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SUPPLEMENTARY MATERIAL

Incipient and subclinical tuberculosis: a narrative review

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Supplementary Table 1. The various studies on early-stage tuberculosis.

Author	Design	Prevalence of subclinical TB	Other characteristics
Frascella et al. [7]	Population-based TB prevalence surveys. Data from 23 national and 5 sub-national TB prevalence surveys across Africa and Asia since 1990	About 36.1% to 79.7% (median, 50.4%) among the bacteriologically confirmed TB. Asian countries: 49.4% (IQR, 38.8%–52.4%) African countries: 56.4% (IQR, 42.8%-68.5%)	Chest radiography was positive in median 89% (73%–98%) cases of bacteriologically confirmed TB, including subclinical TB cases.
Stuck et al. [18]	Meta-analysis of subclinical TB based on individual participants' data from 12 nationally representative surveys in Africa and Asia between 2007 and 2020. The study estimated the prevalence among three case definitions of subclinical TB: no persistent cough; no cough at all; or no symptoms	Unadjusted proportion of subclinical TB: 59.1% (95% CI 55.8–62.3) for no persistent cough and 39.8% (36.6–43.0) for no cough of any duration. Adjusted proportions: 82.8% (95% CI 78.6–86.6) for no persistent cough and 62.5% (56.6–68.7) for no cough at all.	
Hamada et al. [19]	Meta-analysis from 16 national and sub-national TB prevalence surveys conducted in Asian and African countries. Sample size: 740,815 individuals	The prevalence of subclinical TB ranged from 15.1% to 56.7% (median: 38.1%).	On multivariate analysis: current smoking associated with subclinical TB (OR 1.67, 95% CI 1.27–2.40)
Onozaki et al. [20]	Population-based TB prevalence surveys from Asian countries (1990-2012) Data from 18 TB prevalence surveys were included.	40% to 79% of bacteriologically-positive TB cases reported negative TB symptoms on screening.	Chest X-ray screening was positive in all patients.
Frascella et al. [7]	Five regional TB surveys from Tamil Nadu, India	Median prevalence of subclinical TB of 43.1% (IQR 36–55%)	
The Indian National TB Prevalence Survey (2019-2021) [21]	Population-based cross-sectional study	42.6% of the TB cases	Poor healthcare-seeking behavior among 63.6% of symptomatic

Oni et al. [22]	Cross-sectional hospital-based study in Cape Town, South Africa. Study individuals: 274 asymptomatic treatment-naïve HIV-1 infected persons.	Prevalence: 8.5% (95% CI 5.1% to 13.0%).	About 70% of subclinical TB patients were smear negative, compared to 16% in patients with symptomatic TB (P<0.001).
Gunasekera et al. [13]	Population-based survey among the South African communities of the Zambia, South Africa Tuberculosis and AIDS Reduction trial.	The crude prevalence of TB was 2222.1 cases per 100,000 population (95% CI 2053.4–2388.5), and 44.7% of them were subclinical.	A significant association between current tobacco smoking (OR 2.37, 95% CI 1.41–3.99) and HIV-positive status (OR 3.26, 95% CI 2.31–4.61) with subclinical TB
Tang et al. [23]	Retrospective hospital-based study from a low prevalence setting in China	Out of 380 patients 18.2%, had subclinical TB.	The risk of subclinical TB is higher among younger patients. A lower neutrophil-to-lymphocyte ratio and a significantly lower Beijing genotype were found in the subclinical TB group.
Bajema et al. [24]	Hospital-based study. Study subjects included untreated adults with HIV presenting for outpatient care in Durban, South Africa.	Subclinical TB: 23% of all TB cases among untreated HIV	Subclinical TB had an intermediate degree of immunosuppression, with a median CD4 count of 136 (72–312) cells/mm.^{3}
Min et al. [25]	Prospective cohort study from South Korea. Subjects: adult patients aged 19 years with pulmonary TB between 2016 and 2018.	Among 420 enrolled patients, 19.3% had subclinical TB.	On multivariable analysis, age <65 years was significantly associated with subclinical disease. A significantly lower proportion of smear positivity, culture positivity, and multiple lobe involvement in patients with subclinical disease compared to active TB.
Carter et al. [26]	Cross-sectional, secondary analysis of baseline data from the intervention arm of a household cluster randomized trial. Study subjects: household contacts (HHCs) of index TB patients in two South African provinces.	The prevalence of subclinical TB among HHCs was 2.3% (95% CI 1.7–3.1%) compared to 1.0% (95% CI 0.6–1.5%) prevalence for symptomatic pulmonary TB.	The prevalence of subclinical TB is higher in HIV-infected patients compared to HIV-uninfected patients. (4.0% versus 1.9; p = 0.018).
Mtei et al. [27]	Data from the DARDAR Study conducted in	The prevalence of active TB and subclinical TB was	Isoniazid preventive therapy was advised to the majority of subclinical TB initially.

	Tanzania. Eligible subjects: 498 ambulatory, HIV-positive adults with a CD4 cell count of ⩾200 cells/mm3 screened for active TB	71% and 29%, respectively.	
Rickman et al. [28]	Tshepiso Study in Soweto, South Africa. Subjects: 235 HIV-infected pregnant women with TB (and matched HIV-positive, TB-negative pregnant controls) from 2011 to 2014.	The prevalence of subclinical TB among 162 women initially recruited as TB-negative controls: 4.3%.	Higher risk of adverse effects in infants born to HIV-infected mothers with subclinical TB compared with TB-negative mothers.