

Impact of COVID-19 on tuberculosis mortality in Japan: a retrospective analysis of national surveillance data from 2017 to 2022

Lisa Kawatsu

kawatsul513er@gmail.com

Nagasaki University

Kazuhiro Uchimura

Japan Anti Tuberculosis Association

Research Article

Keywords: COVID-19, TB mortality, epidemiology, surveillance data

Posted Date: March 18th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-8948359/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at BMC Public Health on June 15th, 2026.
See the published version at <https://doi.org/10.1186/s12889-026-27978-x>.

Abstract

Background

The coronavirus disease 2019 (COVID-19) pandemic and the associated public health and social measures have disrupted tuberculosis (TB) services globally. However, the impact of the pandemic on TB mortality in Japan has not been examined. This study assessed trends in TB mortality before and during the COVID-19 pandemic and evaluated whether being diagnosed during the pandemic influenced TB mortality.

Methods

We analyzed anonymized, individual-level cohort data for all patients notified with active TB to the national TB surveillance system between 1 January 2017 and 31 December 2022. TB mortality rates were estimated for the pre-COVID-19, pre-Omicron, and Omicron variant-dominant periods. Cox proportional hazards models incorporating a time-varying covariate were used to examine the association between COVID-19 period and TB mortality for the entire cohort and for patients aged 0–64 years and ≥ 65 years, with a follow-up period of 365 days. Covariates included age, sex, country of birth, diabetes status, diagnosis, mode of detection, delay, and insurance status.

Results

TB mortality increased from 10.1 (95% confidence interval [CI] 9.7–10.4) to 12.7 per 100 person-years (95% CI 12.0–13.5) between the pre-COVID-19 and Omicron periods. This increase was driven primarily by patients aged ≥ 65 years, whose mortality rose from 15.2 (95% CI 14.7–15.8) to 18.5 per 100 person-years (95% CI 17.4–19.7). Being diagnosed during the Omicron variant-dominant period was identified as an independent predictor of TB mortality among those aged ≥ 65 years (adjusted hazard ratio [aHR] 1.10, 95% CI 1.03–1.18, $p = 0.007$) but not among those aged 0–64 years (aHR 1.09, 95% CI 0.78–1.53, $p = 0.606$).

Background

The coronavirus disease 2019 (COVID-19) pandemic and the wide-ranging public health, economic, and social measures implemented in response have affected the epidemiology of many diseases, including tuberculosis (TB). According to the WHO Global TB report, the world has experienced 18% reduction in the number of TB cases notified in 2020, compared with 2019, 15% reduction in the number of people treated for drug-resistant tuberculosis, and 21% decrease in the number of people receiving preventive therapy for latent tuberculosis infection¹. Treatment outcomes also deteriorated, with an estimated 1.32 million TB deaths in 2020 – the first year-over-year increase in TB mortality since 2005¹. Several modeling studies have similarly indicated the potential impact of COVID-19 on TB mortality. For example, Cilloni et al. predicted that globally, TB mortality could return to the level reported in 2013², whereas Hogan et al. estimated that TB mortality could increase by up to 20% between 2020 and 2025³.

Japan achieved low-burden TB status during the pandemic, with a notification rate of 9.2 per 100,000 population in 2021⁴. Its TB epidemiology is unique compared with that of other high-income countries, where the majority of the TB burden is now borne by the young migrant population while in Japan, approximately 70% of newly reported patients are Japan-born elderly individuals aged ≥ 65 years⁴. Naturally, older adults experience markedly poorer TB treatment outcomes; among patients notified in 2020, the proportion of deaths was 2.7% among those aged 0–64 years but 38.6% among those aged ≥ 65 years⁴. COVID-19 has also disproportionately affected older adults in Japan. As of May 2023, when COVID-19 was downgraded from Class 5 to Class 2 under Japan's Infectious Diseases Control Law, approximately 34 million cases and 7.4 million deaths had been reported, with individuals aged ≥ 65 years accounting for 95.7% of COVID-19 deaths⁵. Despite this, the extent to which COVID-19 may have influenced TB mortality in Japan—particularly among older adults—remains unknown. This study therefore aimed to examine trends in TB mortality by different age groups before and during the COVID-19 pandemic and explore the effects, if any, of being diagnosed during the COVID-19 pandemic on TB mortality via national TB surveillance data.

Methods

Study design, study population and data sources

We conducted a retrospective observational study using anonymized, individual-level data from the Japan Tuberculosis Surveillance System (JTBS). Details of the system have been described elsewhere⁶, however, briefly, TB is classified as a Class 2 infectious disease in Japan, requiring all physicians—regardless of practice setting—to report diagnosed cases of active TB immediately to the local health authority. Upon notification, the local health authority staff enter patient information into the JTBS. Records remain in the system for up to two years, as mandated by Japan's Infectious Diseases Control Law, which requires follow-up of TB patients for a maximum of two years after treatment completion. Patients are deregistered earlier if they die, transfer out, or are deemed not to require further follow-up (e.g., misdiagnosis). For the purpose of our study, we utilized cohort data from all patients notified with active TB between 1st January 2017 and 31st December 2022. The data were accessed from March 30, 2025, for 6 months.

Operational definitions

The primary outcome was death due to TB, as recorded in the JTBS. Because the “treatment outcome” variable does not specify cause of death⁷, TB-specific mortality was identified using the mandatory field “reason for deregistration,” which classifies deaths as either “TB death” or “non-TB death.” All non-TB deaths and other deregistration reasons were treated as censored observations.

The time to TB death was defined as the number of days from the day the patient was notified to the JTBS (available as the variable “date of notification”) to the day the patient was reported to have died

(available as the variable “date of death”). If the date of death was missing, then we used the date when the patient was deregistered (available as the variable “date of deregistration from the JTBS”) as a proxy.

Exposure variable

The main exposure was the COVID-19 period at the time of TB notification, categorized into:

1. **Pre-COVID-19 period** (January 2017–June 2019):
Patients were assumed to have completed treatment before COVID-19 emerged in Japan.
2. **Pre-Omicron period** (July 2019–November 2021):
Community exposure to COVID-19 was limited; fewer than 5% of the population had been infected⁸.
3. **Omicron variant-dominant period** (December 2021–December 2022):
COVID-19 transmission was widespread, with approximately 27% of the population infected⁸.

Other covariates included age (years), sex, country of birth, TB diagnosis category, diabetes status, mode of detection, diagnostic delay (time from symptom onset to first clinical visit), and insurance status.

(Fig. 1). <**Fig. 1. Newly notified and cumulative number of COVID-19 cases in Japan, 2020–2022.** Newly reported and cumulative number of COVID-19 cases in Japan in the “pre-Omicron” and “Omicron” variant-dominant periods between 2020 and 2022 (those notified in the “pre-COVID” era are not shown) >

Statistical analysis

R version 4.4.1⁹ was used for all the statistical analyses. Descriptive statistics were summarized as means with standard deviations or frequencies with percentages. TB mortality rates were calculated using total person-years as the denominator for each COVID-19 period. Temporal trends in TB mortality across the three periods were assessed using a Cochran–Armitage trend test.

Cox proportional hazards regression models were fitted to estimate crude and adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs). Multicollinearity among covariates was assessed via the variance inflation factor (VIF). Proportional hazards assumptions were evaluated via Schoenfeld residuals.

Age, treated as a continuous variable, violated the proportional hazards assumption and was therefore modeled as a time-varying covariate via the *tt()* function in the Cox model. Categorical covariates that violated the proportional hazards assumption were adjusted for through stratification via the *strata()* option. Statistical significance was defined as $p < 0.05$.

Analyses were conducted for the entire cohort and separately for patients aged 0–64 years and those aged ≥ 65 years to assess potential age-specific differences in the association between the COVID-19 period and TB mortality.

Results

Sociodemographic characteristics and changes over the study period

During the study period, a total of 81,332 patients were newly notified as having active TB to the JTBS, of whom cohort data were available for analysis for 81,003 (99.6%). Patient characteristics by COVID-19 period are summarized in Table 1.

Across the three periods, the proportion of patients aged ≥ 65 years increased from 66.8% in the pre-COVID-19 period to 70.2% in the Omicron period ($p < 0.001$). The proportion of those with extrapulmonary TB (EPTB) also increased (22.6% to 27.0%, $p < 0.001$). Regarding the mode of detection, the proportion of patients identified during outpatient visits or hospitalization increased from 81.8% to 84.0% ($p < 0.001$).

While the proportion of those with shorter delays (< 2 weeks) decreased from 27.7% to 25.9% ($p < 0.001$), this decrease was not as much accompanied by an increase in the proportion of those with longer delays but rather an increase in those whose delay information was unknown (22.8% to 28.8%, $p < 0.001$). The proportion of patients who were uninsured, categorized as “other,” or had unknown insurance status also increased modestly (2.8% to 4.1%, $p < 0.001$).

Table 1
Characteristics of the study participants by COVID-19 period.

	Pre-Covid		Covid: pre-Omicron		Covid: Omicron	
	Jan 1, 2017- Jun 30, 2019		Jul 1, 2019- Nov 30, 2021		Dec 1, 2021-Dec 31, 2022	
	n	%	n	%	n	%
Total	39,374	100	30,460	100	11,169	100.0
Mean age in years (SD)	68.2 (± 21.7)		69.1 (± 21.7)		70.0 (± 21.5)	
Age groups						
0 to 64 years old	13,084	33.2	9,670	31.7	3,327	29.8
65 years old or above	26,290	66.8	20,790	68.3	7,842	70.2
Sex						
Male	23,522	59.7	17,876	58.7	6,681	59.8
Female	15,852	40.3	12,584	41.3	4,488	40.2
Country of birth						
Japan-born	34,266	87.0	26,280	86.3	9,546	85.5
Foreign-born	3,950	10.0	3,442	11.3	1,342	12.0
Unknown	1,158	2.9	738	2.4	281	2.5
Comorbidity - diabetes						
Yes	5,678	14.4	4,588	15.1	1,797	16.1
No	29,667	75.3	22,129	72.6	7,877	70.5
Unknown	4,029	10.2	3,743	12.3	1,495	13.4
Diagnosis						
Sputum smear positive PTB	14,774	37.5	11,079	36.4	4,086	36.6
Other bacteriologically positive PTB	11,629	29.5	8,771	28.8	3,113	27.9
Clinical PTB	4,069	10.3	2,886	9.5	954	8.5
EPTB	8,902	22.6	7,724	25.4	3,016	27.0
Mode of detection						
SD: standard deviation, PTB: pulmonary TB, EPTB: extrapulmonary TB, ¶ Either at outpatient visit or during hospitalization for diseases other than TB						

	Pre-Covid		Covid: pre-Omicron		Covid: Omicron	
	Jan 1, 2017- Jun 30, 2019		Jul 1, 2019- Nov 30, 2021		Dec 1, 2021-Dec 31, 2022	
	n	%	n	%	n	%
Screening	5,022	12.8	3,626	11.9	1,307	11.7
Contact investigation	1,475	3.7	874	2.9	275	2.5
Upon hospital visit/during hospitalization [Ⓢ]	32,219	81.8	25,442	83.5	9,385	84.0
Others or unknown	658	1.7	518	1.7	202	1.8
Delay						
< 2 weeks	10,897	27.7	8,257	27.1	2,894	25.9
≥ 2 weeks, < 1 month	3,280	8.3	2,316	7.6	814	7.3
≥ 1 month, < 3 months	4,307	10.9	2,939	9.6	1,059	9.5
> 3 months	2,203	5.6	1,547	5.1	603	5.4
Unknown	8,988	22.8	7,947	26.1	3,214	28.8
No symptoms	9,699	24.6	7,454	24.5	2,585	23.1
Insurance status						
Insured	35,672	90.6	27,629	90.7	9,975	89.3
Receiving social welfare	2,580	6.6	1,969	6.5	739	6.6
Not insured, others or unknown	1,122	2.8	862	2.8	455	4.1
SD: standard deviation, PTB: pulmonary TB, EPTB: extrapulmonary TB, [Ⓢ] Either at outpatient visit or during hospitalization for diseases other than TB						

Trends in TB mortality and Kaplan–Meier estimates of TB mortality for different COVID-19 periods

Table 2 presents TB mortality by age group and COVID-19 period. Overall, the proportion of those deregistered from the JTBS due to TB death increased from 8.1% in the pre-COVID-19 period to 9.9% in the Omicron period. The proportion of TB deaths was consistently much higher among patients aged ≥ 65 years than among those aged 0–64 years.

TB mortality rates increased significantly across the three periods. Among all ages, mortality rose from 10.1 (95% confidence interval [CI] 9.7–10.4) to 12.7 per 100 person-years (95% CI 12.0–13.5) ($p <$

0.0001). The increase was driven almost entirely by older adults: mortality among those aged ≥ 65 years increased from 15.2 (95% CI 14.7–15.8) to 18.5 per 100 person-years (95% CI 17.4–19.7) ($p < 0.0001$). In contrast, mortality among those aged 0–64 years remained low and stable across periods (1.5 to 1.6 per 100 person-years). (see also Fig. 2). <**Figure 2. Trends in TB mortality from the pre-COVID-19 period to the COVID-19 period by age group.** The mortality rates for the overall population, those aged 0–64 years and those aged 65 years and above, for the pre-COVID-19, pre-Omicron and Omicron variant-dominant periods>

Table 2
TB mortality among different age groups by COVID-19 period.

	Pre-Covid		Covid: pre-Omicron		Covid: Omicron	
	Jan 1, 2017- Jun 30, 2019		Jul 1, 2019- Nov 30, 2021		Dec 1, 2021-Dec 31, 2022	
	n	%	n	%	n	%
All ages						
Total	39,374	100.0	30,460	100.0	11,169	100.0
Of whom, deleted from JTBS	13,962	35.5	11,081	36.4	4,440	39.8
Of whom, deleted due to TB death	3,199	8.1	2,722	8.9	1,104	9.9
Person years	31,802		24,382		8,681	
TB mortality/100 person years (95% CI)	10.1 (9.7–10.4)		11.2 (10.8–11.6)		12.7 (12.0-13.5)	
0–64 years old						
Total	13,084	100.0	9,670	100.0	3,327	100.0
Of whom, deleted from JTBS	2,811	21.5	2,023	20.9	789	23.7
Of whom, deleted due to TB death	173	1.3	112	1.2	48	1.4
Person years	11,926		8,861		2,983	
TB mortality/100 person years (95% CI)	1.5 (1.2–1.7)		1.3 (1.0-1.5)		1.6 (1.2–2.1)	
65 years old and above						
Total	26,290	100.0	20,790	100.0	7,842	100.0
Of whom, deleted from JTBS	11,151	42.4	9,058	43.6	3,651	46.6
Of whom, deleted due to TB death	3,026	11.5	2,610	12.6	1,056	13.5
Person years	19,876		15,522		5,698	
TB mortality/100 person years (95% CI)	15.2 (14.7–15.8)		16.8 (16.2–17.5)		18.5 (17.4–19.7)	
JTBS: Japan Tuberculosis Surveillance System; TB: tuberculosis; CI: confidence interval						

Kaplan–Meier curves showed that most TB deaths occurred within the first 100 days after notification, particularly among patients aged ≥ 65 years. Median survival time was not reached in any group. Mean survival times decreased slightly across periods for all age groups, with the largest decline observed among older adults (328 days in the pre-COVID-19 period to 321 days in the Omicron period). Log-rank tests indicated significant differences in survival across COVID-19 periods for the overall cohort and for those aged ≥ 65 years, but not for those aged 0–64 years. (Figs. 3a-3c). <Figures 3a-3c. Kaplan–Meier survival estimates for TB mortality by COVID-19 period. (3a) Estimates for the whole cohort, (3b) those aged 0–64 years, and (3c) those aged 65 years and above>

Baseline characteristics of patients who died due to TB versus survived

Baseline characteristics of patients who died due to TB and those who survived are shown in Table 3. Compared with survivors, patients who died were more likely to be older, Japan-born, diagnosed with sputum smear-positive pulmonary TB, have diabetes, and be detected during hospital visits or hospitalization. These patterns were consistent across age-stratified analyses.

Table 3
Baseline characteristics of patients who died due to TB versus survived.

	All ages		0–64 years old		65 years old and above	
	Non TB death	TB death	Non TB death	TB death	Non TB death	TB death
Age, in years	NA	NA	NA	NA	NA	NA
Sex						
Female	30,129	2,858	10,401	50	19,728	2,808
Male	43,849	4,167	15,347	283	28,502	3,884
Country of Birth						
Foreign-born	8,671	63	8,332	27	339	36
Japan-born	63,393	6,699	16,940	293	46,453	6,406
Unknown	1,914	263	476	13	1,438	250
Diagnosis						
EPTB	18,205	1,437	5,193	42	13,012	1,395
Sputum smear positive PTB	25,637	4,302	7,721	246	17,916	4,056
Other bacteriologically positive PTB	22,363	1,150	8,255	33	14,108	1,117
Clinical PTB	7,773	136	4,579	12	3,194	124
Comorbidity - diabetes						
No	54,965	4,708	21,112	182	33,853	4,526
Yes	10,876	1,187	1,979	49	8,897	1,138
Unknown	8,137	1,130	2,657	102	5,480	1,028
Mode of detection						
Contact investigation	2,599	25	1,776	0	823	25
Upon hospital visit/during hospitalization	60,282	6,764	16,193	291	44,089	6,473
Screening	9,883	72	7,286	8	2,597	64
Others or unknown	1,214	164	493	34	721	130
Delay*						
PTB: pulmonary TB, EPTB: extrapulmonary TB, * Either at outpatient visit or during hospitalization						

	All ages		0–64 years old		65 years old and above	
	Non TB death	TB death	Non TB death	TB death	Non TB death	TB death
No symptoms	19,344	394	9,464	6	9,880	388
Less than 2 weeks	19,563	2,485	4,907	66	14,656	2,419
More than 2 weeks and less than 1 month	5,820	590	1,905	22	3,915	568
More than 1 month and less than 3 months	7,536	769	2,708	47	4,828	722
More than 3 months	3,989	364	1,768	51	2,221	313
Unknown	17,726	423	4,996	141	12,730	2,282
Insurance status						
With insurance	67,047	6,229	23,283	176	43,764	6,053
On social welfare	2,184	255	1,204	97	980	158
No insurance or unknown	4,747	541	1,261	60	3,486	481
COVID period						
Pre-COVID	36,175	3,199	12,911	173	23,264	3,026
COVID pre-Omicron	27,738	2,722	9,558	112	18,180	2,610
COVID Omicron	10,065	1,104	3,279	48	6,786	1,056
PTB: pulmonary TB, EPTB: extrapulmonary TB, * Either at outpatient visit or during hospitalization						

Effect of being diagnosed during the COVID-19 pandemic on TB mortality

Results of the Cox proportional hazards models are presented in Table 4. Among all ages, being diagnosed during the Omicron period was associated with a significantly higher risk of TB death compared with the pre-COVID-19 period (aHR 1.10, 95% CI 1.02–1.18, $p = 0.010$). No significant association was observed for the pre-Omicron period (aHR 1.04, 95% CI 0.99–1.10, $p = 0.147$).

Age was a strong predictor of TB mortality in all models. When modeled as a time-varying covariate, the effect of age increased over time, particularly among patients aged ≥ 65 years (aHR 1.01, 95% CI 1.01–1.01, $p < 0.001$). In age-stratified analyses, the association between COVID-19 period and TB mortality differed markedly by age group. Among patients aged 0–64 years, neither the pre-Omicron nor Omicron periods were associated with increased TB mortality. In contrast, among those aged ≥ 65 years, being

diagnosed during the Omicron period was an independent predictor of TB death (aHR 1.10, 95% CI 1.03–1.18, $p = 0.007$), whereas the pre-Omicron period was not.

Table 4
Hazard ratios for being diagnosed during the COVID-19 pandemic for TB mortality

All ages	Non-TB death	TB death	cHR	aHR	95% CI	p value
Age, in years	NA		1.07	1.04	1.03–1.04	< 0.001
Age, in years adjusted as TVC	NA		NA	1.01	1.01–1.01	< 0.001
Pre-COVID	36,175	3,199	Reference			
COVID: pre-Omicron	27,738	2,722	1.10	1.04	0.99–1.10	0.147
COVID: Omicron	10,065	1,104	1.24	1.10	1.02–1.18	0.010
0–64 years old						
Age, in years	NA		1.09	1.05	1.03–1.09	< 0.001
Age, in years adjusted as TVC	NA		NA	1.00	0.99–1.01	0.365
Pre-COVID	12,911	173	Reference			
COVID: pre-Omicron	9,558	112	0.88	0.89	0.69–1.14	0.357
COVID: Omicron	3,279	48	1.10	1.09	0.78–1.53	0.606
65 years old and above						
Age, in years	NA		1.08	1.04	1.03–1.05	< 0.001
Age, in years adjusted as TVC	NA		NA	1.01	1.01–1.01	< 0.001
Pre-COVID	23,264	3,026	Reference			
COVID: pre-Omicron	18,180	2,610	1.09	1.05	0.99–1.10	0.103
COVID: Omicron	6,786	1,056	1.19	1.10	1.03–1.18	0.007

TB: tuberculosis, cHR: crude hazard ratio, aHR: adjusted hazard ratio, CI: confidence interval, TVC: time-varying covariate

Discussion

This nationwide retrospective study examined trends in TB mortality in Japan before and during the COVID-19 pandemic and assessed whether being diagnosed during the pandemic influenced TB mortality. Using six years of national surveillance data, we found that TB mortality increased during the pandemic, particularly during the Omicron variant-dominant period. Importantly, this increase was driven

almost entirely by older adults, who constitute the majority of TB patients in Japan. Among individuals aged ≥ 65 years, being diagnosed during the Omicron period was independently associated with a higher risk of TB death, whereas no such association was observed among those aged 0–64 years.

At the onset of the pandemic, Japan classified COVID-19 as a Class 2 infectious disease, the same category as TB, requiring mandatory reporting and intensive public health follow-up^{10,11}. This reallocation of public health resources raised concerns that TB services might be disrupted, with early reports suggesting evidence of reductions in TB case detection and delays in care¹², which were consistent with global observations.

However, several studies have eventually noted that Japan's public health and medical systems remained relatively resilient during the initial pandemic waves, and TB services largely remained functional^{13–16}. Thus, although a decline in case detection was observed in Japan, it may not have aggravated treatment outcomes via reduced access to care, as was reported in some countries^{17,18}. This may explain why being diagnosed during the pre-Omicron period was not associated with increased TB mortality in our analysis.

In contrast, the Omicron period was characterized by unprecedented numbers of COVID-19 cases, despite the variant's lower intrinsic virulence. The sheer volume of infections likely strained healthcare capacity and increased the probability of co-infection with COVID-19 among TB patients. International cohort studies have shown that COVID-19 co-infection has been associated with worse TB outcomes, including higher mortality, particularly among older adults and those with comorbidities^{19,20}. Although we could not assess co-infection directly due to the absence of COVID-19 clinical data in the JTBS, the elevated mortality observed during the Omicron period may reflect the combined effects of increased exposure to COVID-19, healthcare system strain, and the vulnerability of Japan's predominantly older TB population. Beyond direct co-infection, indirect effects of the pandemic may also have contributed to increased TB mortality among older adults. Prolonged social restrictions, reduced physical activity^{21,22}, and worsening mental health^{23–25}—well-documented consequences of the pandemic in Japan—may have disproportionately affected older individuals, potentially exacerbating frailty and impairing their ability to adhere to TB treatment. Poor activities of daily living and depression are known risk factors for adverse TB outcomes^{26–29}, including mortality. These broader societal impacts may therefore have played a role in the observed increase in TB deaths during the later stages of the pandemic.

Our findings underscore the unique vulnerability of older adults with TB in Japan. Even before the pandemic, TB mortality among older adults was substantially higher than among younger individuals. The additional pressures introduced by the pandemic appear to have amplified this disparity. As Japan continues to experience population aging, strengthening TB care for older adults—including early detection, comprehensive clinical management, and social support—will be essential, particularly during public health emergencies.

This study has several limitations. First, because the analysis relied solely on national TB surveillance data, we lacked clinical information on COVID-19 infection and vaccination status. Although several cohort studies from other countries have examined the impact of COVID-19 co-infection and vaccination on TB outcomes, such data are not available in Japan because the JTBS does not include COVID-19–related clinical information. Consequently, we were unable to assess these associations in our dataset. Other important confounders known to influence TB outcomes—such as malnutrition, smoking, and chronic obstructive pulmonary disease—were also unavailable and therefore unmeasured.

Second, the classification of “TB death” and “non-TB death” depends entirely on physicians’ reporting to public health centers. Given Japan’s extremely low autopsy rate compared with other high-income countries, both under- and over-reporting of TB deaths, as well as misclassification, may have occurred³⁰. These issues may have been exacerbated during periods of heightened healthcare strain, such as the COVID-19 pandemic. Moreover, the JTBS does not record the causes of “non-TB death,” meaning that some TB-related deaths may have been misclassified as non-TB deaths.

Third, survivor bias may have influenced period-specific mortality estimates. Patients diagnosed earlier in the pandemic had longer potential follow-up and may have been more likely to survive into later periods, potentially distorting comparisons across COVID-19 periods. In addition, HIV status was missing for the vast majority of patients. Given the well-established association between HIV infection and TB mortality, the absence of this information represents a major limitation and may have resulted in residual confounding.

Despite these limitations, we believe the use of comprehensive national surveillance data provides valuable insights into TB mortality trends during the COVID-19 pandemic in Japan.

Conclusion

This nationwide analysis demonstrates that TB mortality in Japan increased during the COVID-19 pandemic, with the most pronounced rise occurring during the Omicron variant-dominant period. Importantly, this increase was driven almost entirely by older adults, who already represent the majority of TB patients in Japan and who remain particularly vulnerable to adverse outcomes. Being diagnosed during the Omicron period was independently associated with higher TB mortality among individuals aged ≥ 65 years, whereas no such association was observed among younger adults.

These findings highlight the need for strengthened TB care and support systems for older populations, especially during periods of widespread infectious disease transmission or healthcare system strain. Ensuring continuity of TB services, improving early detection, and addressing the broader health and social vulnerabilities of older adults will be essential for mitigating excess TB mortality during future public health emergencies.

Abbreviations

aHR
adjusted hazard ratio
cHR
crude hazard ratio
CI
confidence interval
EPTB
extrapulmonary tuberculosis
JTBS
Japan TB Surveillance
PTB
pulmonary tuberculosis
SD
standard deviation
TB
tuberculosis
TVC
time-varying covariate

Declarations

Ethics approval and consent to participate: The study was conducted in accordance with the Declaration of Helsinki. The protocol was reviewed, and approval was deemed unnecessary by the Institutional Review Board of Nagoya City University, as the study utilized only anonymous surveillance data.

Consent for publication: NA

Availability of data and materials: The JTBS raw data are not publicly available according to the policies of the Ministry of Health, Labor and Welfare, Japan. The datasets used for this current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This work was supported by JSPS KAKENHI Grant Number C23K09709.

Author contributions: LK conceptualized the study and led the manuscript development, including data analysis. KU was a major contributor to the discussion. All the authors have read and approved the final manuscript.

Acknowledgment: NA

References

1. WHO Global. tuberculosis report 2020. Geneva: World Health Organization.
2. Cilloni L, Fu H, Vesga JF, Dowdy D, Pretorius C, Ahmedov S, et al. The potential impact of the COVID-19 pandemic on the tuberculosis epidemic: a modelling analysis. *EClinicalMedicine*. 2020;24:28:100603. 10.1016/j.eclinm.2020.100603.
3. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. *Lancet Glob Health*. 2020;8(9):e1132–41. 10.1016/S2214-109X(20)30288-6.
4. The Tuberculosis Surveillance Center. Statistics of TB. Available from: <https://jata-ekigaku.jp/english/statistics-of-tb>. Accessed 21 September, 2025.
5. Ministry of Health. Labour and Welfare, Japan. De-ta kara wakaruru shinngata korona kannsensho jouhou (Data on COVID-19). In Japanese. Available from: <https://covid19.mhlw.go.jp/>. Accessed 21 September, 2025.
6. Tuberculosis Surveillance Center. Tuberculosis in Japan annual report 2021. Available from: <https://jata-ekigaku.jp/english/annual-reports>. Accessed 21 September, 2025.
7. Uchimura K, Ngamvithayapong-Yanai J, Kawatsu L, Ohkado A, Yoshiyama T, Ito K, et al. Permanent employment or public assistance may increase tuberculosis survival among working-age patients in Japan. *Int J Tuberc Lung Dis*. 2015;19(3):312–8. 10.5588/ijtld.14.0104.
8. Kinoshita R, Miyamoto S, Sakuraba S, Sugihara J, Suzuki M, Suzuki T, et al. Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence, Japan, 2023. *Emerg Infect Dis*. 2024;30(6):1267–70. 10.3201/eid3006.231454.
9. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2023.
10. Uchida K. Hokenjo no kannsennshou kikananritaiseino kyouka – COVID-19 taisaku no kadai mo fukumete (Strengthening the infectious disease crisis management system of public health centers-including the challenges of COVID-19 measures). *Japanese J Public Health Pract*. 2021;85(11):751–6. <https://doi.org/10.11477/mf.1401209731>.
11. Machida M, Wada K. Public health responses to COVID-19 in Japan. *Global Health Med*. 2022;30(4):78–82. 10.35772/ghm.2022.01025.
12. Uchimura K. Medium-term impact of the COVID-19 pandemic on the epidemiology of tuberculosis in Japan. Presentation Asia Pac Soc Respirol, 2024. Presentation no. A018-004.
13. Tashiro A, Shaw R. COVID-19 Pandemic Response in Japan: What Is behind the Initial Flattening of the Curve? *Sustainability*. 2020; 12(13):5250. <https://doi.org/10.3390/su12135250>
14. Legido-Quigley H, Asgari N, Teo YY, Leung GM, Oshitani H, Fukuda K, et al. Are high-performing health systems resilient against the COVID-19 epidemic? *Lancet*. 2020;14(10227):848–50. 10.1016/S0140-6736(20)30551-1.
15. Nomura S, McEnany M, Sugawara J, Noritake R, Miyata H. Sustainability and Resilience in Japan's Health System. London; 2022. Available from: <https://hgpi.org/en/wp->

- content/uploads/sites/2/Report_PHSSR_Japan_2022_ENG.pdf Accessed December 26, 2025.
16. Tomioka K, Yamada M, Uno K, Araki I, Hirohata H, Nagai H, et al. Hokenjo ni okeru shingata korona uirusu kansensho heno taiou: kinki hokenjochokai chousa houkoku. *Japanese Soc Public Health*. 2022;69(6):473–82. <https://doi.org/10.11236/jph.21-096>.
 17. Magro P, Formenti B, Marchese V, Gulletta M, Tomasoni LR, Caligaris S, et al. Impact of the SARS-CoV-2 epidemic on tuberculosis treatment outcome in Northern Italy. *Eur Respir J*. 2020;56(4):2002665. 10.1183/13993003.02665-2020.
 18. Wang X, He W, Lei J, Liu G, Huang F, Zhao Y. Impact of COVID-19 Pandemic on Pre-Treatment Delays, Detection, and Clinical Characteristics of Tuberculosis Patients in Ningxia Hui Autonomous Region, China. *Front Public Health*. 2021;9:644536. 10.3389/fpubh.2021.
 19. Mollaligh H, Chala D, Beyen D. Clinical Features and Treatment Outcome of Coronavirus and Tuberculosis Co-Infected Patients: A Systematic Review of Case Reports. *Infect Drug Resist*. 2022;15:4037–46. 10.2147/IDR.S370837.
 20. Wang Q, Guo S, Wei X, Dong Q, Xu N, Li H, et al. Global prevalence, treatment and outcome of tuberculosis and COVID-19 coinfection: a systematic review and meta-analysis (from November 2019 to March 2021). *BMJ Open*. 2022;12:e059396. 10.1136/bmjopen-2021-059396.
 21. Teraoka K, Ysuiji T, Jindo T, Tokunaga S, Okura T. Changes in the physical fitness of elderly people in the COVID-19 pandemic: An examination using performance tests. *Japanese J Japan Geriatr Soc*. 2022;59:91–500. <https://doi.org/10.3143/geriatrics.59.491>.
 22. Yamada M, Kimura Y, Ishiyama D. Effect of the COVID-19 epidemic on physical activity in community-dwelling older adults in Japan: A cross-sectional online survey. *J Nutr Health Aging*. 2020;24:948–50. 10.1007/s12603-020-1424-2.
 23. Fujita K, Inoue A, Kuzuya M, Uno C, Huang CH, Umegaki H, Onishi J. Mental Health Status of the Older Adults in Japan During the COVID-19 Pandemic. *J Am Med Dir Assoc*. 2021;22(1):220–1. 10.1016/j.jamda.2020.11.023.
 24. Matsuzono K, Mashiko T, Ana Y, Koide R, Yoshizumi H, Fujimoto S. Impact of COVID-19 pandemic on mortality and cognitive function of dementia patients: Tochigi Dementia Cohort Study. *J Neurol Sci*. 2024;456:122840. 10.1016/j.jns.2023.122840.
 25. Matsui T, Mitsuma S, Nagata A, Matsushita S, Asahi T. Accelerated cognitive decline after the COVID-19 pandemic in a community population of older persons with cognitive impairment: A 4-year time series analysis in the Tokyo Metropolis area. *Geriatr Gerontol Int*. 2023;23(3):200–4. 10.1111/ggi.14543.
 26. Osawa T, Watanabe M, Morimoto K, Yoshiyama T, Matsuda S, Fujiwara K, et al. Activities of Daily Living, Hypoxemia, and Lymphocytes Score for Predicting Mortality Risk in Patients With Pulmonary TB. *Chest*. 2024;165(2):267–77. 10.1016/j.chest.2023.09.008.
 27. Horita N, Miyazawa N, Yoshiyama T, Kojima R, Omori N, Kaneko T, et al. Poor performance status is a strong predictor for death in patients with smear-positive pulmonary TB admitted to two Japanese hospitals. *Trans R Soc Trop Med Hyg*. 2013;107(7):451–6. 10.1093/trstmh/trt037.

28. Ruiz-Grosso P, Cachay R, de la Flor A, Schwalb A, Ugarte-Gil C. Association between tuberculosis and depression on negative outcomes of tuberculosis treatment: a systematic review and meta-analysis. PLoS ONE. 2020;15(1):e0227472. 10.1371/journal.pone.0227472.

29. Ambaw F, Mayston R, Hanlon C, Alem A. Depression among patients with tuberculosis: determinants, course and impact on pathways to care and treatment outcomes in a primary care setting in southern Ethiopia-a study protocol. BMJ Open. 2015;5(7):e007653. 10.1136/bmjopen-2015-007653.

30. Ishihara K, Iwase H. Reform of the death investigation system in Japan. Medicine, Science and the Law. 2020; 60(3): 216–222. 10.1177/0025802420916590

Figures

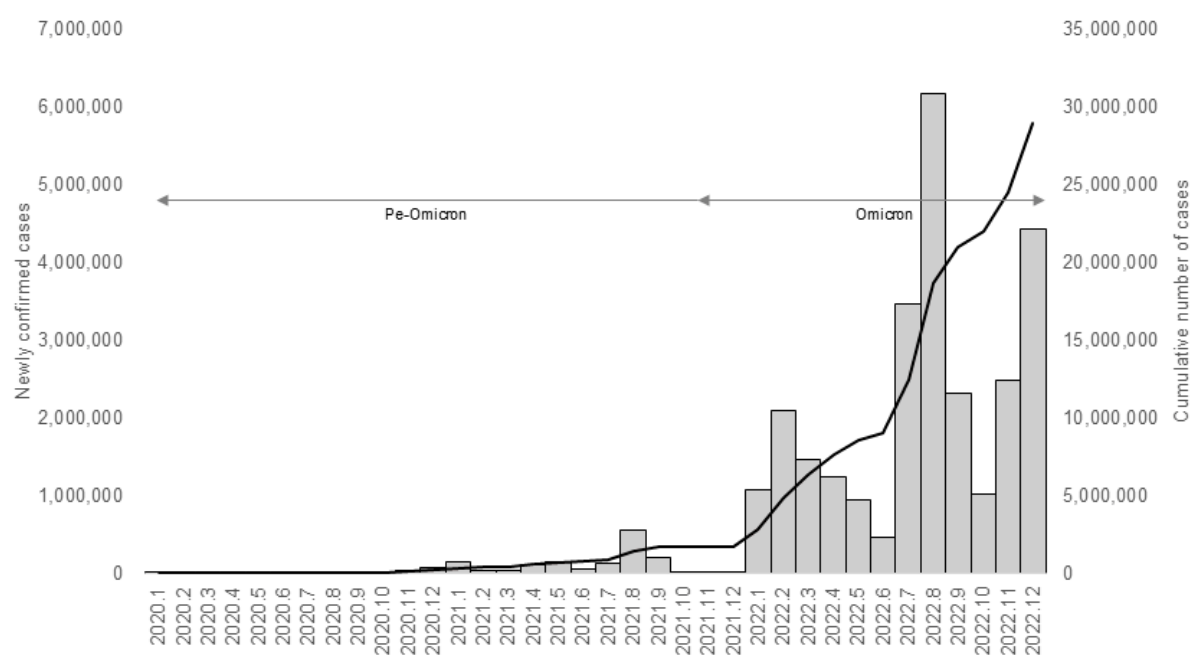


Figure 1

Newly notified and cumulative number of COVID-19 cases in Japan, 2020--2022. Newly reported and cumulative number of COVID-19 cases in Japan in the “pre-Omicron” and “Omicron” variant-dominant periods between 2020 and 2022 (those notified in the “pre-COVID” era are not shown)

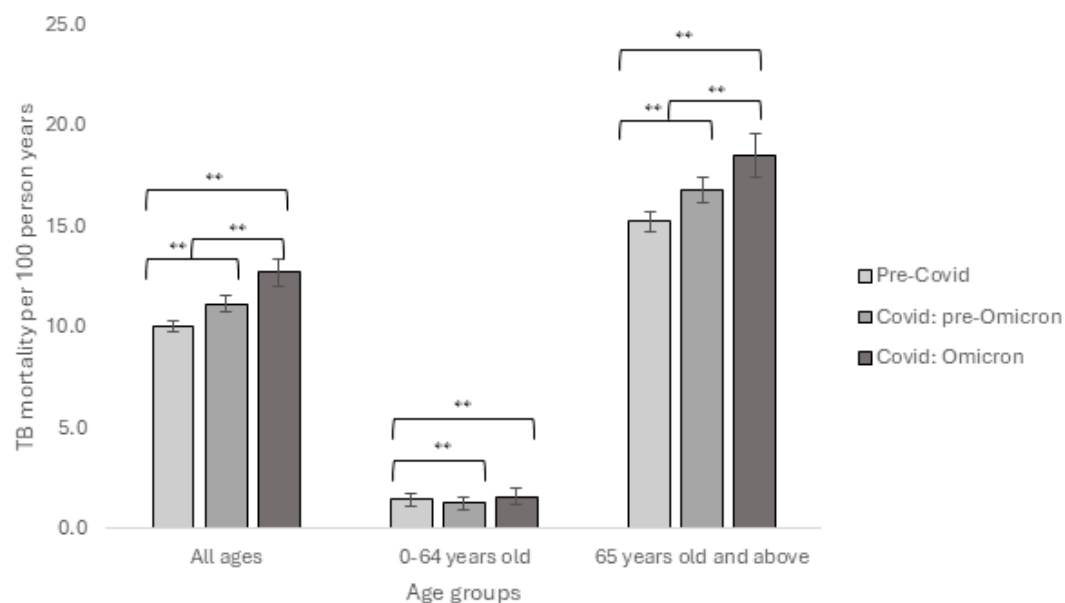


Figure 2

Trends in TB mortality from the pre-COVID-19 period to the COVID-19 period by age group. The mortality rates for the overall population, those aged 0–64 years and those aged 65 years and above, for the pre-COVID-19, pre-Omicron and Omicron variant-dominant periods

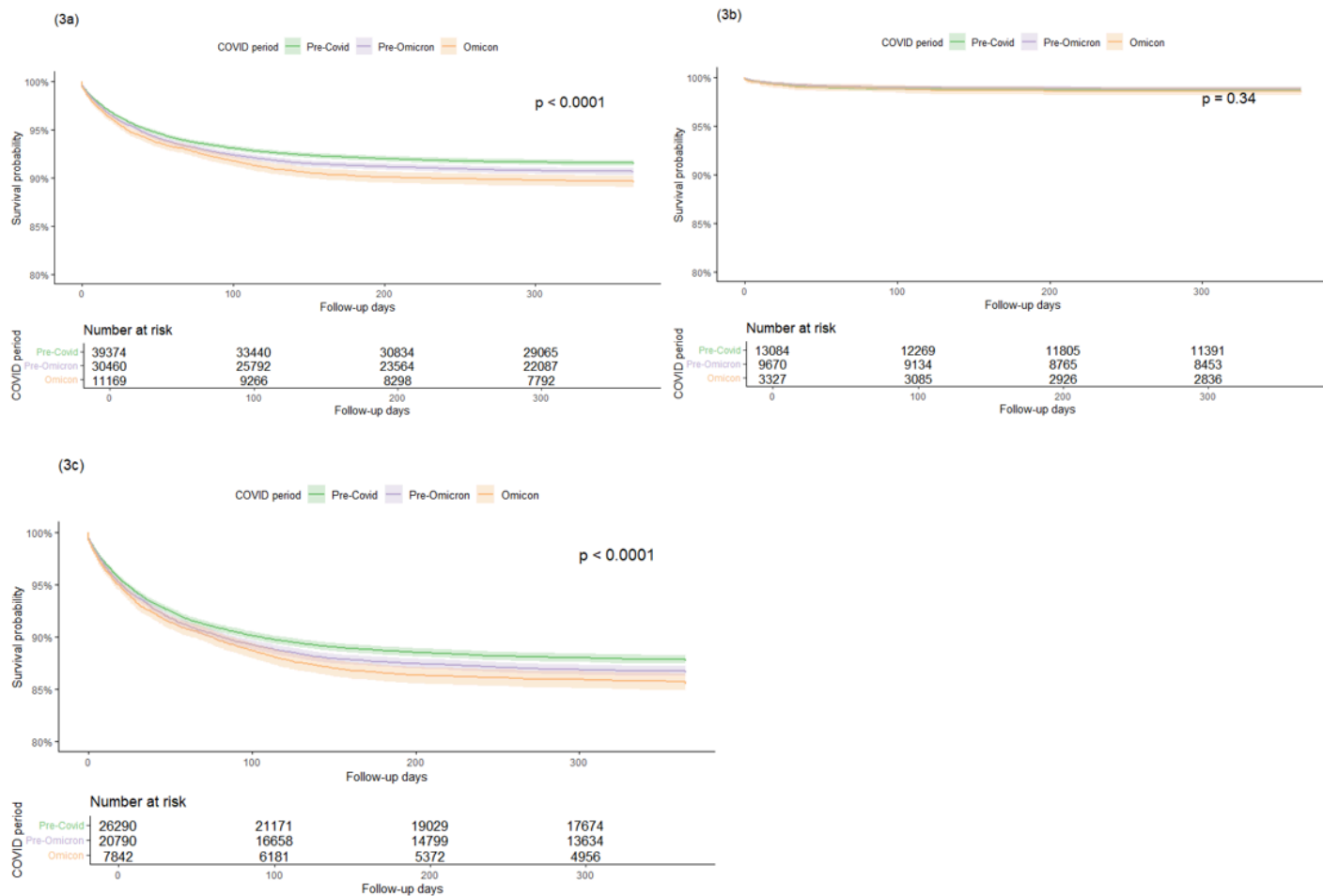


Figure 3

Kaplan–Meier survival estimates for TB mortality by COVID-19 period. (3a) Estimates for the whole cohort, (3b) those aged 0-64 years, and (3c) those aged 65 years and above