The impact of population ageing on tuberculosis incidence, mortality, and case fatality in South Korea: a nationwide retrospective study

Seung Won Lee[1,8], Doosoo Jeon[2,8], Hongjo Choi[3], Chiwook Chung[4], Jeongha Mok[5], Dawoon Jeong[6], Hojoon Sohn[6] and Young Ae Kang[1,7]

[1]Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, Republic of Korea. [2]Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, Republic of Korea. [3]Division of Health Policy and Management, Korea University College of Health Science, Seoul, Republic of Korea. [4]Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Republic of Korea. [5]Department of Internal Medicine, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Republic of Korea. [6]Department of Preventive Medicine, Seoul National University, Seoul, Republic of Korea. [7]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea. [8]These authors contributed equally.

Corresponding author: Young Ae Kang (mdkang@yuhs.ac)

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Population ageing complicates TB control by increasing fatality rates and slowing incidence and mortality declines. Tailored interventions that specifically address older adults' needs are essential to overcome these challenges. https://bit.ly/42IjEWK

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Abstract

Background This study investigated the effect of population ageing on the epidemiology of tuberculosis (TB) in South Korea.

Methods We conducted a retrospective cohort study using an integrated database from three national databases. We analysed trends in age-specific TB incidence, mortality, case fatality rates and risk factors for all-cause mortality among 328 637 patients with drug-susceptible TB from 2011 to 2020.

Results From 2011 to 2020, the proportion of patients aged ⩾65 years increased from 30.5% to 50.7% of TB cases and from 74.3% to 86.8% of deaths. The TB incidence rate decreased from 90.3 to 39.5 per 100 000 (average annual per cent change (AAPC) −8.5%; 95% confidence interval (CI) −9.2 to −7.7). The crude mortality rate remained largely unchanged, shifting from 4.6 to 5.4 per 100 000 (AAPC 1.6%; 95% CI −0.1 to 3.1). The case fatality rate increased from 5.1% to 13.5% (AAPC 11.3%; 95% CI 10.5 to 12.1). Although incidence and mortality declined across all age groups, the rate of decline slowed with increasing age. Patients aged ⩾80 years showed the slowest decline in incidence (AAPC −4.3%; 95% CI −5.4 to −3.5) and stagnation in mortality (AAPC 0.5%; 95% CI −1.4 to 2.2).

Conclusions This study highlights the challenges of population ageing on TB control, including increasing case fatality rates and slower declines in TB incidence and mortality. These findings call for a reassessment of current strategies to address the needs of the elderly.

Introduction

Tuberculosis (TB) has resumed its position as the world's leading cause of death by a single pathogen, temporarily overtaken by COVID-19 [1]. The World Health Organization (WHO) estimated 10.8 million new TB cases and 1.25 million TB-related deaths in 2023 [1]. From 2015 to 2023, global TB incidence and mortality rates decreased by 8.3% and 23%, respectively. However, these reductions fell short of the WHO's "End TB Strategy" targets, which aim for a 50% reduction in incidence and a 75% reduction in mortality by 2025 [2].

Population ageing is a consequence of demographic transition occurring worldwide [3]. Initially observed in high-income countries, this shift is now significantly impacting low- and middle-income countries as well. Although increased human lifespan is a major public health achievement, population ageing has emerged as a growing challenge in global TB control [4–7]. A recent global study has indicated that overall incidence and mortality from TB has gradually declined across all age groups [8]. However, the rate of decline has been uneven across age groups, with older adults showing slower progression. This disparity highlights the urgent need for age-specific strategies that focus on the elderly population.

South Korea is undergoing one of the most rapid population ageing processes worldwide and is expected to become a "super-aged society" by 2025, with individuals aged ⩾65 years comprising 20% of the total population [9]. In 2023, South Korea reported 19 540 TB cases (38.2 per 100 000 people) [10] and 1322 TB-related deaths in 2022 (2.6 per 100 000 people) [11]. Despite an overall reduction in TB incidence, recent studies have shown that the case fatality rate (CFR) has gradually increased [12, 13]. This paradox is likely attributable to the ageing TB population. Analysing recent trends in age-specific TB incidence and mortality in South Korea offers valuable insights into the impact of population ageing on TB epidemiology. As global population ageing progresses, these findings could help inform TB control strategies in other countries undergoing or anticipating similar demographic shifts.

In this study, we aimed to evaluate trends in age-specific incidence, mortality, CFR and risk factors for all-cause mortality during treatment in drug-susceptible TB patients using an integrated TB database created by linking three national databases.

Methods

Data sources and study population

This retrospective cohort study was based on an integrated database created by linking data from three national databases in South Korea: 1) the Korea Tuberculosis Surveillance System (KTB-Surv) between 2011 and 2022; 2) the National Health Information Database (NHID) between 2010 and 2022; and 3) the Causes of Death Statistics databases between 2010 and 2022. A detailed description of these databases and the collected variables is provided in the supplementary material.

The study cohort included patients with drug-susceptible TB who were notified between 1 January 2011 and 31 December 2020. The initial cohort comprised 415 937 TB cases reported from 2011 to 2021. We excluded individuals with drug-resistant TB, incomplete data and those diagnosed in 2021, resulting in a final study population of 328 637 patients (supplementary figure S1).

The study protocol was approved by the Institutional Review Board of Severance Hospital (4-2022-0595) and Korea National Health Insurance Service Medical Request Review Committee (NHIS-2022-1-737). The requirement for informed consent was waived because this was a retrospective study, and the data used were anonymised.

Analysis

Definition and measurement of outcomes

We analysed the trends in overall and age-specific TB incidence, mortality and CFR in a drug-susceptible TB cohort. TB incidence was defined as the number of notified patients with TB. TB death was defined as events of dying from any cause during the treatment period. We further classified deaths using the Causes of Death Statistics database, with codes A15–A19 designated as TB-related, while all other codes were considered non-TB-related. The primary focus of this study was all-cause mortality, with supplemental consideration given to TB-related and non-TB-related mortalities. This approach was chosen to address the 28.2% discrepancy observed between the Causes of Death Statistics and KTB-Surv in classifying TB-related deaths within our cohort [14]. Moreover, previous studies have highlighted the challenges in accurately determining the causes of death during TB treatment [15].

Crude TB incidence and mortality rates were calculated by dividing the number of reported cases and deaths by the mid-year population expressed per 100 000 individuals. The CFR was defined as the percentage of all-cause deaths during the treatment period among all reported TB cases in the same year. This definition differs slightly from that of the traditional CFR, which specifically measures deaths attributable to TB. Age-standardised TB incidence and mortality were calculated using direct standardisation, with South Korea's 2005 population as a reference. Age-specific incidence, mortality and CFR were assessed by categorising the age groups as 0–24, 25–44, 45–64, 65–79 and ⩾80 years.

Risk factor analysis

We analysed the characteristics of the deceased patient group and identified the risk factors for all-cause mortality by comparing this group with a combined group of patients with treatment success and failure. The definitions of the covariates used in the analysis are described in the supplementary material.

Statistical analysis

Annual trends in TB incidence, mortality and CFR were analysed using the Joinpoint Regression Program, Version 5.2.0 (Statistical Research and Applications Branch, National Cancer Institute) [16]. The t-test or Mann–Whitney U-test was used to compare continuous variables, while the chi-square test or Fisher's exact test was used to compare categorical variables. A Cox proportional hazards model was constructed to estimate the hazard ratio (HR) of the risk factors associated with mortality. Variables with p-values <0.2 in the univariate analysis were entered into the multivariate models. All p-values were two-tailed, and p-value <0.05 was deemed statistically significant. All statistical analyses were performed using the SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC, USA) and STATA/MP version 17 (Stata Corp LLC, College Station, TX, USA).

Results

Annual trends in overall incidence, mortality and CFR

The crude TB incidence rate decreased significantly from 90.3 per 100 000 population in 2011 to 39.5 per 100 000 population in 2020, with an average annual per cent change (AAPC) of −8.5% (95% confidence interval (CI): −9.2 to −7.7) (table 1) (figure 1). The age-standardised incidence rate declined more rapidly, with an AAPC of −11.5% (95% CI: −12.2 to −11.0). The crude mortality rate increased from 4.6 per 100 000 people in 2011 to a peak of 6.4 per 100 000 people in 2016 (annual per cent change (APC): 6.6%), followed by a gradual decline to 5.4 per 100 000 people in 2020 (APC: −4.4%). As a result, the overall change from 2011 to 2020 was not statistically significant, with an AAPC of 1.6% (95% CI: −0.1 to 3.1). In contrast, the age-standardised mortality rate progressively decreased throughout the study period, with an AAPC of −4.3% (95% CI: −5.7 to −2.9). However, the CFR increased significantly from 5.1% in 2011 to 13.5% in 2020, with an AAPC of 11.3% (95% CI: 10.5 to 12.1).

The proportion of patients aged ⩾65 years increased from 30.5% to 50.7% in incidence (AAPC: 5.7%, 95% CI: 5.4 to 6.1) and from 74.3% to 86.8% in mortality (AAPC: 1.7%, 95% CI: 1.3 to 2.0) between 2011 and 2020. The proportion of patients aged ⩾80 years increased more rapidly than that of patients aged 65–79 years in both TB incidence and mortality.

Annual trends in age-specific incidence, mortality and CFR

Table 2 presents the results of the Joinpoint analysis of trends in age-specific incidence, mortality and CFRs from 2011 to 2020; detailed data are provided in supplementary tables S2–S4. Figure 2 also shows the trend in age-specific incidence, mortality and CFRs from 2011 to 2020. The incidence decreased across all age groups; however, the rate of decline progressively slowed with age. The greatest reduction in

TABLE 1 Annual incidence, mortality and case fatality among patients with drug-susceptible tuberculosis, 2011–2020

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	AAPC, % (95% CI)
Tuberculosis incidence											
Notified cases, n	45 097	42 012	37 699	36 255	33 135	31 954	29 409	27 553	24 699	20 490	−8.1# (−8.9 to 7.4)
Crude incidence rate, /10^6	90.3	83.7	74.8	71.4	65.0	62.4	57.3	53.4	47.7	39.5	−8.5# (−9.2 to −7.7)
Age-standardised incidence rate, /10^6	81.7	73.8	64.6	60.0	53.0	49.1	43.4	38.6	33.3	26.8	−11.5# (−12.2 to −11.0)
Proportion of ⩾65 years, %	30.5	33.3	34.9	36.8	39.0	41.9	43.8	47.3	49.0	50.7	5.7# (5.4 to 6.1)
65–79 years	22.1	23.6	23.9	24.4	25.1	25.7	25.9	26.8	26.9	27.4	2.4# (1.9 to 2.7)
⩾80 years	8.3	9.6	10.9	12.4	13.9	16.2	17.9	20.6	22.1	23.3	12.1# (11.8 to 12.4)
Tuberculosis death											
Death cases, n	2312	2616	2611	3064	3091	3296	3110	3161	2998	2774	2.0# (0.3 to 3.6)
Case fatality rate, %	5.1	6.2	6.9	8.5	9.3	10.3	10.6	11.5	12.1	13.5	11.3# (10.5 to 12.1)
Crude mortality rate, /10^6	4.6	5.2	5.2	6.0	6.1	6.4	6.1	6.1	5.8	5.4	1.6 (−0.1 to 3.1)
Age-standardised mortality rate, /10^6	3.6	3.8	3.6	4.0	3.7	3.8	3.3	3.2	2.7	2.5	−4.3# (−5.7 to −2.9)
Proportion of ⩾65 years, %	74.3	78.5	78.7	80.3	81.3	83.5	84.5	84.8	86.1	86.8	1.7# (1.3 to 2.0)
65–79 years	39.5	41.9	38.9	38.5	35.5	33.4	32.7	30.5	28.9	29.6	−4.1# (−5.3 to −2.9)
⩾80 years	34.8	36.7	39.9	41.7	45.8	50.1	51.8	54.3	57.2	57.2	5.9# (5.1 to 6.7)

AAPC: average annual percentage change. #: significantly different from zero (p<0.05).

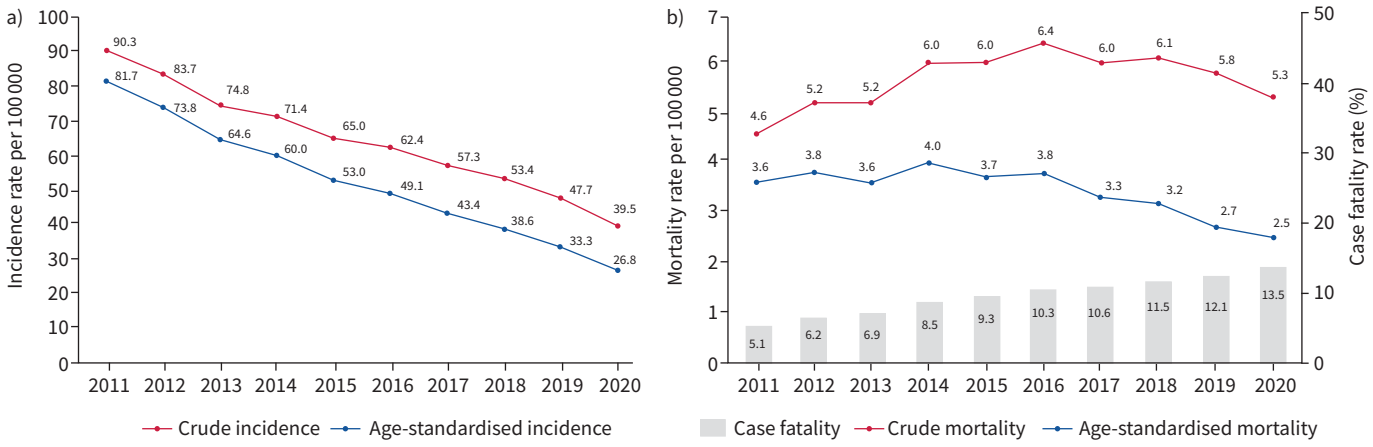

FIGURE 1 Trends in tuberculosis a) incidence and b) mortality rate among patients with drug-susceptible tuberculosis, 2011–2020.

incidence was observed in the 0–24- and 25–44-year age groups, while patients aged ⩾80 years experienced the slowest decline, with an AAPC of −4.3% (95% CI: −5.4 to −3.5).

The mortality rates showed a similar age-dependent trend. While the overall mortality remained stagnant during the study period, a significant decline was observed in the later periods across all age groups. In the 65–79-year age group, a significant decline began in 2014 (APC: −8.7%) while in the ⩾80-year age

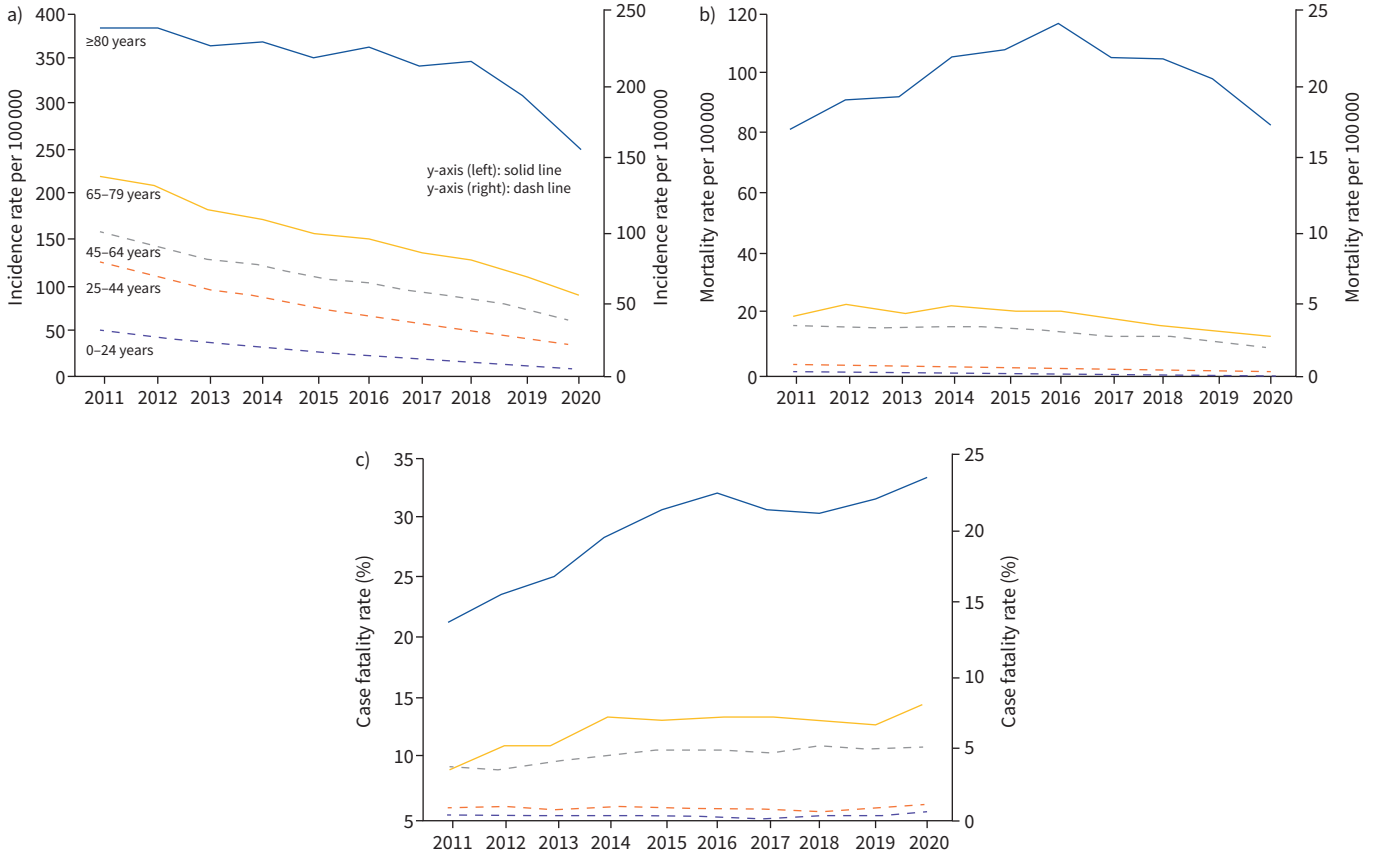

FIGURE 2 Trend in age-specific tuberculosis a) incidence, b) mortality and c) case fatality rates among patients with drug-susceptible tuberculosis, 2011–2020.

TABLE 2 Joinpoint analysis of trends in incidence, mortality and case fatality among patients with drug-susceptible tuberculosis, 2011–2020

	Period 1			Period 2			Entire period (2011–2020)	
	Years	APC %	95% CI	Years	APC %	95% CI	AAPC %	95% CI
Incidence rate								
0–24	2011–2015	−13.9#	(−16.4 to −6.3)	2015–2020	−20.1#	(−25.9 to −18.4)	−17.4#	(−18.8 to −15.9)
25–44	2011–2017	−12.0#	(−12.5 to −11.5)	2017–2020	−16.9#	(−18.2 to −15.5)	−13.7#	(−14.0 to −13.49)
45–64	2011–2018	−8.2#	(−8.7 to −7.4)	2018–2020	−16.0#	(−18.6 to −12.4)	−10.0#	(−10.5 to −9.5)
65–79	2011–2018	−7.3#	(−8.1 to −5.7)	2018–2020	−16.0#	(−20.6 to −11.1)	−9.3#	(−10.3 to −8.4)
⩾80	2011–2018	−1.4	(−2.3 to 0.0)	2018–2020	−13.8#	(−18.8 to −8.3)	−4.3#	(−5.4 to −3.5)
Overall	2011–2018	−7.0#	(−7.69 to −5.5)	2018–2020	−13.3#	(−17.1 to −9.4)	−8.5#	(−9.2 to −7.7)
Mortality rate								
0–24							−12.3#	(−20.9 to −2.7)
25–44							−12.6#	(−15.8 to −9.4)
45–64	2011–2015	0.4	(−3.0 to 7.3)	2015–2020	−9.8#	(−14.2 to −7.4)	−5.4#	(−6.8 to −3.9)
65–79	2011–2014	4.5	(−2.3 to 18.9)	2014–2020	−8.7#	(−13.6 to −6.5)	−4.5#	(−6.6 to −2.4)
⩾80	2011–2016	7.1#	(3.9 to 12.4)	2016–2020	−7.2#	(−14.0 to −3.3)	0.5	(−1.4 to 2.2)
Overall	2011–2016	6.6#	(4.0 to 11.2)	2016–2020	−4.4#	(−10.7 to −1.2)	1.6	(−0.1 to 3.1)
Case fatality rate								
0–24	2011–2017	−6.7	(−51.4 to 84.5)	2017–2020	47.4	(−26.0 to 190.8)	8.7	(−7.7 to 24.2)
25–44	2011–2018	−2.7#	(−17.2 to −8.1)	2018–2020	22.8	(−1.4 to 44.6)	2.5	(−2.5 to 5.7)
45–64	2011–2015	8.7#	(6.2 to 13.2)	2015–2020	1.1	(−1.8 to 2.9)	4.4#	(3.4 to 5.5)
65–79	2011–2014	12.1#	(6.2 to 24.5)	2014–2020	0.8	(−10.1 to 5.2)	4.4#	(2.4 to 6.3)
⩾80	2011–2015	9.4#	(6.8 to 14.0)	2015–2020	0.9	(−2.0 to 2.6)	4.6#	(3.5 to 5.7)
Overall	2011–2014	18.7#	(15.3 to 23.6)	2014–2020	7.7	(−0.6 to 8.6)	11.3#	(10.5 to 12.1)

APC: annual percentage change; AAPC: average annual percentage change. #: significantly different from zero ($p<0.05$).

group, the decline started in 2016 (APC: −7.2%). When analysed by cause of death, TB-related mortality declined much more rapidly in both age groups (65–79 years: APC −14.2% and ⩾80 years: APC −13.6%) than non-TB-related mortality (65–79 years: APC −7.9% and ⩾80 years: APC −1.3%) (supplementary table S5). Conversely, the CFR in both age groups increased until 2014–2015, and then remained stagnant (supplementary table S6).

Baseline characteristics of patients who died during treatment

During the study period, 29 033 of the 328 637 patients (8.8%) died, with a median time to death of 52 days (interquartile range (IQR) 16–122) from treatment initiation. The median age of deceased patients was 79 years (IQR 70–85), with 82.1% aged ⩾65 years. Table 3 compares baseline characteristics of deceased patients by age group (⩾65 *versus* <65 years). In the older age group, a higher proportion of women, patients with extrapulmonary TB and those with smear-negative results were observed. This group also had more comorbidities, with a median Charlson Comorbidity Index (CCI) score of 4 (IQR 2–5) compared to a score of 3 (IQR 2–4) in the younger group ($p<0.001$).

Risk factor for all-cause death during treatment

Independent risk factors for all-cause mortality included advanced age, male sex (adjusted hazard ratio (aHR): 1.57; 95% CI: 1.53–1.60), positive smear results (aHR: 1.51; 95% CI: 1.47–1.55), lower household income (aHR: 1.60 for the lowest income group; 95% CI: 1.54–1.66) and the presence of comorbidities (table 4). Compared to the 0–24-year age group (reference), the risk of mortality increased progressively with age, reaching an aHR of 77.52 (95% CI: 60.23–99.79) for patients aged ⩾80 years. Age stratification at 65 years revealed similar risk factors for both younger (<65 years) and older (⩾65 years) cohorts, except for reporting institutions. Treatment at public–private mix (PPM) institutions reduced mortality risk in the older cohort (aHR: 0.86; 95% CI: 0.83–0.88) but increased it in the younger cohort (aHR: 1.26; 95% CI: 1.19–1.35).

Discussion

This study provides meaningful insights into how population ageing impacts TB epidemiology. Over the past decade in South Korea, patients aged ⩾65 years have become the age group with the highest TB incidence and mortality, exerting the greatest influence on overall TB epidemiology. The proportion of patients aged ⩾65 years increased from 30.5% in 2011 to 50.7% in 2020, and the share of deaths during TB treatment increased from 74.3% to 86.8% over the same period. This ageing trend in the TB

TABLE 3 Baseline characteristics of patients who died during treatment for drug-susceptible tuberculosis, stratified by age 65 years

	All ages	Age <65 years	Age ⩾65 years	p-value
Patients, n	29 033	5183	23 850	
Age years, median (IQR)	79 (70–85)	56 (50–60)	81 (76–86)	<0.001
Time to death days, median (IQR)	52 (16–122)	51 (15–137)	52 (17–119)	0.155
Sex, male	18 347 (63.19)	4302 (83)	14 045 (58.89)	<0.001
Region				<0.001
Seoul	4414 (15.2)	992 (19.14)	3422 (14.35)	
Metropolitan	6776 (23.34)	1359 (26.22)	5417 (22.71)	
Others	17 843 (61.46)	2832 (54.64)	15 011 (62.94)	
Household income				<0.001
0 (Lowest)	4387 (15.11)	1126 (21.72)	3261 (13.67)	
1	4517 (15.56)	1076 (20.76)	3441 (14.43)	
2	3280 (11.3)	993 (19.16)	2287 (9.59)	
3	3834 (13.21)	812 (15.67)	3022 (12.67)	
4	4728 (16.28)	693 (13.37)	4035 (16.92)	
5 (Highest)	8287 (28.54)	483 (9.32)	7804 (32.72)	
Lesion of tuberculosis				<0.001
Pulmonary/mix	24 006 (82.69)	4390 (84.7)	19 616 (82.25)	
Extrapulmonary	5027 (17.31)	793 (15.3)	4234 (17.75)	
Tuberculosis history				<0.001
New	25 328 (87.24)	4367 (84.26)	20 961 (87.89)	
Retreatment	3705 (12.76)	816 (15.74)	2889 (12.11)	
AFB smear				<0.001
Negative	13 722 (47.26)	2122 (40.94)	11 600 (48.64)	
Positive	12 494 (43.03)	2548 (49.16)	9946 (41.7)	
Unknown	2817 (9.7)	513 (9.9)	2304 (9.66)	
Institution				<0.001
Non-PPM	9346 (32.19)	1462 (28.21)	7884 (33.06)	
PPM	15 002 (51.67)	3022 (58.31)	11 980 (50.23)	
Non-PPM+PPM	4685 (16.14)	699 (13.49)	3986 (16.71)	
CCI score, group				<0.001
0	994 (3.42)	405 (7.81)	589 (2.47)	
1	2677 (9.22)	761 (14.68)	1916 (8.03)	
2	4452 (15.33)	986 (19.02)	3466 (14.53)	
3 or above	20 910 (72.02)	3031 (58.48)	17 879 (74.96)	
CCI score, median (IQR)	4 (2–5)	3 (2–4)	4 (2–5)	<0.001
Comorbid disease				
Cardiovascular disease	8130 (28)	697 (13.45)	7433 (31.17)	<0.001
Cerebrovascular disease	12 643 (43.55)	1206 (23.27)	11 437 (47.95)	<0.001
Cancer	6685 (23.03)	1388 (26.78)	5297 (22.21)	<0.001
Diabetes mellitus	14 896 (51.31)	2624 (50.63)	12 272 (51.45)	0.287
COPD	10 031 (34.55)	1168 (22.54)	8863 (37.16)	<0.001
End-stage renal disease	878 (3.02)	206 (3.97)	672 (2.82)	<0.001
HIV	82 (0.28)	61 (1.18)	21 (0.09)	<0.001

Data are presented as n (%) unless indicated otherwise. AFB: acid-fast bacilli; PPM: public–private mix; CCI: Charlson comorbidity index; HIV: human immunodeficiency virus.

population is likely responsible for the stagnation in overall crude mortality and the consistent increase in treatment-phase CFR despite a steady decline in the overall TB incidence rate. Age-specific analyses demonstrated that the elderly had the greatest impact on recent trends in TB epidemiology. Although TB incidence and mortality rates have decreased across all age groups, the decline has been slower among patients aged ⩾65 years, particularly those aged ⩾80 years. This finding aligns with global trends [3] but underscores the more rapid shift of the TB burden towards older populations, highlighting the impact of population ageing in South Korea.

The ageing TB population is more pronounced in countries where population ageing coincides with a decline in TB incidence [17]. Age-specific TB incidence reflects shifts in a country's overall TB epidemic. In TB-endemic regions with high ongoing transmission, TB incidence is highest among younger adults

TABLE 4 Risk factors for all-cause mortality in patients with drug-susceptible tuberculosis stratified by age 65 years

	All ages		Age <65 years		Age ⩾65 years	
	aHR	(95% CI)	aHR	(95% CI)	aHR	(95% CI)
Patients, n	29 033		5183		23 850	
Sex						
Male	1.57	(1.53–1.60)	1.89	(1.75–2.04)	1.52	(1.48–1.56)
Female	1.00		1.00		1.00	
Age group, years						
0–24	1.00		1.00			
25–44	2.96	(2.27–3.85)	2.53	(1.94–3.29)		
45–64	11.36	(8.82–14.63)	6.70	(5.19–8.64)		
65–79	29.50	(22.92–37.98)			1.00	
⩾80	77.52	(60.23–99.79)			2.63	(2.56–2.70)
Region						
Seoul	1.00		1.00		1.00	
Metropolitan	1.01	(0.97–1.05)	0.99	(0.91–1.08)	1.00	(0.96–1.05)
Others	0.99	(0.96–1.03)	1.04	(0.97–1.12)	0.97	(0.93–1.00)
Household income						
0 (Lowest)	1.60	(1.54–1.66)	3.40	(3.04–3.79)	1.37	(1.31–1.43)
1	1.19	(1.14–1.23)	1.81	(1.62–2.02)	1.12	(1.08–1.17)
2	1.15	(1.11–1.20)	1.75	(1.57–1.95)	1.10	(1.05–1.15)
3	1.08	(1.04–1.12)	1.39	(1.24–1.56)	1.08	(1.03–1.13)
4	1.03	(1.00–1.07)	1.27	(1.13–1.42)	1.03	(0.99–1.07)
5 (Highest)	1.00		1.00		1.00	
Lesion of tuberculosis						
Pulmonary/mix	0.96	(0.92–0.99)	0.87	(0.79–0.96)	0.98	(0.94–1.02)
Extrapulmonary	1.00		1.00		1.00	
Tuberculosis history						
New case	1.00		1.00		1.00	
Retreatment	1.00	(0.97–1.04)	1.06	(0.98–1.14)	0.98	(0.94–1.02)
AFB smear						
Negative	1.00		1.00		1.00	
Positive	1.51	(1.47–1.55)	2.24	(2.10–2.38)	1.39	(1.35–1.43)
Unknown	0.91	(0.87–0.95)	0.85	(0.76–0.95)	0.93	(0.89–0.98)
Institution						
Non-PPM	1.00		1.00		1.00	
PPM	0.92	(0.90–0.95)	1.26	(1.19–1.35)	0.86	(0.83–0.88)
Non-PPM+PPM	0.97	(0.94–1.01)	1.21	(1.11–1.33)	0.92	(0.89–0.96)
Comorbidities						
Cardiovascular disease	1.65	(1.60–1.69)	2.01	(1.84–2.19)	1.62	(1.57–1.66)
Cerebrovascular disease	1.25	(1.22–1.28)	1.38	(1.29–1.48)	1.22	(1.18–1.25)
Cancer	1.71	(1.66–1.76)	3.47	(3.26–3.70)	1.49	(1.45–1.54)
Diabetes mellitus	1.35	(1.32–1.39)	1.79	(1.69–1.90)	1.25	(1.22–1.29)
COPD	1.07	(1.05–1.10)	1.32	(1.24–1.41)	1.04	(1.01–1.07)
End-stage renal disease	2.60	(2.42–2.78)	2.34	(2.02–2.71)	2.50	(2.31–2.70)
HIV	2.58	(2.08–3.21)	2.69	(2.09–3.47)	1.75	(1.14–2.69)

aHR: adjusted hazard ratio; AFB: acid-fast bacilli; PPM: public–private mix; HIV: human immunodeficiency virus.

due to recent infections. However, as TB incidence decreases and transmission slows, TB rates increase among older adults due to the re-activation of latent infections. This trend has been observed in the historical experiences of lower-incidence countries such as Japan [18], the USA [19] and the UK [20]. As TB incidence decreases and population ageing progresses worldwide, the ageing TB population is expected to become a global trend.

The growing burden of older adults among TB cases presents a significant challenge for both individual case management and national TB control [21, 22]. Older adults often present with atypical symptoms and are more likely to have comorbidities that complicate diagnosis and treatment [23]. In our study, the patients aged ⩾65 years had a higher proportion of extrapulmonary TB, smear-negative results and more comorbidities compared to the patients aged <65 years, which is consistent with the findings in other

studies [24]. This demographic shift can lead to delayed diagnosis and treatment, resulting in prolonged periods of infectiousness and greater opportunities for transmission, particularly in settings such as nursing homes or hospitals [25]. Additionally, older adults are more prone to treatment complications and adverse drug reactions, which can lead to higher rates of treatment failure and mortality [26]. These factors contribute to an increased burden on healthcare systems and make it more difficult to achieve TB eradication goals.

The high CFR, as shown in this study, is the most prominent impact of population ageing on TB epidemiology. The CFR is a critical metric for evaluating the effectiveness of TB control measures. The WHO has set global targets for reducing the CFR to 10% by 2020 and further to 6.5% by 2025, with an optimal target of <5% [2]. However, in this study, the CFR continuously increased reaching 13.5% in 2020, despite an overall decline in crude mortality. This paradox occurs because TB mortality is determined by both incidence rates and the CFR, as already observed in low-incidence settings [27]. In some of the low-incidence settings, population ageing did not result in a higher CFR, likely due to the offsetting effect of younger immigrant populations within the TB cohort [28]. These findings suggest that, in an ageing society, relying on the CFR alone as a performance indicator may lead to an incomplete assessment of TB control effectiveness.

In this study, CFR increased not only in patients aged ⩾80 years but also in middle-aged (45–64 years) and early elderly (65–79 years) groups. This trend likely reflects a broader demographic shift in TB incidence beyond ageing, particularly in low-incidence settings. As overall TB incidence declines, TB cases are increasingly concentrated among vulnerable populations, such as individuals with comorbidities and those of lower socioeconomic status. This shift in disease burden may contribute to the elevated CFR observed in these age groups. In our risk factor analysis, specific comorbidities (*e.g.*, cancer) and low-income status were associated with relatively higher hazard ratios for mortality in patients aged <65 years compared to those aged ⩾65 years. Similar findings have been reported in high-income, low-incidence settings [13, 29], highlighting the need for integrated TB control strategies tailored to these vulnerable populations.

The most concerning impact of population ageing is the potential slowdown in the decline of overall TB incidence and mortality rates [18]. This study found that the decrease in TB incidence and mortality rates progressively slowed with increasing age, which is consistent with findings from a global study [8]. However, a significant decline in all-cause mortality rates among the elderly population has been observed in recent years. This decline is likely due to the combined effects of decreased TB incidence and improved TB-related mortality. TB-related mortality declined rapidly in the 65–79-year age group (APC: −14.2%) starting in 2014 and the ⩾80-year age group (APC: −13.6%) beginning in 2016. In contrast, among the ⩾80-year age group, the non-TB-related CFRs continued to increase and non-TB-related mortality remained stagnant during the same period. These findings suggest the need for integrated healthcare strategies that address both TB and chronic comorbidities to further reduce overall mortality in ageing populations [4].

To identify the specific risk factors for all-cause mortality in older adults, we conducted an age-stratified analysis. While no significant differences in risk factors emerged between patients aged ⩾65 years and <65 years, the HR for most factors were lower in the older group, highlighting age as the strongest predictor of mortality. Notably, in the ⩾80-year age group, the aHR for mortality was 78 times higher than that in the 0–24-year age group, aligning with UK data [30]. Independent risk factors included male sex, smear positivity and comorbidities, consistent with previous studies [31]. Interestingly, mortality risk among patients aged ⩾65 years was lower at PPM institutions than at non-PPM institutions, suggesting that effective case management in PPM settings may reduce mortality in older adults. Further research is needed to confirm this association and clarify the underlying mechanisms.

As the decline in TB incidence and mortality slows due to population ageing, this reality calls for a reassessment of current TB control strategies. Active case-finding strategies targeting vulnerable older adults are essential. Since 2018, South Korea has initiated a nationwide TB screening programme for high-risk individuals over 65 years of age, including bedridden older adults, using mobile chest radiography and sputum testing [32]. In 2021 and 2022, the project detected 120 and 132 TB cases, respectively. With this enhanced case-finding approach, shifting the focus to treating latent tuberculosis infection (LTBI) in older adults is becoming increasingly important. In ageing populations with declining TB incidence, the epidemic is primarily driven by LTBI re-activation. LTBI treatment in older adults has been deprioritised due to concerns about adverse events from traditional regimens. However, recent guidelines recommend safer, shorter rifapentine-containing regimens, making treatment more feasible [33, 34]. Additionally, reducing

non-TB-related mortality among elderly TB patients should be a priority [35]. Integrated care strategies addressing both TB and comorbidities could improve health outcomes and reduce mortality in this vulnerable population.

One of the strengths of this study is its population-based design, offering a comprehensive view of TB trends in South Korea. Although rapid ageing in South Korea may limit direct generalisability, the study provides valuable insights into the relationship between population ageing and TB epidemiology. As many countries experience simultaneously ageing and declining TB incidence, these findings can inform preparations for similar transitions globally. This study included most notified TB patients in South Korea but differed from registry-based national statistics in key aspects. By focusing on patients with drug-susceptible TB and their mortality during treatment, we conducted a detailed analysis of a homogeneous group. The integrated database enabled evaluation of clinical factors associated with mortality risk. However, the study's retrospective design and reliance on routinely collected data present limitations. Defining TB deaths as all-cause mortality during treatment may have overestimated the CFR by including deaths not directly caused by TB. This rationale is explained in the Methods section. Nonetheless, since the ultimate goal of TB treatment is to reduce overall mortality, regardless of cause, this approach provides a broader perspective on TB epidemiology and potential solutions.

In conclusion, this study underscores the significant challenges posed by population ageing to TB epidemiology in rapidly ageing societies. The increasing CFR, coupled with the slower reduction in TB incidence and mortality among older adults, may hinder progress towards achieving TB elimination targets. This demographic shift calls for a fundamental reassessment of current TB control strategies to address the specific needs of the elderly population.

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Data availability: The release of data by the researchers is not legally permitted. All data are available from the database of the National Health Insurance Sharing Service (NHISS) (https://nhiss.nhis.or.kr/bd/ay/bdaya001iv.do). NHISS allows the data to be used by any researcher who agrees to abide by research ethics at some cost. The data for this article can be accessed and downloaded from the website after agreeing to abide by the ethical rules.

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Ethics statement: The study protocol was approved by the Institutional Review Board of Severance Hospital (4-2022-0595) and Korea National Health Insurance Service Medical Request Review Committee (NHIS-2022-1-737). The requirement for informed consent was waived because this was a retrospective study, and the data used were anonymised.

Author contributions: SWL, Doosoo Jeon, HC and YAK conceptualised the study and designed the research methodology. JM, CC, Dawon Jeong, HS conducted data collection and managed resources. SWL and Doosoo Jeon prepared the initial draft of the manuscript. HC, JM, CC, Dawon Jeong, HS participated in data interpretation and provided professional guidance on the manuscript. All authors provided input into interpretation of the results and content of the paper. SWL, Doosoo Jeon, and YAK had full access to all data in the study and verified the data and are responsible for the integrity and accuracy of the data and the decision to submit the manuscript. All authors critically reviewed, revised, and approved the final manuscript.

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