Obstacles and prospects in a holistic approach to tuberculosis eradication: A systematic review

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Abstract

Background: Tuberculosis (TB) remains one of the major public health issues in Indonesia, ranking third globally in the number of TB cases after India and China. Despite global and national efforts to combat the disease, significant challenges persist, including Multidrug-Resistant Tuberculosis (MDR-TB), limited early detection, patient non-compliance with treatment, and widespread social stigma. The Indonesian government has implemented the National Strategy for TB Prevention and Control, which focuses on early detection, appropriate treatment, and TB transmission prevention through comprehensive approaches such as Directly Observed Treatment, Short-course (DOTS), and the use of rapid diagnostic technologies like Xpert MTB/RIF. However, to achieve the target of TB elimination by 2030, in line with the Sustainable Development Goals (SDGs), further and more coordinated efforts are required.

Purpose: To examine the epidemiology of TB worldwide and in Indonesia, the challenges in implementing TB eradication programs, and the strategic measures needed to accelerate TB elimination.

Method: A systematic review approach in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Articles were sourced from online databases such as PubMed, Google Scholar and Science Direct. The review was organized according to the PICOS framework. The keywords used in the search included "tuberculosis eradication" "patient's experience" and "one health approach" and "literacy" and "pharmacokinetics" and "quality of life" and "patient's perspective". Articles were selected based on specific inclusion criteria: the last three years (2021-2024), written in English and Indonesian.

Results: Indonesia faces challenges in managing TB by 2030, with 845,000 new cases and increasing MDR-TB prevalence. The COVID-19 pandemic has exacerbated the issue, with a critical healthcare system, stigma, and economic hardships affecting diagnosis and treatment. Digital healthcare technology and public-private partnerships can help improve diagnosis and treatment. Community-based efforts and new therapeutic treatment protocols can improve patient health and healthcare systems.

Conclusion: With strong governmental commitment, support from international organizations, and active community participation, Indonesia is expected to achieve TB elimination by 2030. Enhancing health system capacity, adopting innovative technologies, and sustaining public education will be crucial in addressing the challenges and opportunities in fully eradicating TB.

Keywords: Early Detection; Elimination; Program, Tuberculosis.

INTRODUCTION

Tuberculosis remains a global concern, with 10.6 million new cases reported in 2021, 1.6 million deaths, and 450,000 MDR-TB cases, making it one of the largest preventable causes of mortality. The World Health Organisation highlights the complexity and cost of treatment for this infectious disease (Calderon, Perry, Thi, & Stevens, 2023). Tuberculosis is most prevalent in South-east Asia, Sub-Saharan Africa, and the Western Pacific, with India, China, and Indonesia having the largest global burden. Socioeconomic factors like poverty, overcrowding, and lack of healthcare access contribute to high incidences. Vulnerable populations, such as those with HIV and healthcare workers, are more susceptible. Drug resistance, particularly in countries with inadequate treatment infrastructure, prolongs therapy duration, increases costs, and decreases treatment success (Bathia, Rijal, Sharma, Islam, Vassal, Bhargava, & Raviglione, 2023).

Indonesia faces a high prevalence of tuberculosis, with an estimated 824,000 new cases annually by 2022, equivalent to 312 cases per 100,000 people. The mortality rate is high, with over 93,000 deaths in 2021 (Baratau, 2024). Despite government health facilities offering free treatment, many patients receive delayed diagnosis or do not finish, causing further transmission. Multidrug-resistant tuberculosis is a growing threat, with around 24,000 cases annually. This is more challenging to treat and requires a longer course of treatment. Drug resistance is primarily due to inappropriate medication use or early patient withdrawal. The presence of drug resistance makes tuberculosis management in Indonesia more challenging and requires a more rigorous strategy, including close monitoring of patients (Zhao, Butala, Luc, Feinn, & Murray, 2022).

The high prevalence of tuberculosis among HIV patients in Indonesia is a significant factor in the spread of the disease. This is due to compromised immune systems and the prevalence of TB-HIV co-infection, which complicates treatment (Wijiseno, Arini, & Listiowati, 2023). Unfavorable socioeconomic conditions, such as high poverty rates, urban overcrowding, and limited access to health services, further exacerbate the TB epidemic.

Despite government measures, challenges remain in early detection, treatment adherence, and addressing vulnerable populations to eliminate tuberculosis in Indonesia by 2030. These factors contribute to the disease's spread and hinder progress towards eradicating the disease (Sofiana, Ayu, Wardani, Puspaningrum, & Hadianti, 2022).

Indonesia's National Tuberculosis Control Program focuses on decreasing the incidence and death rates associated with Mycobacterium tuberculosis, a leading cause of mortality in the country. Despite accessible treatments and preventive initiatives, tuberculosis continues to be a significant public health challenge. Committed to achieving the Sustainable Development Goals, Indonesia aims to eliminate tuberculosis by 2030 through the National Strategy for TB Prevention and Control. This plan emphasizes on early detection, effective treatment, management of drug-resistant cases, and prevention of transmission, with active community involvement. (Main, Hussain, Maniar, Safdar, Mohiuddin, Riaz, & Ralph, 2022). The Directly Observed Treatment Short Course (DOTS) technique, developed in 1995, is one of the most important programs in Indonesia. The WHO promotes DOTS as a global strategy for successful treatment of TB. The National Strategy for TB Prevention and Control includes early identification, proper treatment, control of drug-resistant tuberculosis, prevention, and community education. Both the Indonesian government and international agencies support the plan (Kardani, & Subandiyah, 2020).

The Sustainable Development Goals aim to eliminate tuberculosis by 2030, aiming for a 90% reduction in incidence and 95% reduction in mortality rates. To achieve these goals, Indonesia has initiated national policies and programs, including providing free medical services, increasing diagnostic laboratory capacity, and encouraging community participation in detecting cases and supervising treatment (Adi, 2024). These strategies also involve preventing transmission at the community level through health education and counseling programs. The programs target vulnerable groups, such as HIV-positive individuals, health workers, and those with low socioeconomic situations, who are at a higher

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risk of contracting tuberculosis and potentially developing consequences from the disease (Hidayati, Indrayati, Nurhan, Rozi, Irbah, Desfitra, & Hayuningtyas, 2024).

The management of tuberculosis in Indonesia is challenging due to factors such as unequal access to health services, logistical constraints in drug distribution, stigma towards those affected, and low public education about early detection and treatment. The increasing number of drug-resistant cases further complicates the situation (Bea, Lee, Choi, Huh, Jung, & Shin, 2023). To improve control, Indonesia needs to adopt a more innovative, efficient, and inclusive approach. Strategies include increasing the health system's capacity, strengthening regulations, and providing communities with tools for early identification and comprehensive treatment. Trans-sectoral cooperation, community participation, and international assistance are expected to help achieve the goal of eliminating tuberculosis in accordance with global commitments and improve community quality of life (Ha, & Duong, 2023).

The tuberculosis control program in Indonesia faces significant challenges, including inequal access to medical treatments, patient dissatisfaction with treatment, and a high social stigma associated with the disease. Patients in remote areas, particularly in eastern Indonesia, often lack proper medical facilities, leading to delayed diagnosis and treatment. Additionally, patients often stop treatment before it is completed, increasing the risk of drug resistance (Burugina Nagaraja, Thekkur, Satyanarayana, Tharyan, Sagli, Tonsing, & Sachdewa, 2021). The distribution of drugs, shortage of skilled health personnel in rural areas, and high stigma contribute to these issues. To combat these challenges, efforts must be made to educate the public and organize campaigns. Despite significant progress in early detection, treatment, and disease prevention, issues like medication resistance, adherence to therapy, and vulnerable populations need to be addressed. Indonesia aims to eliminate tuberculosis by 2030 with a comprehensive strategy and strong cooperation between the government, communities, and foreign partners (Zafar Ulah, Shresta, Malik, & Roy, 2022).

RESEARCH METHOD

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The process began with formulating clinical questions relevant to the topic, guided by the PICOS criteria: P (problem, patient, or population), I (intervention, prognostic factor, or exposure), C (comparison or control), O (outcome), and S (study design). For this review, the criteria were defined as follows: P - Tuberculosis, I - Intervention (with no intervention specified), C - No comparison group, O - Tuberculosis eradication, and S - study designs including qualitative, quantitative, and mixed methods.

The systematic search used the keywords: "Tuberculosis Eradication," "Patient's Experience," "One Health Approach," "Literacy," "Pharmacokinetics," "Quality of Life," and "Patient's Perspective." Articles were included if they were published in English or Indonesian within the past three years (2021–2024). Articles published before 2021 were excluded.

The search yielded 42 articles from PubMed, 31 from Google Scholar, and 20 from ScienceDirect. After applying the inclusion and exclusion criteria, eight articles were selected for further analysis.

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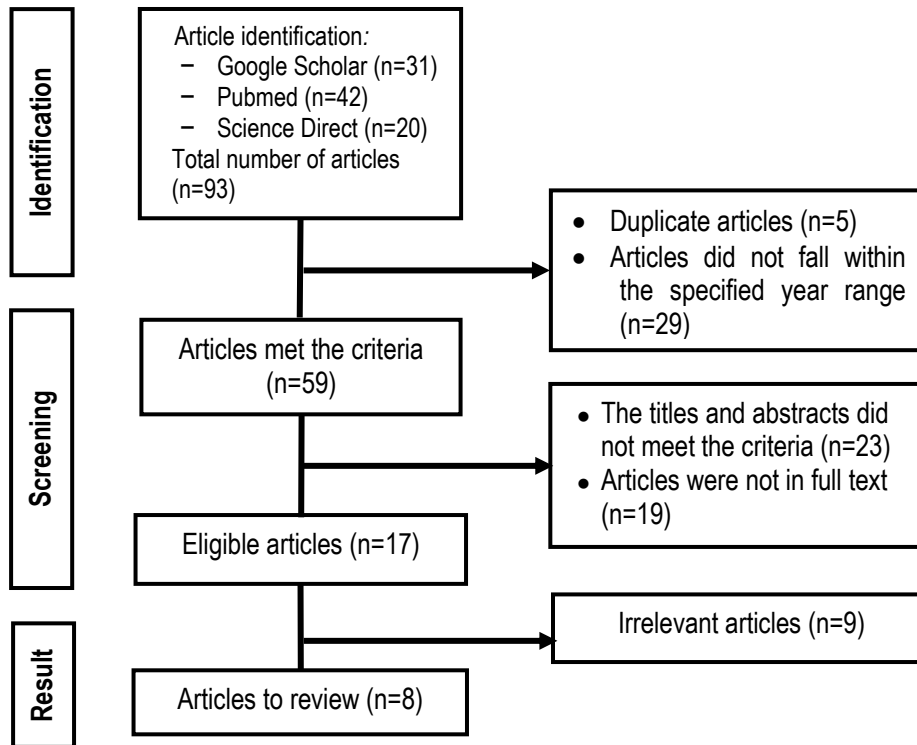
RESEARCH RESULTS

Figure 1. PRISMA Flow Diagram

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Table 1. The Main Characteristics of Included Studies

Author (Year) (Country)	Purpose	Method	Results
(Sutrisno et al., 2022) (Indonesia)	Investigating the experiences of tuberculosis patients throughout the recovery process in relation to the risk factors contributing to their depression.	A qualitative study employing a phenomenological approach was conducted. Using purposive sampling, nine participants were recruited from five public health centers in the Sleman district. The participants were pulmonary tuberculosis patients undergoing treatment in either the intensive or continuous phase and were identified as having depression through screening with the Beck Depression Inventory-II Questionnaire. Data were collected through in-depth interviews and analyzed using inductive content analysis.	Five themes were identified as variables contributing to depression in individuals with pulmonary tuberculosis: a) denial of fate, b) stigma associated with tuberculosis, c) concomitant conditions, d) lack of familial support, and e) job loss.
(Sofiana et al., 2022) (Indonesia)	To identify the risk variables affecting the quality of life of tuberculosis patients in Sleman Regency, Special Region of Yogyakarta, Indonesia.	A cross-sectional analytical observational investigation. The respondents were tuberculosis patients in the second trimester who were undergoing treatment at all health care center in Sleman Regency, Yogyakarta Special Region, Indonesia, in 2020. Purposive sampling was employed in the sampling process. The WHO quality of life (WHOQOL-BREF) questionnaire assessed quality of life, whereas the Morisky Medication Adherence Scale evaluated knowledge, self-efficacy, familial support, and medication adherence.	The Chi-square test was employed to analyse the data. Self-efficacy (sig=0.013; RP=2.295) and medication adherence (sig=0.014; RP=8.333) were associated with the quality of life of tuberculosis patients. Knowledge (sig=0.384; RP=0.709) and family support (sig=0.227; RP=0.419) were not correlated with the quality of life of tuberculosis patients.
(Baratau, 2024) (Indonesia)	To elucidate the attitudes, views, and experiences of many stakeholders, such as community members, educators, and policymakers, to	Utilizing a mixed-methods approach, integrating qualitative and quantitative data collection techniques. Initial data indicate that the program has effectively enhanced literacy skills among participants, with claimed advancements in reading and writing capabilities.	Community involvement has played a pivotal role in the program's success, as participants exhibited a strong sense of ownership and dedication to its goals. Cultural adaptation has also been essential, with program

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Author (Year) (Country)	Purpose	Method	Results
	inform the creation of more successful and culturally attuned literacy programs in the region.		materials and delivery tailored to reflect local traditions, values, and languages. The implications of these findings for future literacy initiatives in North Toraja and similar cultural settings are explored.
(Pradipta et al., 2021) (Indonesia)	Investigating obstacles to effective tuberculosis treatment from the patients' viewpoint, with the objective of identifying viable patient-centered care techniques to enhance tuberculosis treatment outcomes in Indonesia.	A qualitative study was performed in an area of Indonesia characterized by elevated tuberculosis prevalence. Individuals from diverse backgrounds, including tuberculosis patients, physicians, nurses, pharmacists, tuberculosis activists, and tuberculosis program coordinators at the district and primary care levels, underwent comprehensive interviews and focus group discussions. All interviews and focus group discussions were transcribed verbatim from audio and visual recordings, and the corresponding transcriptions were utilized for data analysis. Barriers were established by analyzing the patterns and co-occurrences of the codes. The reliability and credibility of the information were determined by information saturation, participant validation, and triangulation methods. The data were processed inductively using Atlas.ti 8.4 software and reported in accordance with the COREQ 32-item guidelines.	The hurdles were categorized into three themes: socio-demographics and economy; knowledge and perception; and tuberculosis treatment. We identified five primary connected hurdles across all themes: insufficient tuberculosis knowledge, stigmatization, distance to healthcare facilities, adverse drug reactions, and loss of household income.
(Herawati et al., 2021) (Indonesia)	To identify the anti-tuberculosis medications utilized in hospitals and to ascertain the inconsistencies in the continuity of tuberculosis treatment.	This retrospective cross-sectional study utilized medical records of adult patients and was undertaken in two district tertiary care facilities. Only 35 of 136 patient records from Hospital A and 33 of 85 records from Hospital B satisfied the inclusion criteria.	The predominant systemic anti-infective agents identified in the investigation were ceftriaxone (51.80 DDD/100 patient-days) utilized in Hospital A and isoniazid (59.53 DDD/100 patient-days) employed in Hospital

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Author (Year) (Country)	Purpose	Method	Results
			B. The quantity of rifampicin prescriptions was inferior to that of isoniazid. Each patient received an average of two DDD per 100 patient-days, indicating insufficient dosage for effective treatment.
(Syamsir et al., 2023) (Indonesia)	To investigate the experiences of tuberculosis patients who finished their treatment during the COVID-19 pandemic.	This qualitative study was conducted utilizing a content analysis technique from May to July 2022. A total of 14 tuberculosis patients who consented to participate in this study were identified using purposive sampling. Comprehensive interviews were performed utilizing semi-structured guidelines, concluding with the attainment of information saturation. Data analysis was conducted simultaneously to ascertain the primary themes. The NVIVO software package, version 12, was employed for data analysis.	Multiple significant themes emerged from the study, illuminating various facets of the lives of tuberculosis patients during the COVID-19 epidemic. Themes include (1) Barriers to Tuberculosis Diagnosis during the COVID-19 Pandemic; (2) Challenges in Tuberculosis Treatment during the COVID-19 Pandemic; and (3) Support Resources for Tuberculosis Treatment during the pandemic era.
(Juliasih et al., 2024) (Indonesia)	To examine the factors influencing transmission behaviour among tuberculosis patients in Surabaya, Indonesia.	Employing a cross-sectional design, with 144 tuberculosis patients from three community health center in Surabaya, selected using simple random sampling. Variables such as knowledge level, supportive behaviour, and medication adherence were examined, and data collection was conducted with a structured questionnaire. Furthermore, statistical approaches were employed for data analysis to ascertain the significance of variables.	The findings indicated that knowledge (P-value <0.001), supportive behaviour (P-value = 0.001), and medication adherence (P-value = 0.004) significantly influenced transmission prevention behaviour in tuberculosis patients.

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Author (Year) (Country)	Purpose	Method	Results
(Soedarsono et al., 2023) (Indonesia)	Assessing the impact of demographic, clinical, and genetic factors that contribute to heterogeneity in RIF pharmacokinetic characteristics among Indonesian tuberculosis patients.	A total of 210 Indonesian individuals with tuberculosis (300 plasma samples) participated in this investigation. Clinical data, including haplotypes *1a, *1b, and *15 of the solute carrier organic anion transporter family member-1B1 (SLCO1B1), as well as RIF concentrations, were analyzed. The population pharmacokinetic model was constructed with a non-linear mixed effects approach.	A one-compartment model utilizing allometric scaling effectively characterized the pharmacokinetics of RIF. Age and the SLCO1B1 haplotype *15 shown a substantial correlation with variations in apparent clearance (CL/F). In patients aged 40 and above, every 10-year increment in age correlated with a 10% reduction in CL/F (7.85 L/h). Patients possessing the SLCO1B1 haplotype *15 exhibited a 24% reduction in clearance (CL/F) relative to individuals with the wild-type genotype. Visual prediction checks and non-parametric bootstrap analysis demonstrated satisfactory model performance.

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DISCUSSION

Indonesia faces numerous challenges in eradicating tuberculosis by 2030, in line with the global end TB strategy. The main obstacle is the high prevalence of active TB and multidrug-resistant TB (MDR-TB), which is resistant to the most potent first-line anti-TB medications. Around 24,000 people develop MDR-TB annually, complicating treatment and increasing costs. MDR-TB requires extended therapy with second-line medications, which are more expensive, have severe adverse effects, and have reduced efficacy rates. Extensively drug-resistant tuberculosis, a more severe form of drug resistance, also poses a threat to tuberculosis elimination initiatives, requiring substantial resources, extended treatment periods, and more complex medical procedures (Adnyana, Utomo, Eliatin, & Sudaryati, 2023).

Indonesia's tuberculosis case detection rate is low, with only 67% of cases identified in 2020. This under-detection is attributed to factors like limited healthcare access, lack of public awareness, and stigma. The WHO recommends using quick molecular diagnostic tests like GeneXpert, but many healthcare facilities still use outdated techniques like sputum microscopy. This results in patients not receiving accurate diagnoses, postponing therapy commencement. Insufficient access to advanced testing technologies and outdated techniques further exacerbates the issue (Cannon, Oladimeji, & Goon, 2021). Tuberculosis is a stigmatized illness in Indonesia, particularly in rural areas, due to misconceptions about its exclusiveness to impoverished or immoral individuals. This stigma often deters individuals from seeking care, leading to delayed treatment and increased risk of transmission. The stigma also affects the workplace, where individuals may face prejudice or jeopardize their employment due to their diagnosis. The fear of social ostracism and economic instability further complicates tuberculosis management, hindering prompt diagnosis and treatment (Malik, Hussain, Maniar, Safdar, Mohiuddin, Riaz, & Khowaja, 2022).

Indonesia's healthcare system faces challenges in eliminating tuberculosis due to its vast terrain, lack of facilities, and inadequate healthcare professionals. Rural and isolated regions often face delays in treatment and inadequate care. Despite the universal health coverage initiative, Jaminan Kesehatan Nasional (JKN), which expanded access to healthcare, coverage gaps persist, particularly among marginalized and low-income groups. The costs of tuberculosis care, including transportation, diagnostic assessments, and pharmaceuticals, continue to be a significant barrier for many patients (Winardi, Wahyuni, Hidayat, WIrawan, Nurwidya, Uddin, & Yusup, 2022).

Adherence to tuberculosis treatment is crucial for preventing medication resistance and achieving positive outcomes. However, in Indonesia, adherence remains a significant barrier due to the extended treatment regimen, financial constraints, and lack of support. Premature termination of treatment also poses a risk, increasing the risk of drug-resistant tuberculosis and facilitating disease transmission (Fuady, Hutarnamon, Herlinda, Luntungan, & Wingfield, 2024). Indonesia has the potential to accelerate tuberculosis elimination through the increasing accessibility of novel diagnostic instruments and more effective treatment protocols. Quick molecular diagnostics like GeneXpert can improve diagnosis accuracy, especially for drug-resistant strains. Novel treatment protocols like the WHO's MDR-TB regimen can reduce treatment duration and improve patient adherence (Qureshi, Faiz, & Khalid, 2023).

Community involvement is crucial for successful tuberculosis eradication, especially in rural areas. Indonesia has implemented community-based programs to train health workers, improve treatment outcomes, and enhance case detection. Digital health technologies, such as mobile health platforms and electronic medication adherence monitoring, can improve diagnosis, treatment compliance, and follow-up care. The Indonesian government is exploring these technologies, and additional investment could significantly contribute to the eradication of tuberculosis (Dongo, Graham, Nsonga, Wabwire-Mangen, Maleche-Obimbo, Mupere, & Zawedde-Muyanja, 2021).

Indonesia can improve its tuberculosis control initiatives through public-private partnerships. Private healthcare providers play a crucial role in screening and treatment, but often lack integration into the national TB control program. By fostering

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collaborations between the public health system and private providers, Indonesia can ensure adequate care for patients and reduce disease transmission (Ginting, Aldila, & Febriana, 2024). Mitigating the stigma around tuberculosis is also essential for enhancing screening, diagnosis, and treatment compliance. Public health programs should raise awareness about the disease, its curability, early diagnosis, and its impact on individuals, especially in rural and conservative areas where traditional beliefs and norms significantly influence health-seeking behaviors (Reuter, Beko, Memani, Furin, Daniels, Rodriguez, & Mohr-Holland, 2022).

To eradicate tuberculosis, social determinants like poverty, overcrowded living conditions, malnutrition, and limited access to clean air and sanitation must be addressed. This is particularly important for marginalized groups, such as those in poverty, those with weakened immune systems, and urban slum dwellers. Enhancing living conditions and access to basic health services can mitigate tuberculosis transmission and improve health outcomes (Carnino, Schwob, Neofytos, Lazo-Porras, Chappuis, & Eperon, 2021). Collaboration across sectors like housing, education, sanitation, and nutrition is crucial for addressing these issues. Investment in research and development is vital for enhancing control and eradication efforts. Indonesia, with the largest tuberculosis burden, can contribute significantly to global research by enhancing its involvement in clinical trials and joint research efforts. Additionally, collaborations and financial support can help advance vaccine development, diagnostics, and treatment protocols (Otchere, Aboagye, Arthur, & Asante-Poku, 2024)..

The elimination of tuberculosis requires the enhancement of healthcare personnel's capabilities, particularly in rural and isolated areas of Indonesia. Healthcare practitioners lack the necessary training and resources to diagnose and treat the disease accurately. Regular professional development and training for physicians, nurses, and community health workers is crucial for providing prompt and appropriate care (Lin, Liu, Zhang, Cai, Hu, Xiao, Harries, 2021). Educating healthcare professionals on TB symptoms, using diagnostic tools, and handling drug-resistant cases can improve care quality. Access to current treatment protocols and

medications can also enhance their management and reduce disease transmission. Comprehensive surveillance systems are essential for monitoring disease trends, detecting drug-resistant strains, and managing all cases. Data-driven decision-making can help tailor control plans to local needs (Yulianti, 2024).

HIV is a significant risk factor for tuberculosis (TB) development, and in Indonesia, the co-infection of TB and HIV poses a significant issue. Individuals with compromised immune systems face a higher risk of developing active TB. To address this, integrated healthcare systems are needed, providing comprehensive screening, diagnosis, and treatment for both conditions (Chawla, Burugina Nagaraja, Siddalingaiah, Sanju, Shenoy, Kumar, & Reddy, 2021). Integrated TB-HIV programs, which offer simultaneous antiretroviral medication, can improve health outcomes and reduce death rates. A multisectoral strategy, including government ministries, NGOs, the commercial sector, and civil society, is crucial for eradicating TB. Collaborative initiatives across education, housing, sanitation, and employment can reduce TB transmission and improve health outcomes (Yusuf, & Abidemi, 2023).

Civil society organizations and patient advocacy groups play a crucial role in promoting awareness of tuberculosis, mitigating stigma, and enhancing access to care. In Indonesia, NGOs and community-based organizations have contributed to TB control initiatives by providing information, screening services, and medical assistance. Involving TB sufferers in advocacy can help diminish stigma and dismantle myths. Indonesia can benefit from global partnerships with international organizations like the WHO, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and the Stop TB Partnership, which offer technical aid, financial support, and strategic direction. Additionally, Indonesia's prominence in regional forums like ASEAN presents potential for transnational tuberculosis control initiatives (Natalia, Zahirah, Widjaja, & Ernawati, 2024).

Indonesia faces challenges in eradicating tuberculosis, including drug-resistant cases, inadequate detection, healthcare system limitations, stigma, and socio-economic barriers. Opportunities include increased access to innovative diagnostics, digital health technology, and public-private sector

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cooperation. Addressing socioeconomic determinants, enhancing healthcare infrastructure, engaging communities, and mobilizing support are key. A comprehensive approach targeting stigma, integrating care, and investing in research is crucial for achieving tuberculosis elimination by 2030 (Ponnampalli, & Birudukota, 2023)..

CONCLUSION

Indonesia faces challenges in eradicating tuberculosis, including drug-resistant cases, inadequate detection, healthcare system limitations, stigma, and socio-economic barriers. Opportunities include increased access to innovative diagnostics, digital health technology, and public-private sector cooperation. Addressing socioeconomic determinants, enhancing healthcare infrastructure, engaging communities, and mobilizing support are key. A comprehensive approach targeting stigma, integrating care, and investing in research is crucial for achieving tuberculosis elimination by 2030.

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