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Association between Tuberculosis Infection and Dementia Burden: A Systematic Review

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Association between Tuberculosis Infection and Dementia Burden: A Systematic Review

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Abstract

Background: Research has linked systemic infections and neuroinflammation with dementia, and experimental studies have suggested potential neurological effects of tuberculosis (TB). Whether TB is associated with subsequent dementia remains unclear. It is also uncertain whether coexisting dementia is associated with poorer TB treatment outcomes. Clarifying these relationships may inform long-term cognitive follow-up and treatment support for people with TB.

Methods: We systematically searched PubMed/MEDLINE, Embase, and Scopus on 29 June 2026, without date or language restrictions. Observational studies examining incident dementia following TB or TB mortality and treatment outcomes according to dementia status were eligible. Risk of bias was assessed using the Newcastle–Ottawa Scale, and findings were synthesized narratively in accordance with Synthesis Without Meta-analysis (SWiM) guidance.

Results: Of 2,693 database records screened, six observational studies were included, two from Taiwan, two from South Korea, one from Japan, and one from the United States. Two Taiwanese cohorts reported increased risks of all-cause dementia (aHR, 1.21; 95% CI, 1.06–1.38) and Alzheimer's disease (aHR, 1.43; 95% CI, 1.01–2.02), respectively. A South Korean cohort reported increased risks of all-cause dementia (aHR, 1.12; 95% CI, 1.05–1.19), Alzheimer's disease (aHR, 1.11; 95% CI, 1.03–1.20), and vascular dementia (aHR, 1.48; 95% CI, 1.16–1.89). Among patients with TB, a Korean cohort reported lower cure rates in patients with dementia (38.9% vs. 56.3%; aOR for non-cure, 1.74; 95% CI, 1.34–2.26) and higher TB-related mortality (7.0% vs. 3.0%). A Japanese study reported higher in-hospital mortality (aOR, 3.20; 95% CI, 1.15–8.88), while a US study reported higher odds of treatment noncompletion (aOR, 5.05; 95% CI, 1.33–20.32).

Conclusions: TB was associated with an increased risk of subsequent dementia, including Alzheimer's disease and vascular dementia. Among patients with TB, coexisting dementia was associated with higher mortality and worse treatment outcomes. Larger longitudinal studies are needed to clarify these associations.

Introduction

Tuberculosis (TB) and dementia are major global health challenges. The WHO Global TB Report 2025 estimates 10.7 million incident TB cases (131 per 100,000 population) and 1.23 million deaths [1]. Dementia affects approximately 57 million people, over 60% of them in low- and middle-income countries, with nearly 10 million new cases annually; Alzheimer's disease accounts for an estimated 60-70% [2].

Infections outside the brain may contribute to later neurodegeneration. A nationwide study linked hospital-treated infections to higher risk of dementia, including Alzheimer's and vascular dementia, over 25-30 years [3], and a 2025 meta-analysis of 16 cohorts found a similar association [4]. For TB, experimental studies report gliosis, protein aggregation, neuronal loss, and neuroinflammation [5,6]. Proposed mechanisms include blood-brain barrier dysfunction and persistent glial activation [7-9], and hippocampal involvement has led to the suggestion of a tuberculosis-related hippocampal syndrome [10]. However, it remains unclear whether TB is associated with subsequent dementia, or whether comorbid dementia worsens mortality and treatment outcomes among people with TB.

We therefore systematically reviewed the observational evidence addressing two complementary epidemiological directions: (1) whether TB is associated with an increased risk of incident dementia, including Alzheimer's disease and vascular dementia, and (2) whether pre-existing dementia is associated with higher mortality or poorer treatment outcomes among patients with TB. We assessed the direction, consistency, and limitations of the evidence for each association, alongside its biological plausibility.

Methods

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement

(PRISMA) [11]. The protocol was prospectively registered in Open Science Framework (OSF).

Search strategy

We searched PubMed/MEDLINE, Embase, and Scopus for observational studies reporting tuberculosis infection and dementia on 29 June 2026. Two main concepts, tuberculosis and dementia, were combined to develop the following search string: [("Tuberculosis" OR "Tuberculosis, Pulmonary" OR "Mycobacterium tuberculosis" OR "tubercul*" OR "TB") AND ("Dementia" OR "Alzheimer Disease" OR "Vascular Dementia" OR "dement*" OR "Alzheimer" OR "cognitive impairment" OR "cognitive decline")]. No restrictions were applied based on publication language or publication date. Appendix 1 reports the search string for each database.

Study Selection

We applied a series of inclusion criteria. Articles were included if they were: (1) enrolling patients with tuberculosis, primarily pulmonary tuberculosis, (2) reporting at least one outcome of interest, namely incident dementia following TB, mortality among patients with TB, or treatment outcomes according to dementia status, and (3) including an appropriate comparator group depending on the outcome reported by the study: non-tuberculosis patients for studies reporting dementia risk, or tuberculosis patients with and without dementia for studies reporting mortality or TB treatment outcomes. Cross-sectional studies, case reports and case series were excluded. Records identified through database searching were merged and de-duplicated using Zotero. Two reviewer teams (AN and AS) and (HG, MG, and HI) independently screened titles and abstracts, and subsequently full texts, according to these eligibility criteria, with disagreements resolved by discussion.

Outcome Definition

Three outcome domains were extracted: (1) incident dementia following TB; (2) mortality among patients with TB; and (3) TB treatment outcomes according to dementia status. Dementia ascertainment methods varied across studies and included administrative diagnostic coding and medical-record or chart-based information. Dementia outcomes included all-cause dementia [12,13], Alzheimer's disease [13,14], and vascular dementia [13]. Mortality outcomes comprised TB-related mortality [15] and in-hospital mortality [16]. Treatment outcomes included cure or non-cure [15] and treatment noncompletion [17].

Data Extraction and Synthesis

Two reviewers (AN and HG) independently extracted data from all eligible studies. The extracted data included study characteristics; population characteristics; exposure and comparator definitions; outcome definitions; effect estimates. Extracted data were synthesized narratively in accordance with the Synthesis Without Meta-analysis (SWiM) reporting guideline [18].

Quality assessment

Risk of bias of included studies was independently assessed by two reviewers (AN and HG), with disagreements resolved by discussion. Because all included studies were observational studies, the Newcastle–Ottawa Scale (NOS) [19] was used to appraise study quality. Overall study quality was categorized using commonly applied AHRQ criteria [20]. Good quality was defined as 3–4 stars in the selection domain, 1–2 stars in comparability, and 2–3 stars in outcome. Fair quality was defined as 2 stars in selection, 1–2 stars in comparability, and 2–3 stars in outcome.

Poor quality was assigned when a study received 0–1 star in selection, 0 stars in comparability, or 0–1 star in outcome.

Results

The screening process of studies is illustrated in Figure 1. A total of 2,693 non-duplicate records were screened for eligibility. After title/abstract screening, 5 studies were assessed for full-text evaluation, and 3 studies met the inclusion criteria. Forward and backward citation searching identified 3 additional studies, bringing the total to 6 studies included in the review (Figure 1).

Study Characteristics

Six retrospective observational studies conducted in Taiwan [12,14], South Korea [13,15], Japan [16], and the United States [17] were included. Their reported sample sizes ranged from 279 to 100,364 participants. Three studies examined the association between TB and subsequent dementia [12–14], while the remaining three investigated TB-related outcomes according to dementia status [15–17]. The populations varied in age and sex distribution. Peng et al. [12] reported a mean age of 59.7 ± 18.2 years and 31.0% female participants in the TB group, whereas Yeo et al. [13] reported that 66% of participants were older than 60 years and 42% were female. Su et al. [14] did not report age or sex characteristics. The three studies examining TB outcomes among patients with and without dementia involved older populations: Kim et al. [15] reported a mean age of 76.2 ± 11.4 years overall, with mean ages of 81.4 and 75.7 years in the dementia and non-dementia groups, respectively; Saiki et al. [16] reported a median age of 76 years; and Wu et al. [17] included 172 participants aged 65 years or older, of whom 101 were aged at least 75 years. Female participants accounted for 45.49% of the overall Kim cohort, 36.2% of the Saiki cohort, and 31.4% of the older adults in Wu et al. The study periods and follow-up durations also varied. Peng et al. [12] reported a mean follow-up of 5.9

years, while Yeo et al. [13] reported a mean follow-up of 3.5 ± 2.2 years. Su et al. [14] included TB diagnoses made between 1998 and 2011, with follow-up through 2013. Kim et al. [15] covered 2021–2022, Saiki et al. [16] covered 2008–2016, and Wu et al. [17] covered 2016–2019, reporting a median TB treatment duration of 202 days. Regarding outcomes, the first three studies assessed incident all-cause dementia, Alzheimer's disease, and/or vascular dementia [12–14]. The remaining studies examined TB treatment cure and TB-related mortality [15], in-hospital mortality [16], and TB treatment noncompletion [17].

Risk of Bias

The risk of bias assessment is presented in Table 2. Five studies [12-15,17] were judged to have an overall good quality rating. Among these, three [12,13,17] scored 9 of 9 stars, one [15] scored 8 of 9 stars, and one [14] scored 7 of 9 stars. The remaining study [16] was judged to have an overall fair quality rating, scoring 7 of 9 stars, with two of four selection stars.

Risk of Dementia

Three studies investigated the association between tuberculosis infection and subsequent dementia risk, consistently reporting an increased risk among individuals with a history of TB. Peng et al. (2015) found that patients with pulmonary TB had a significantly higher risk of developing all-cause dementia compared with individuals without TB (aHR = 1.21, 95% CI: 1.06–1.38) over a mean follow-up of 5.9 years [12]. Similarly, Su et al. (2018) reported an increased risk of Alzheimer's disease among patients with pulmonary TB (aHR = 1.43, 95% CI: 1.01–2.02) [14]. Further evidence was provided by Yeo et al. (2024), whose nationwide Korean cohort demonstrated significantly higher risks of all-cause dementia (aHR = 1.12, 95% CI: 1.05–1.19), Alzheimer's disease (aHR = 1.11, 95% CI: 1.03–1.20), and

vascular dementia (aHR = 1.48, 95% CI: 1.16–1.89) among TB survivors compared with matched controls [13]. The strongest association was observed for vascular dementia. Overall, all three studies reported positive associations between TB infection and subsequent dementia, although differences in study populations, follow-up periods, and dementia subtypes should be considered when interpreting the findings (Table 3).

Mortality and treatment outcomes

Three studies investigated the association between coexisting dementia and TB-related outcomes, reporting higher mortality and poorer treatment outcomes among patients with dementia. Kim et al. (2024) reported higher TB-related mortality among patients with dementia than among those without dementia (7.0% vs. 3.0%). Treatment cure rates were also lower in the dementia group. The article reported cure rates of 38.9% and 56.3%, respectively. In adjusted analysis, dementia was associated with higher odds of treatment non-cure (aOR = 1.74, 95% CI: 1.34–2.26) [15]. Similarly, Saiki et al. (2019) identified dementia as an independent predictor of in-hospital mortality among patients hospitalized with smear-positive pulmonary TB (aOR = 3.20, 95% CI: 1.15–8.88) [16]. Wu et al. (2022) also reported that dementia was associated with higher odds of TB treatment noncompletion among older adults (aOR = 5.05, 95% CI: 1.33–20.32). However, the wide confidence interval indicates considerable uncertainty surrounding this estimate [17]. Collectively, these findings suggest that coexisting dementia is associated with poorer TB outcomes, although differences in outcome definitions and study precision should be considered when interpreting the results (Table 3).

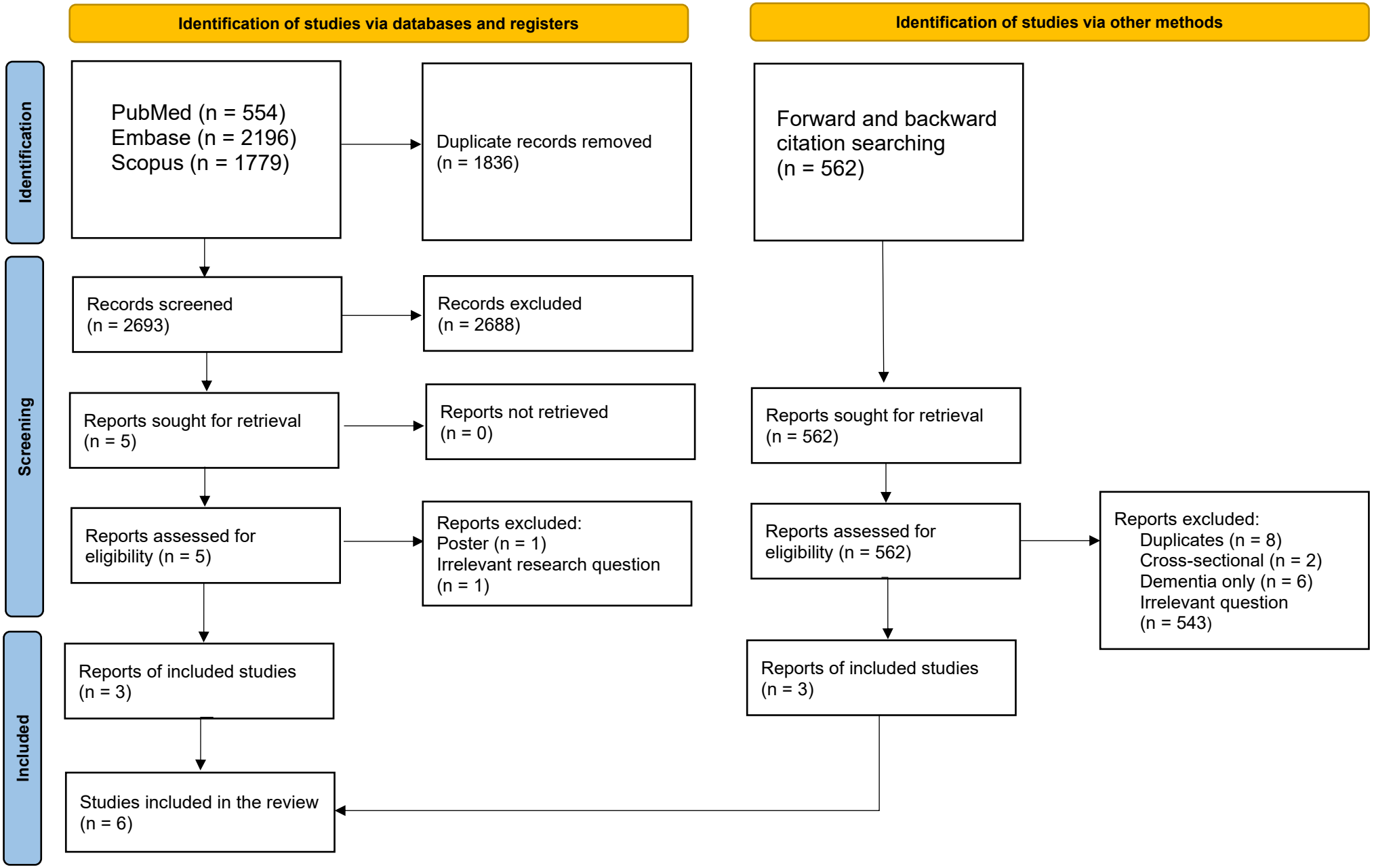


Figure 1. PRISMA-2020 flow diagram of study selection

Table 1. Study Characteristics

Study	Country	Study design	Sample size	Age characteristics	Female	Study period / follow-up	Outcomes
Peng et al. (2015) [12]	Taiwan	Retrospective observational study	32,363 (TB: 6,473; controls: 25,890)	Mean: 59.7 ± 18.2 years (TB group)	31.0% (TB group)	Mean follow-up: 5.9 years	Incident all-cause dementia
Su et al. (2018) [14]	Taiwan	Retrospective observational study	56,272 (TB: 6,260; controls: 50,012)	Not reported	Not reported	TB diagnoses: 1998–2011; follow-up through 2013	Incident Alzheimer's disease
Yeo et al. (2024) [13]	South Korea	Retrospective observational study	100,364 (TB: 50,182; controls: 50,182)	66% aged over 60 years	42%	Mean follow-up: 3.5 ± 2.2 years	All-cause dementia, Alzheimer's disease, vascular dementia
Kim et al. (2024) [15]	South Korea	Retrospective observational study	2,992 (dementia: 270; no dementia: 2,722)	Mean: 76.2 ± 11.4 years overall; 81.4 years with dementia and 75.7 years without dementia	45.49% overall; 56.67% with dementia and 44.38% without dementia	2021–2022	TB treatment cure and TB-related mortality
Saiki et al. (2019) [16]	Japan	Retrospective medical-record-based observational study	279	Median: 76 years	36.2%	2008–2016 (nine-year study period)	In-hospital mortality
Wu et al. (2022) [17]	United States	Retrospective observational study	517 overall; 172 aged ≥65; 169 with available charts; 163 in adjusted analysis	Population aged ≥65 years; 101 of 172 were ≥75 years	31.4% among older adults	2016–2019; median treatment duration: 202 days	TB treatment noncompletion

Table 2. Risk of Bias Assessment by the Newcastle-Ottawa Scale (NOS)

Study	1. Representativeness of exposed cohort	2. Selection of non-exposed cohort	3. Ascertainment of exposure	4. Outcome not present at start	SELECTION stars (max 4)	1a. Controls age, sex? (Y/N)	1b. Controls other factors? (Y/N)	COMPARABILITY stars (max 2)	1. Assessment of outcome	2. Follow-up long enough	3. Adequacy of follow-up	OUTCOME stars (max 3)	TOTAL stars (max 9)	AHRQ rating
Peng et al. 2015	a	a	a	a	**4**	Y	Y	**2**	b	a	a	**3**	**9**	**Good**
Su et al. 2018	a	a	a	b	**3**	N	Y	**1**	b	a	a	**3**	**7**	**Good**
Yeo et al. 2024	a	a	a	a	**4**	Y	Y	**2**	b	a	a	**3**	**9**	**Good**
Kim et al. 2024	a	a	a	a	**4**	Y	Y	**2**	b	b	a	**2**	**8**	**Good**
Saiki et al. 2019	c	a	a	b	**2**	Y	Y	**2**	b	a	a	**3**	**7**	**Fair**
Wu et al. 2022	a	a	a	a	**4**	Y	Y	**2**	b	a	b	**3**	**9**	**Good**

NOS entries are coded as follows:
(a) criterion fulfilled; (b) criterion not fulfilled or insufficiently reported; and (c) criterion not applicable.

Table 3. Study Outcomes

Outcome	Study	Estimated effect size	Main findings
Incident dementia	Peng et al., 2015 [12]	aHR = 1.21 (95% CI: 1.06–1.38)	TB was associated with a higher risk of incident all-cause dementia.
	Su et al., 2018 [14]	aHR = 1.43 (95% CI: 1.01–2.02)	TB was associated with a higher risk of Alzheimer's disease.
	Yeo et al., 2024 [13]	All-cause dementia: aHR = 1.12 (95% CI: 1.05–1.19); Alzheimer's disease: aHR = 1.11 (95% CI: 1.03–1.20); vascular dementia: aHR = 1.48 (95% CI: 1.16–1.89)	TB was associated with higher risks of all-cause dementia, Alzheimer's disease, and vascular dementia. The strongest association was observed for vascular dementia.
Mortality and treatment outcomes	Kim et al., 2024 [15]	TB-related mortality: 7.0% vs. 3.0%; cure rate: 38.9% vs. 56.3% (17.4 percentage points lower in the dementia group); aOR for non-cure = 1.74 (95% CI: 1.34–2.26)	Dementia was associated with higher TB-related mortality and a lower treatment cure rate.
	Saiki et al., 2019 [16]	aOR = 3.20 (95% CI: 1.15–8.88)	Coexisting dementia was associated with higher odds of in-hospital mortality among patients with pulmonary TB.
	Wu et al., 2022 [17]	aOR = 5.05 (95% CI: 1.33–20.32)	Dementia was associated with higher odds of TB treatment noncompletion among older adults.

Discussion

This systematic review synthesized observational evidence addressing two complementary epidemiological directions in the relationship between tuberculosis (TB) and dementia. First, three cohorts consistently associated TB with an increased risk of subsequent dementia, including Alzheimer's disease and vascular dementia, with adjusted hazard ratios ranging from 1.12 to 1.48. Second, three studies found that pre-existing dementia was associated with poorer TB-related clinical outcomes, including higher mortality, lower cure rates, and treatment non-completion. However, the evidence remains limited to a small number of observational cohorts and therefore cannot establish causality.

Our findings are consistent with a broader epidemiological literature linking serious infections with later dementia. A 2025 systematic review and meta-analysis of 16 cohort studies found that hospitalization with infection was associated with increased risks of all-cause dementia, Alzheimer's disease, and vascular dementia [4]. A nationwide New Zealand register study of 1.7 million people likewise found that hospital-treated infections were associated with subsequent dementia over up to 30 years, including Alzheimer's and vascular dementia, after adjustment for several pre-existing and socioeconomic factors [3]. Although these studies did not cover TB specifically, they do show comorbid infection as a risk factor for developing dementia and cognitive decline. Experimental studies suggest that systemic inflammation may disrupt the blood–brain barrier and activate glial cells [7–9], while TB-related hippocampal abnormalities have also been proposed [10]. The associations are biologically plausible as pulmonary tuberculosis infection stimulates T lymphocytes alongside activated macrophages [21,22]. This host-pathogen interaction induces a severe systemic surge of proinflammatory cytokines [21,22]. The elevation of these cytokines creates a high-grade systemic inflammatory environment that spills into systemic circulation [22,23]. Cytokines

activate brain endothelial cells, triggering the upregulation of matrix metalloproteinases that degrade endothelial basement membranes and extracellular matrices [24,25]. Cytokines can also stimulate NF-κB signaling, upregulating BACE1 expression and enhancing γ-secretase activity [25-27]. Aβ peptides act as physiological antimicrobial peptides within the innate immune system, oligomerizing to entrap invading bacterial and viral pathogens [3,28,29], however, systemic infection disrupts this physiological protective role, leading to excessive Aβ production and persistent plaque deposition [3,24].

There are also potential implications for patients who have dementia and develop TB. The included studies found higher mortality and poorer cure outcomes in this group [15-17]. Evidence on TB in older adults indicates that treatment can be complicated by adverse effects, drug interactions, and adherence difficulties, and cognitive impairment may further complicate treatment completion [30]. WHO guidance emphasizes individualized, patient-centered support for adherence in older adults, including caregiver involvement when physical or cognitive limitations affect treatment delivery [31]. These observations support closer supportive care, but the current evidence does not demonstrate that dementia independently causes treatment failure or justify changes to standard TB therapy.

Several limitations reduce the certainty of these conclusions. Only six studies met the criteria, and they evaluated different outcome domains, limiting direct comparability and preventing meaningful quantitative pooling. The studies also differed substantially in sample size, follow-up duration, population characteristics, and dementia definitions. Most studies relied on ICD-coded diagnoses, which may lead to outcome misclassification and provide limited information on dementia severity or subtype. Generalizability is also constrained because most cohorts were from East Asia. Finally, one included study was available as a conference abstract, limiting the assessment of its methodology and reducing confidence in its findings.

Conclusion

TB was associated with an increased risk of subsequent dementia, including Alzheimer's disease and vascular dementia. Among patients with TB, coexisting dementia was associated with higher TB-related and in-hospital mortality, lower cure rates and treatment noncompletion. However, these findings are based on only six observational studies with heterogeneous populations and outcome definitions. Larger, well-designed longitudinal studies are needed to clarify whether TB contributes to neurodegeneration or primarily identifies individuals already vulnerable to dementia.

Other Information

Statement of Ethics

This systematic review exclusively utilized data from previously published studies and did not involve the collection or analysis of individual patient-level data. Therefore, ethical approval and informed consent were not required. Ethical approval and informed consent for the original studies had been obtained by the respective investigators, as reported in the published articles.

Conflict of Interest Statement

The authors have no conflicts of interest to declare

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Author Contributions

AN contributed to protocol development, independent title, abstract and full-text screening, independent data extraction, risk-of-bias assessment, data synthesis, and manuscript drafting. HG contributed to independent title, abstract and full-text screening, independent data extraction, risk-of-bias assessment, and manuscript revision. MG, HI, and AS contributed to independent title, abstract and full-text screening and manuscript revision. AT contributed to manuscript writing and revision. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

All data analyzed in this study were obtained from previously published research, with the relevant sources cited in the article. No original individual-level data were collected. The datasets compiled during this study, including extracted study data and risk-of-bias assessments, are available from the corresponding author upon reasonable request.

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Supplementary Material

Appendix 1. Search String for each database

PubMed

("Tuberculosis"[Mesh] OR "Tuberculosis, Pulmonary"[Mesh] OR "Mycobacterium tuberculosis"[Mesh] OR tubercul*[tiab] OR TB[tiab]) AND ("Dementia"[Mesh] OR "Alzheimer Disease"[Mesh] OR "Vascular Dementia"[Mesh] OR dement*[tiab] OR Alzheimer*[tiab] OR "cognitive impairment"[tiab] OR "cognitive decline"[tiab])

Embase

('tuberculosis'/exp OR 'tuberculosis, pulmonary'/exp OR 'mycobacterium tuberculosis'/exp OR tubercul*:ti,ab OR TB:ti,ab) AND ('dementia'/exp OR 'alzheimer disease'/exp OR 'vascular dementia'/exp OR dement*:ti,ab OR alzheimer*:ti,ab OR 'cognitive impairment':ti,ab OR 'cognitive decline':ti,ab)

Scopus

(TITLE-ABS-KEY(tuberculosis OR tubercul* OR TB OR "Mycobacterium tuberculosis")) AND (TITLE-ABS-KEY(dementia OR Alzheimer* OR "vascular dementia" OR dement* OR "cognitive impairment" OR "cognitive decline"))

Appendix 2. Agreement between the two reviewers

Inter-reviewer agreement was assessed using Cohen's kappa (κ). Agreement was fair during title and abstract screening ($\kappa = 0.34$) and almost perfect during full-text screening ($\kappa = 1.00$).