JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S9

National Tuberculosis (TB) Control and Prevention Program in Medina City

Abdullah Abdullatef M Alqurafi[1], Hasan Ali Althobyane[1], Omar Redah O Alsobahi[1], Ahmed Fidhi Alrehaili[1], Anas Ameen Fallatah[2], Ibraheem Maqbool Q Alawfi[3], Turki Suwaylim B Alsaedi[4], Sami Owaid K Aljabri[5], Mohammed Abdulwahed S Majidah[6], Badr Zaid Alamri[5]

1. Consultant, Family Medicine, KSA.
2. Registrar, Family Medicine, KSA.
3. Health Administration Specialist, KSA.
4. Nursing Administration Senior Specialist, KSA.
5. Nursing Technician, KSA.
6. Health Education Specialist, KSA.

ABSTRACT

The National Tuberculosis (TB) Control and Prevention Program in Medina City implements a comprehensive strategy to address TB, aligning with international guidelines set by the American Thoracic Society, the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America (IDSA), emphasizing evidence-based approaches for TB management and diagnosis. The program differentiates recommendations based on patients' risk levels, employing Interferon-Gamma Release Assays (IGRA) as the preferred diagnostic method over Tuberculin Skin Tests (TST) for certain age groups and BCG-vaccinated individuals. For active TB diagnosis, the program uses Acid-Fast Bacilli (AFB) smear microscopy combined with mycobacterial cultures and Nucleic Acid Amplification Testing (NAAT), allowing rapid identification and assessment of drug-resistant strains. Treatment and prevention measures include Directly Observed Treatment, Short-course (DOTS) to enhance medication adherence, free access to second-line drugs for multidrug-resistant TB, and proactive monitoring of treatment side effects to ensure patient compliance.

Preventive strategies, such as the BCG vaccination for infants, stringent infection control in healthcare settings, public awareness initiatives, and regular screenings for high-risk groups, play pivotal roles in reducing TB transmission. The program emphasizes targeted testing and treatment of latent TB infections, leveraging a combination of IGRA and TST methods tailored to each patient’s needs. Through extensive surveillance and data collection, Medina’s program identifies treatment gaps, tracks drug resistance trends, and informs resource allocation. Moreover, the program collaborates with international organizations, focusing on research, capacity building, and addressing social determinants influencing TB transmission. These efforts illustrate Medina’s commitment to TB elimination by integrating diagnostic, preventive, and treatment strategies within a robust public health framework.

KEYWORDS: Tuberculosis control, latent tuberculosis infection, diagnostic

1. Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a significant public health concern globally, with individuals presenting either active TB disease or latent tuberculosis infection (LTBI), where the infection exists without evident clinical symptoms. Medina City's National TB Control and Prevention Program aligns its guidelines with a task force supported by the American Thoracic Society, the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America (IDSA), using a graded evaluation system (GRADE) for clinical recommendations [1]. The primary goal of the National TB Program is to reduce the incidence and mortality of TB through a combination of preventive, diagnostic, and treatment interventions. The program also aims to provide universal access to TB care, focusing on early detection and treatment of active TB cases, managing drug-resistant TB, and preventing TB transmission within the community. This objective aligns with Saudi Arabia's commitment to the WHO's End TB Strategy, which targets a 90% reduction in TB deaths and an 80% reduction in TB incidence by 2030.These guidelines are tailored for high-resource settings with low TB incidence and aim to assist clinicians in diagnosing and managing TB effectively (table 1).

Table 1. Interpretation of strong and conditional recommendations for the TB control and prevention program

Recommendation Type	Patients	Healthcare Providers	Policy Makers
Strong Recommendation	Most patients would prefer the recommended course of action, with only a few who may not.	Most patients should receive the recommended intervention. Following these guidelines can be used as a quality measure or performance standard. Decision aids are generally not needed to ensure patients' values and preferences align with the recommendation.	The recommendation is suitable to be implemented as policy in most scenarios.
Conditional (Weak) Recommendation	While many patients may opt for the suggested approach, a substantial number may choose differently.	Acknowledge that individual choices may vary, and healthcare providers should guide each patient to a decision that respects their personal values and preferences. Decision aids might support patients in making informed decisions consistent with their values.	Significant discussion and input from multiple stakeholders will be necessary to implement as policy.

LTBI diagnostic recommendations

For individuals likely infected with Mtb and at low or moderate risk of progressing to active TB, we recommend diagnostic testing for LTBI, prioritizing Interferon-

Gamma Release Assays (IGRA) over Tuberculin Skin Tests (TST) for individuals aged five years or older. IGRA is preferred in cases where individuals have received Bacille Calmette-Guérin (BCG) vaccination or are unlikely to return for TST readings. However, TST remains an acceptable alternative when IGRA is unavailable or cost-prohibitive [2].

For individuals at high risk of TB progression, no specific preference is suggested between TST and IGRA due to limited data. Medina's program supports the CDC's stance that those at low risk for Mtb infection should generally not be tested for LTBI, except where required by legal or credentialing bodies. For children under five years, TST is recommended, though IGRA may be considered for children over three if preferred by experts [3].

Table 2: Recommendations for testing for LTBI for the national tuberculosis control and prevention program

Group	Testing Strategy	Considerations
Likely to be Infected High Risk of Progression (TST ≥ 5mm)	Adults - Preferred: IGRA or TST - Consider dual testing if a positive result would confirm diagnosis. Children < 5 years of age - Preferred: TST - Acceptable: IGRA or TST - Consider dual testing for a confirmed positive result.	- High-risk exposure settings - BCG vaccination prevalence - Test availability - Patient acceptance and preferences - Program resources
Likely to be Infected Low to Intermediate Risk of Progression (TST ≥ 10mm)	- Preferred: IGRA where available - Acceptable: IGRA or TST	- Resource limitations - Test accuracy concerns - Scheduling flexibility for TST follow-up
Unlikely to be Infected (TST ≤ 15mm)	Testing for LTBI is generally not recommended. If testing is required: - Preferred: IGRA - Acceptable: Either IGRA or TST - Consider retesting if an initial positive result is found	- Cost and resource allocation - Low prevalence environments - Legal or policy requirements for testing in specific cases

TB disease testing recommendations

To enhance TB diagnosis, particularly in suspected cases of pulmonary TB, Medina's guidelines recommend conducting Acid-Fast Bacilli (AFB) smear microscopy on respiratory samples. AFB smear testing should be accompanied by both liquid and solid mycobacterial cultures to improve diagnostic accuracy. In cases where sputum samples are difficult to obtain or yield negative AFB smears, sputum induction or flexible bronchoscopy may be employed to secure a sample [4].

The guidelines also endorse nucleic acid amplification testing (NAAT) for initial respiratory samples, especially when AFB smear results are positive, to facilitate rapid TB diagnosis. Rapid molecular drug susceptibility testing for rifampin or isoniazid is recommended for patients with prior TB treatment, exposure in countries with high TB rates, or known multi-drug-resistant TB contacts [5].

For suspected extrapulmonary TB, Medina's program advises mycobacterial culture of fluid samples, AFB smear microscopy, and histological examination, with NAAT as a supplementary test when applicable. Adenosine deaminase (ADA) and interferon-gamma (IFN-γ) levels in pleural or peritoneal fluids may also support TB diagnosis in extrapulmonary cases [6].

Medina City's guidelines serve as a reference for healthcare providers involved in TB care, encouraging diagnostic decisions that prioritize patient outcomes and efficient TB management. However, these guidelines are not exhaustive; clinicians are encouraged to interpret them flexibly, adjusting for individual patient scenarios to optimize care delivery. These guidelines complement, rather than replace, clinical judgment and should not be enforced as a strict standard, allowing for comprehensive and adaptive patient care [7].

These recommendations align with WHO guidelines for high-burden TB contexts, making them adaptable to broader TB control needs across diverse healthcare settings. Medina's National TB Control and Prevention Program, in implementing these recommendations, aims to enhance TB control efforts while respecting local healthcare capacities and requirements.

Table 3. Diagnostic algorithm for TB testing, specifically regarding rapid testing for MTB detection and rifampicin resistance evaluation. This type of algorithm is often used in healthcare settings to streamline the diagnostic pathway for suspected TB patients, ensuring they receive appropriate and timely treatment.

Step	MTB Xpert Test	Culture/DST	Decision
Collect specimen and perform smear microscopy and Xpert	Initiate test for MTB and rifampicin resistance	Preserve second sample for culture and DST	Proceed with Xpert testing for MTB detection
MTB Smear - Not Detected	Re-evaluate clinically; additional testing	Consider additional tests as per guidelines	Further testing based on clinical judgment
MTB Smear - AFB +/-	Evaluate for MDR-TB risk factors	Use clinical judgment	Assess MDR-TB risk and take appropriate action
MTB Smear - AFB +/-, MTB Xpert Test Detected	Treat with first-line regimen; repeat Xpert if needed	Monitor and evaluate based on risk factors	Monitor rifampicin resistance results
Rifampicin Resistance - Not Detected	Treat with first-line regimen	Regular monitoring	Continue first-line TB regimen
Rifampicin Resistance - Detected	Follow Algorithm 1 to interpret	Specialized care referral	Initiate MDR-TB treatment plan
Patient at high risk of MDR-TB	Refer to DR-TB treatment center	Initiate second-line treatment if necessary	Refer high-risk cases to specialized care
Patient at low risk of MDR-TB	Repeat Xpert MTB/RIF	Continue first-line regimen if no resistance	Repeat testing if resistance is suspected

How to use these guidelines?

These guidelines are designed to assist healthcare providers in making informed decisions regarding the diagnostic evaluation of patients with possible LTBI or active TB. They are not intended to set a rigid standard of care. The recommendations serve as a framework for clinical decision-making, recognizing that individual patient situations can vary significantly. Therefore, clinicians, patients, stakeholders, and third-party payers should not interpret these recommendations as absolute rules. Each recommendation includes qualifying

remarks to facilitate accurate interpretation. It is essential that these remarks are included when quoting or referencing the guidelines to maintain their context and intent [8].

Committee selection

The committee members were selected based on their expertise in TB-related clinical and research areas. Additional criteria included participation in organizations the IDSA, or employment at the CDC Division of Tuberculosis Elimination. Committee members were free from disqualifying conflicts of interest, which were managed according to the policies of the participating organizations. To streamline the guideline development process, the committee was divided into subcommittees, each responsible for drafting sections on specific topics: LTBI, clinical and radiological aspects of TB diagnosis, microbiological evaluation for TB, and pediatric TB diagnosis [9].

2. Methods

Each subcommittee focused on addressing key diagnostic questions by conducting a practical evidence synthesis for each topic. They first sought studies that compared diagnostic interventions and measured clinical outcomes. In cases where such data was unavailable, the subcommittees evaluated diagnostic accuracy studies or relied on the collective clinical experience of committee members. Recommendations were developed using the GRADE approach, which considers factors like the quality of evidence, balance of benefits and harms, patient preferences, resource use, and feasibility. Subcommittee members reached consensus through open discussion, and voting was only used if consensus could not be reached—though this was not necessary for any of the recommendations [10].

Diagnostic Tests

The guidelines discuss two primary diagnostic methods for LTBI:

Tuberculin Skin Test (TST): The TST detects immune response to Mtb via a delayed hypersensitivity reaction. It is administered by injecting a protein derived from Mtb under the skin, with results evaluated 48-72 hours later. The interpretation depends on the patient's risk factors, with reaction sizes of ≥5 mm, ≥10 mm, or ≥15 mm indicating infection based on specific exposure or health conditions. The TST is beneficial due to its simplicity, low cost, and portability. However, it requires trained personnel, a follow-up visit, and may yield false positives in individuals with BCG vaccination or false negatives in immunosuppressed patients [11].

Interferon-Gamma Release Assays (IGRAs): IGRAs are blood tests that measure the release of IFN-γ in response to Mtb-specific antigens. These tests are generally more specific than the TST, particularly for those vaccinated with BCG, as they do not cross-react with the vaccine. There are two main commercially available IGRAs: QuantiFERON-TB gold in tube and T-SPOT.TB. While IGRAs offer the advantage of a single-visit test and greater specificity, they are more expensive and require phlebotomy, making them challenging for some populations, such as children [12].

Benefits and Limitations

TST Benefits and Limitations: The TST is simple and affordable, making it suitable for use in remote or low-resource settings. It does not require specialized equipment and has established definitions for conversion, making it reliable for serial testing. However, it demands skilled personnel for proper administration and reading, may yield false positives due to BCG vaccination, and requires a second visit for interpretation [13].

IGRA Benefits and Limitations: IGRAs provide more specific results for Mtb infection and do not cross-react with BCG, making them ideal for BCG-vaccinated populations. They are completed in a single visit, reducing the need for follow-up. Despite these benefits, IGRAs are costly, require blood samples (posing a challenge in children), and show variability in results, especially near diagnostic cutoffs. Additionally, limited evidence is available on the impact of IGRA-based treatment on preventing TB progression [14].

Diagnostic approach: testing for suspected LTBI

Currently, there is no definitive test for diagnosing LTBI, so our recommendations are based on the probability of Mtb infection and the risk of progression to active TB disease if LTBI is present. The likelihood of infection and progression risk guide testing decisions. While our literature review did not find direct comparisons of different LTBI diagnostic methods regarding clinical outcomes, evidence indicates that treating LTBI can prevent the development of active TB, thus reducing both individual and public health risks [15].

Benefits of treating LTBI

Treating LTBI is essential because it prevents progression to active TB, which poses significant health risks, including the spread of TB in high-risk settings like hospitals, shelters, and prisons. Studies estimate that individuals with LTBI have a 4–6% lifetime risk of progressing to active TB, with a higher risk shortly after exposure. For example, in populations like household contacts of TB patients and persons with immunocompromising conditions, treating LTBI has been shown to reduce TB incidence. Although treatment benefits for lower-risk populations may be relatively minor, early intervention is critical in high-risk groups with, especially among those living or working in close-contact settings or with immune-compromising conditions [16].

Testing methods: IGRA vs. TST

For individuals over five years old who are likely infected with Mtb and have a low or intermediate risk of disease progression, the choice between IGRAs and TSTs depends on factors like the person's vaccination history and follow-up feasibility. Research suggests that IGRAs generally offer greater specificity in individuals vaccinated with BCG, which is common, due to IGRAs' ability to target antigens not found in BCG and most non-tuberculosis mycobacteria [17].

Recommendation Summary

1. Recommendation for IGRA use: For individuals likely infected with Mtb who have a low or moderate progression risk and are either BCG-vaccinated or unlikely to return for TST readings, we recommend IGRA testing. The reliability of IGRA, combined with its reduced false-positive rate in BCG-vaccinated individuals, makes it the preferred option. However, TST remains a practical alternative in cases where IGRA is unavailable or cost-prohibitive.

2. Conditional recommendation for IGRA in all others: For individuals without BCG vaccination or with reliable follow-up, IGRA is still suggested due to better accuracy, but TST remains an acceptable alternative in cases where practicality, accessibility, or costs influence the testing choice.

Justification for extending IGRA recommendation to individuals aged 5 and older

In young children, TB poses a higher risk of rapid progression and severe disease, which decreases with age. From age five onward, children's immune response to TB aligns more closely with that of adults, making IGRA testing suitable and practical. Thus, the program extends IGRA recommendations to children aged five and older, ensuring early detection and intervention to curb the risk of active TB progression in this demographic [18].

Quantitative interpretation and limitations

Both IGRA and TST are valuable tools in detecting infection with Mtb for the National Tuberculosis Control and Prevention Program. However, neither test can differentiate active TB from LTBI. Thus, it is essential to rule out active TB disease before beginning LTBI treatment. This involves assessing symptoms indicative of active TB, performing a chest radiograph, and, if necessary, conducting further testing for confirmation based on radiographic signs such as airspace opacities, pleural effusions, or cavities [19].

The quantitative interpretation of these tests presents challenges. In TST, results are primarily qualitative, categorized as positive or negative. While a reaction of over 15 mm may suggest Mtb infection, quantitative variations are generally not factored in, and repeat TST testing is discouraged if there was a prior positive result. This limitation restricts understanding of TST result variability over time. For IGRA, the measurement of IFN-γ responses allows for some quantifiable insight. However, these levels may fluctuate due to biological variations, host immunity changes, or even exposure to other antigens. While such changes could indicate ongoing infection, they may also result from test variability, making the interpretation of quantitative IGRA data complex. The FDA accepts a variance of 11% for IGRA results, but optimal interpretation points remain a subject of ongoing research [20].

Understanding test discordance

TST and IGRA results sometimes disagree, particularly among those vaccinated with BCG. TST-positive/IGRA-negative results are common in BCG-vaccinated individuals; however, strong TST-positive reactions over 15 mm have also been seen in IGRA-negative cases. This discordance may arise from past immune responses or immune system differences between TST's delayed hypersensitivity and IGRA's

blood assay. Such cases can complicate LTBI diagnosis in low-risk groups where discordant results might indicate false positives [21].

Programmatic considerations for LTBI testing

The benefits of targeted LTBI testing rely on the careful integration of these tests within the TB control program rather than the test itself. Programmatic factors—such as cost, test availability, BCG exposure prevalence in the population, and the logistics of patient follow-up—play a significant role in choosing between IGRA or TST. Additionally, the training and experience of healthcare personnel in the program are crucial to ensuring accurate test administration and result interpretation [22].

Testing for high-risk groups

For individuals over five years who are likely infected with Mtb and have a high risk of progression to TB (e.g., those with HIV, abnormal chest radiographs, or under immunosuppressive therapy), both TST and IGRA show limitations. Studies indicate that both tests have reduced sensitivity in immunocompromised individuals, with IGRAs generally providing higher sensitivity than TST in HIV-positive patients (up to 100% for IGRA versus 43% for TST). Because of the variability in test sensitivity, no strong preference is recommended between IGRA and TST as a first-line diagnostic for LTBI in high-risk individuals [23].

Alternative testing strategy for high-risk populations

If initial testing is negative in high-risk patients, a second test can be considered to reduce false negatives. For instance, if the IGRA test is negative, follow-up with a TST, or vice versa, can increase sensitivity. While this approach may reduce specificity, it is an acceptable tradeoff for high-risk individuals where missing an LTBI diagnosis could result in severe outcomes [24].

Testing in low-risk populations

For individuals unlikely to be infected with Mtb, IGRA is preferable due to its higher specificity, particularly in low-prevalence areas. If a positive result occurs, a second confirmatory test is advised to reduce the likelihood of false positives. Testing low-risk individuals for LTBI should generally be avoided unless required by legal or institutional mandates, as false positives may lead to unnecessary therapy and its associated risks [25].

Testing in children under five years of age

TST is recommended for children under five years old due to limited evidence of IGRA sensitivity in this age group. For young children, avoiding false negatives (to ensure prompt treatment if LTBI is present) is critical given their high risk of rapid progression to active TB. While IGRAs are potentially more specific, the lack of supporting evidence in young children, along with high rates of indeterminate results and practical issues in blood sampling, favor the use of TST [26].

3. Summary of Recommendations

1. IGRA over TST in low-risk populations: For low-risk individuals, IGRA is recommended due to higher specificity, though a second confirmatory test is advised if the initial result is positive.

2. TST for children under five: TST is preferred for young children due to limited data supporting IGRA efficacy in this group.

3. Alternative testing for high-risk individuals: When testing high-risk individuals with initial negative results, a second test may be warranted to reduce the chance of missed LTBI diagnosis.

Essential diagnostic tests for TB and drug resistance

Seven main diagnostic tests support TB detection and drug resistance management within the laboratory network (summarized in Table 3). These tests should be available to all healthcare providers involved in TB care, as well as to public health agencies overseeing TB control. For suspected cases of pulmonary TB, sputum smears for AFB and NAATs provide rapid confirmation. Both should be performed with minimal delay after specimen collection, enabling timely treatment and necessary infection control measures, such as patient isolation [27].

Table 4. Core laboratory tests for TB detection

Test	Estimated Time for Results
Nucleic acid amplification test (NAAT-TB)	1 day
NAAT resistance markers (NAAT-R)	1–2 days
Acid-fast bacilli (AFB) microscopy	1 day
Growth detection (Liquid medium)	Average 10–14 days
Growth detection (Solid medium)	Average 3–4 weeks
Mycobacterium tuberculosis identification by DNA probe/HPLC	1 day after growth
First- and second-line drug susceptibility testing	1–4 weeks

Recommendations for AFB smear microscopy

AFB smear microscopy remains a recommended test for initial TB screening. Studies indicate that performing three AFB smears offers a sensitivity of around 70%, with each additional sample slightly increasing sensitivity. However, a positive AFB smear alone does not confirm TB, and a negative result does not exclude it. Thus, the recommendation is to use AFB smears as a preliminary test, with at least three samples to improve diagnostic sensitivity.

Combination of liquid and solid mycobacterial cultures

In suspected TB cases, both liquid and solid mycobacterial cultures are recommended. Liquid cultures detect TB bacteria more rapidly (13-15 days) than solid cultures (up to 25 days) but may be prone to contamination. Solid cultures provide a safeguard, as some TB isolates only grow on solid media. This dual approach increases the likelihood of accurate and timely TB detection.

Use of NAAT for early TB detection

NAAT is recommended for patients suspected of pulmonary TB, especially for cases where AFB smears are positive. NAAT distinguishes TB from non-TB mycobacteria, aiding rapid diagnosis. In cases where AFB smears are negative, NAAT can provide preliminary evidence of TB if clinical suspicion is moderate to high. However, NAAT is a supplementary test and cannot replace culture for final confirmation.

Rapid molecular testing for drug susceptibility

Rapid molecular drug susceptibility testing (DST) is advised for patients with risk factors for drug-resistant TB. This includes individuals previously treated for TB, those from regions with higher TB prevalence, contacts of multi-drug-resistant TB (MDR-TB) patients, and people with HIV. Rapid DST helps identify drug resistance to rifampin (and sometimes isoniazid) and allows timely treatment adjustments, critical for managing drug-resistant TB effectively [28].

Diagnostic considerations for children with suspected TB

For children with suspected TB, collecting respiratory specimens (e.g., gastric aspirates, induced sputum) for culture is suggested. While obtaining a positive culture in pediatric cases is challenging, it is essential for accurate diagnosis and DST. Gastric aspirates may have higher diagnostic yields in infants and symptomatic children, while sputum induction can be used when appropriate for older children [29].

Sputum induction vs. bronchoscopy in adults

For adults suspected of TB who cannot produce sputum or have negative AFB smear results, sputum induction is recommended over bronchoscopy. Sputum induction has shown to be equally or more effective in TB detection, is less invasive, and more cost-effective. Bronchoscopy should only be considered if sputum induction is unsuccessful or if alternative diagnoses are being considered [30].

Limitations and Cautions

1. AFB smears and culture requirements: AFB smears are useful for preliminary screening but not definitive; follow-up cultures are essential.

2. Sample quality and specimen collection: Proper specimen volume (5–10 mL for sputum) and techniques (e.g., concentration and fluorescence microscopy) enhance accuracy.

3. Rapid testing for drug resistance: While rapid DST provides quick insights, it should be confirmed with conventional culture-based DST, especially in low MDR-TB prevalence areas.

4. Pediatric testing: For young children, negative culture results do not exclude TB, and clinicians should treat empirically when necessary.

Recommendations for TB diagnostic approaches and evidence-based rationale for TB control program

1. Sputum induction vs. bronchoscopic sampling for initial TB diagnosis: For adults with suspected pulmonary TB, especially those unable to produce sputum naturally or whose initial tests are negative, it is advised to prioritize sputum induction over flexible bronchoscopy as the first diagnostic method. Evidence suggests sputum induction has a comparable or superior diagnostic yield to bronchoscopy, is more cost-effective, and involves fewer risks. While bronchoscopy may offer a quicker presumptive TB diagnosis through biopsy, the overall benefits of sputum induction make it the preferred initial approach [31].

2. Flexible bronchoscopy when sputum induction fails: If induced sputum fails to yield samples in TB-suspected cases, flexible bronchoscopy is recommended. This method provides a diagnostic yield of 50-100%, even for patients with HIV, and can support early TB diagnosis and differentiation from other diseases. For cases requiring prompt intervention, a transbronchial biopsy may complement other bronchoscopic techniques to establish a faster diagnosis, particularly when other respiratory samples are unattainable [32].

3. Post-Bronchoscopy sputum collection for TB testing: For patients undergoing bronchoscopy, it is advisable to collect sputum samples post-procedure for additional TB testing. Such samples may yield important diagnostic information when examined under AFB smear microscopy and cultured for TB bacteria, thus enhancing diagnostic accuracy [33].

4. Bronchoscopy in suspected miliary TB cases: In cases where miliary TB is suspected, flexible bronchoscopy remains critical if no other accessible lesions are present for sampling. This recommendation applies especially when patients cannot produce sufficient sputum for testing, and bronchoscopy can help differentiate TB from other diseases. The method also allows for quick, presumptive diagnoses, which are essential for timely and effective treatment [34].

5. Testing for extrapulmonary TB involves multiple diagnostic approaches, given the variability and complexity of the disease. Methods such as cell counts, ADA, and free IFN-γ measurements provide supportive evidence for TB diagnosis in pleural, cerebrospinal, and peritoneal fluids. Given the moderate sensitivity and high specificity of ADA and IFN-γ tests, they are recommended for use in suspected extrapulmonary TB cases as they contribute to an accurate diagnosis [35].

6. Role of AFB smear and mycobacterial cultures: AFB smear microscopy, though limited in sensitivity for extrapulmonary TB, is a valuable test for early diagnosis due to its high specificity. Mycobacterial cultures remain essential for TB confirmation and DST, which ensures appropriate treatment. False-negative results are possible with both tests, so further investigation may be necessary when results are inconclusive [36].

7. Use of NAAT for early TB detection: NAAT is recommended for rapid TB diagnosis, as it provides reliable results within hours. It should be used alongside traditional mycobacterial culture, as NAAT cannot replace cultures for DST

purposes. This rapid testing option is particularly advantageous in clinical scenarios requiring quick action [37].

8. Genotyping for TB transmission tracking: Genotyping TB strains from patients can enhance tracking and understanding of TB transmission. By analyzing DNA patterns, genotyping can assist in identifying clusters and transmission networks, providing critical data for targeted public health interventions [38].

Treatment and medication management:

The treatment and medication management approach in Saudi Arabia's National TB Program is meticulously designed to ensure patient adherence and successful treatment outcomes. One of the foundational strategies employed is the WHO-recommended Directly Observed Treatment, Short-course (DOTS). This strategy involves healthcare workers directly observing patients as they take their medication, which is particularly crucial for TB because the treatment regimen is extensive, often lasting six months or more. DOTS helps improve adherence by ensuring that patients do not miss doses, which is vital because incomplete or inconsistent treatment can lead to drug resistance. By engaging healthcare workers in this process, the program builds a support system that fosters regular check-ins and addresses patient concerns, increasing the likelihood of successful treatment outcomes [39].

In addition to standard TB treatment,

program addresses multidrug-resistant tuberculosis (MDR-TB), a more complex and challenging form of the disease. MDR-TB occurs when the TB bacteria become resistant to the two most powerful first-line drugs, requiring patients to undergo more extended treatment with second-line drugs. Recognizing the severity and complexity of MDR-TB, the program provides specialized second-line medications at no cost to patients, easing the financial burden and promoting treatment adherence. These drugs often come with a longer treatment duration and require close monitoring to ensure the infection is managed effectively. In Medina, as in other regions, the availability of these medications is part of the broader commitment to comprehensive care, allowing patients access to the resources necessary to combat drug-resistant forms of TB effectively [40].

The management of side effects related to TB medications is another critical aspect of the program. TB drugs, especially those used to treat MDR-TB, can produce significant side effects, including nausea, fatigue, and, in severe cases, organ damage. To mitigate these adverse effects and support patient compliance, specialized TB clinics provide thorough patient support services. These clinics offer monitoring systems to identify and manage side effects early, allowing for adjustments in treatment as needed. By providing access to healthcare professionals trained in TB care, patients receive personalized support that can alleviate the physical and emotional challenges associated with long-term medication. This support network not only enhances the quality of care but also improves overall patient adherence, ultimately reducing the incidence of drug-resistant TB [41].

The program's free provision of TB medications reflects Saudi Arabia's commitment to equitable healthcare, ensuring that all individuals, regardless of financial means,

have access to life-saving treatments. This approach aligns with the global public health goal of making essential medicines universally accessible, particularly for communicable diseases like TB, which pose significant public health risks if left untreated. By eliminating the financial barriers to medication access, the program empowers patients to complete their full treatment regimens, reducing transmission risks and contributing to the country's broader TB control objectives. In essence, the treatment and medication management strategies in TB program demonstrate a comprehensive, patient-centered approach that addresses both medical and socio-economic factors, promoting sustained health outcomes and advancing the national goal of TB elimination [42].

Dosage Recommendations for Antituberculosis Drugs

First-Line Drugs

1. Isoniazid (INH): Available in tablet, elixir, and injection forms, typically paired with pyridoxine (vitamin B6) for patients at risk of neuropathy, such as pregnant women and those with chronic conditions. Dosage for adults is usually 300 mg daily and can reach up to 900 mg for intermittent doses (e.g., twice or thrice weekly).

2. Rifampin: Available as a capsule and IV solution, with adult dosages around 600 mg daily or adjusted for intermittent doses. Children receive 10-20 mg/kg, with the upper end of this range recommended for daily use.

3. Rifabutin: Primarily used in adults with a typical dose of 300 mg daily, but no intermittent dosage recommendations.

4. Rifapentine: Administered in 150 mg tablets, suitable for weekly dosing in children over 12 years and adults, though not FDA-approved for younger children.

5. Pyrazinamide and Ethambutol: Used in both adults and children; doses are typically higher in children on a per-kilogram basis.

Second-Line Drugs

1. Cycloserine and Ethionamide: Both drugs are recommended for daily use, with dosages adjusted based on tolerance, often starting at lower doses and gradually increased.

2. Streptomycin, Amikacin/Kanamycin, Capreomycin: Injectable agents requiring close monitoring in patients with renal issues; typical adult dosage is 15 mg/kg daily or 25 mg/kg intermittently, with similar recommendations for children.

3. Levofloxacin and Moxifloxacin: Fluoroquinolone antibiotics are given daily, with levofloxacin dosed up to 1000 mg in adults and moxifloxacin dosed at 400 mg daily.

Special Considerations and Recommendations

- Renal Impairment: Doses are often reduced or administered less frequently in patients with compromised renal function.

- Intermittent Dosing: While daily dosing is preferred, intermittent regimens (such as twice or thrice weekly) may be considered under certain conditions, particularly for those with drug-susceptible TB who are not HIV-infected and have low relapse risk.

Preventive measures:

Preventive measures are a cornerstone of the National TB Program, with initiatives aimed at reducing the incidence of TB and preventing its spread across communities, including in Medina. One of the primary preventive measures is the administration of the BCG vaccine to infants. The BCG vaccine has been shown to provide significant protection against severe forms of TB, particularly in children, and is a standard part of immunization protocols in many countries with a high TB burden. The early administration of BCG helps establish immunity in the most vulnerable populations and is an essential step in the country's strategy to curb the spread of TB. By targeting infants, the program creates a layer of protection that not only benefits individuals but also contributes to overall community health by reducing the potential number of active TB cases in the future [43].

In addition to vaccination, infection control measures are rigorously implemented in healthcare facilities, where the risk of TB transmission is often heightened. Healthcare settings are typically environments where TB patients seek diagnosis and treatment, making infection control critical to protecting healthcare workers, patients, and visitors from exposure. Measures such as proper ventilation, the use of protective masks, and isolation rooms for active TB cases are implemented to reduce the risk of transmission. These protocols are especially crucial in regions like Medina, where healthcare facilities may experience a high influx of patients, including those visiting for religious purposes. By reinforcing these infection control standards, the program minimizes the risk of healthcare-associated TB transmission, which is a vital aspect of comprehensive TB prevention [44].

Public awareness campaigns in Medina and other cities play a significant role in the program’s preventive efforts, aiming to educate the community on TB symptoms, modes of transmission, and the importance of early diagnosis and treatment. These campaigns, often conducted through local media, health seminars, and community outreach programs, help dispel myths about TB and encourage individuals to seek medical advice if they experience symptoms such as persistent cough, fever, and weight loss. Early diagnosis not only benefits the individual by allowing for timely treatment but also helps prevent the spread of TB to others. Public awareness initiatives are essential in combating the stigma that can be associated with TB, promoting a culture of openness and support that encourages people to access healthcare services without fear of judgment or discrimination [45].

The program also focuses on high-risk individuals, particularly healthcare workers and those residing in overcrowded settings, who are at an elevated risk of contracting TB due to their exposure levels. Healthcare workers, who frequently interact with TB patients, are provided with regular screenings and preventive treatment options as part of occupational health practices [46]. These preventive treatments, including prophylactic medication for those exposed to active TB cases, are designed to

prevent the development of the disease. Similarly, people living in overcrowded environments, such as migrant communities or densely populated areas in Medina, undergo periodic TB screenings. This proactive approach helps identify latent TB cases before they progress to active, contagious TB, further supporting the program's preventive goals.

Overall, TB prevention measures encompass a multi-faceted approach that addresses the needs of both individual and community health. Through vaccination, infection control in healthcare facilities, public education, and targeted screening of high-risk populations, the program establishes a robust framework for preventing TB transmission [47]. These efforts collectively contribute to the program's larger objective of reducing the TB burden and moving towards the goal of TB elimination across the country. By addressing preventive needs in a culturally and contextually relevant manner, the National TB Program demonstrates a comprehensive approach to safeguarding public health.

The Surveillance and Data Collection efforts of National TB Program play an instrumental role in the systematic monitoring of TB cases and assessing treatment outcomes. Through a robust and centralized surveillance system, each reported TB case is carefully tracked from diagnosis to treatment completion, providing critical insights into the effectiveness of the national TB control strategies [48]. This systematic tracking allows healthcare professionals and policymakers to assess treatment efficacy, adherence rates, and identify potential gaps in the program’s approach. For example, in a city like Medina, data-driven insights may indicate higher TB rates due to certain population factors, such as a high volume of visitors and residents in close-contact settings, enabling the program to intensify interventions where they are most needed. The data collected also informs resource allocation, directing financial and logistical support to regions with higher TB burdens, and ensures efficient use of resources in a way that maximizes impact.

In addition to monitoring treatment outcomes, the program keeps a close eye on treatment completion rates, recurrence, and drug resistance trends. Treatment completion is a crucial metric, as incomplete TB treatment can lead to drug-resistant TB strains, a significant public health challenge. By tracking recurrence rates, the program can assess the durability of its treatment regimens and identify cases where follow-up may be required. Monitoring drug resistance trends allows the program to adjust its treatment protocols to combat drug-resistant TB effectively [49]. This data-driven approach not only strengthens the program’s immediate response but also informs long-term strategies and interventions, making Saudi Arabia’s National TB Program adaptive and responsive to changing patterns in TB epidemiology.

The program also places a strong emphasis on Research and Capacity Building to continually improve TB management strategies. Research initiatives focus on understanding TB prevalence across various demographics, investigating drug resistance patterns, and developing effective models for engaging communities in TB prevention and treatment. By conducting localized research, the program can tailor its strategies to the specific needs of regions like Medina, ensuring that interventions are relevant and impactful. Additionally, healthcare providers involved in the program receive specialized training on TB diagnosis, treatment protocols, and

patient management. This capacity-building effort enhances healthcare delivery by ensuring that medical professionals are well-equipped with the latest knowledge and skills to provide optimal TB care. Training extends to the proper handling of drug-resistant TB cases, managing side effects, and maintaining a patient-centered approach, all of which are essential for effective TB control.

Multisectoral Collaboration is another cornerstone of the National TB Program, reflecting the understanding that TB is influenced by various social, economic, and environmental factors. The program collaborates with sectors such as education, immigration, and social welfare to address social determinants that contribute to TB risk [50]. For example, collaboration with the education sector may involve TB awareness campaigns in schools, while immigration policies might include TB screenings for incoming residents. Social welfare programs are also leveraged to support vulnerable groups, such as low-income individuals and those living in crowded settings, who are more susceptible to TB infection. These partnerships address the root causes of TB transmission and create a supportive environment that promotes overall community health.

Moreover, the program's partnerships with international organizations, including the WHO and the Global Fund, bring in additional technical expertise, resources, and funding. These collaborations strengthen the program's capacity to meet its objectives and provide a platform for sharing best practices and accessing global innovations in TB management. The technical assistance from these international bodies helps Saudi Arabia maintain alignment with global standards and ensures that the program is equipped to address complex challenges, such as the rise of MDR-TB. By leveraging multisectoral and international support, the National TB Program in Saudi Arabia not only enhances its operational capacity but also ensures a holistic approach to TB prevention and control, positioning itself as a comprehensive and adaptive model in global TB management.

4. Conclusion

These guidelines are designed to facilitate informed, evidence-based decision-making in the diagnostic assessment of patients with suspected or latent tuberculosis in Medina City. They are not designed to provide a strict standard of care but to offer a basis for informed clinical decisions. Healthcare providers, consumers, payers, stakeholders, and legal entities should not construe these guidelines as obligatory protocols. These guidelines are intended to inform, rather than prescribe, patient care, acknowledging the variety of clinical situations.

The implementation of these guidelines must be tailored to each patient's specific situation, and physicians are urged to utilize their professional discretion. Qualifying statements accompanying each advice are essential for accurate interpretation and must be provided verbatim when citing or interpreting these recommendations. This adaptability guarantees that the guidelines stay pertinent and efficacious within the unique clinical and public health framework of Medina City.

References

Schünemann HJ, Osborne M, Moss J, et al. (2009). Managing conflict of interest in professional societies. Am J Respir Crit Care Med, 180(5), 564-580.
Schünemann HJ, Oxman AD, Brozek J, et al. (2008). Grading quality of evidence for diagnostic tests. BMJ, 336(7653), 1106-1110.
Schünemann HJ, Jaeschke R, Cook DJ, et al. (2006). Grading evidence quality in ATS guidelines. Am J Respir Crit Care Med, 174(5), 605-614.
World Health Organization. (2015). Global tuberculosis report. Geneva, Switzerland: WHO.
Edlin BR, Tokars JI, Grieco MH, et al. (1992). Multidrug-resistant tuberculosis outbreak among HIV patients. N Engl J Med, 326(23), 1514-1521.
Gandhi NR, Moll A, Sturm AW, et al. (2006). XDR TB in HIV patients in South Africa. Lancet, 368(9547), 1575-1580.
Scott C, Kirking HL, Jeffries C, et al. (2015). Tuberculosis trends in the U.S., 2014. MMWR Morb Mortal Wkly Rep, 64(10), 265-269.
Bennett DE, Courval JM, Onorato I, et al. (2008). TB infection prevalence in the U.S. Am J Respir Crit Care Med, 177(3), 348-355.
US Institute of Medicine. (2000). Ending neglect: The elimination of tuberculosis in the U.S. Washington, DC: National Academy Press.
American Thoracic Society. (2000). Targeted tuberculin testing and treatment of LTBI. MMWR Recomm Rep, 49(RR-6), 1-51.
Huebner RE, Schein MF, Bass JB Jr. (1993). The tuberculin skin test. Clin Infect Dis, 17(6), 968-973.
Pai M, Denkinger CM, Kik SV, et al. (2014). Gamma interferon release assays for TB detection. Clin Microbiol Rev, 27(1), 3-20.
Kendig EL Jr, Kirkpatrick BV, Carter WH, et al. (1998). Underreading tuberculin skin tests. Chest, 113(4), 1175-1177.
Centers for Disease Control and Prevention. (2005). Preventing TB transmission in healthcare. MMWR Recomm Rep, 54(RR-17), 1-141.
Black CA. (1999). Delayed hypersensitivity theories. Dermatol Online J, 5(1), 7.
Cole ST, Brosch R, Parkhill J, et al. (1998). Biology of Mycobacterium tuberculosis. Nature, 393(6685), 537-544.
Andersen P, Andersen AB, Sørensen AL, Nagai S. (1995). Immunity to TB in mice. J Immunol, 154(7), 3359-3362.
Mustafa AS, Amoudy HA, Wiker HG, et al. (1998). TB antigen-specific T-cell responses. Scand J Immunol, 48(5), 535-543.
Mustafa AS, Oftung F, Amoudy HA, et al. (2000). Human T cell lines for TB. Clin Infect Dis, 30(Suppl 3), S201-S205.
Harboe M, Oettinger T, Wiker HG, et al. (1996). ESAT-6 in Mycobacterium species. Infect Immun, 64(1), 16-22.
Mahairas GG, Sabo PJ, Hickey MJ, et al. (1996). Genetic differences in Mycobacterium. J Bacteriol, 178(5), 1274-1283.
Berthet FX, Rasmussen PB, Rosenkrands I, et al. (1998). TB operon encoding ESAT-6. Microbiology, 144(Pt 11), 3195-3203.
Bothamley GH, Rudd RM. (1994). TB serological assay using monoclonal antibody. Eur Respir J, 7(2), 240-246.
Colangeli R, Spencer JS, Bifani P, et al. (2000). TB-specific hypersensitivity in guinea pigs. Infect Immun, 68(2), 990-993.
Dillon DC, Alderson MR, Day CH, et al. (2000). Immunodiagnostic antigen CFP-10 in TB. J Clin Microbiol, 38(9), 3285-3290.
Arend SM, de Haas P, Leyten E, et al. (2005). ESAT-6 and CFP-10 in Mycobacterium isolates. J Infect Dis, 191(7), 1301-1310.
Geluk A, van Meijgaarden KE, Franken KL, et al. (2002). Immunological cross-reactivity in TB. Infect Immun, 70(5), 2544-2548.
Geluk A, van Meijgaarden KE, Franken KL, et al. (2004). TB cross-reactivity study. Scand J Immunol, 59(1), 66-70.
Millington KA, Gooding S, Hinks TS, et al. (2010). TB immune profiles post-cure. J Infect Dis, 202(12), 1685-1689.
Hinks TS, Dosanjh DP, Innes JA, et al. (2009). Region-specific immune profiles in TB. Infect Immun, 77(12), 5486-5492.

Kik SV, Franken WP, Arend SM, et al. (2009). IGRA tests in immigrant TB contacts. Int J Tuberc Lung Dis, 13(7), 820-828.

Lalvani A, Nagvenkar P, Udwadia Z, et al. (2001). T-cell response in urban Indians. J Infect Dis, 183(4), 469-477.

Ferrara G, Losi M, D'Amico R, et al. (2006). IGRA blood tests in routine TB diagnosis. Lancet, 367(9519), 1328-1334.

Ferrara G, Losi M, Meacci M, et al. (2005). IGRA tests for TB in clinical use. Am J Respir Crit Care Med, 172(5), 631-635.

Lee JY, Choi HJ, Park IN, et al. (2006). Commercial interferon-gamma assays. Eur Respir J, 28(1), 24-30.

van Zyl-Smit RN, Zwerling A, Dheda K, Pai M. (2009). TB testing variability. PLoS One, 4(6), e8517.

Connell TG, Curtis N, Ranganathan SC, et al. (2006). IGRA assay for TB in children. Thorax, 61(8), 616-620.

Richeldi L. (2006). Update on TB diagnosis. Am J Respir Crit Care Med, 174(7), 736-742.

Treatment and Control (References 39–50)

Marks SM, Taylor Z, Qualls NL, et al. (2000). Outcomes of TB contact investigations. Am J Respir Crit Care Med, 162(6), 2033-2038.

Reichler MR, Reves R, Bur S, et al. (2002). LTBI treatment in TB contacts. South Med J, 95(4), 414-420.

Hirsch-Moverman Y, Daftary A, Franks J, Colson PW. (2008). Adherence to LTBI treatment. Int J Tuberc Lung Dis, 12(11), 1235-1254.

American Thoracic Society. (2000). Diagnostic Standards and Classification of TB. Am J Respir Crit Care Med, 161(4), 1376-1395.

Black CA. (1999). Delayed hypersensitivity theories. Dermatol Online J, 5(1), 7.

American Academy of Pediatrics. (2015). Committee on Infectious Diseases Red Book. 30th ed. Elk Grove Village, IL: AAP.

Gandhi NR, Moll A, Sturm AW, et al. (2006). XDR TB in HIV patients in South Africa. Lancet, 368(9547), 1575-1580.

Munro SA, Lewin SA, Smith HJ, et al. (2007). Patient adherence to TB treatment. PLoS Med, 4(7), e238.

Centers for Disease Control and Prevention. (2014). Managing TB patients and improving adherence. Atlanta, GA: CDC.

Wright CM, Westerkamp L, Korver S, Dobler CC. (2015). Community-based DOT for TB. BMC Infect Dis, 15(1), 210.

Liu SY, Li JH, Schluger NW. (2005). DOT and timely treatment in TB patients. Int J Tuberc Lung Dis, 9(8), 884-889.