Journal of Communicable Diseases
Volume 57, Issue 3 - 2025, Pg. No. 182-190
Peer Reviewed & Open Access Journal

Review Article

Is Isolation of Open Active Pulmonary Tuberculosis Cases the Last Mile Strategy to Achieve Tuberculosis Elimination in India?

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DOI: https://doi.org/10.24321/0019.5138.202585

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How to cite this article:
Chadhar K, Kishore J, Jani A, Shekhar C, Jani K K, Gupta N. Is Isolation of Open Active Pulmonary Tuberculosis Cases the Last Mile Strategy to Achieve Tuberculosis Elimination in India? J Commun Dis. 2025;57(3):182-190.

Date of Submission: 2025-06-02
Date of Acceptance: 2025-09-18

A B S T R A C T

Tuberculosis (TB), despite extensive global efforts for elimination, continues to pose significant public health challenges, particularly in high-burden countries like India. This review explored the TB cases for a minimum period of 2 weeks as a critical strategy to curb transmission and achieve TB elimination targets. Analysing historical and current epidemiological data, we discussed the burden of TB and its transmission dynamics, emphasising the role of early detection and isolation in halting community spread. Multidrug-resistant TB (MDR-TB) and associated co-morbidities such as diabetes, undernutrition, and tobacco and alcohol use exacerbate challenges in TB control. We presented isolation policies, modelled on the success of infection control strategies during the COVID-19 pandemic, as pivotal interventions, particularly in managing MDR-TB and extensively drug-resistant TB (XDR-TB). Recommendations included targeted use of isolation, enhanced ventilation, respiratory hygiene, and community education to mitigate household and community transmission. The role of community health workers, such as ASHAs and ANMs, is critically examined to ensure their involvement maximises TB care without increasing the risk of transmission. Key strategies include implementing evidence-based harm reduction in crowded settings through maximised natural ventilation and strict respiratory hygiene. Critically, these measures must be integrated into the National TB Elimination Programme (NTEP) through structural support, such as training community health workers to conduct home assessments, establishing community-based short-stay isolation centers, and making psychosocial support a routine component of care. By integrating robust public health measures with comprehensive psychosocial and financial support, the path toward TB elimination, while challenging, becomes increasingly feasible and equitable.

Keywords: Tuberculosis, isolation, transmission, MDR-TB, infection control, household contacts, disease elimination

Introduction

Twenty years before Robert Koch delivered his Nobel Lecture in 1905, tuberculosis was not even considered an infectious disease, although Jean Antoine Villemin's work, along with the experimental investigations by Cohnheim and Salomonsen, had already hinted that this belief was incorrect. However, it was the discovery of the tubercle bacillus that firmly established the aetiology of tuberculosis and confirmed that it is a biological agent, and thus an infectious yet preventable, disease. Even after almost 140 years, TB still continues to kill its hosts or render serious morbidity to a large number of people. A multitude of strategies are in play to combat this disease and achieve the national and global targets of elimination. In this review, we ponder over the strategy of isolation of active (open) cases to halt the transmission of TB in the community.

Burden of TB

Tuberculosis incidence varies widely across regions, with higher rates observed in developing countries. In 2022, an estimated 10.6 million people (95% UI: 9.9–11.4 million) developed TB globally, an increase from 10.3 million in 2021 and 10.0 million in 2020. The estimated TB incidence rate for 2022 was 133 cases per 100,000 population per year (95% UI: 124–143). The prevalence of TB remains substantial, particularly in countries with high HIV rates and inadequate healthcare infrastructure. It is estimated that approximately 30% of the world's population has latent TB. Notably, thirty high TB burden countries accounted for 87% of the global TB cases in 2022, with two-thirds of the total cases concentrated in eight countries: India (27%), Indonesia (10%), China (7.1%), the Philippines (7.0%), Pakistan (5.7%), Nigeria (4.5%), Bangladesh (3.6%), and the Democratic Republic of the Congo (3.0%). In terms of mortality, TB caused an estimated 1.30 million deaths worldwide in 2022 (95% UI: 1.18–1.43 million), a slight decrease from the 1.4 million deaths recorded in both 2020 and 2021, and nearly returning to the 2019 levels. (WHO Global TB report). India in particular is to bear the largest burden of TB in the world. The national prevalence of all forms of TB among all age groups in India was found to be 312 per 100,000 population (with a confidence interval of 286 - 337) for the year 2021. The highest prevalence was observed in Delhi with 747 per 100,000 population, while the lowest was in Gujarat with 137 per 100,000 population.[1]

In the aftermath of the pandemic and guided by the "National Strategic Plan (NSP) 2017-2025," the National TB Elimination Programme (NTEP) intensified its efforts in 2022, aiming to eradicate TB by 2025. This renewed focus led to numerous achievements and the implementation of innovative strategies and interventions benefiting both patients and the community. Despite a temporary decline in TB notifications in 2020 and 2021, NTEP not only increased but surpassed previous numbers. The year 2022 stands as a significant milestone for TB surveillance in India, with a record high notification of 2.42 million cases, representing a 13% increase compared to 2021. This corresponds to a case notification rate of approximately 172 cases per 100,000 population. Additionally, 2022 witnessed the highest number of private TB case notifications to date, totalling 730,000. The total number of MDR/RR patients diagnosed in 2022 was 63,801. The programme's success in identifying missed TB patients was driven by bolstering both passive and active case-finding efforts. Consequently, the presumptive TB examination rate (PTBER) for the country increased to 1,281 per 100,000 population in 2022, marking a 68% rise from 763 in 2021. However the road to elimination still seems like pipe dream given the high burden and related bio-social factors which pose a challenge to achieve the set targets. Given the current insufficient decline in global tuberculosis incidence (8.7%) and mortality (19%), it is unlikely that the END TB strategy will achieve its milestones of a 50% reduction in incidence and a 75% reduction in mortality by 2025.[2]

Transmission of TB

Elimination of a disease is defined as halting the transmission of the disease thus stopping the incidence of the disease.[3] The transmission of TB among humans primarily occurs via airborne particles when individuals with active pulmonary TB cough, sneeze, or speak, with the bacteria remaining viable in the air for several hours. *Mycobacterium tuberculosis* is considered the quintessential example of aerosol transmission via small airborne particles (<5 µm) that persist in the air and contaminate poorly ventilated spaces.[4] From an infection control and public health perspective, airborne transmission is generally more challenging to manage. While coughing and sneezing are commonly recognised as bodily functions that generate aerosols, singing, speaking, and breathing also produce these particles.[5] Although particles containing culturable bacilli are traditionally deemed infectious, it is now understood that particles with non-culturable bacilli[6,7] may also pose an infectious risk.[8] For successful transmission, the infectious particle containing *M. tuberculosis* must reach the small terminal airways deep in the lung, which are conducive to infection.[9,10] Due to the clandestine nature of the disease in early period of infection and multiple pathways of transmission, much remains to be known about this century old disease. It is also pertinent that the key to eliminating TB lies in understanding the transmission dynamics and points where appropriate interventions can be done.

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202585

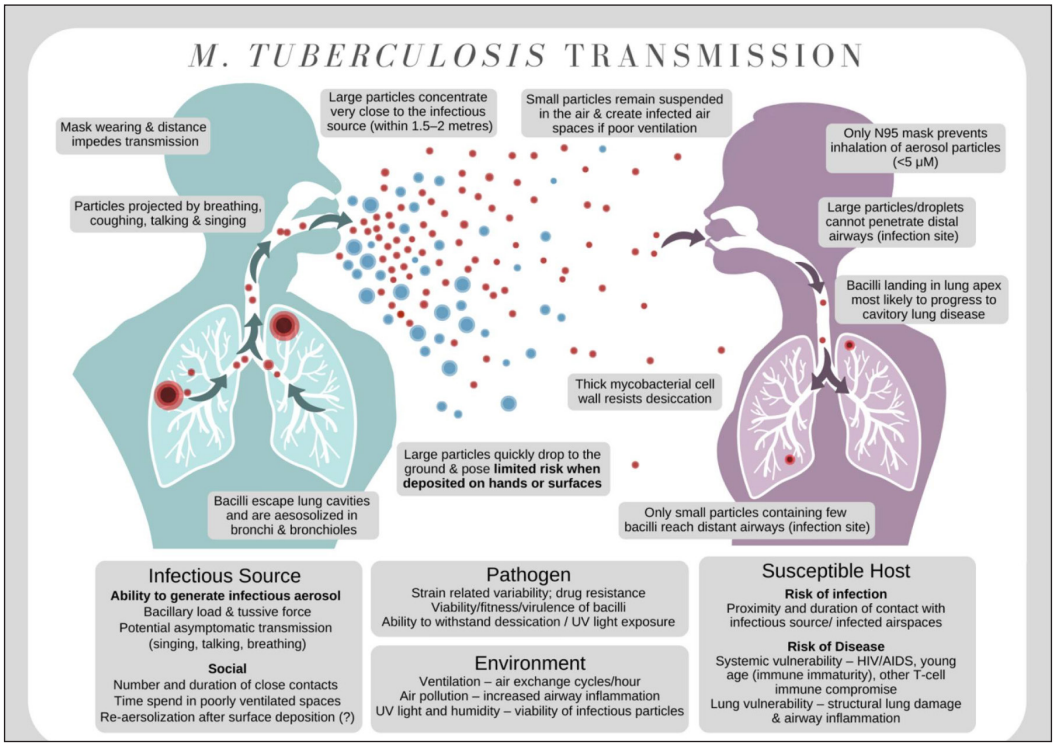

Figure 1.Transmission of M. tuberculosis among humans[10]

Risk of infection and disease among household contacts of patient with TB

Programmatic definitions of household contact include persons living in the same house and eating from the same kitchen as the index case for ≥one night or for frequent or extended periods during the day during the 3 months before diagnosis in the index case.

Individuals exposed to an infectious household member or a so called open case are at a significantly high risk of acquiring *M. tuberculosis* infection and developing tuberculosis disease.[11] Open cases are the once who are sputum positive, i.e., infectious beacuse excreting mycobactirea. Inffective drugs can render dam as non infectious or sputum negative with in two week. So open cases should be isolated for atleast two weeks to stop the TB transmission In Vietnam, household contacts were found to have a 2.5-fold increased risk of developing any form of tuberculosis and a 6.4-fold increased risk of developing sputum smear-positive disease compared to community members without household TB contact. [12] Implementing household contact tracing and tuberculosis preventive therapy (TPT) offers substantial benefits, particularly for vulnerable young children, who face the highest risk of developing tuberculosis disease.[13,14] A recent study involving nearly 140,000 child household contacts revealed that 19% of young children with a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) developed tuberculosis within the following two years.[14] The WHO recommends active case finding and the use of TPT among household tuberculosis contacts to reduce diagnosis time and limit ongoing transmission. However, the epidemiological impact of these measures on a population scale has yet to be demonstrated.[14-16]

A cohort study[17], conducted between 2014 and 2019 in South India, aimed to determine the prevalence and risk factors associated with latent tuberculosis infection (LTBI) among 1523 household contacts (HHCs) of pulmonary TB patients found that nearly all HHCs had shared a residence with the index case (IC) for over a year, with 25% sharing the same bed. The prevalence of LTBI among these HHCs was 52.6% (95% CI: 50.1–55.1%). Through mixed-effects generalised linear modelling it was determined that HHCs aged 19–64 years (adjusted incidence rate ratio (aIRR) = 1.2; 95% CI: 1.1–1.3; p = 0.02), those older than 65 years (aIRR = 1.4; 95% CI: 1.1–1.9; p = 0.02), and those sharing the same bed with the IC (aIRR = 1.2; 95% CI: 1.1–1.3; p = 0.04) were significant independent determinants of LTBI. A retrospective record review[18] evaluated the yield of active case finding among household contacts of newly diagnosed smear-positive TB patients. Of the 643 household contacts of 280 index TB patients, using chest X-rays followed by symptom screening, 71 (13%) had abnormal radiographs, and 70% of these were symptomatic. TB was diagnosed in 29 (5.3%) contacts, with 79% being sputum smear positive. The number needed to screen (NNS) was 19 overall and 2 among those with abnormal X-rays. Factors associated with abnormal radiographs included age over 44 years, male gender, and being siblings of the index case, while

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202585

the 15–44 age group was significantly linked to developing TB. The study concluded that active screening, particularly using chest X-rays with symptom screening, effectively improves TB case detection among household contacts.

Multidrug- resistant TB and comorbidities associated with TB

Tuberculosis at times stops responding to the conventional drugs used in treatment; such a situation occurs when the bacilli develop resistance to anti-tubercular drugs. This resistance can either develop in situ due to incomplete or incorrect treatment or be transmitted from a patient who is infected by a resistant bacillus. The burden of MDR-TB in India is significant. The first national drug resistance survey[19] conducted in 2014-15, indicated that among all TB patients, the prevalence of multidrug-resistant TB (MDR-TB) was 6.19%, with 2.84% in new and 11.60% in previously treated patients. Additionally, 21.82% of MDR-TB patients showed resistance to fluoroquinolones, and 3.58% to second-line injectable drugs. Extensively drug-resistant TB (XDR-TB) was found in 1.3% of MDR-TB patients. Overall, 28.0% of TB patients exhibited resistance to any first- or second-line drugs, with higher resistance rates among previously treated patients. Isoniazid resistance was 11.06% in new patients and 25.09% in previously treated patients, while pyrazinamide resistance was 6.95% and 8.77%, respectively. The national MDR-TB rates align with previous state-level surveys, highlighting significant drug resistance across various settings. Untreated MDR-TB is almost always fatal, but before the patients succumb to resistant forms of TB, a high amount of transmission had already occurred among the contacts thus bringing public health in the foray. Detection of MDR-TB is largely dependent on drug sensitivity and testing services. NTEP employs a universal drug sensitivity testing strategy, hence all diagnosed cases have to undergo molecular testing for drug sensitivity often limiting to only rifampicin. The impact of different drug-susceptibility patterns and HIV status on TB transmission risk is not entirely understood. Patients with multidrug-resistant TB (MDR-TB) typically take longer to convert their sputum to non-infectious compared to those with drug-susceptible TB, likely due to the limited effectiveness of second-line drugs. Consequently, MDR-TB patients remain infectious for extended periods, even after treatment initiation, increasing the risk of transmission within households. Therefore, additional infection control measures are necessary for managing MDR-TB patients at home to mitigate these risks.

Programmatic challenges hamper a hundred percent rate of testing; thus, it suggests that such cases should be isolated at priority till a clear diagnosis is made and appropriate treatment started.

Among other challenges that TB elimination faces is prevalence of co-morbidities that affect the course of disease significantly. Undernutrition is the biggest risk factor, to which 34% and 19% of TB cases can be attributed to in India[20] and globally[21] respectively. Nutritional supplementation schemes including food baskets and cash transfers are envisaged to tackle this socio-economic challenge and branches out to affect other risk factors that contribute to significant morbidity and mortality among patients with TB. Another co-morbid condition is diabetes mellitus, where undermined immune states result in development of tuberculosis and further making treatment difficult. Patients with co-morbid diabetes, have high pill burden which can possibly affect the compliance with treatment of both diabetes and TB introducing a catch 22 situation. This also pressurises the health system, hence bi-directional screening among both diabetes and TB patients is introduced in program mode in the country.

Other co-morbidities like tobacco and alcohol consumption affect TB incidence and treatment significantly. Moreover, focus should also be thrown on mental health issues and stigma related to TB which are less talked about from an interventional point of view. A retrospective analysis[22] in South India identified diabetes mellitus (30.9%) as the most prevalent risk factor for pulmonary tuberculosis (PTB) among 207 patients, with PTB being more common in men and those over 40 years old. Occupation analysis revealed higher PTB prevalence in blue-collar and white-collar workers. Another study[23] across 18 TB program units in India found that male gender, history of TB treatment, and adult age were significant risk factors for TB, while treatment history was crucial for rifampicin-resistant TB. A cross-sectional study[24] in South India's Kancheepuram district highlighted that diabetes, pre-diabetes, and hypertension significantly increase the risk of LTBI progressing to active TB, suggesting the need for targeted health interventions.

Isolation as a strategy to combat transmission of TB

COVID-19 pandemic has reminded us about the effectiveness of simple yet effective strategies such as isolation and quarantine. TB shares the property of aerosol transmission and TB is no less of a pandemic in itself. Hence the question is often asked, what should be the isolation policy for active (open) TB cases? The answer lies in the transmission dynamics of the disease earlier. While in a well-ventilated, hygienic and non-crowded environment, the chances of transmission significantly reduce, however the patients who dwell in this environment are often outliers. Since the transmission is largely person to person, emphasis on isolation of patients of open active TB with appropriate infection control measures including sputum disposal should be a given. Several countries implement isolation

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202585

policies for TB patients to prevent transmission and ensure effective treatment. For instance, in Australia, particularly in Queensland, TB patients, especially those with smear-positive pulmonary TB, are required to follow strict infection control measures, including airborne precautions and isolation, either in healthcare settings or at home, until they are deemed non-infectious.[25] The European Centre for Disease Prevention and Control (ECDC) also provides guidance on managing contacts of MDR TB and XDR TB patients, emphasizing the importance of isolation and infection control measures to prevent the spread of TB in healthcare and community settings. Additionally, the World Health Organization (WHO) recommends comprehensive infection prevention and control measures, including the isolation of TB patients, to reduce transmission. These guidelines are part of a broader strategy to manage and control TB globally. These policies reflect a concerted effort to address TB transmission through isolation and other infection control measures, highlighting the importance of strict adherence to these protocols to protect public health.

Modelling study to assess the impact of early case detection and isolation on MDR-TB incidence employed a 15-day isolation period post-treatment initiation for active TB cases, with parameters derived from current literature. Results indicated that achieving over 90% TB case identification within four weeks of symptom onset, combined with a 15-day isolation strategy with 50% effectiveness, could reduce MDR-TB incidence by 10% over a decade. Complete prevention of transmission could halt MDR-TB's rise within ten years, though the reduction would be less than 20% in this period. The success of transmission reduction measures critically depends on timely and accurate case identification, emphasizing the need for increased investment in early detection efforts to mitigate the high costs and adverse effects associated with MDR-TB treatment.[26] Another model suggested that that TB may be eliminated by 2035 in India if the treatment success rate could be achieved to 95%, by contact tracing and isolating at least 50% of MDR-TB. A systematic review[27] of seven before-and-after studies found that the use of surgical masks by individuals with infectious TB led to a 14.8% reduction in TB infection rates within a hospital setting. Surgical masks can similarly be used in home settings to further limit the spread of infection. Other evidence suggests similar methods to disrupt transmission.[28,29]

Role of Community Health Workers in TB Care

Should ASHA and ANMs be Involved in TB Care? Accredited Social Health Activists (ASHAs) and Auxiliary Nurse Midwives (ANMs) play crucial roles in TB care, including drug distribution and patient education. However, their direct involvement in managing open cases is debated due to the risk of transmission to other vulnerable populations. They are often involved in providing community based health services to pregnant mothers and under-five children. The transmission dynamics suggest that the particles containing tubercle bacilli can latch onto the body surfaces of healthcare workers and can be carried to healthy population groups often involving mother and child. Hence ANMs and ASHAs should take extra precautions when visiting to an open case of TB. They should take universal precaution to deal with such cases. They can provide domiciliary support to patients who have crossed the infective period. Their role in community mobilization and awareness generation for TB should not be hampered. However, further research is required to strengthen this claim and incorporated in the program for uniform application across the country.

Patient-Centered Mandate for Tuberculosis Isolation in India

India's goal to eliminate tuberculosis (TB) by 2025 is threatened by the severe non-clinical consequences of the disease and its management. [30] While isolating infectious patients is a public health necessity, its implementation often imposes devastating economic, psychological, and social burdens that undermine treatment and recovery. A patient-centered approach must therefore address this human cost by moving beyond medication to actively supporting patients through the challenges of isolation.

Challenges in Infection Control in Crowded Settings

For many in India, particularly in crowded urban and rural homes, effective isolation is a significant logistical challenge. However, evidence-based harm reduction is achievable. The World Health Organization (WHO) emphasizes simple, low-cost infection control measures that can significantly reduce transmission risk in resource-limited settings. [31]

Key Strategies Include

- **Maximizing Natural Ventilation:** As TB bacteria are dispersed in well-ventilated environments, opening windows and using fans to create cross-ventilation is a critical measure.
- **Strict Cough Hygiene:** Patients must be educated on proper cough etiquette, including covering the mouth and nose and the safe disposal of used tissues.
- **Sleeping Arrangements:** In households where a separate room is unavailable, the patient should sleep alone in a well-ventilated area, positioned to cough away from others.

Socio-Psychological Burden of Isolation

The mental health toll on TB patients is severe. A systematic review found the prevalence of depression among TB patients in India to be 37% [33], a rate strongly associated with poor medication adherence. This psychological

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202585

distress is overwhelmingly driven by social stigma rooted in misinformation. Qualitative studies document patient experiences of social exclusion and verbal abuse.[34]

This stigma is compounded by catastrophic financial loss. Patients lose an average of 83 workdays, costing households 20-30% of their annual income. [35, 36] While the government's Nikshay Poshan Yojana provides some financial relief, it is often insufficient to prevent families from selling assets or borrowing money to survive. [37]

Integrating Isolation Support into the National TB Elimination Programme (NTEP)

To be effective, isolation cannot be a passive recommendation; it must be an active, supported component of the NTEP. Recommendations include:

- **Conducting Home Assessments:** Community health workers should be trained to assess home environments to determine the feasibility of safe isolation and provide tailored guidance.
- **Establishing Community-Based Isolation Options:** For patients unable to isolate at home, the program should partner with local bodies to create dedicated short-stay community isolation centers.
- **Integrating Psychosocial Support:** Mental health screening and tele-counselling services must be integrated into routine care for all isolated patients, not just as an optional service.[38]

The Modern Role of the Sanatorium

The role of institutional isolation also merits consideration. While long-stay sanatoriums are a historical model, specialized facilities retain a vital, modern function. The TB Sanatorium in Bhowali, for example, now operates as a short-stay center for stabilizing complex cases, managing co-morbidities, and treating drug-resistant TB (DR-TB). [39]

These centers offer a model for a critical unmet need within the NTEP: providing a safe, medically supervised environment for highly infectious patients or those from households where safe home isolation is impossible. A patient-centered approach demands that isolation be viewed not as a simple instruction but as a complex clinical, social, and economic intervention. By investing in practical guidance, robust psychosocial support, and dedicated facilities for those most in need, India can mitigate the human cost of TB and accelerate its progress toward elimination.

Recommendations

Studies from India in the 1950s as discussed earlier indicated that the primary risk for TB infection arises from close contact with an infectious individual before diagnosis.[26,27] Whether the patient remains at home or moves to a sanatorium has minimal impact on household transmission if the patient receives effective treatment. Early case detection is crucial for reducing household TB transmission and should align with national TB control policies. Infection control behaviour-change campaigns should be incorporated into community education to emphasize early identification, treatment adherence, and proper TB infection control practices such as cough etiquette and respiratory hygiene. TB bacilli are resilient organisms and can survive for months in dust particles. The most important source of infection is active, open pulmonary TB cases that release bacilli not only by direct droplet spread but also indirectly during early treatment until they become bacteriologically negative. A particularly grave aspect is the long survival of these bacilli in dust. Besides the isolation of open cases, therefore, disinfection of the environment, object, and dust is also requisite until the patients become non-infectious or non-bacilli carriers.

To minimize household exposure, it is recommended that

- Homes be well-ventilated, particularly rooms where infectious TB patients spend time.
- The house should be clean and dust free with provision of disinfection.
- Those who cough should practice proper respiratory hygiene,
- Smear-positive open active TB patients should spend as much time outdoors as possible,
- Sleep alone in a well-ventilated room
- Avoid congregate settings and public transport.

It is recommended that the National TB Elimination Programme (NTEP) develop and disseminate clear, pictorial guidelines on these practical infection control measures for families and community health workers.

Promoting community awareness of infection control is essential regardless of the TB drug susceptibility profile, as many cases of multidrug-resistant TB (MDR-TB) remain undiagnosed but continue to be transmitted within the community. When promoting infection control awareness in the community, it is crucial to ensure the quality of information, education, and communication to prevent exacerbating the stigma associated with TB. Efforts must be balanced with the potential benefits of community education, such as garnering social support to reduce TB transmission and fostering sustainable healthy behaviours. Effective communication should aim to provide accurate information while encouraging an understanding and supportive environment to help mitigate stigma. WHO has suggested that while being culture positive, MDR-TB patients who cough should always practice cough etiquette (including use of masks) and respiratory hygiene when in contact with people. Ideally, health service providers should wear particulate respirators when attending patients in enclosed spaces. Ideally, family members living with

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202585

HIV, or family members with strong clinical evidence of HIV infection, should not provide care for patients with culture-positive MDR-TB. If there is no alternative, HIV-positive family members should wear respirators, if available. Children below five years of age should spend as little time as possible in the same living spaces as culture-positive MDR-TB patients. Such children should be followed up regularly with TB screening and, if positive, drug-susceptibility testing and treatment. While culture positive, XDR-TB patients should be isolated at all times, and any person in contact with a culture positive XDR-TB patient should wear a particulate respirator. If at all possible, HIV-positive family members, or family members with a strong clinical evidence of HIV infection, should not share a household with culture positive XDR-TB patients. If possible, potential renovation of the patient's home should be considered, to improve ventilation (e.g. building of a separate bedroom, or installation of a window or wind catcher, or both).[30] These measures however need to be employed keeping in mind the feasibility, if not possble, other alternative methods should be used.

Conclusion

In summation, the journey toward tuberculosis (TB) elimination demands a multifaceted approach, with the isolation of open active cases emerging as a pivotal strategy. Despite the vast strides made since Koch's discovery, TB continues to challenge public health worldwide, particularly in high-burden countries like India. The crux of effective TB control lies in early detection, rigorous isolation protocols, and comprehensive care, including attention to multidrug-resistant strains and co-morbid conditions like undernutrition, diabetes and HIV. Community health workers play an essential role, though their direct involvement with infectious cases must be carefully managed to prevent further spread. Ultimately, while the road to eradication is fraught with challenges, a concerted effort grounded in scientific rigor and community engagement can transform this seemingly Sisyphean task into a triumphant reality.

Conflict of Interest: None

Source of Funding: None

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: None

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DOI: https://doi.org/10.24321/0019.5138.202585