Objective: To determine the characteristics associated with mortality in patients with culture-positive pulmonary tuberculosis (PTB) in Airin, Osaka City, Japan.

Methods: The characteristics of patients with culture-positive PTB registered between 2015 and 2018 in Airin, Osaka City, Japan, were compared between those who died of all causes before or during treatment and those who completed treatment.

Results: Of the 241 culture-positive PTB patients eligible for this study, 170 completed treatment, with negative sputum culture tests, and 62 died. The all-cause case fatality rate was 26.7% (62/232). Multivariate analysis showed that mortality was associated with age ≥70 years, having a positive sputum smear, a body mass index of <18.5 and serious comorbidities such as cancer and heart and renal disease. Detection of tuberculosis (TB) by screening or in an outpatient department (OPD) for other diseases was inversely associated with mortality.

Discussion: Detection of PTB by chest X-ray screening and during regular visits to OPDs for other diseases was associated with non-fatal TB and might contribute to early case finding. Therefore, current active TB case finding and health education on regular visits to physicians for other diseases should be strengthened further for the urban poor population of Osaka City, Japan.

In 2018, Osaka City had the highest TB notification rate of all cities in Japan, at 29.3 per 100 000 population, and the highest rate (298 per 100 000) was in the small, densely populated area of Airin (21 500/0.62 km²). The annual reduction in the TB incidence rate in Airin during 2013–2018 was 5%, similar to the national average. The TB case fatality rate in Airin during 2015–2018 was 25.9% for all age groups, 15.5% for patients aged 0–69 years and 41.7% for patients aged ≥70 years.

Airin was a residential area during the country’s period of economic growth between the 1950s and the 1980s, accommodating Japan’s largest population of day labourers, including factory, dock and construction workers. Its peak population was in 1960, when there were 30 306 residents. During the economic recession...
Factors associated with mortality in tuberculosis patients

Shimouchi et al

The aim of this study was to guide interventions to reduce mortality from TB by determining the characteristics associated with mortality in patients with culture-positive PTB in Airin, Osaka City, between 2015 and 2018.

METHODS

Study population

TB is a notifiable disease under the Infectious Disease Control Law in Japan; thus, physicians must report all TB cases to their local government. PTB patients registered in Airin between January 2015 and December 2018 were included in the study if they were alive at diagnosis, examined by chest X-ray and were culture-positive. Culture-positive PTB was defined as the presence of Mycobacterium tuberculosis in cultured sputum identified by immune-chromatography or nucleic acid amplification. Notifications of extrapulmonary TB were excluded, as most were not bacteriologically proven. Eligible PTB patients with coexisting extrapulmonary TB such as lymphadenitis and pleuritis were included.

Patients who moved out of Osaka City during the treatment period, in whom treatment failed (i.e. culture reversed from negative to positive or was persistently positive during treatment) or who were lost to follow-up were excluded from the analysis.

Data collection

In routine practice, public health nurses (PHNs) at local public health centres record data on individual TB patients on structured patient cards, which are then entered onto an electronic spreadsheet. The data include sex, age, social condition, chest X-ray findings, bacteriological test results, mode of case detection and comorbidities. During interviews with the cases, PHNs also collect information such as height and body weight.

Determination of death

In Japan, a TB patient’s attending physician is solely responsible for diagnosing the cause of death as TB-specific or non-TB-specific. In Osaka City, attending physicians
Factors associated with mortality in tuberculosis patients

Shimouchi et al

and medical staff at the Public Health Office have monthly meetings at each hospital where TB patients are treated to discuss and agree on the cause of each TB patient’s death (TB or non-TB) for official records. Furthermore, by police request, any death of unknown cause identified in Osaka City is investigated by the Osaka Coroner’s Office, by inspection or autopsy.

Variables

The outcome variables for this study were (1) treatment success: treatment completed and culture negative, “cured” for smear-positive patients and “treatment completion” for smear-negative patients; and (2) death: patients who died of any cause before or during treatment.

Possible explanatory variables were: sex (male, female); age (<70, ≥70 years); homelessness (yes, no); cavity finding on chest X-ray (present, absent); bacteriological test results: sputum smear on Ziehl-Neelsen staining (positive, negative) and susceptibility to all five first-line anti-TB medicines, isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide (yes, no); body mass index (BMI) (<18.5, ≥18.5 kg/m²); detection by “active screening” (yes, no), diabetes mellitus (present, absent); and other serious comorbidities (yes, no).

“Detection by active screening” was defined as diagnosis from a chest X-ray during active screening or at an outpatient visit for other diseases. This was compared with all other detection categories, e.g. at an outpatient visit for TB symptoms or during hospitalization for other diseases.

As diabetes mellitus was not shown to be associated with TB disease in a previous case–control study in Airin in 2015–2018, this was analysed separately from other comorbidities.

Analysis

To ascertain associations between the explanatory variables and mortality, univariate analysis was conducted with the χ² test. Three separate analyses were conducted against treatment success: all deaths, early deaths (defined as death before or within the first 2 months of TB treatment) and late deaths (defined as death during the third month of treatment or later). The characteristics of TB-specific and non-TB-specific deaths were also compared. Variables with P < 0.1 were included in binomial multivariate logistic regression analysis, and adjusted odds ratios (aOR) were calculated.

Backward stepwise selection was applied to the binomial multivariate analysis. P < 0.05 was considered statistically significant. The univariate analysis was performed in Microsoft Excel® 2016, and binomial multivariate analysis was performed with SPSS version 11.0J for Windows (SPSS Inc., Chicago, IL, USA).

Ethical considerations

The Ethical Review Committee of the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan, approved the study protocol (authorization number: RIT/IRB 2019–20). Informed consent was not obtained from eligible TB patients, as it is not required by the research ethics guidelines of the Japanese Government when research is conducted retrospectively from de-individualized, anonymous data collected routinely by legal requirement.

RESULTS

Between January 2015 and December 2018, 342 TB patients were registered in Airin. One was diagnosed with TB at autopsy, two were clinically diagnosed and died before chest X-ray examination and 18 had extrapulmonary TB. Of the remaining 321 PTB patients who underwent a chest X-ray, 241 were culture-positive and 80 were culture-negative. Of the 241 culture-positive PTB cases, nine were transferred out of Osaka City, and none had treatment failure or was lost to follow-up. Therefore, 232 culture-positive PTB patients were included in the analysis (Fig. 1).

The mean age of the study participants was 66.4 years (range, 19–97), 95.7% (n = 222) were male, 51.9% (n = 121) were enrolled in PAP, and 29.2% (n = 68) were homeless. There were two foreign-born patients.
### Table 1. Serious comorbidities included in the study of enrolled pulmonary tuberculosis patients, Airin, Osaka City, Japan, 2015–2018

| Cancer            | Affected organ: stomach, liver, lung, colon, bladder, larynx                                                                 |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------|
| Heart             | Atrial fibrillation, acute cardiac ischaemia, cardiac bypass surgery, angina pectoris, chronic heart failure, dilated cardiomyopathy, sequelae of rheumatic fever |
| Lung              | Pulmonary fibrosis, emphysema, chronic obstructive pulmonary disease, tracheostomy, asbestosis                                |
| Digestive organ   | Hepatic disorder, alcoholic liver disorder, liver cirrhosis, hepatic failure, alcoholic pancreatitis, peritonitis, intestinal ileus, gastrostomy, gastrectomy |
| Kidney            | Renal failure, nephrotic syndrome                                                                                                |
| Brain             | Sequelae of cerebral infarction                                                                                               |
| Neurological disorder | Parkinson disease                                                                                                           |
| Systemic          | Anaemia, chronic thyroiditis, disuse syndrome                                                                                |

### Fig. 1. Flowchart of PTB case selection for analysis

TB: tuberculosis; PTB: pulmonary tuberculosis; EPTB: extrapulmonary tuberculosis.
### Table 2. Univariate and multivariate analyses of characteristics associated with all deaths, early deaths and late deaths in pulmonary tuberculosis patients in Airin, Osaka City, 2015–2018

| Characteristic | Treatment success (n = 170) n (%) | All deaths (n = 62) | Early deaths (n = 29) | Late deaths (n = 33) |
|----------------|----------------------------------|---------------------|----------------------|---------------------|
|                | Univariate analysis P | Multivariate analysis aOR (95% CI) | P | Univariate analysis P | Multivariate analysis aOR (95% CI) | P | Univariate analysis P | Multivariate analysis aOR (95% CI) | P |
| **Sex**        |                                |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Male           | 166 (97.1) 57 (91.9) 0.089 0.19 (0.02-1.55) 0.122 28 (96.6) 0.883 29 (89.7) 0.019 0.11 (0.01-1.01) 0.051 | | | | | | | | | |
| Female         | 5 (2.9) 5 (8.1) 1 (3.4) 0.089 0.19 (0.02-1.55) 0.122 28 (96.6) 0.883 29 (89.7) 0.019 0.11 (0.01-1.01) 0.051 | | | | | | | | | |
| **Age**        |                                |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| ≥70            | 53 (31.2) 37 (59.7) <0.001 2.66 (1.11-6.35) 0.027 19 (65.5) <0.001 4.39 (1.32-14.63) 0.016 18 (54.5) 0.010 2.01 (0.73-5.54) 0.176 | | | | | | | | | |
| <70            | 117 (68.8) 25 (40.3) 10 (34.5) 15 (45.5) | | | | | | | | | |
| **Country of birth** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Japan          | 168 (98.8) 62 (100) 0.391 29 (100) 0.557 33 (100) 0.532 | | | | | | | | | |
| Other          | 2 (1.2) 0 (0) 0 (0) | | | | | | | | | |
| **Homeless**   |                                |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 54 (31.8) 14 (22.6) 0.174 6 (20.7) 0.230 8 (24.2) 0.402 | | | | | | | | | |
| No             | 116 (68.2) 48 (77.4) 23 (79.3) 25 (75.8) | | | | | | | | | |
| **Cavity on chest X-ray** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 55 (32.4) 29 (46.8) 0.043 1.97 (0.81-4.80) 0.134 15 (51.7) 0.043 3.06 (0.90-10.46) 0.073 14 (42.4) 0.254 | | | | | | | | | |
| No             | 115 (67.6) 33 (53.2) 14 (48.3) 19 (57.6) | | | | | | | | | |
| **Sputum smear** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Positive       | 107 (62.9) 55 (88.7) <0.001 5.03 (1.51-16.80) 0.008 25 (86.2) 0.014 3.82 (0.79-18.32) 0.094 30 (90.9) 0.002 7.79 (1.53-39.76) 0.013 | | | | | | | | | |
| Negative       | 63 (37.1) 7 (11.3) 4 (13.7) 3 (9.1) | | | | | | | | | |
| **Susceptibility to isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 150 (88.2) 55 (88.7) 0.921 25 (86.2) 0.757 30 (90.9) 0.657 | | | | | | | | | |
| No             | 20 (11.8) 7 (11.3) 4 (13.8) 3 (9.1) | | | | | | | | | |
| **Body mass index (kg/m²)** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| <18.5          | 49 (29.5) 31 (59.6) <0.001 2.77 (1.17-6.53) 0.020 14 (63.6) <0.001 3.33 (1.03-10.72) 0.044 17 (56.7) 0.004 2.66 (0.98-7.25) 0.056 | | | | | | | | | |
| ≥18.5          | 117 (70.5) 21 (40.4) 8 (36.4) 13 (43.3) | | | | | | | | | |
| Unknown        | 4 (2.4) 10 (17.2) 7 (34.3) 3 (9.1) | | | | | | | | | |
| **Diabetes mellitus** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 37 (21.8) 12 (20.3) 0.818 5 (18.5) 0.702 7 (21.9) 0.989 | | | | | | | | | |
| No             | 133 (78.2) 47 (79.7) 22 (81.5) 25 (78.1) | | | | | | | | | |
| Unknown        | 3 | 2 | 1 | | | | | | | |
| **Other serious comorbidity** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 41 (24.1) 38 (61.3) <0.001 5.56 (2.24-13.81) <0.001 18 (62.1) <0.001 6.15 (1.79-21.13) 0.004 20 (60.6) <0.001 6.45 (2.85-17.68) <0.001 | | | | | | | | | |
| No             | 129 (75.9) 24 (38.7) 11 (37.9) 13 (39.4) | | | | | | | | | |
| **Detected by screening, including at outpatient department for other diseases** |                             |                     |                      |                     |                                 | |                             | |                                 | |                             | |                             | |                             | |
| Yes            | 94 (55.3) 3 (4.8) <0.001 0.06 (0.02-0.24) <0.001 1 (3.4) <0.001 0.06 (0.01-0.49) 0.009 2 (6.1) <0.001 0.06 (0.01-0.32) <0.001 | | | | | | | | | |
| No             | 76 (44.7) 59 (95.2) 28 (96.6) 31 (93.9) | | | | | | | | | |
Factors associated with mortality in tuberculosis patients

Treatment was completed by 170 patients, and 62 patients died before or during TB treatment, for a case fatality rate of 26.7%. There were 29 (46.7%) early deaths, including 3 (4.8%) before treatment, and

| Characteristic                                      | TB-specific deaths n (%) | Non-TB-specific deaths n (%) | Univariate analysis P | Multivariate analysis aOR (95% CI) | P  |
|-----------------------------------------------------|--------------------------|------------------------------|-----------------------|----------------------------------|----|
| Sex                                                 |                          |                              |                       |                                  |    |
| Male                                                | 35 (100%)                | 23 (85%)                     | 0.019                 |                                  |    |
| Female                                              | 0 (0%)                   | 4 (15%)                      |                       |                                  |    |
| Age (years)                                         |                          |                              |                       |                                  |    |
| ≥70                                                 | 21 (60%)                 | 16 (59%)                     | 0.953                 |                                  |    |
| <70                                                 | 14 (40%)                 | 11 (41%)                     |                       |                                  |    |
| Homeless                                            |                          |                              |                       |                                  |    |
| Yes                                                 | 9 (26%)                  | 5 (19%)                      | 0.502                 |                                  |    |
| No                                                  | 26 (74%)                 | 22 (81%)                     |                       |                                  |    |
| Cavity on chest X-ray                               |                          |                              |                       |                                  |    |
| Present                                             | 20 (57%)                 | 9 (33%)                      | 0.062                 | 2.26 (0.73–6.94)                 | 0.155|
| Absent                                              | 15 (43%)                 | 18 (67%)                     |                       |                                  |    |
| Sputum smear                                        |                          |                              |                       |                                  |    |
| Positive                                            | 33 (94%)                 | 22 (81%)                     | 0.114                 |                                  |    |
| Negative                                            | 2 (6%)                   | 5 (19%)                      |                       |                                  |    |
| Susceptible to isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide | | | | | |
| Yes                                                 | 31 (89%)                 | 24 (89%)                     | 0.969                 |                                  |    |
| No                                                  | 4 (11%)                  | 3 (11%)                      |                       |                                  |    |
| Body mass index                                     |                          |                              |                       |                                  |    |
| <18.5                                               | 16 (59%)                 | 15 (60%)                     | 0.957                 |                                  |    |
| ≥18.5                                               | 11 (41%)                 | 10 (40%)                     |                       |                                  |    |
| Unknown                                             | 8                        | 2                            |                       |                                  |    |
| Diabetes mellitus                                   |                          |                              |                       |                                  |    |
| Yes                                                 | 5 (15%)                  | 7 (27%)                      | 0.265                 |                                  |    |
| No                                                  | 28 (85%)                 | 19 (73%)                     |                       |                                  |    |
| Unknown                                             | 2                        | 1                            |                       |                                  |    |
| Other serious comorbidity                           |                          |                              |                       |                                  |    |
| Yes                                                 | 18 (51%)                 | 20 (74%)                     | 0.070                 | 0.32 (0.10–1.03)                 | 0.057|
| No                                                  | 17 (49%)                 | 7 (26%)                      |                       |                                  |    |
| Detected by screening, including at outpatient department for other diseases | | | | | |
| Yes                                                 | 2 (6%)                   | 1 (4%)                       | 0.715                 |                                  |    |
| No                                                  | 33 (94%)                 | 26 (96%)                     |                       |                                  |    |
| Early death                                         |                          |                              |                       |                                  |    |
| Yes                                                 | 21 (60%)                 | 8 (30%)                      | 0.017                 | 3.95 (1.29–12.07)                | 0.016|
| No                                                  | 14 (40%)                 | 19 (70%)                     |                       |                                  |    |

The conditions included those listed in the Charlson comorbidity index and the Elixhauser comorbidity score as well as alcoholic pancreatitis, peritonitis, intestinal ileus and Parkinson disease (Table 1).
33 (53.2%) late deaths. Of the 59 patients who died during treatment, 55 (93.2%) were hospitalized from the beginning of treatment until death. Two were discharged from hospital but were readmitted when their general condition deteriorated just before death. Five died in the community.

The binomial multivariate analysis showed that, in comparison with treatment success, death of PTB patients was significantly associated with age ≥70 years, sputum smear positivity, underweight (BMI <18.5) and presence of serious comorbidity. Detection of TB at screening was inversely associated with mortality. All these variables, apart from sputum smear positivity, were also significantly associated with early death in PTB patients. In the comparison of treatment success and late deaths of PTB patients, positive sputum smear and serious comorbidity were significantly associated with late death, and detection by TB screening was inversely associated with mortality (Table 2).

Of the 62 deaths, 35 were TB-specific and 27 non-TB-specific. Of the TB-specific deaths, 60.0% (21/35) were early deaths. In the multivariate analysis of patient characteristics for TB-specific and non-TB-specific deaths, TB-specific deaths were associated only with early death (aOR: 3.95, 95% confidence interval: 1.29; 12.07) (Table 3).

DISCUSSION

The all-cause case fatality rate among culture-positive PTB patients in Airin, Osaka City, between 2015 and 2018 was 26.7%. Multivariate analysis showed that age ≥70 years, a positive sputum smear, BMI <18.5 and serious comorbidity were associated with mortality in PTB patients. Detection by active screening or during an OPD visit for another disease was inversely associated with mortality in PTB patients. The frequency of characteristics did not differ between TB-specific and non-TB-specific deaths, TB-specific deaths were associated only with early death (aOR: 3.95, 95% confidence interval: 1.29; 12.07) (Table 3).

Of the fatal PTB cases in Airin, 93% were in a hospital from the beginning of treatment until death. Almost all (92%) of the cases during the study period received daily DOT in the Airin TB programme. None of the TB patients in the study failed treatment or were lost to follow-up; therefore, none of the deaths was due to treatment interruption or non-adherence, which may have contributed to deaths in other studies.8

About half of the fatalities among PTB patients were early deaths, occurring before or within the first 2 months of treatment. Similar findings were reported in Australia,6 Denmark,12 Taiwan (China),16 Spain,17 the Republic of Korea,18 the United Kingdom19 and Finland.20 We also found that a higher proportion of early deaths were TB-specific rather than non-TB-specific, which suggests that patients who survive >2 months of TB treatment have better outcomes, and late deaths are due more commonly to causes other than TB.

Advanced age is well recognized as a risk factor for morbidity and mortality from TB because of weakening of both the innate and adaptive immune systems.21 The presence of comorbidity has also been identified as the most common characteristic of death from TB in other developed countries, such as Australia,6 Denmark,12 Finland,20 the Netherlands,22 Spain,17 Singapore,23 the Republic of Korea,18 Taiwan (China)9,11,24 and the USA.10 Older people tend to be more vulnerable to comorbidity, as suggested by a one-day survey of the prevalence of morbidity in 2017 conducted by random stratified sampling in 6402 hospitals (76% of hospitals in Japan), which showed that the rate of comorbidity among people aged ≥65 years was 17 times higher than among those aged 20–24 years.25 In our study, both older age and having a comorbidity were associated with PTB mortality.

A BMI of <18.5 was significantly associated with all deaths and with early deaths of PTB patients in this study but not with late deaths of PTB patients. A similar finding was made in a study in Taiwan (China).16 Undernutrition impairs cell-mediated immunity, which increases vulnerability to specific infectious diseases, including TB.26,27 A BMI of <18.5 defines underweight and is a good proxy indicator of undernutrition. A literature review of cohort studies in the USA, Europe, India, Bangladesh and East Asia showed that being underweight was associated with a significantly higher risk for all-cause mortality.28

In contrast, our study showed that having a positive sputum smear status was associated with all deaths and late deaths in PTB patients but not with early deaths in these patients. A review of individual patient records in our study showed that about half of smear-negative

https://ojs.wpro.who.int/
Factors associated with mortality in tuberculosis patients

Shimouchi et al

with non-fatal TB, perhaps because they contributed to early case finding. Therefore, current active TB case finding and health education on regular visits to physicians for any disease should be further strengthened in the urban poor setting in Osaka City, Japan. Attending physicians should be advised to take periodic chest X-rays for aged patients with serious comorbidities or low BMI, regardless of symptoms and even in other parts of Osaka City if the facilities are available.

Acknowledgement

The authors are grateful to the public health nurses of Nishinari District Public Health Offices for their hard work and data collection.

Funding

This research was partly supported by the Research Programme on Emerging and Re-emerging Infectious Diseases of the Japan Agency for Medical Research and Development, AMED (reference number: 19fk0108063s0202).

Conflict of interest

None declared.

References

1. The End TB Strategy. Geneva: World Health Organization; 2015. Available from: https://www.who.int/teams/global-tuberculosis-programme/the-end-tb-strategy, accessed 12 July 2021.

2. Tuberculosis control in Nishinari District: Report of special TB project in Nishinari District (in Japanese). Osaka: Nishinari Public Health Office; 2020. Available from: https://www.osaka-pha.or.jp/suisin_02/pdf/shimoutiakira.pdf, accessed 12 July 2021.

3. Statistics of TB. 2019. Tokyo: Japan Anti-Tuberculosis Association; 2019. Available from: https://www.jata.or.jp/rit/ekigaku/en/statistics-of-tb/, accessed 12 July 2021.

4. Mizuuchi T, Hirakawa T, Tominaga T, editors. Fifty years’ history of the Osaka Prefecture Urban Hostels’ Association: Global Center of Excellence Report Series 17. Osaka: Osaka City University; 2011. (in Japanese). Available from: https://www.ur-plaza.osaka-cu.ac.jp/wp-content/uploads/2016/06/GCOE_Report17.pdf, assessed 12 July 2021.

5. 2015 population census. Osaka City: Statistics Bureau, Ministry of Internal Affairs and Communications, Japan; 2021. Available from: https://www.e-stat.go.jp/en/stat-search, accessed 12 July 2021.

6. Walpola HC, Siskind V, Patel AM, Konstantinos A, Derhy P. Tuberculosis-related deaths in Queensland, Australia, 1989-1998: characteristics and risk factors. Int J Tuberc Lung Dis. 2003 Aug;7(8):742–50. pmid:12921150
7. Shuldiner J, Leventhal A, Chemtob D, Mor Z. Mortality of tuberculosis patients during treatment in Israel, 2000-2010. Int J Tuberc Lung Dis. 2014 Jul;18(7):818–23. doi:10.5858/ijtlid.13.0591 pmid:24902558

8. Nahid P, Jarlsberg LG, Rudoy I, de Jong BC, Unger A, Kawamura FY, et al. Factors associated with mortality in patients with drug-susceptible pulmonary tuberculosis. BMC Infect Dis. 2011 Jan 3;11(1):1. doi:10.1186/1471-2334-11-1 pmid:21199579

9. Yen YF, Chuang PH, Yen MY, Lin SY, Chuang P, Yuan MJ, et al. Association of body mass index with tuberculosis mortality in the United States, 2009–2013. Public Health Rep. 2017 May;132(3):366–75. doi:10.1177/0033354916696817 pmid:28394707

10. Wu YC, Lo HY, Yang SL, Chu DC, Chou P. Comparing the factors correlated with tuberculosis and non-tuberculosis-specific deaths in different age groups among tuberculosis-related deaths in Taiwan. PLoS One. 2015 Mar 3;10(3):e0118929. doi:10.1371/journal.pone.0118929 pmid:25734444

11. Holden IK, Lillebaek T, Andersen PH, Wejsce C, Johansen IS. Characteristics and predictors for tuberculosis mortality in Denmark from 2009 through 2014: A retrospective cohort study. PLoS One. 2020 Jun 4;15(6):e0231821. doi:10.1371/journal.pone.0231821 pmid:32497102

12. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol. 2004 Dec;57(12):1288–94. doi:10.1016/j.jclinepi.2004.03.012 pmid:15617995

13. Li B, Evans D, Faris P, Dean S, Quan H. Risk adjustment performance of Charlson and Elixhauser comorbidities in ICD-9 and ICD-10 administrative databases. BMC Health Serv Res. 2008 Jan 14;8(1):12. doi:10.1186/1472-6963-8-12 pmid:18194561

14. Shimouchi A, Tsuda Y, Komukai J, Matsumoto K, Yoshida H, Ohkado A. Characteristics of individuals with tuberculosis in an urban, poor population in Osaka City, Japan – a case-control study. 2020;11(1):22–8. doi:10.5365/wpsar.2018.9.1.005. pmid:32963888

15. Lai HH, Lai YJ, Yen YF, Y YF. Association of body mass index with timing of death during tuberculosis treatment. PLoS One. 2017 Jan 3;12(1):e0170104. doi:10.1371/journal.pone.0170104 pmid:28085951

16. Rodrigo T, Casals M, Caminero JA, Garcia-Garcia JM, Jiménez-Fuentes MA, Medina JF, Millet JP, Ruiz-Manzano J, Caylá J, Working Group of the Integrated Programme of Tuberculosis Research. Factors associated with mortality during the intensive phase of anti-tuberculosis treatment. PLoS one. 2016 Aug 3;11(8):e0159925. doi:10.1371/journal.pone.0159925 pmid:27487189

17. Min J, Kim JS, Kim HW, Shin AJ, Koo HK, Lee SS, et al. Clinical profiles of early and tuberculosis-related mortality in South Korea between 2015 and 2017: a cross-sectional study. BMC Infect Dis. 2019 Aug 22;19(1):735. doi:10.1186/s12879-019-4365-9 pmid:31438876

18. Pedrazzoli D, Kranzer K, Thomas HL, Lalor MK. Trends and risk factors for death and excess all-cause mortality among notified tuberculosis patients in the UK: an analysis of surveillance data. ERJ Open Res. 2019 Dec 16;5(4):00125. doi:10.1183/23120541.00125-2019 pmid:31857993

19. Korhonen V, Lyytikäinen O, Ollgren J, Soini H, Vasankari T, Ruutu P. Risk factors affecting treatment outcomes for pulmonary tuberculosis in Finland 2007-2014: a national cohort study. BMC Public Health. 2020 Aug 17;20(1):1250. doi:10.1186/s12889-020-09360-7 pmid:32807112

20. Byng-Maddick R, Noursadeghi M. Does tuberculosis threaten our ageing populations? BMC Infect Dis. 2016 Mar 11;16(1):119. doi:10.1186/s12879-016-1451-0 pmid:26966654

21. Borgdorff MW, Veen J, Kaisisvaara NT, Nagelkerke N. Mortality among tuberculosis patients in The Netherlands in the period 1993-1995. Eur Respir J. 1998 Apr;11(4):816–20. doi:10.1183/09031936.98.11040816 pmid:9623682

22. Low S, Ang LW, Cutter J, James L, Chee CBE, Yang YT, et al. Mortality among tuberculosis patients on treatment in Singapore. Int J Tuberc Lung Dis. 2009 Mar;13(3):328–34. pmid:19275792

23. Yen YF, Yen MY, Shih HC, Hu BS, Ho BL, Li LH, et al. Prognostic factors associated with mortality before and during anti-tuberculosis treatment. Int J Tuberc Lung Dis. 2013 Oct;17(10):1310–6. doi:10.5588/ijtld.12.0888 pmid:24025383

24. Byng-Maddick R, Noursadeghi M. Does tuberculosis threaten our ageing populations? BMC Infect Dis. 2016 Mar 11;16(1):119. doi:10.1186/s12879-016-1451-0 pmid:26966654

25. Outline of patient survey 2017. Tokyo: Ministry of Health, Labour and Welfare; 2017. Available from: https://www.mhlw.go.jp/toukei/list/10-20.html, accessed 12 July 2021.

26. Chandra RK. Nutritional deficiency and susceptibility to infection. Bull World Health Organ. 1997;59(2):167–77. pmid:980017

27. Chandra RK. Nutritional and functional deficiency in T helper cells in protein energy malnutrition. Clin Exp Immunol. 1983 Jan;51(1):126–32. pmid:6219837

28. Legal KM, Kit BK, Graubard BL. Body mass index categories in observational studies of weight and risk of death. Am J Epidemiol. 2014 Aug 1;180(3):288–96. doi:10.1093/aje/kwu111 pmid:24893710

29. Farah MG, Tverdal A, Steen TW, Heldal E, Brantsaeter AB, Bjune G. Treatment outcome of new culture positive pulmonary tuberculosis in Norway. BMC Public Health. 2005 Feb 7;5(1):14. doi:10.1186/1471-2458-5-14 pmid:15698472