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Active and Latent Tuberculosis Among Household Contacts of Pulmonary Tuberculosis Patients: Epidemiology, Determinants and Diagnostic Approaches: A Narrative Review

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Abstract

***Background:** Household contacts of pulmonary tuberculosis (TB) patients constitute a high-risk population for both active tuberculosis and latent tuberculosis infection (LTBI) because of prolonged and repeated exposure to infectious individuals. Understanding the burden, determinants, diagnostic approaches, and preventive strategies in this group is essential for effective tuberculosis control.*

***Objective:** To review the current evidence on the epidemiology, determinants, diagnosis, and prevention of active tuberculosis and LTBI among household contacts of pulmonary tuberculosis patients.*

***Methods:** A narrative review of published literature was conducted, focusing on studies evaluating the prevalence of active TB and LTBI, associated risk factors, diagnostic modalities, and preventive interventions among household contacts.*

***Results:** The prevalence of active tuberculosis among household contacts ranges from approximately 1% to 12%, while LTBI prevalence frequently exceeds 40% and may surpass 60% in high-burden settings. LTBI is considerably more common than active disease, representing a substantial reservoir for future tuberculosis cases. Evidence indicates that transmission and disease progression are influenced by a complex interaction of exposure-related and host-related factors. Prolonged exposure, smear positivity of the index case, overcrowding, and delayed diagnosis primarily influence infection acquisition, whereas progression to active disease is more strongly associated with age, diabetes mellitus, smoking, immune status, and nutritional status. Advances in molecular diagnostics, chest radiography, interferon-gamma release assays, and newer antigen-specific skin tests such as Cy-TB have improved opportunities for early detection. Recent studies also demonstrate that nutritional supplementation and tuberculosis preventive therapy can significantly reduce the risk of disease progression among household contacts.*

***Conclusion:** Household contacts represent a major reservoir of latent infection and a population at substantial risk of active tuberculosis. Effective tuberculosis control requires comprehensive household contact investigation integrating active case finding, LTBI screening, preventive therapy, nutritional support, and risk-factor modification. Strengthening these strategies will be essential for reducing transmission and accelerating progress toward tuberculosis elimination.*

***Key words:** Tuberculosis; latent tuberculosis infection; household contacts; contact investigation; risk factors; Cy-TB; tuberculosis preventive therapy; active case finding.*

Introduction

Tuberculosis (TB) remains a major global public health challenge and continues to be one of the leading causes of death from a single infectious agent. According to the World Health Organisation (WHO), an estimated 10.7 million people developed Tuberculosis worldwide in 2024, with India contributing the largest share of global burden. Despite significant advances in diagnosis, treatment, and prevention, Tuberculosis continues to impose substantial health, social, and economic consequences, particularly in low- and middle-income countries[1,2].

Transmission of *Mycobacterium tuberculosis* occurs primarily through inhalation of infectious aerosols generated by individuals with pulmonary TB. Consequently, household contacts of pulmonary TB patients represent one of the highest-risk populations for both TB infection and disease because of prolonged and repeated exposure within shared living environments. Factors such as overcrowding, poor ventilation, delayed diagnosis of the index case, and adverse socio-economic conditions further increase the risk of transmission within households[3].

Following exposure, individuals may develop either active TB or latent tuberculosis infection (LTBI). Active TB is associated with clinical disease, morbidity, mortality, and ongoing transmission, whereas LTBI represents a state of persistent immune sensitisation to *M. tuberculosis* without

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clinical evidence of disease. Although individuals with LTBI are asymptomatic and non-infectious, they constitute an important reservoir for future active TB. Household contacts consistently demonstrate substantially higher rates of both active TB and LTBI than the general population, making them a key target for TB control programmes[4,5].

The burden of TB among household contacts is influenced by a complex interaction of exposure-related, environmental, and host-related factors. Bacillary load of the index case, duration and intensity of exposure, crowding, ventilation, age, nutritional status, diabetes mellitus, HIV infection, smoking, and socio-economic conditions have all been implicated as determinants of infection and disease progression. While exposure-related factors primarily influence acquisition of infection, host-related factors appear to play a greater role in progression from latent infection to active disease[6-8].

Early identification of active TB and LTBI among household contacts has become a cornerstone of global TB control strategies. Systematic contact investigation, supported by advances in molecular diagnostics, interferon-gamma release assays (IGRAs), and newer antigen-specific skin tests such as Cy-TB, provides opportunities for earlier detection and preventive intervention[9,10].

Given the substantial burden of active TB and LTBI among household contacts, a comprehensive understanding of their epidemiology, determinants, diagnostic approaches, and preventive strategies is essential. This narrative review synthesizes current evidence on active and LTBI among household contacts of pulmonary TB patients, with particular emphasis on factors influencing transmission, disease progression, diagnosis, and prevention.

Methodology

A narrative review was conducted to evaluate the burden, determinants, diagnostic approaches, and preventive strategies related to active tuberculosis (TB) and latent tuberculosis infection (LTBI) among household contacts of pulmonary TB patients. Relevant English-language literature was identified through searches of PubMed, Scopus, Google Scholar, Embase, and the Cochrane Library.

The search strategy included combinations of Medical Subject Headings (MeSH) terms and keywords such as "tuberculosis", "latent tuberculosis infection", "household contacts", "contact investigation", "active tuberculosis", "risk factors", "Mantoux test", "interferon-gamma release assay", "Cy-TB", and "preventive therapy". Additional articles were identified through manual review of reference lists and relevant international guidelines.

Original research articles, systematic reviews, meta-analyses, randomised controlled trials, observational studies, and guidelines from organisations including the World Health Organisation (WHO) and the National Tuberculosis Elimination Programme (NTEP) were considered. Studies reporting data on active TB, LTBI, risk factors, diagnostic methods, or preventive interventions among household contacts were prioritized.

The evidence was synthesized thematically and organised into key domains including disease burden, determinants, diagnostic approaches, preventive therapy, and challenges in household contact investigation, with emphasis on areas of consensus, controversy, and future research needs.

Burden of Active Tuberculosis Among Household Contacts

Household contacts of pulmonary TB patients represent one of the highest-risk groups for active TB because of prolonged exposure to infectious aerosols within shared living environments. Numerous studies have demonstrated that systematic contact investigation identifies a substantial number of previously undiagnosed TB cases, emphasizing its importance in TB control programmes.

Evidence from systematic reviews and meta-analyses indicates that active TB among household contacts is not uncommon. Morrison *et al*[4] reported a pooled prevalence of 4.5% among close contacts in low- and middle-income countries, while Seid *et al*[11] reported a prevalence of 3.29% across sub-Saharan Africa. These findings suggest that approximately one in every 20 - 30 household contacts may have active disease, highlighting the value of routine contact investigation.

Considerable variation in prevalence has been reported across different settings. Daniel *et al*[12] observed an active TB prevalence of 2.72% among household contacts in Ethiopia, whereas studies from Brazil and other African countries have generally reported rates between 1% and 4%. In India, Singh *et al*[13] documented active TB in 6.9% of household contacts and demonstrated that new cases continued to emerge during follow-up, emphasizing the importance of longitudinal surveillance. Similarly, Chawla *et al*[14] reported tuberculosis in 12.1% of household contacts following active case finding, among the highest prevalence estimates reported in the literature.

The observed variability likely reflects differences in diagnostic methods, follow-up duration, infectiousness of index cases, HIV prevalence, nutritional status, socio-economic conditions, and household environmental factors. Studies incorporating active case finding, microbiological confirmation, and longitudinal follow-up generally report higher yields than cross-sectional or symptom-based screening approaches.

Despite these differences, a consistent finding across studies is that household contacts carry a substantially greater burden of active TB than the general population. This observation supports current WHO and national tuberculosis programme recommendations advocating systematic household contact investigation for early case detection and interruption of transmission. Overall, the available evidence demonstrates that active TB remains an important public health concern among household contacts and highlights the need for comprehensive screening, periodic follow-up, and targeted preventive interventions.

LTBI prevalence varies considerably across settings, ranging from approximately 20% to over 60%. In India, Sangma *et al*[15] reported an LTBI prevalence of 26.36%, while Praveen *et al*[16] observed a prevalence of 43.6% among contacts of sputum-positive pulmonary tuberculosis patients. Similarly, Barik *et al*[17] reported an LTBI prevalence of 20.4% using a combination of tuberculin skin testing and interferon-gamma release assays. Higher prevalence estimates have been reported from other regions, including Indonesia, where Karbito *et al*[18] documented LTBI in 63.8% of household contacts. Likewise, Moosazadeh *et al*[5] reported an LTBI prevalence of 42.8% and demonstrated that household contacts had a markedly higher risk of active TB than the general population.

Table I: Key studies reporting active tuberculosis among household contacts of pulmonary tuberculosis patients.

Study	Country	Study Design	Sample Size	Active TB Prevalence	Key Findings
Morrison *et al*[4]	Multiple LMICs	Systematic review and meta-analysis	Multiple studies	4.50%	Household contacts have substantially higher active TB burden than the general population
Seid *et al*[11]	Sub-Saharan Africa	Systematic review and meta-analysis	95 studies	3.29%	Confirmed significant burden of active TB among household contacts across Africa
Daniel *et al*[12]	Ethiopia	Cross-sectional	344 contacts	2.72%	Active case finding identified previously undiagnosed TB cases among contacts
Chawla *et al*[14]	India	Prospective observational	356 contacts	1.97%	Active contact investigation improved case detection
Singh *et al*[13]	India	Prospective cohort	548 contacts	6.90%	Demonstrated both co-prevalent and incident TB among household contacts
Pinto *et al*[31]	Brazil	National cohort study	420,854 contacts	2.12%	Household contacts had significantly elevated TB risk compared with the general population

LMICs: Low- and Middle-Income Countries.

Burden of Latent Tuberculosis Infection Among Household Contacts

Latent tuberculosis infection (LTBI) represents the largest reservoir of *Mycobacterium tuberculosis* infection worldwide and plays a central role in sustaining the TB epidemic. Although individuals with LTBI are asymptomatic and non-infectious, they remain at risk of progressing to active disease, particularly in the presence of immunosuppression or other risk factors. Consequently, identification and management of LTBI among household contacts have become key components of TB control strategies.

Household contacts experience substantially higher rates of latent infection than the general population because of prolonged exposure to infectious cases. Morrison *et al*[4] estimated that approximately 51.5% of household contacts in low- and middle-income countries have LTBI, indicating that more than half of exposed individuals acquire infection following close contact with an infectious case. This finding highlights the magnitude of the latent reservoir within households.

The wide variation in LTBI prevalence reflects differences in diagnostic methods, exposure intensity, index case infectiousness, household crowding, ventilation, socio-economic conditions, and background community transmission. Several studies have identified prolonged daily exposure, shared sleeping spaces, overcrowding, and diabetes mellitus as important predictors of LTBI acquisition. Karbito *et al*[18] demonstrated significantly higher infection rates among contacts exposed for more than five hours daily and among those living in overcrowded households, emphasizing the importance of exposure-related factors.

From a public health perspective, LTBI among household contacts presents both a challenge and an opportunity. While latent infection constitutes a major reservoir for future TB cases, it also provides an important target for preventive interventions. Systematic identification of LTBI through contact investigation, followed by appropriate TB preventive therapy, remains a cornerstone of the WHO End TB Strategy and national TB elimination programmes.

Overall, the available evidence demonstrates that LTBI is highly prevalent among household contacts and occurs far more frequently than active disease. The consistently elevated burden observed across diverse settings highlights the importance of routine contact investigation, accurate diagnostic approaches, and implementation of preventive strategies aimed at reducing future TB incidence.

whereas older adults may be at increased risk owing to immunosenescence and associated comorbidities. Adult contacts often demonstrate higher LTBI prevalence because of greater cumulative exposure.

Sex-related differences have been reported across studies. Acuña-Villaorduña *et al*[9] observed a higher

Table II: Key studies reporting latent tuberculosis infection among household contacts of pulmonary tuberculosis patients.

Study	Country	Study Design	Sample Size	LTBI Prevalence	Key Findings
Morrison *et al*[4]	Multiple LMICs	Systematic review and meta-analysis	Multiple studies	51.50%	More than half of household contacts had LTBI
Moosazadeh *et al*[5]	Iran	Systematic review and meta-analysis	Multiple studies	42.80%	Confirmed elevated LTBI burden among household contacts globally
Seid *et al*[11]	Ethiopia	Cross-sectional	668 contacts	42.80%	Demonstrated substantial LTBI prevalence in a high-burden setting
Sangma *et al*[15]	India	Cross-sectional	330 contacts	26.36%	Lower LTBI prevalence compared with many international studies
Praveen *et al*[16]	India	Cross-sectional	220 contacts	43.60%	Diabetes mellitus and exposure-related factors influenced LTBI risk
Barik *et al*[17]	India	Cross-sectional	235 contacts	20.40%	LTBI prevalence varied according to diagnostic modality used
Karbito *et al*[18]	Indonesia	Cross-sectional	138 contacts	63.80%	One of the highest LTBI prevalence rates reported; prolonged exposure and crowding were major determinants
Odera *et al*[32]	Kenya	Cross-sectional	175 contacts	55.70%	High LTBI burden among exposed household contacts

LMICs: Low- and Middle-Income Countries.

Determinants of Active and Latent Tuberculosis Among Household Contacts

The occurrence of active TB and LTBI among household contacts is influenced by a complex interaction of host-related, exposure-related, environmental, and socio-economic factors. While exposure to an infectious index case is a prerequisite for transmission, only a proportion of exposed individuals acquire infection, and an even smaller proportion subsequently progress to active disease. This variability reflects differences in susceptibility arising from demographic characteristics, nutritional status, comorbidities, living conditions, and intensity of exposure. Understanding these determinants is essential for identifying high-risk contacts, improving risk stratification, and designing targeted interventions for TB prevention and control.

(A) Host-Related Determinants

Several host-related factors influence susceptibility to TB infection and progression to active disease among household contacts. Age is an important determinant, although its effect differs for latent infection and active disease. Young children are particularly vulnerable to progression because of immature immune responses,

likelihood of LTBI among male contacts, while Velen *et al*[7] identified male sex as an independent predictor of active TB. Conversely, some studies have reported higher LTBI prevalence among female contacts, suggesting that gender-related differences may vary according to local socio-cultural and exposure patterns.

Comorbid conditions substantially increase TB risk. Diabetes mellitus has emerged as one of the strongest predictors of both LTBI and active disease among household contacts. Velen *et al*[7] reported more than a threefold increase in TB risk among diabetic contacts, while Praveen *et al*[16] similarly identified diabetes as an important determinant of LTBI. Other conditions including HIV infection, chronic kidney disease, and immunosuppressive states may also increase susceptibility to infection and disease progression.

Behavioural factors further contribute to risk. Smoking has been consistently associated with active TB among household contacts, with Velen *et al*[7] demonstrating a threefold increase in disease risk among current smokers. Household smoking exposure and excessive alcohol consumption have also been linked to increased TB risk through their adverse effects on respiratory defenses, immunity, and nutritional status.

Overall, age, sex, comorbidities, and behavioural factors significantly influence both acquisition of infection and progression to active disease. Identification of high-risk contacts based on these characteristics may improve the effectiveness of contact investigation and targeted preventive interventions.

(B) Exposure-Related Determinants

Exposure to an infectious TB patient is the fundamental prerequisite for transmission, and the intensity, duration, and proximity of exposure are among the strongest determinants of both LTBI and active TB among household contacts.

Duration of exposure has been consistently associated with increased infection risk. Acuña-Villaorduña *et al*[9] demonstrated a dose – response relationship between exposure duration and LTBI prevalence, with infection risk increasing significantly beyond 250 hours of exposure. Similarly, Karbito *et al*[18] reported nearly fivefold higher odds of LTBI among contacts exposed to index cases for more than five hours per day, highlighting the importance of prolonged exposure.

Physical proximity also plays a crucial role. Sharing a bedroom with an infectious patient has been associated with significantly higher LTBI prevalence, likely due to increased cumulative aerosol exposure. Acuña-Villaorduña *et al*[9] further reported that contacts sharing sleeping spaces with index cases had higher infection rates than other household members.

Characteristics of the index case substantially influence transmission. Exposure to sputum smear-positive patients, bilateral pulmonary disease, and extensive radiological involvement has been associated with increased LTBI risk, reflecting the role of bacillary burden and disease severity in household transmission[9]. Delayed diagnosis and prolonged symptomatic periods further increase transmission opportunities. Velen *et al*[7] demonstrated that a longer duration of cough in the index case independently increased the risk of TB among household contacts.

Exposure to multiple infectious individuals may further amplify transmission. Acuña-Villaorduña *et al*[9] reported significantly higher LTBI prevalence among contacts exposed to more than one index case, while Laghari *et al*[19] identified prolonged daily exposure (>18 hours/day) and the presence of another TB case within the household as important predictors of secondary TB.

Overall, duration and proximity of exposure, infectiousness of the index case, treatment delay, and exposure to multiple tuberculosis patients are major determinants of transmission within households. These findings support prioritisation of close and highly exposed contacts for active case finding, LTBI screening, and preventive interventions.

(C) Environmental and Household Determinants

Environmental and household conditions play a critical role in TB transmission by influencing the concentration and circulation of infectious aerosols within shared living spaces. Household contacts residing in overcrowded, poorly ventilated, and socio-economically disadvantaged environments are at increased risk of both LTBI and active TB.

Household crowding is among the strongest environmental determinants of transmission. Karbito *et al*[18] demonstrated that contacts living in overcrowded bedrooms had more than fivefold higher odds of LTBI, while Laghari *et al*[19] identified overcrowding as a significant predictor of secondary tuberculosis. Limited living space increases close contact with infectious individuals and reduces opportunities for adequate air exchange.

Ventilation is another key determinant. Poorly ventilated households facilitate accumulation of airborne bacilli, increasing the likelihood of transmission. Singh *et al*[20] reported inadequate ventilation in more than half of TB-affected households, highlighting the persistence of unfavorable indoor environmental conditions in high-burden settings. Similarly, inadequate sunlight exposure, often a marker of poor housing quality, has been associated with increased TB vulnerability[20].

Indoor air pollution and household smoking exposure further contribute to risk. Biomass fuel combustion, tobacco smoke, and other indoor pollutants impair respiratory defenses and may facilitate both infection and disease progression. Laghari *et al*[19] identified household smoking exposure as an independent predictor of secondary TB among contacts.

Household size and the presence of multiple TB cases within the same residence also influence transmission dynamics. Larger households increase the number of susceptible individuals exposed to infectious patients, while multiple TB cases within a household may reflect intense transmission networks. Laghari *et al*[19] reported that the presence of another TB case within the household was among the strongest predictors of secondary disease.

Overall, crowding index, poor ventilation, inadequate housing conditions, limited sunlight exposure, indoor

air pollution, and larger household size significantly contribute to TB transmission among household contacts. Addressing these environmental factors alongside biomedical interventions may substantially reduce household transmission and strengthen TB control efforts.

(D) Socio-economic Determinants

TB is closely linked to poverty and social deprivation, with socio-economic conditions influencing exposure risk, nutritional status, healthcare access, and disease outcomes. Among household contacts, socio-economic disadvantage not only increases the likelihood of infection but also contributes to progression from latent infection to active disease.

Poverty remains one of the most consistently reported determinants of TB. Individuals from low-income households often experience overcrowding, poor ventilation, undernutrition, and limited access to healthcare services. Singh *et al*[20] reported that most tuberculosis-affected individuals belonged to economically disadvantaged households characterised by poor living conditions, low educational attainment, and inadequate access to essential services. Similarly, Laghari *et al*[19] identified low family income as a significant predictor of secondary TB among household contacts.

Educational status also influences TB risk by affecting awareness of symptoms, transmission, preventive measures, and healthcare-seeking behaviour. Lower educational attainment may delay diagnosis, reduce treatment adherence, and limit participation in contact investigation programmes. In addition, restricted access to healthcare services due to cost, distance, and limited availability of diagnostic facilities can further delay case detection and treatment initiation. Singh *et al*[20] identified these barriers as common obstacles to timely TB care.

The economic consequences of TB often perpetuate a cycle of poverty and disease. Wingfield *et al*[21] demonstrated that TB-related costs frequently reached catastrophic levels for affected households and were associated with poorer treatment outcomes. Importantly, socio-economic support interventions improved treatment success and uptake of preventive therapy among household contacts.

Beyond material deprivation, stigma and social exclusion may discourage individuals from seeking care or participating in contact screening, thereby contributing to delayed diagnosis and continued transmission. Overall, poverty, low income, limited education, poor healthcare access, economic hardship, and stigma are important determinants of TB among household contacts and should be addressed alongside biomedical interventions to achieve effective disease control.

(E) Nutritional Determinants

Nutrition is one of the most important and potentially modifiable determinants of TB susceptibility and disease progression. The relationship between TB and undernutrition is bidirectional: undernutrition increases vulnerability to TB through impaired immune function, while active disease further worsens nutritional status through increased metabolic demands and reduced dietary intake.

Adequate nutritional status is essential for effective immune responses against *Mycobacterium tuberculosis*. Undernutrition impairs macrophage function, T-cell responses, and granuloma formation, thereby increasing the risk of progression from latent infection to active disease. Evidence suggests that nutritional status influences disease progression more strongly than the initial acquisition of infection. The TB LION study[22] further demonstrated that undernutrition adversely affects both innate and adaptive immune responses involved in controlling *M. tuberculosis*.

Strong evidence supporting nutrition as a determinant of TB among household contacts comes from the landmark RATIONS trial. Bhargava *et al*[23] evaluated nutritional supplementation among more than 10,000 household contacts in India and reported a 39% reduction in overall TB incidence and a 48% reduction in microbiologically confirmed pulmonary TB among supplemented contacts. These findings provide compelling evidence that improving nutritional status can reduce progression from infection to active disease.

Additional support comes from the TB LENS study[24], which reported improvements in weight gain, physical functioning, well-being, and household food security following nutritional supplementation among household contacts. Observational studies have similarly demonstrated higher rates of active TB among undernourished contacts, suggesting that nutrition acts both as an independent risk factor and as a mediator of broader socio-economic influences on TB outcomes[33,34].

Overall, current evidence identifies nutrition as a critical determinant of tuberculosis among household contacts. Unlike many other risk factors, nutritional status is modifiable, and emerging evidence indicates that nutritional interventions can substantially reduce TB

incidence. Incorporating nutritional assessment and support into household contact investigation programmes may therefore represent an important strategy for TB prevention and control.

Table III: Key studies evaluating determinants of active tuberculosis and latent tuberculosis infection among household contacts.

Study	Country	Study Design	Sample Size	Outcome Assessed	Significant Determinants Identified
Acuña-Villaorduña *et al*[9]	USA and Canada	Prospective	3040 contacts multicentric cohort	LTBI	Age >5 years, male sex, foreign birth, smear-positive index case, bilateral disease, shared bedroom, exposure to multiple index cases, longer exposure duration
Velen *et al*[7]	Vietnam	Nested case-control	1254 contacts	Active TB	Male sex, urban residence, previous TB, diabetes mellitus, smoking, prolonged cough duration in index case
Karbito *et al*[18]	Indonesia	Cross-sectional	138 contacts	LTBI	Overcrowded bedrooms, prolonged exposure (>5 hours/day), occupation
Laghari *et al*[19]	Pakistan	Cross-sectional analytical	2397 contacts	Secondary TB	Overcrowding, household smoking, prolonged exposure (>18 hours/day), low income, presence of another TB case in household
Praveen *et al*[16]	India	Cross-sectional	220 contacts	LTBI	Female sex, diabetes mellitus, exposure to retreatment (Category II) index cases
Sangma *et al*[15]	India	Cross-sectional	330 contacts	LTBI	Female gender of index case associated with higher LTBI prevalence
Singh *et al*[20]	India	Cross-sectional	100 TB patients	TB Risk Context	Poor ventilation, inadequate sunlight exposure, indoor smoke, low income, poor education, limited healthcare access
Wingfield *et al*[21]	Peru	Prospective cohort and household-randomised intervention	876 patients; 282 households	TB outcomes and prevention	Poverty, catastrophic costs, socio-economic deprivation; socio-economic support improved preventive therapy uptake and treatment success
Bhargava *et al* (RATIONS Trial)[23]	India	Cluster-randomised controlled trial	10,345 contacts	Incident TB	Nutritional supplementation reduced tuberculosis incidence by 39%
Cintron *et al* (TB LION)[24]	India	Prospective interventional study	760 contacts	TB progression risk	Undernutrition, impaired immune responses, low BMI
Carwile *et al* (TB LENS)[22]	India	Qualitative study	Household contacts	Nutritional determinants	Nutritional supplementation improved weight, wellbeing, and perceived disease resilience

Diagnosis of Active and Latent Tuberculosis Among Household Contacts

Early identification of active TB and LTBI among household contacts is a cornerstone of TB control strategies. Because household contacts are at substantially increased risk of both infection and disease, systematic screening enables timely diagnosis, initiation of treatment, implementation of preventive therapy, and interruption of transmission.

(A) Diagnosis of Active Tuberculosis

The diagnosis of active TB among household contacts follows a structured approach combining clinical, radiological, and microbiological evaluation. Current recommendations from the World Health Organisation (WHO) and India's National Tuberculosis Elimination Programme (NTEP) emphasize systematic contact investigation, beginning with symptom screening and chest radiography. Common symptoms suggestive of active tuberculosis include persistent cough, fever, weight loss, night sweats, and fatigue. However, symptom screening alone has limited sensitivity, particularly among household contacts who may have early or subclinical disease. Consequently, chest radiography is increasingly recommended as a complementary screening tool, including for asymptomatic contacts whenever feasible[25,26].

Individuals with suggestive symptoms and/or abnormal chest radiographic findings undergo microbiological evaluation. Nucleic acid amplification tests (NAATs), including Cartridge-Based Nucleic Acid Amplification Test (CBNAAT/Xpert MTB-RIF) and Truenat, are currently recommended as frontline diagnostic tools because they provide rapid detection of *Mycobacterium tuberculosis* and information regarding rifampicin resistance[25]. Sputum smear microscopy and mycobacterial culture continue to

serve as important adjunctive investigations, particularly in resource-constrained settings or for drug-susceptibility testing. The integration of clinical assessment, chest radiography, and microbiological confirmation improves case detection and ensures exclusion of active disease before preventive interventions are considered[26].

(B) Diagnosis of Latent Tuberculosis Infection

Unlike active TB, LTBI is characterised by immunological sensitisation to *Mycobacterium tuberculosis* in the absence of clinical, radiological, or microbiological evidence of disease. Therefore, LTBI cannot be diagnosed through direct detection of bacilli and instead relies on immunological testing following exclusion of active TB[25].

The Tuberculin Skin Test (TST/Mantoux test) remains the most widely used tool for LTBI detection worldwide and continues to be the principal test employed under routine programmatic conditions in many high-burden countries. The test measures delayed hypersensitivity to purified protein derivative (PPD) and is inexpensive, simple, and field-friendly[27]. However, its specificity is reduced in Bacillus Calmette-Guérin (BCG)-vaccinated populations and may be affected by exposure to non-tuberculous mycobacteria. Additionally, false-negative results may occur in immunocompromised or malnourished individuals[28].

Interferon-gamma release assays (IGRAs) offer greater specificity by utilizing *M. tuberculosis*-specific antigens such as ESAT-6 and CFP-10, which are absent from BCG strains. These tests are less affected by prior BCG vaccination and generally demonstrate higher specificity than the Mantoux test, although their widespread use may be limited by cost and laboratory requirements. Recent evidence suggests that newer assays such as QuantiFERON-TB Gold Plus and T-SPOT.TB provide improved diagnostic performance in selected populations[29].

In recent years, antigen-specific skin tests such as Cy-TB have emerged as promising alternatives that combine the operational simplicity of skin testing with the specificity of IGRA technology. Cy-TB utilizes recombinant ESAT-6 and CFP-10 antigens and has demonstrated high specificity with diagnostic performance comparable to laboratory-based IGRAs. Because it can be administered and interpreted similarly to the Mantoux test while avoiding many of its specificity limitations, Cy-TB has generated considerable interest for large-scale screening of household contacts in high-burden settings[30].

Despite advances in diagnostic technologies, no currently available test can reliably distinguish LTBI from incipient or active TB. Consequently, all LTBI testing must be interpreted in conjunction with clinical assessment and exclusion of active disease. Effective diagnosis among household contacts therefore requires an integrated approach combining symptom screening, radiological evaluation, microbiological testing, and appropriate immunological assessment according to individual risk profiles and available resources.

Future directions, knowledge gaps and challenges

Despite substantial advances in TB control, important gaps remain in the understanding and management of active TB and LTBI among household contacts. Existing evidence consistently demonstrates a high burden of both infection and disease in this population; however, significant heterogeneity in study design, diagnostic approaches, follow-up duration, and epidemiological settings limits direct comparison of findings and reduces the generalizability of available data.

One of the most important knowledge gaps relates to the prediction of disease progression. Current diagnostic tools can identify LTBI but cannot reliably distinguish individuals who will remain asymptomatic from those who will subsequently develop active disease. The development of predictive biomarkers, host immune signatures, and risk-stratification models capable of identifying contacts at highest risk of progression remains a major research priority.

Diagnostic limitations also continue to pose challenges. While newer tests such as interferon-gamma release assays and antigen-specific skin tests including Cy-TB have demonstrated improved specificity compared with the traditional Mantoux test, evidence regarding their long-term predictive value, operational feasibility, and cost-effectiveness in large-scale household contact screening programmes remains limited. Further multicentric studies are required to evaluate their performance across diverse populations and epidemiological settings.

Although several determinants of tuberculosis among household contacts have been identified, the relative contribution and interaction of host-related, environmental, and exposure-related factors are not yet fully understood. Future studies should focus on developing comprehensive risk prediction models incorporating demographic, clinical, socio-economic, nutritional, and exposure-related variables to facilitate targeted screening and preventive interventions.

Nutrition represents another important area requiring further investigation. Recent interventional studies have demonstrated that nutritional supplementation can

significantly reduce TB incidence among household contacts; however, the optimal composition, duration, delivery mechanisms, and cost-effectiveness of nutritional interventions remain uncertain. Additional research is needed to better define the immunological pathways through which nutritional status influences susceptibility to infection and disease progression.

Implementation challenges also warrant further attention. Despite strong recommendations for contact investigation and tuberculosis preventive therapy, uptake and completion rates remain suboptimal in many high-burden settings. Operational research focusing on barriers to screening, treatment adherence, stigma reduction, healthcare accessibility, and community engagement is essential to improve programme effectiveness.

Future TB control strategies should move toward a more integrated and person-centred approach. Combining active case finding, LTBI screening, preventive therapy, nutritional support, socioeconomic interventions, and digital health technologies may substantially improve outcomes among household contacts. The integration of artificial intelligence-assisted radiography, molecular diagnostics, electronic contact tracing systems, and individualised risk assessment tools offers promising opportunities to enhance the efficiency and effectiveness of household contact investigation programmes.

Addressing these knowledge gaps through well-designed multicentric studies, longitudinal cohorts, implementation research, and interventional trials will be critical for refining tuberculosis prevention strategies and accelerating progress toward national and global TB elimination goals.

Conclusion

Household contacts of pulmonary TB patients represent one of the most vulnerable populations in the TB epidemic, bearing a substantially higher burden of both active TB and LTBI than the general population. Evidence from diverse geographical settings consistently demonstrates that a significant proportion of household contacts either harbor latent infection or develop active disease, highlighting their central role in ongoing transmission dynamics.

The occurrence of TB among household contacts is influenced by a complex interplay of host-related, exposure-related, environmental, socio-economic, and nutritional determinants. While factors such as prolonged exposure, household crowding, poor ventilation, poverty, and limited healthcare access increase the likelihood of infection, host characteristics including age, comorbidities, smoking, and particularly undernutrition play a critical role in determining progression from latent infection to active disease. Emerging evidence from nutritional intervention studies further suggests that improving nutritional status can significantly reduce TB incidence among exposed individuals.

Early identification of active TB through systematic contact investigation, combined with accurate detection of latent infection using Mantoux testing, interferon-gamma release assays, and newer antigen-specific tests such as Cy-TB, provides an important opportunity for timely intervention. Integration of effective diagnostic strategies with tuberculosis preventive therapy has the potential to substantially reduce future disease burden and interrupt transmission within households.

Achieving TB elimination goals will require strengthening household contact investigation programmes, expanding access to preventive therapy, addressing underlying social and nutritional determinants, and adopting innovative diagnostic and risk-stratification approaches. A comprehensive, person-centered strategy targeting household contacts is therefore essential for reducing tuberculosis transmission and accelerating progress toward national and global TB elimination targets.

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