be utilized to categorize the entire sample into homogeneous subgroups based on their growth patterns. Due to the complexity of the multi-process LGM and the limitations of the sample size, the Maximum Likelihood Ratio (MLR) estimator may fail to converge. To address this issue, the Bayesian approach can be employed.

In our literature review, we did not find any study that simultaneously estimated the global growth trajectories of HIV/AIDS and TB while considering the heterogeneity among countries and territories. Therefore, the objective of this study was to cluster and model the concurrent worldwide patterns of HIV/AIDS and TB mortality rates from 1990 to 2021 using longitudinal k-means and Bayesian multi-process LGM. The findings of this study may help to improve our understanding of the growth trajectories in HIV/AIDS and TB mortality rates. Additionally, categorizing countries based on their patterns can provide valuable insights into the importance of implementing strategies for groups of countries that not only reduce mortality rates but also contribute to achieving the Sustainable Development Goals (SDGs).

Methods

In this longitudinal study, the global mortality rates of HIV/AIDS and TB in 1990, 1995, 2000, 2005, 2010, 2015, and 2021 were retrieved from the Global Burden of Disease (GBD) platform [25]. Due to the fact that the patterns of TB and especially HIV/AIDS were nonlinear and required segment-by-segment estimation, for simplicity in interpretation the data was extracted based on every five-year time point. The GBD is the most comprehensive platform that provides mortality and other measurements for almost all major diseases and injuries globally, regionally, and nationally. In this study, the total number of deaths and mortality rates per 100,000 population for HIV/AIDS and TB were obtained from the GBD database (https://vizhub.healthdata.org/gbd-results) for 204 countries and territories. Although the total number of deaths for TB and HIV/AIDS was reported, the main outcome considered in the statistical analysis was the mortality rate per 100,000 population.

The statistical analysis was initiated by conducting a Bayesian multi-process nonlinear LGM to estimate the overall mortality rate patterns of HIV/AIDS and TB simultaneously. The utilization of the multi-process nonlinear LGM model stemmed from its capacity to concurrently assess the growth trajectories of two interrelated outcomes [20]. Moreover, by treating the factor loadings on the slopes as free time scores, the model can effectively capture both linear and nonlinear patterns across different outcomes concurrently [20]. The conceptual diagram of the multi-process nonlinear LGM with seven time-point repeated measures is illustrated in Fig. 1.

In Fig. 1, the rectangles in the HIV/AIDS trajectory part illustrate the growth process of HIV/AIDS mortality rates, while the rectangles in the TB trajectory part represent the growth process of TB mortality rates from 1990 to 2021. The oval shapes in Fig. 1 represent the latent intercepts and slopes. These growth factors indicate the initial amount of the outcome variables (latent intercepts) and the rate of change of the outcome variables over time (latent slopes) [20]. The covariances between latent factors are represented by two-sided arrows in Fig. 1. The covariance between the intercept and slope reveals the association between the initial level of the outcome and the rate of outcome change. Furthermore, the covariance between the latent intercepts of the two growth trajectories provides information about the association between the two outcomes at the beginning of the study time. Additionally, the covariance between the latent slopes indicates the association between the rates of change in the two outcomes [20]. In this study, for

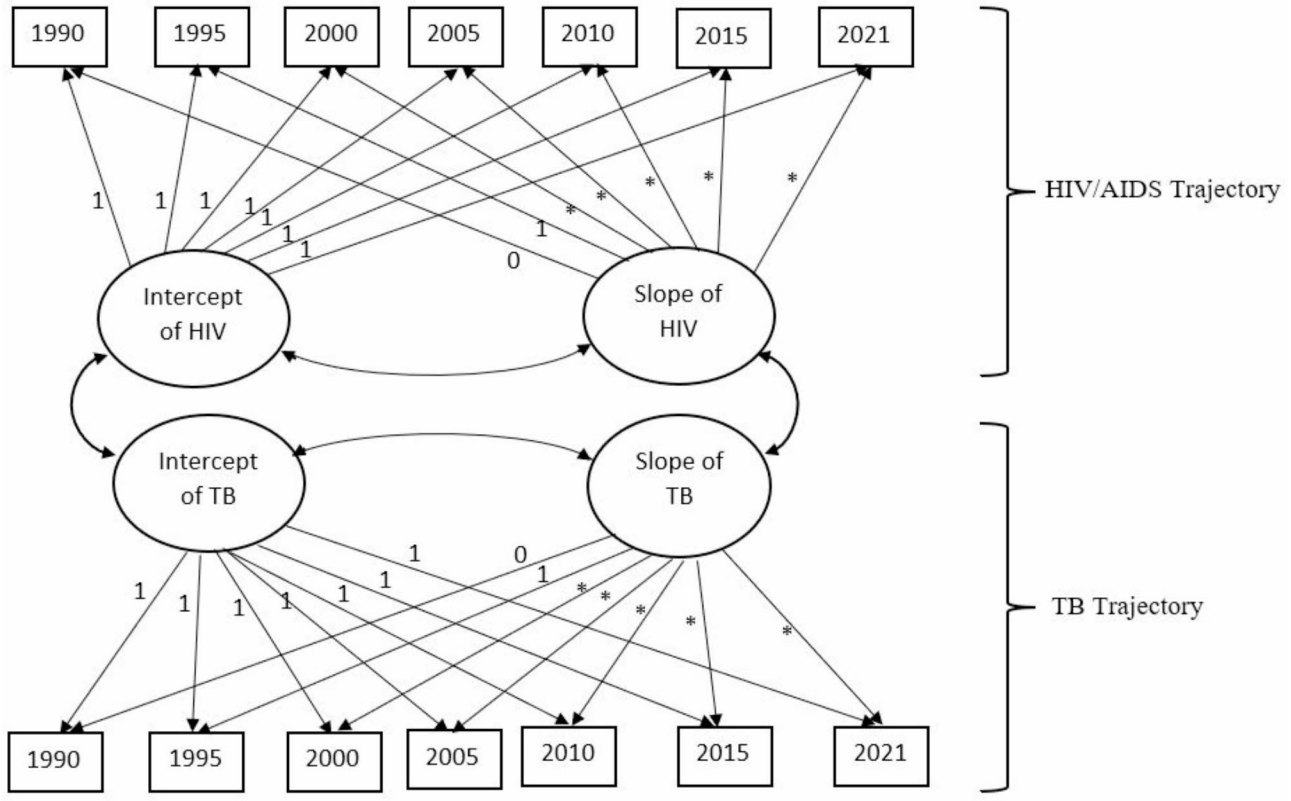

Fig. 1 The conceptual diagram of the parallel-process Latent Growth Model (LGM)

simplicity of interpretation, the standardized covariances (or correlations) were reported instead of regular covariances. As we can see in Fig. 1, the factor loadings on the intercept are fixed at 1.0 to estimate the initial level of the outcome variable, while the factor loadings on the slope determine the shape of the growth process. If the factor loadings have equal distances, the growth process is linear; otherwise, it is non-linear [20]. In this study, both the TB and HIV/AIDS mortality rates demonstrated a non-linear growth process. Therefore, the factor loadings on the slope are treated as free time scores, with the first two-time scores fixed at 0 and 1 for the model identification, and the remaining factor loadings estimated based on the data. In the free time score approach, the slope of each segment or time interval in the model depends on the estimated factor loadings, which can result in different slopes for each segment. The multi-process LGM detailed in Eq. (1).

$$\begin{aligned} y_{ti}^{m} &= \eta_{0i}^{y_m} + \lambda_{t}^{y_m} \eta_{1i}^{y_m} + \epsilon_{ti}^{y_m} \\ \eta_{0i}^{y_m} &= \eta_{0}^{y_m} + \zeta_{0i}^{y_m} \\ \eta_{1i}^{y_m} &= \eta_{1}^{y_m} + \zeta_{1i}^{y_m} \end{aligned} \tag{1}$$

In Eq. (1), y_{ti}^{m} represents the ith observed outcome measure at time point t for the mth outcome measure. $\lambda_{t}^{y_m}$ denotes the factor loadings, which determine the shape of the growth process as linear or nonlinear. $\epsilon_{ti}^{y_m}$ stands for the error term at time t, while $\eta_{0i}^{y_m}$ and $\eta_{1i}^{y_m}$ signify the random intercepts and slopes for the mth outcome growth process. The latent growth factors $\eta_{0}^{y_m}$ and $\eta_{1}^{y_m}$ are the model estimated overall mean level of the initial outcome and the average rate of outcome change over time, respectively. additionally, $\zeta_{0i}^{y_m}$ and $\zeta_{1i}^{y_m}$ stands for residuals in the model [20].

In the next step, the longitudinal k-means clustering approach was used to categorize 204 countries and territories based on the HIV/AIDS and TB mortality rate patterns. Longitudinal k-means clustering for joint trajectories is a non-parametric and non-model-based approach that can cluster samples based on their growth trajectories of multiple response variables [24]. In k-means clustering, the fundamental assumption is that clusters are homogeneous, meaning that each cluster is characterized by a central point called the centroid. This centroid represents the average position of all the data points within that cluster. When new data points are assigned to clusters, their membership is determined based on their proximity to the nearest centroid. This proximity is calculated using a distance metric and the data point is assigned to the cluster whose centroid is closest to it. This process of assigning data points to clusters based on the nearest centroid is what defines

the k-means clustering algorithm [26]. In this study, the HIV/AIDS and TB mortality rates are two longitudinal variables that are jointly associated with each other. This k-means clustering method is designed specifically for longitudinal data to cluster multiple variable trajectories over a specific period of time [24]. The Calinski-Harabasz criterion was used to establish the ideal number of clusters. This metric assesses the proximity of an object to its specific cluster (cohesion) in comparison to other clusters (separation). Cohesion is calculated by evaluating the distances from data points within a cluster to its centroid, while separation is determined by the distances between cluster centroids and the global centroid [27]. The highest value of Calinski-Harabasz criterion indicating the ideal number of clusters [24]. Finally, the Bayesian multi-process nonlinear LGM was conducted to estimate the growth patterns of HIV/AIDS and TB mortality rates in each cluster. The Potential Scale Reduction (PSR) criterion was utilized to assess convergence the Bayesian multi-process LGM models. A PSR value less than 1.05 indicated convergence [28]. The longitudinal k-means clustering approach was performed using the kml3d package in R software. Additionally, Mplus 8.3 software was utilized to run Bayesian multi-process LGM, and ArchGIS 10.8 software was used to demonstrate the geographic distribution of worldwide countries based on their cluster membership. It is important to mention that during the preparation of this work, the authors used the ChatGPT AI tool to translate from Persian to English, rewrite sentences, and correct grammar to enhance clarity and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the publication's content.

Table 1 Total number of deaths and average mortality rate of HIV/AIDS and TB from 1990 to 2021

Year	HIV/AIDS		TB	
	Total number of mortalities	Mean (SD)	Total number of mortalities	Mean (SD)
1990	305,945	10.942 (35.276)	1,778,869	30.609 (40.237)
1995	835,480	30.442 (82.930)	1,754,173	28.758 (37.968)
2000	1,369,802	48.417 (130.936)	1,733,573	25.762 (34.345)
2005	1,575,236	48.181 (134.705)	1,612,718	22.543 (31.542)
2010	1,190,883	31.411 (83.287)	1,428,028	18.997 (28.315)
2015	898,290	23.714 (61.396)	1,288,262	16.157 (25.057)
2021	718,079	16.903 (42.142)	1,162,796	13.339 (21.208)

Results

Table 1 presents the total number of global HIV/AIDS and TB mortalities, as well as the mean and Standard Deviation (SD) of HIV/AIDS and TB mortality rates per 100,000 population from 1990 to 2021. The results from Table 1 indicate that the average mortality rates of TB exhibited a decreasing pattern throughout the study period. On the other hand, the average mortality rates of HIV/AIDS displayed a nonlinear pattern. It initially increased from 10.94 persons per 100,000 in 1990 to 48.42 persons per 100,000 in 2000, and subsequently followed a decreasing trend, reaching 16.90 persons per 100,000 in 2021.

As observed in Table 1, there were instances, such as in 2021, where the total number of mortalities for TB exceeded those for HIV/AIDS, while the mean mortality rate for TB was lower than that for HIV/AIDS. This discrepancy can be attributed to the fact that countries with larger populations in East Asia, such as India, Pakistan, and Bangladesh, had higher mortality rates for TB compared to HIV/AIDS. Conversely, countries with smaller populations in Africa, such as Lesotho, Eswatini, and Botswana, exhibited higher mortality rates for HIV/AIDS than TB. It is worth noting that this study focused on the mortality rate per 100,000 rather than the total mortality count.

In the next step, the overall patterns of HIV/AIDS and TB mortality rates were estimated using the Bayesian multi-process LGM, with the PSR achieving 1.046 by iteration 22,900. According to Table 2, the intercepts for the HIV/AIDS and TB models were 11.168 and 30.184, respectively, indicating the number of mortality rates per 100,000 population at the beginning of the study. The interpretation of the intercept is quite straightforward, but the interpretation of the slope depends on the magnitude of the factor loadings. For instance, the slope of HIV/AIDS was 16.104, and the factor loadings for time points 1990 to 2021 were as follows: 0, 1, 2.126, 2.288, 1.212, 0.724, and 0.353, respectively. Therefore, the slope of each segment was calculated as follows: $16.104(1-0) = 16.104$, $16.104(2.126\text{-}1) = 18.133$, $16.104(2.288-2.126) = 2.609$, $16.104(1.212-2.609) = -22.498$, $16.104(0.724-1.212) = -7.859$, and $16.104(0.353-0.724) = -5.974$. The positive slopes in the first three segments indicate an increasing pattern, while the negative slopes indicate a decreasing pattern in the last three segments. The segment slopes of the HIV/AIDS and TB models were calculated and are shown in Table 2. All of the estimated negative slopes for TB in the model indicate a decreasing pattern of TB death rates from 1990 to 2021, with the most significant decrease observed in the segment 2000–2005, with a slope of -3.918. For the HIV/AIDS model, there was a significant correlation coefficient of 0.670 between the slope and intercept, indicating that higher HIV/AIDS mortality

Table 2 The bayesian multi-process LGM of HIV/AIDS and TB mortality rates results

Estimates	Parameter		HIV/AIDS			TB		
			Mean (PSD**)			Mean (PSD)		
Coefficients	Intercept		11.168 (2.224) *			30.184 (2.886) *		
	Slope		16.104 (3.901) *			-1.040 (0.357) *		
Correlations	Slope and Intercept		0.670 (0.068) *			-0.821 (0.024) *		
	Both of the intercepts		0.433 (0.061) *					
	Both of the slopes		-0.166 (0.070) *					
Number of iterations to achieve PSR < 1.05			22,900					
Factor Loadings								
Year		1990	1995	2000	2005	2010	2015	2021
HIV/AIDS	Score	0	1	2.126	2.288	1.212	0.724	0.353
	Slope	---	16.104	18.133	2.609	-22.498	-7.859	-5.974
TB	Score	0	1	4.138	7.906	11.190	13.274	15.016
	Slope	---	-1.040	-3.263	-3.918	-3.415	-2.167	-1.812

* Significant at 0.05 level

** PSD: Posterior Standard Deviation

rates at the beginning are associated with a higher slope, and vice versa. On the other hand, the significant correlation between the slope and intercept of TB was − 0.821, suggesting that higher TB mortality rates in the initial stage are associated with a lower slope. In addition, the correlation between the two intercepts of HIV/AIDS and TB in the model was 0.433, leading to the conclusion that higher mortality rates of either HIV/AIDS or TB at the baseline are associated with higher mortality rates of the other disease at that time. In contrast, the correlation between the two slopes was − 0.166, leading to the conclusion that the steepest trends of either HIV/AIDS or TB are associated with lower trends in mortality rates of the other disease. In other words, this quantity indicated the direction of the two slopes, which were represented based on the factor loading scores. As seen from Table 2, the factor loading scores for HIV/AIDS increased from 1990 to 2000, saw a slight increase from 2000 to 2005, and then its direction decreased from 2005 to 2021. In contrast, the direction of factor loadings for TB was increasing throughout the entire study period. Therefore, the direction of slopes (or we can say the strengths of the changes) was increasing for TB, while it was almost decreasing for HIV/AIDS during the study period.

In the next step, the longitudinal k-means clustering approach was employed to categorize the 204 countries based on the joint trajectories of two outcomes, HIV/AIDS and TB mortality rates, from 1990 to 2021. The Calinski-Harabasz criterion yielded the highest value for three clusters, indicating that the optimal number of clusters was three. Figure 2 shows the mean of HIV/AIDS and TB mortality rates from 1990 to 2021 for each cluster. Cluster A, with 149 countries, had the lowest mortality rates, and Cluster C, with 10 countries, had the highest mortality rates for both HIV/AIDS and TB. The pattern of HIV/AIDS in Cluster C was non-linear. Additionally, Cluster B, with 45 countries, had an almost nonlinear mortality rate trend for HIV/AIDS.

Finally, the Bayesian multi-process nonlinear LGM was employed in each cluster, and the results are reported in Table 3. The convergence (PSR < 1.05) was attained after 11,800 iterations for cluster A, 3200 iterations for cluster B, and 2600 iterations for cluster C. Cluster A had the lowest initial mortality rates for HIV/AIDS and TB. For HIV, the segment's slopes were 1.828 and 0.550 for the periods 1990–1995 and 1995–2000, respectively. However, the segment's slopes for HIV were negative from 2000 to 2021. In terms of TB mortality rates within cluster A, the slopes were negative. The lowest decreasing slope was − 0.475 observed during 1990–1995, while the highest decreasing slope was − 1.205 observed during 2005–2010. Cluster B had a high initial TB mortality rate (intercept = 86.550) and exhibited the steepest decline among all clusters from 1990 to 2021. In contrast, HIV/AIDS mortality rates in Cluster B followed a nonlinear pattern, increasing with slopes of 26.036 and 13.039 during 1990–1995 and 1995–2000, respectively, and then decreasing with slopes of -8.354, -18.270, -12.076, and − 9.864 from 2000 to 2021. Cluster C had the highest initial mortality rates for HIV and TB and the steepest slopes for HIV mortality rates from 1995 to 2021. In contrast, the slopes of TB mortality rates were nearly zero throughout the study period, indicating a constant pattern from 1990 to 2021. Figure 3; Table 4 illustrate the geographic distribution of countries worldwide based on their cluster membership.

Discussion

The overall growth trajectories of HIV/AIDS and TB mortality rates for 204 countries and territories were estimated simultaneously from 1990 to 2021. By utilizing the Bayesian multi-process nonlinear LGM, we were able to

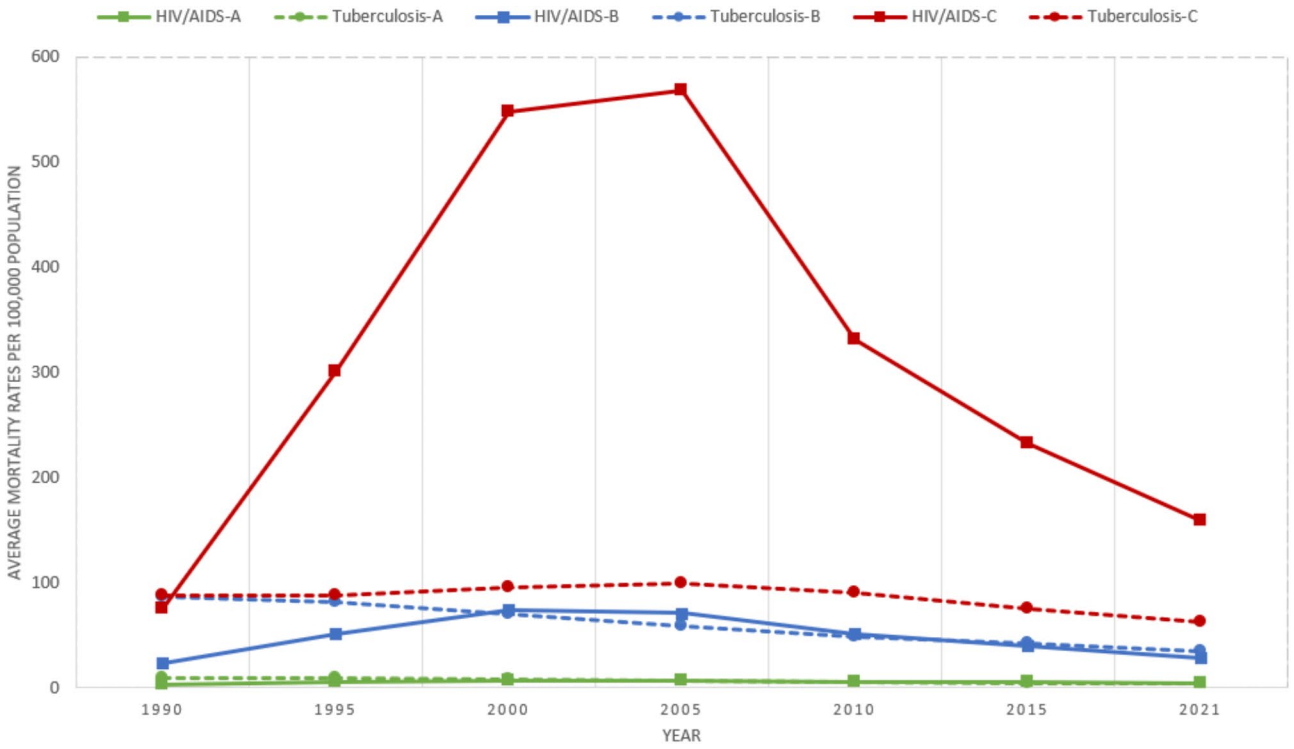

Fig. 2 The mortality rates of HIV/AIDS and TB in each cluster from 1990 to 2021

concurrently estimate the patterns of HIV/AIDS and TB mortality rates in segments with five-year intervals. This approach allowed us to assign a distinct slope to each segment, reflecting the growth trajectories specific to that period. For instance, in Table 2, the segment slopes of HIV/AIDS mortality rates for the 1990–1995 and 1995–2000 intervals were 16.104 and 18.133, respectively. In contrast, the segment slopes of TB mortality rates for the same intervals were – 1.040 and – 3.263, respectively. This indicates that HIV/AIDS mortality rates increased by 16.104 and 18.133 individuals per 100,000 population during the 1990–1995 and 1995–2000 intervals, while TB mortality rates decreased by -1.040 and – 3.263 individuals per 100,000 over the same periods. Based on the results in Table 2, the overall trend of HIV/AIDS mortality rates nonlinearly increased from 1990 to 2005 and then decreased from 2005 to 2021. The highest increasing and decreasing slopes were observed in the segments of 1995–2000 and 2005–2010, respectively. The correlation between slope and intercept was positive for HIV/AIDS, indicating that countries with higher HIV/AIDS mortality rates in 1990 had a higher slope of mortality rates during the study period. In contrast, the overall TB mortality rates exhibited a decreasing slope in all segments, with the steepest decreasing pattern observed in the segment of 2000–2005. The correlation between slope and intercept was negative for TB, indicating that countries with higher TB mortality rates had a lower slope of TB mortality rates from 1990 to 2021. Previous studies have indicated that despite a steady decline in the incidence of HIV since the mid-1990s, HIV-related mortality reached its highest point in 2006 with 1.95 million deaths [29]. However, since then, HIV mortality has progressively decreased, reaching 630,000 deaths worldwide in 2022 [7]. Since the 1990s, the burden of the HIV/AIDS has undergone significant changes due to the implementation of HIV antiretroviral therapy (ART) and other successful interventions [30]. On the other hand, global TB mortality rates have shown a gradual decline over the years, with the World Health Organization reporting in 2017 a 37% decrease since 2000 [31]. Despite this decline, with an estimated 1.6 million deaths in 2021, TB remains a major cause of death, surpassing the number of deaths caused by HIV/AIDS [32]. One of the United Nations objectives outlined in the Sustainable Development Goals (SDGs) is to eradicate the worldwide TB epidemic [33]. In order to achieve this goal, the End TB Strategy has established specific targets concerning TB mortality. These targets include a 35% reduction in TB mortalities by 2020, with the ultimate goal of achieving a 95% reduction by 2035 [33]. Despite the declining global TB mortality rates, it is anticipated that many countries will not be able to meet these targets by 2035 [34]. To identify various groups of countries with effective efforts and programs for the eradication of HIV/AIDS and TB, the longitudinal k-means clustering approach was employed.

Table 3 Bayesian multi-process LGM of HIV/AIDS and TB mortality rates results

Estimates	Parameter	Cluster A		Cluster B		Cluster C	
		n = 149		*n* = 45		*n* = 10	
		HIV/AIDS	TB	HIV/AIDS	TB	HIV/AIDS	TB
		Mean (PSD**)	Mean (PSD)	Mean (PSD)	Mean (PSD)	Mean (PSD)	Mean (PSD)
Coefficients	Intercept	4.959 (0.715) *	8.855 (0.921) *	38.436 (9.401) *	86.550 (5.699) *	67.148 (23.232) *	88.739 (16.376) *
	Slope	1.828 (0.672) *	-0.475 (0.160) *	26.036 (10.104) *	−4.231 (2.462) *	0.760 (0.550) *	0.001 (0.227)
Correlations	Slope and Intercept	0.818 (0.035) *	-0.929 (0.013) *	0.621 (0.165) *	-0.805 (0.064) *	-0.094 (0.427)	-0.347 (0.299)
	Both of the intercepts	0.209 (0.082) *		-0.06 (0.166)		0.909 (0.965)	
	Both of the slopes	-0.112 (0.087)		-0.052 (0.169)		0.456 (0.298)	
Number of iterations to achieve PSR < 1.05		11,800		3200		2600	

Factor Loadings

Cluster	Disease		1990	1995	2000	2005	2010	2015	2021
A	HIV/AIDS	Score	0	1	1.302	0.848	0.139	-0.070	-0.345
		Slope	---	1.828	0.550	-0.830	-1.296	-0.382	-0.503
	TB	Score	0	1	2.554	4.645	7.181	9.135	10.691
		Slope	---	-0.475	-0.738	-0.993	-1.205	-0.928	-0.739
B	HIV/AIDS	Score	0	1	1.501	1.173	0.471	0.007	-0.372
		Slope	---	26.036	13.039	-8.536	-18.270	-12.076	-9.864
	TB	Score	0	1	3.782	6.627	9.004	10.465	11.905
		Slope	---	-4.231	-11.771	-12.037	-10.057	-6.181	-6.088
C	HIV/AIDS	Score	0	1	536.749	621.593	347.604	230.057	133.303
		Slope	---	0.760	407.169	64.481	-208.232	-89.336	-73.533
	TB	Score	0	1	30.009	86.077	109.494	109.593	101.387
		Slope	---	0.001	0.029	0.056	0.023	0.000	-0.008

* Significant at 0.05 level

** PSD: Posterior Standard Deviation

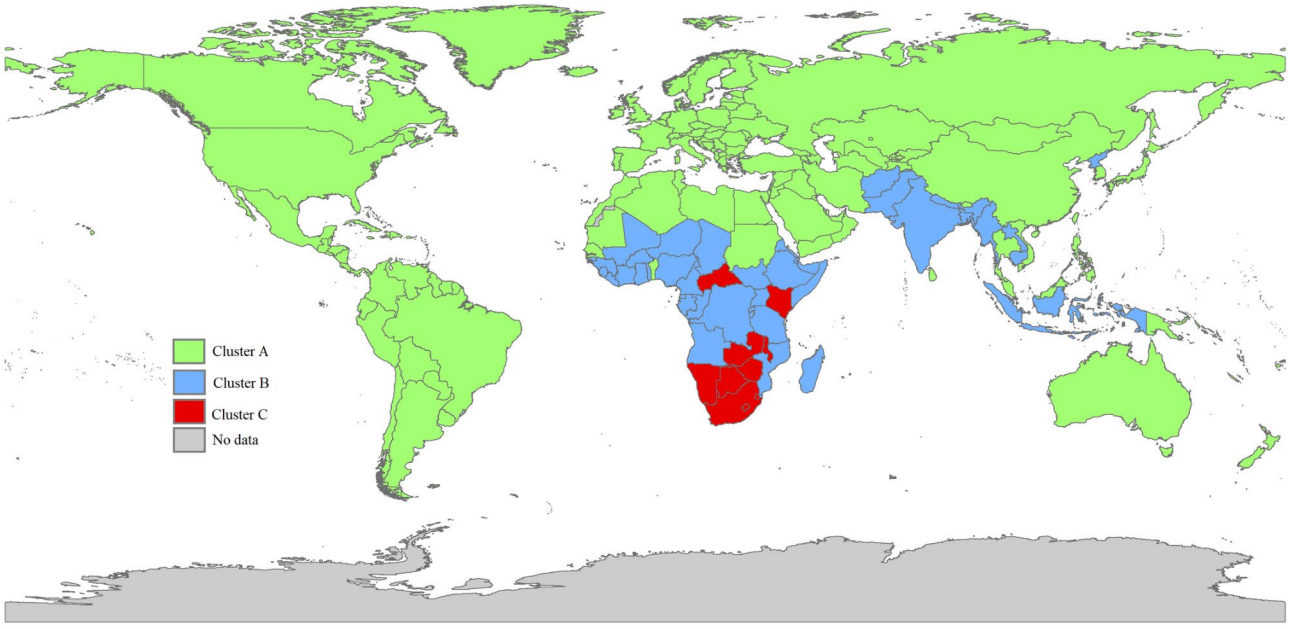

Fig. 3 The geographic distribution of worldwide countries based on their cluster membership

Table 4 Cluster membership of worldwide countries

Cluster	Countries and territories
A	Albania, Algeria, American Samoa, Andorra, Antigua and Barbuda, Argentina, Armenia, Australia, Austria, Azerbaijan, Bahamas, Bahrain, Barbados, Belarus, Belgium, Belize, Benin, Bermuda, Bhutan, Bolivia, Bosnia and Herzegovina, Brazil, Brunei Darussalam, Bulgaria, Cabo Verde, Canada, Chile, China, Colombia, Cook Islands, Costa Rica, Croatia, Cuba, Cyprus, Czechia, Denmark, Dominica, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Fiji, Finland, France, Georgia, Germany, Greece, Greenland, Grenada, Guam, Guatemala, Guyana, Haiti, Honduras, Hungary, Iceland, Iran, Iraq, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kazakhstan, Kuwait, Kyrgyzstan, Latvia, Lebanon, Libya, Lithuania, Luxembourg, Malaysia, Maldives, Malta, Mauritania, Mauritius, Mexico, Micronesia, Monaco, Mongolia, Montenegro, Morocco, Nauru, Netherlands, New Zealand, Nicaragua, Niue, North Macedonia, Northern Mariana Islands, Norway, Oman, Palau, Palestine, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Poland, Portugal, Puerto Rico, Qatar, Republic of Korea, Republic of Moldova, Romania, Russian Federation, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Samoa, San Marino, Sao Tome and Principe, Saudi Arabia, Senegal, Serbia, Seychelles, Singapore, Slovakia, Slovenia, Solomon Islands, Spain, Sri Lanka, Sudan, Suriname, Sweden, Switzerland, Syrian Arab Republic, Taiwan, Tajikistan, Thailand, Tokelau, Tonga, Trinidad and Tobago, Tunisia, Turkey, Turkmenistan, Ukraine, United Arab Emirates, United Kingdom, United States of America, United States Virgin Islands, Uruguay, Uzbekistan, Vanuatu, Venezuela, Viet Nam, Yemen
B	Afghanistan, Angola, Bangladesh, Burkina Faso, Burundi, Cambodia, Cameroon, Chad, Comoros, Congo, Côte d'Ivoire, Democratic People's Republic of Korea, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, India, Indonesia, Kiribati, Lao People's Democratic Republic, Liberia, Madagascar, Mali, Marshall Islands, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Rwanda, Sierra Leone, Somalia, South Sudan, Timor-Leste, Togo, Tuvalu, Uganda, United Republic of Tanzania
C	Botswana, Central African Republic, Eswatini, Kenya, Lesotho, Malawi, Namibia, South Africa, Zambia, Zimbabwe

Our findings revealed the existence of heterogeneity in the patterns of HIV/AIDS and TB mortality rates among these countries, leading to the clustering of the 204 countries and territories into three subgroups. To gain a comprehensive understanding of HIV/AIDS and TB mortality rates, it is crucial to examine the distinct patterns exhibited by each subgroup.

According to the results of the longitudinal k-means clustering method, Cluster A included 149 countries from around the world, excluding regions such as Sub-Saharan Africa and Southeast Asia, as well as specific countries like India, Pakistan, Bangladesh, and the Democratic People's Republic of Korea. Cluster A had the highest proportion of the study population (73%) and exhibited the lowest initial mortality rates for both HIV/AIDS and TB. Moreover, it displayed the lowest nonlinear growth trajectories for HIV/AIDS compared to the other clusters. The results of Bayesian multi-process LGM showed that the HIV/AIDS mortality rates increased from 1990 to 2000 and then followed an almost stable decreasing pattern until 2021. On the other hand, the TB mortality rates exhibited a decreasing growth pattern from 1990 to 2021. Earlier research findings suggested that the peak of global HIV mortality occurred in 2006, resulting in 1.95 million deaths [11, 29, 35]. Subsequently, there was a decline to 0.95 million deaths by

2017 and further to 0.63 million deaths by 2022 [7, 29]. The significant increase in the availability of antiretroviral therapy (ART) has contributed to a decline in HIV mortality rates [36]. By 2015, the global coverage of ART had reached 46%, resulting in a noteworthy 26% decrease in annual HIV-related deaths since 2010 [36]. Furthermore, the global TB mortality rate decreased annually by 1.2 to 4.1% over the period of 1990–2017 due to progress made in care and prevention [37, 38]. It is worth mentioning that the decreasing pattern of HIV/AIDS mortality rates for cluster A started from segment 2000–2005. A previous study has shown that the decreasing pattern of the worldwide HIV death rate began in 2006 [29].

Cluster B consists of 45 countries, including African countries (specifically western, central, and eastern countries), as well as Southeast Asian countries, Afghanistan, India, Pakistan, and Bangladesh. These nations are commonly labeled as countries with limited social resources and lower levels of economic advancement [18]. Based on the Bayesian multi-process LGM results, the mortality rates of HIV and TB were initially high, with the HIV growth pattern sharply increasing nonlinearly from 1990 to 2000 and then steadily decreasing, while the TB mortality rates showed a decreasing pattern over the study period. The steepest increasing and decreasing patterns of HIV mortality rates were observed in the segments 1990–1995 and 2005–2010, respectively, and the steepest decreasing pattern of TB was estimated in the segment 2000–2005. Significant advancements have been made in reducing the impact of HIV/AIDS since reaching its highest point in 2005 [35]. However, the number of individuals affected by HIV remained highest in the WHO South-East Asia and African regions. In 2015, Sub-Saharan Africa accounted for 75% of new cases, with South Asia following at 8.5% and Southeast Asia at 4.7% [14]. As a result, HIV/AIDS continues to pose a significant public health threat in these regions. Key factors contributing to HIV prevalence in South Asia comprise sexual transmission, drug use, stigma, and restricted access to prevention and treatment resources due to financial limitations and governmental support challenges [39]. Additionally, research has demonstrated that non-adherence of newborns to HIV management guidelines plays a substantial role in the propagation of the virus [40]. In sub-Saharan Africa, various socioeconomic factors such as education, marital status, the presence of diverse HIV strains, economic marginalization and poverty, high prevalence of sexually transmitted infections (STIs) and other opportunistic infections, patterns of sexual networking and contact, multiple concurrent sexual partners, lack of male circumcision, overcrowded prisons, the role of core groups like commercial sex workers, and population mobility all contribute to the complex dynamics of HIV transmission in the region [41, 42]. Education and ART coverage played critical roles in decreasing HIV incidence rates in Sub-Saharan Africa between 2000 and 2015, underscoring the complex interplay between social determinants and behavioral risk factors [43]. It is crucial to prioritize education regarding HIV transmission and prevention, along with widespread testing and immediate treatment for individuals who test positive. Furthermore, along with HIV, the majority of TB cases were reported in the regions of Africa (24%) and Southeast Asia (44%) in 2018 [44]. Together, these two regions constituted roughly about 70% of the total new TB cases reported globally [44]. However, with the implementation of interventions such as ART and isoniazid preventive treatment (IPT) to prevent the progression to active TB in populations with high co-infection of TB and HIV, the WHO reported a decrease in TB incidence in Africa and other regions [44].

Cluster C included Southern African countries, Kenya, and the Central African Republic, which had the highest mortality rates for both HIV/AIDS and TB at the initial stage. It also exhibited a steep increasing growth trajectory of HIV/AIDS mortality rates from 1990 to 2005, followed by a decrease from 2005 to 2021. In contrast, the TB mortality rates remained high with no significant changes observed during the study period. A small and nonsignificant growth factor (Slope = 0.001) for TB, with a PSD of 0.227, indicates a wider confidence interval for the small slope. This uncertainty may be attributed to the small sample size in this cluster. Despite a decline in overall HIV-related mortality, WHO reports that 39 million individuals continue to live with HIV/AIDS, which remains the leading cause of death for over 600,000 people annually, primarily concentrated in sub-Saharan Africa [7]. While the inadequate healthcare systems in developing countries, particularly in Africa, contributed to the severity of the outbreak, it is important to note that there were other factors that also played a role in the HIV/AIDS pandemic [11]. The effectiveness of preventive measures, including condom use, prevention of mother-to-child transmission, voluntary male medical circumcision, and community awareness campaigns, have not met the anticipated success, possibly due to unresolved systemic issues [11]. The prevalence of HIV in South Africa has had a profound effect on the burden of TB [34]. A systematic review study conducted in South Africa highlighted the high mortality rates among TB patients, particularly those with HIV, drug-resistant TB, and prior TB treatment [45]. These findings underscore the importance of implementing targeted interventions to address these specific risk factors and improve patient outcomes. The significant reduction in TB-related mortality can largely be attributed to the increased availability and provision of ART [34].

The COVID-19 pandemic has significantly disrupted healthcare systems globally, adversely affecting the management of HIV/AIDS and TB [46]. A systematic review indicated that TB notifications dropped by up to 80% in some regions due to healthcare disruptions and lockdown measures [47]. COVID-19 negatively impacted TB case notifications and HIV testing in Ghana, leading to significant declines in TB cases and HIV tests [48]. In Nagpur, India, notable declines in HIV testing and treatment adherence were observed, highlighting service gaps and challenges in patient engagement [49]. The interplay between these diseases has led to increased challenges in diagnosis, treatment, and care. Despite these challenges, proactive measures are essential to recover lost ground in HIV and TB management, emphasizing the need for resilient healthcare systems.

Chronic infectious diseases such as hepatitis B virus (HBV), and human papillomavirus (HPV) can significantly influence mortality rates in populations affected by HIV/AIDS and tuberculosis (TB). For instance, HBV infection during pregnancy has been associated with high maternal and perinatal fatality rates, particularly in low-resource settings, complicating immune responses and worsening clinical outcomes [50, 51]. Similarly, HPV prevalence in certain regions, such as western Kazakhstan, highlights its role in cervical cancer development, which may further exacerbate health disparities in vulnerable populations [52]. These studies underscore the importance of considering comorbidities when analyzing global HIV/AIDS and TB mortality trends, as they may contribute to immune dysfunction and complicate treatment outcomes. Furthermore, biomarkers play a pivotal role in understanding and predicting clinical outcomes [53]. For example, in HIV/AIDS, CD4 cell counts and viral load are critical biomarkers for assessing disease progression and treatment efficacy, while in tuberculosis (TB), sputum smear microscopy and molecular tests such as Xpert MTB/RIF are essential for diagnosis and monitoring. Integrated healthcare strategies targeting these comorbidities alongside HIV/AIDS and TB, as well as related biomarkers, could enhance early detection and intervention, potentially reducing overall mortality rates.

Strengths and limitations

The main strength of this study was its ability to address the heterogeneity in the patterns of HIV/AIDS and TB mortality rates simultaneously. Furthermore, by using the Bayesian nonlinear LGM, we were able to concurrently estimate the patterns of HIV/AIDS and TB mortality rates segment by segment. Nevertheless, it is important to acknowledge some drawbacks of the study. In certain high HIV/AIDS prevalence settings, TB cases are predominantly identified in ART clinics. This scenario may lead to a high correlation between HIV/AIDS and TB, potentially affecting the accuracy of our estimations. Moreover, the quality of the GBD dataset varied among countries, with some data being estimated through modeling techniques. The GBD uses a variety of sources, such as censuses, household surveys, civil registration and vital statistics, disease registries, health service utilization, air pollution monitors, satellite imaging, disease notifications, and other relevant sources [54]. However, the presence of variability in the numerous sources utilized for data collection and estimation poses a potential risk of introducing biases into the analysis. Furthermore, the GBD database only provides data from 1990 to 2021, and there is a lack of available data for the years 2022 and 2023. Another limitation was the inability to incorporate socioeconomic factors such as HDI (Human Development Index), income, education, and migration into the model due to limitations in the Mplus software. Therefore, to enhance the study's impact, future research should prioritize utilizing data from diverse sources like the WHO, which may provide more current insights into HIV/AIDS and TB mortality rates. Furthermore, integrating socioeconomic factors into the analysis and employing alternative statistical software or methodologies that can accommodate a wider range of variables are crucial for developing a comprehensive understanding of mortality patterns. These efforts will not only address current limitations but also strengthen the reliability and comprehensiveness in understanding the dynamics of HIV/AIDS and TB mortality rates.

Conclusion

Although TB exhibited an overall declining trend in mortality rates from 1990 to 2021, the mortality rate of HIV/AIDS initially increased from 1990 to 2005 but then decreased. However, the rates of change in these trends varied among countries. These variations in HIV/AIDS and TB mortality rates have significant implications for efforts to control both pandemics. Clustered data revealed that Sub-Saharan African countries, especially Southern African countries, and Southeast Asian countries experienced a high burden of HIV/AIDS and TB. While the overall global HIV/AIDS and TB mortality rates declined, Southern African countries had the highest HIV/AIDS and TB mortality rates at the beginning of the study period, with no significant changes observed in TB mortality rates from 1990 to 2021. Moreover, the HIV/AIDS mortality rates remained high in this region. Therefore, to achieve the Sustainable Development Goals (SDGs) of eradicating the global HIV/AIDS and TB epidemics by 2030 and 2035 respectively, it is crucial to prioritize these countries. Improved full integration of TB and HIV services is recommended in Sub-Saharan Africa and Southeast Asian countries (Clusters B and C) to enhance the quality and accessibility of care. Education

and targeted interventions with ART and isoniazid preventive treatment (IPT) are essential to prevent the progression of TB and HIV in high-risk populations with a high rate of co-infection.

Abbreviations

HIV/AIDS	Human immunodeficiency virus/ Acquired immune deficiency syndrome
TB	Tuberculosis
LGM	Latent growth model
SDGs	Sustainable development goals
WHO	World health organization
ART	Antiretroviral treatment
MLR	Maximum likelihood ratio
GBD	Global burden of disease
SD	Standard deviation
PSD	Posterior standard deviation

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Declarations

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Competing interests
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