

## A New Dawn in Tuberculosis Eradication Via Emerging Laboratory Techniques, Vaccines and Treatments

Rosemary Nneka Udeji<sup>1\*</sup>, Chidimma Anthonia Azike<sup>2</sup>, Okoye Nelyn Akunna<sup>3</sup> and Onyinyechukwu Uzoamaka Oka<sup>4</sup>

<sup>1</sup> Ikate Primary Health Centre, Lekki, Lagos State, Nigeria

<sup>2</sup> Department of Medical Laboratory Science, Rivers State University

<sup>3</sup> Department of Hospital Services, Rivers State University

<sup>4</sup> Alex Ekwueme Federal University Teaching Hospital Abakaliki, Ebonyi State

Corresponding author's email address: [rosemaryudeji@gmail.com](mailto:rosemaryudeji@gmail.com)

Received: 6<sup>th</sup> February, 2024

Accepted: 25<sup>st</sup> February, 2024

Published: 28<sup>th</sup> February, 2024

Available: <https://www.nmlsj.org>

Publisher: ScholarlyFeed

Copyright © 2024 Udeji *et al.*

Article distributed under the CC-BY-ND

**Cite as:** Udeji NU, Azike CA, Akunna ON, Oka OU. A New Dawn in Tuberculosis Eradication Via Emerging Laboratory Techniques, Vaccines and Treatments. Nexus Med Lab Sci J. 2024; 1(1):35-45

### Abstract

Tuberculosis (TB) remains a formidable global health challenge, with an estimated 10 million new cases and 1.5 million deaths reported annually. The aim of this review is to critically examine the potential impact of recent innovations on TB prevention, diagnosis, and treatment. Employing a review approach, we searched across multiple databases using relevant keywords and approximately 40 individual literatures were reviewed, we identified key studies published from 2015 to date, revealing a substantial knowledge gap in synthesizing the advancements in laboratory techniques, vaccines, and drugs. The review showcase the remarkable progress in laboratory diagnostics, exemplified by molecular diagnostics and whole-genome sequencing, offering unprecedented accuracy in TB diagnosis. Novel vaccines, including M72/AS01E and adjuvanted BCG, demonstrate promising efficacy, while emerging drugs such as bedaquiline and delamanid mark a paradigm shift in TB treatment. However, challenges such as cost, accessibility, and ethical considerations persist. The synthesis of these innovations into a cohesive strategy holds immense potential to catalyze a new era in TB eradication, paving the way for a substantial reduction in the global TB burden. This review contributes a comprehensive overview of recent advancements and highlights the need for continued research and collaborative efforts to address the multifaceted challenges hindering the widespread implementation of these groundbreaking interventions.

**Keywords:** Hospitalization, Monkeypox, Polymerase Chain Reaction.

## 1.0 Introduction

A significant global health concern, tuberculosis (TB) is estimated to cause 1.5 million deaths and 10 million new cases each year [1]. Conventional techniques, vaccines, and drugs have been the mainstays of TB control initiatives over the years. Still, the shortcomings of these methods combined with the gaps found in earlier studies highlight the need for ongoing innovation in this area. The intricate interactions of factors like drug resistance, co-infections, and socioeconomic determinants continue to obstruct the total eradication of this infectious disease, despite tremendous advancements in diagnosis and treatment over the years. Recent years have seen a surge in research efforts as the world struggles with the ongoing threat of tuberculosis (TB), which has resulted in promising developments in laboratory techniques, vaccines, and drug therapies.

Traditionally, sputum microscopy and culture have been the mainstays of conventional TB diagnostic techniques. These methods have drawbacks, despite their relative effectiveness, including low sensitivity, labor-intensive processes, and difficulties in identifying latent or drug-resistant infections [2]. Comparably, even though it is the only TB vaccine with a license, the Bacillus Calmette-Guérin (BCG) vaccine shows inconsistent protection and varying efficacy, particularly in adult populations [3]. First-line anti-TB drugs are used in a six-month treatment regimen that has been proven to be effective. However, patient adherence can be problematic, which can result in the emergence of drug-resistant strains and relapses [1].

The advancement of novel laboratory techniques has substantially enhanced our ability to accurately diagnose tuberculosis (TB), monitor the illness's course, and unravel its intricate pathogenesis. Molecular diagnostic methods such as polymerase chain reaction (PCR) and nucleic acid amplification tests (NAATs) have revolutionized the diagnosis of tuberculosis because of their fast and reliable results [2]. Moreover, novel imaging modalities such as positron emission tomography (PET) and magnetic resonance imaging (MRI) offer hitherto unseen insights into the temporal and spatial dynamics of tuberculosis (TB) lesions within the host [4]. Using these new methods improves our understanding of tuberculosis and supplies the necessary components for timely intervention and containment.

The pursuit of an efficacious TB vaccine has been a long-standing challenge, and recent developments offer renewed hope. Progress in understanding the complex immunology of Mycobacterium tuberculosis has paved the way for innovative vaccine candidates, such as the M72/AS01E vaccine, demonstrating unprecedented efficacy in clinical trials [3]. These advancements underscore the potential of vaccines not only in preventing active TB but also in providing durable protection, particularly in high-risk populations. The armamentarium against TB has expanded with the emergence of new drug candidates demonstrating improved efficacy and shorter treatment regimens. Anti-TB drug development has made significant strides with the introduction of bedaquiline, a diarylquinoline, and pretomanid, a nitroimidazole, which provide increased potency and shorter treatment durations [5, 6]. These innovative medications are important because they address the urgent problem of multidrug-resistant tuberculosis, which goes beyond just their therapeutic potential.

Prior investigations have revealed significant deficiencies in the current tuberculosis control model, underscoring the necessity for enhanced precision and speed in diagnosis, vaccines with high efficacy, and medication regimens that are more manageable for patients. A robust alternative to BCG has proven to be unavailable, which has fueled the search for novel vaccine candidates with improved immunogenicity and wider protective coverage [3]. Furthermore, worries about the epidemic of drug-resistant tuberculosis have fueled research into finding novel antimicrobial drugs that are more effective and require shorter course of treatment [5].

It is critical to fill in these research gaps as the field of tuberculosis research develops. This thorough review aims to summarize the most recent developments in medication therapies, vaccines, and laboratory techniques while providing a critical evaluation of their possible effects on the eradication of tuberculosis. Emerging strategies offer a promising trajectory for reshaping the global response to tuberculosis (TB) by addressing the limitations identified and building upon the foundations of conventional approaches.

This extensive review's objective is to critically assess and summarize the state of TB eradication strategies today, with an emphasis on the most recent developments in laboratory techniques, vaccines, and drug treatments. This review seeks to

provide a thorough synthesis of the most recent developments in laboratory techniques, vaccines, and drug therapies, highlighting their crucial roles in the global effort to eradicate tuberculosis. It does this by methodically going over the scientific literature and clinical advancements. Through a critical evaluation of these new approaches, we hope to add to the current discussion about tuberculosis control and prevention by providing information that could guide future research agendas and public health initiatives.

## **1.1 Methodology**

### **1.1.1 Search Strategy**

This review assessed relevant literature focusing on emerging laboratory techniques, vaccines, and drug treatments for tuberculosis (TB). The search was conducted across relevant databases, including PubMed, Scopus, and Web of Science. A combination of keywords such as "tuberculosis," "laboratory techniques," "vaccines," and "drug treatments" guided the search strategy. The initial database search yielded a total of 69 potential articles. After removing duplicates, the titles and abstracts of 59 articles were screened for relevance. Following this, a full-text assessment was conducted on 40 articles that met the inclusion criteria. The final selection comprised a diverse range of studies, including clinical trials, observational studies, and reviews, providing a comprehensive overview of the current state of TB research.

### **1.1.2 Selection Criteria**

Inclusion criteria were established to ensure the quality and relevance of the selected literature. Only peer-reviewed articles, clinical trials, and systematic reviews that presented novel findings or contributed valuable insights to the field were considered. Priority was given to studies discussing advancements and identifying research gaps in conventional TB control approaches.

### **1.1.3 Data Extraction and Synthesis**

Data were extracted independently by two reviewers to ensure accuracy and reliability. Any discrepancies or disagreements were resolved through discussion and consensus. The extracted data were organized systematically, facilitating subsequent analysis and synthesis.

The synthesis of data involved a thematic analysis to identify common trends, patterns, and key findings across the selected studies. The laboratory

techniques were categorized into distinct themes based on their applications in TB diagnosis, monitoring, and research. Within each theme, similarities and differences among the techniques were explored.

The synthesis process also included an in-depth examination of the advantages and limitations of each laboratory technique. The goal was to provide a comprehensive overview of the strengths and potential challenges associated with the innovative methods discussed in the review. Furthermore, the synthesis aimed to highlight any emerging trends, novel approaches, or areas where the field of TB laboratory techniques may benefit from further research and development.

Throughout the synthesis, attention was given to variations in study populations, settings, and methodologies to provide a nuanced understanding of the generalizability and applicability of the laboratory techniques across diverse contexts.

### **1.1.4 Ethical Consideration**

As this review involved the analysis of previously published studies, and no primary data collection from human subjects was undertaken, explicit informed consent and ethical approval were not applicable. Ethical approval for the review itself was not sought, as it did not involve human or animal subjects.

## **2.0 Epidemiology and Prevalence of Tuberculosis**

A complex epidemiological landscape shaped by multiple factors, such as socioeconomic conditions, healthcare infrastructure, and the prevalence of risk factors, characterizes tuberculosis (TB), which continues to be a major global public health concern. The World Health Organization (WHO) estimated that there were 1.5 million TB-related deaths worldwide in 2021 and 10 million new cases of TB [1]. The burden of tuberculosis (TB) is still disproportionately high in some areas and populations, even with advancements in lowering incidence and mortality rates.

The prevalence of tuberculosis (TB) varies geographically, with low- and middle-income countries having a higher burden. In 2021, the Western Pacific area, Southeast Asia, and Sub-Saharan Africa accounted for roughly 78% of all tuberculosis cases worldwide [1]. These areas struggle with issues like poverty, congested

housing, and restricted access to healthcare, which add to the prevalence of TB.

Urban areas within countries typically have higher rates of tuberculosis prevalence because of higher population densities and related risk factors. The incidence rate of tuberculosis (TB) was 130 cases per 100,000 people worldwide in 2021, although regional variations greatly affected this number. With 255 cases per 100,000 people, Sub-Saharan Africa had the highest incidence rate, followed by Southeast Asia with 175 cases [1].

A number of socioeconomic and demographic variables increase some populations' susceptibility to tuberculosis. The risk of tuberculosis (TB) is increased by factors like smoking, malnutrition, HIV co-infection, and immunosuppressive illnesses. HIV-positive individuals were estimated to account for 8% of all TB cases worldwide in 2021, highlighting the complex relationship between TB and HIV [1].

One more obstacle to TB control efforts is the emergence of drug-resistant TB. Cases of extensively drug-resistant TB (XDR-TB) and multidrug-resistant TB (MDR-TB) have been reported worldwide; these cases present unique treatment challenges. An estimated 465,000 cases of MDR-TB were reported in 2021, highlighting the continuous risk of drug resistance in the treatment of tuberculosis [1]. The COVID-19 pandemic's effects have further complicated efforts to control tuberculosis. There have been reports of disruptions in TB diagnosis and treatment programs, which could result in a rise in TB incidence and a delay in case detection. It is imperative to address these issues, which call for ongoing international initiatives that prioritize enhancing healthcare systems, expanding access to diagnosis and treatment, and tackling the socioeconomic determinants of tuberculosis.

## **2.1 Laboratory Techniques in Tuberculosis Detection: A Review**

### **2.1.1 Conventional Laboratory Techniques and Their Limitations**

Historically, sputum smear microscopy and culture were the mainstays of conventional laboratory techniques for tuberculosis (TB) diagnosis. Although these techniques have been essential, they have some significant drawbacks. For example, smear microscopy is not very sensitive, especially when paucibacillary TB is present, which can lead to underdiagnosis and a delay in starting treatment [7]. Even though culture-based approaches are

thought to be the best, they can take weeks to produce results, which makes it difficult to implement public health control measures and interventions in a timely manner [8].

Drug-resistant tuberculosis has largely been identified using conventional drug susceptibility testing (DST) techniques, such as the proportion method on solid media. They may not detect hetero-resistance, though, and their slowness makes it difficult to promptly modify treatment plans [9]. These limitations highlighted the need for novel strategies to reduce diagnostic delays, boost sensitivity, and improve our capacity to quickly identify drug resistance.

### **2.1.2 Advancements in TB Laboratory Techniques**

Recent years have seen a dramatic change in laboratory techniques for tuberculosis (TB), thanks to the introduction of cutting-edge techniques that improve monitoring capabilities, diagnostic precision, and our understanding of TB biology.

#### **1. Xpert® MTB/RIF Assay**

TB diagnosis has been transformed by the Xpert® MTB/RIF assay, especially in environments with limited resources. This nucleic acid amplification test, created by Cepheid, allows for the rapid detection of both rifampicin resistance and *Mycobacterium tuberculosis* (MTB) DNA in a matter of hours. Because it is automated, it requires fewer skilled technicians, which makes it appropriate for point-of-care settings. The high sensitivity of the assay overcomes the drawbacks of smear microscopy, even in paucibacillary samples, enabling early treatment initiation and better patient outcomes [10]. Additionally, the Xpert® MTB/RIF Ultra version improves sensitivity and specificity even more, supporting the global initiative to stop the spread of tuberculosis.

#### **2. Whole-Genome Sequencing (WGS)**

Because whole-genome sequencing offers a comprehensive view of the genetic composition of *M. tuberculosis* strains, it has revolutionized research on tuberculosis. By identifying drug resistance mutations, this high-throughput technique helps clinicians create individualized treatment plans. Furthermore, WGS sheds light on population structures and patterns of transmission by providing insights into the evolutionary dynamics of tuberculosis. WGS has produced rich genomic data that has been extremely helpful in

deciphering the intricate biology of tuberculosis and guiding public health initiatives [11].

### **2.1.3 Innovative Methods Improving Detection**

#### **1. Lateral Flow Urine Lipoarabinomannan Assay (LF-LAM)**

The LF-LAM assay tackles the problem of TB diagnosis in immunocompromised people, especially those who are HIV positive. LF-LAM is a quick and non-invasive diagnostic method that was designed as a point-of-care test to identify mycobacterial antigens in urine. The assay is useful for people with advanced HIV disease, where diagnosing tuberculosis is frequently difficult. Improved sensitivity in identifying active tuberculosis has been shown for LF-LAM, which makes it a useful adjunct to the diagnostic toolbox, particularly in environments where access to advanced laboratory infrastructure is restricted [12].

### **2. Advanced Imaging Technologies**

Molecular imaging methods, like magnetic resonance imaging (MRI) and positron emission tomography (PET), have revolutionized our capacity to track the development of tuberculosis lesions. Real-time visualization of tuberculosis pathology is made possible by these non-invasive techniques, which enable a more complex comprehension of the temporal and spatial dynamics of the illness. In particular, PET has demonstrated promise in locating latent and active tuberculosis foci, supporting treatment evaluations, and assisting in the creation of focused interventions [13].

## **2.2 Tuberculosis Vaccines**

### **2.2.1 Conventional TB Vaccines and Their Limitations**

Traditional TB vaccinations, which are mainly based on *Bacillus Calmette-Guérin* (BCG), have been extremely important in preventing tuberculosis (TB), particularly in children [14]. But the drawbacks of BCG and other traditional methods have spurred the creation of novel tactics and vaccines, highlighting the need for advancements in TB vaccination [15].

The most common and contagious form of tuberculosis (TB) in adults is pulmonary TB, for which BCG is effective, but its effectiveness against severe forms in children is inconsistent and frequently diminishes. This restriction makes it

more difficult to prevent tuberculosis [16] and highlights the need for adult populations to receive vaccines with increased efficacy. Another problem is that BCG gradually reduces immunity, making people more vulnerable to tuberculosis as adults. In order to counteract this decline, booster shots or the creation of vaccines that offer long-lasting protection are therefore required, especially for populations that have had prolonged exposure to tuberculosis.

The efficacy of BCG varies significantly among different populations and geographical areas, which presents difficulties in attaining uniform protection [16]. Moreover, BCG primarily targets active tuberculosis, largely ignoring latent tuberculosis infection. Developments in tuberculosis vaccination research endeavor to create vaccines that not only prevent active tuberculosis but also target latent tuberculosis infection, an essential reservoir for potential future disease reactivation [15]. Obstacles in high-burden environments, impacted by variables such as undernourishment, HIV co-infection, and exposure to environmental mycobacteria, highlight the necessity for vaccines that can surmount these challenges and provide reliable protection, particularly in areas with a high TB prevalence [17]. Furthermore, the focus of advancements is highlighted by the incapacity of BCG and certain conventional vaccines to elicit sufficiently strong and long-lasting immune responses, especially in adult populations [18]. The goal of ongoing research into TB vaccines is to produce shots that stimulate more robust and long-lasting immune responses, which are crucial elements of long-term protection against tuberculosis [3]. Finally, the BCG vaccination complicates the diagnosis of tuberculosis (TB) by interfering with diagnostic tests like the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs). As a result, creating vaccines that don't interfere with diagnostic procedures is prioritized [19]. In conclusion, understanding these drawbacks of traditional TB vaccinations encourages researchers to develop new approaches and more potent tactics for the ongoing fight against tuberculosis.

### **2.2.2 Advancements in TB Vaccine Development**

The development of novel TB vaccines has advanced significantly in recent years, indicating a move toward a more focused and all-encompassing strategy.



### 1. M72/AS01E Vaccine

The M72/AS01E vaccine represents a significant advancement in the field of tuberculosis (TB) immunization.

#### Mechanism of Action of M72/AS01E Vaccine

The M72/AS01E vaccine works by inducing a strong immune response against *Mycobacterium tuberculosis* through a specific mechanism. Two TB-specific antigens, Mtb32A and Mtb39A, are included in the vaccine and are prepared with the adjuvant AS01E. Immunostimulants and liposomes combine to form AS01E, which improves the immune system's ability to recognize these antigens and encourages a stronger, longer-lasting response.

Antigen-presenting cells, like dendritic cells, are activated by the antigens and go on to process and deliver peptides specific to tuberculosis (TB) to T cells. By sending out signals that promote T cell activation and proliferation, the AS01E adjuvant intensifies this process. It is the goal of this coordinated humoral and cellular immune response to provide protection from future *M. tuberculosis* exposure [20].

#### Clinical Trials

The M72/AS01E vaccine has undergone several phases of clinical trials aimed at assessing its safety, immunogenicity, and effectiveness. An important step forward in the development of a TB vaccine was made when the Phase 2b controlled trial showed a 54% efficacy in preventing active pulmonary TB in adults with latent TB infection [20]. The goal of ongoing studies and trials is to ascertain the M72/AS01E vaccine's long-term effectiveness, ideal dosage, and suitability for a range of demographics.

### 2. H56:IC31 Vaccine

Aeras and the Statens Serum Institute collaborated to create the H56:IC31 vaccine, which is different from the conventional live attenuated vaccines.

#### Mechanism of Action

To elicit a broad and diverse immune response against *Mycobacterium tuberculosis*, the H56:IC31 vaccine uses a unique mechanism. The vaccine targets various aspects of the tuberculosis pathogen by incorporating multiple TB-specific antigens, such as Ag85B and ESAT-6. These antigens activate T cells, especially CD4+ and CD8+ T cells, which are essential for fighting intracellular infections, by stimulating antigen-presenting cells. By aiding in T cell activation and antigen-presenting cell maturation, the IC31 adjuvant

further strengthens the immune response. This combination seeks to overcome the difficulties brought on by the intricate biology of *Mycobacterium tuberculosis* by eliciting a thorough and long-lasting immune response [15].

#### Clinical Trials

The goal of H56:IC31's early-stage clinical trials has been to determine its immunogenicity and safety profiles. The groundwork for continuing studies into the vaccine's ability to prevent tuberculosis was established by these trials. The vaccine is a promising contender in the search for an efficient TB vaccine because of its capacity to elicit a strong and wide immune response.

### 2.3 Effectiveness of Emerging Tuberculosis Vaccines: A Critical Appraisal

One of the most important factors in the continuous fight against this threat to global health is the efficacy of newly developed tuberculosis (TB) vaccinations. M72/AS01E and H56:IC31, two well-known candidates, have demonstrated promise in early and mid-phase clinical trials, signifying important developments in the field of tuberculosis vaccination.

#### 1. M72/AS01E Vaccine

In adults with latent TB infection, the M72/AS01E vaccine has shown a noteworthy efficacy in preventing active pulmonary TB. A 54% efficacy rate was found in the pivotal Phase 2b controlled trial, indicating that the vaccine has the potential to provide a significant level of protection against tuberculosis [20]. Still up for debate are the drug's long-term efficacy, best dosage methods, and suitability for a range of demographics.

The efficacy of the M72/AS01E vaccine is ascribed to its distinct mode of operation, which utilizes TB-specific antigens in conjunction with the AS01E adjuvant to elicit a focused and enduring immune response. Its performance in real-world settings, in various TB-endemic populations, and in possible interactions with other health interventions are all being evaluated as part of the ongoing investigation into its efficacy.

#### 2. H56:IC31 Vaccine

Early-phase clinical trials have demonstrated promise for the H56:IC31 vaccine, which combines the IC31 adjuvant and multiple TB-specific antigens. Although the primary focus of these trials was safety and immunogenicity, they established the groundwork for assessing the vaccine's efficacy

against tuberculosis in later stages. The vaccine is a strong candidate for additional research because of its mechanism of action, which is intended to elicit a robust and broad immune response [15].

The efficacy of the H56:IC31 vaccine is still being rigorously evaluated in a variety of populations, including those living in areas where tuberculosis is endemic. Given the genetic diversity of the pathogen, the purpose of effectiveness trials is to shed light on the vaccine's potential to protect against different strains of *Mycobacterium tuberculosis*.

## 2.4 Emerging Drugs and Treatments for Tuberculosis

Significant advancements have been made in the creation and authorization of novel drugs and treatments to treat tuberculosis (TB) in recent years.

**1. Bedaquiline:** A diarylquinoline called bedaquiline prevents mycobacterial ATP synthase, which stops *Mycobacterium tuberculosis* (MTB) from producing energy. It proved to be more effective than conventional treatments in treating drug-resistant tuberculosis, converting sputum cultures more quickly and resulting in lower mortality rates [21].

**2. Delamanid:** This nitroimidazole derivative targets the synthesis of mycolic acid, which is essential for maintaining the integrity of the MTB cell wall. With faster sputum culture conversion, recent research has demonstrated its effectiveness in treating multidrug-resistant tuberculosis [22].

**3. Pretomanid:** Mycobacterial DNA synthesis is hampered by the nitroimidazole compound Pretomanid. Treatment of extensively drug-resistant tuberculosis (TB) with the BPaL regimen showed high success rates when combined with bedaquiline and linezolid [23].

**4. Sutezolid:** A derivative of oxazolidinone that prevents MTB from synthesizing proteins. Its advantages over linezolid, such as shorter treatment times and less toxicity, make it a desirable choice for both.

**5. Bacteriophage Therapy:** This technique, which uses viruses to infect and kill bacteria, is becoming more and more popular as a possible addition to tuberculosis treatment. Its effectiveness against

drug-resistant MTB strains has been suggested by recent preclinical studies [25].

**6. Immunomodulatory Therapies:** To strengthen the host immune response against tuberculosis, immunomodulatory therapies, like host-directed therapies (HDTs), are used. To supplement established therapies, agents that target immune checkpoints, such as interferons and monoclonal antibodies, are being investigated [26].

**7. Nitazoxanide:** By interfering with Mtb's energy metabolism, the antiparasitic medication nitazoxanide has demonstrated anti-TB action. Its potential as an adjuvant therapy that improves treatment outcomes has been shown in recent studies [27].

**8. Combinations of Linezolid and Clofazimine:** Linezolid and Clofazimine have both been shown to be effective in reducing the length of tuberculosis treatment. They both have bactericidal and anti-inflammatory qualities. This strategy has the potential to improve patient adherence and lessen the burden of treatment [28].

**9. Aerosolized Therapies:** To improve drug delivery to the site of infection, aerosolized delivery of TB medications, such as liposomal amikacin, is being investigated. By enhancing drug concentrations in the lungs, this strategy may boost treatment effectiveness [29].

**10. Cycloserine Derivatives:** New cycloserine derivatives are being researched with the goal of increasing effectiveness and lowering toxicity. These substances target the synthesis of Mtb cell walls, suggesting that they could be used as substitutes for current medications [30].

## 2.5 Challenges and Limitations in the Implementation of Emerging Techniques, Vaccines, and Drugs in Tuberculosis Eradication

Even though new laboratory techniques, drugs, and vaccines show great promise in the fight against tuberculosis (TB), their application is fraught with difficulties and has several restrictions that should be carefully considered. This section explores the intricacies surrounding these innovations, considering variables like price, accessibility, and possible adverse effects.

### **1. Cost Barriers in Implementing New Laboratory Techniques**

Adopting cutting-edge laboratory techniques frequently has significant financial ramifications. The widespread application of cutting-edge technologies, like whole-genome sequencing and molecular diagnostics, may be hampered by their financial burden in environments with limited resources [31].

### **2. Accessibility Issues in Remote Areas**

Accessibility to medical treatments and diagnostic equipment is still a major concern, especially in isolated or underdeveloped areas. Overcoming logistical obstacles, such as transportation and infrastructure constraints, is necessary to guarantee that novel laboratory methods, vaccines, and medications reach the populations most in need [32].

### **3. Vaccine Distribution Challenges**

Even with the creation of potent TB vaccines, distributing them fairly remains a significant challenge. Inequalities in healthcare infrastructure and distribution networks have the potential to impede the prompt and extensive implementation of vaccines, thereby intensifying pre-existing health disparities [33].

### **4. Side Effects and Adverse Reactions**

One very important factor to take into account is the safety profile of new drugs and vaccines. Patient acceptance and compliance may be impacted by unfavorable reactions and side effects. It is still a challenge to make sure that these novel interventions are safe and well-tolerated for a variety of populations [34].

### **5. Drug Resistance Concerns**

One ongoing problem in the treatment of tuberculosis is the emergence of drug-resistant strains. Although new medications provide hope, the risk of resistance developing calls for vigilant monitoring and surveillance measures [35].

### **6. Socio-cultural Factors Influencing Vaccine Uptake**

Sociocultural factors impact the effectiveness of vaccination campaigns. The acceptance of vaccines may be impacted by cultural beliefs, disinformation, and mistrust of healthcare systems. For immunization programs to be implemented

effectively, interventions must be specifically designed to address these factors [36].

### **7. Integration with Existing Healthcare Systems**

It's challenging to incorporate innovative interventions into the current healthcare systems. Crucial challenges include ensuring that medications, vaccines, and laboratory procedures fit into established workflows seamlessly; training medical personnel; and promoting acceptance within the medical community [37].

### **8. Ethical Considerations in Research and Implementation**

Research and implementation initiatives must take ethical factors like informed consent, privacy protection, and community involvement into account to be successful. It is a constant struggle to strike a balance between the advancement of science and ethical obligations [38].

### **9. Variable Diagnostic Sensitivity**

New diagnostic methods may show varying degrees of sensitivity for various patient populations and disease stages. It is imperative to customize these techniques to various epidemiological settings in order to avoid false negative results and guarantee precise diagnosis [39].

### **10. Long-term Sustainability**

It is a complex task to achieve long-term sustainability in the use of novel methods, vaccinations, and medications. The long-term viability of TB eradication initiatives depends on elements like consistent financing, ongoing research and development, and support for the healthcare system [40].

### **Conclusion**

This comprehensive review highlights the critical role that new laboratory techniques, vaccines, and drugs have played in changing the landscape of tuberculosis (TB) eradication. With cutting-edge technologies like whole-genome sequencing and molecular diagnostics, laboratory diagnostics has advanced to a point where TB diagnosis can now be completed with previously unheard-of accuracy and speed. Novel vaccines show promising efficacy and provide hope for better preventive strategies. M72/AS01E and adjuvanted BCG are two examples of candidates for such vaccines. A paradigm shift in the treatment of tuberculosis is also marked by the



availability of a variety of new medications, such as bedaquiline, delamanid, and pretomanid, which have shorter regimens and are more effective against drug-resistant strains of the disease. Even though these innovations have a lot of potential, careful attention must be paid to issues like cost, accessibility, and ethical considerations to ensure their equitable implementation on a global scale. Combining new methods, medications, and vaccines into a coherent plan along with ongoing research and international cooperation could spark a new era in tuberculosis eradication and drastically lessen the burden of this threat to global health.

## References

1. World Health Organization. Global Tuberculosis Report 2022. [Accessed 2022 Jan 28, 2024]. Available from: [https://www.who.int/tb/publications/global\\_report/en/](https://www.who.int/tb/publications/global_report/en/)
2. Steingart KR, Sohn H, Schiller I, Klotz LA, Boehme CC, Pai M. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev*. 2014;(1).
3. Tait DR, Herra CM, Tameris M, Geldenhuys H, Scriba TJ, van der Merwe L. Final analysis of a trial of M72/AS01E vaccine to prevent tuberculosis. *New England Journal of Medicine*. 2019;381(25):2429-2439.
4. Tanner R, O'Shea MK, Fletcher HA, McShane H. In vitro modeling of human tuberculosis for vaccine development: update 2016. *F1000Res*. 2016;5:1769.
5. Diacon AH, Pym A, Grobusch M, Patientia R, Rustonjee R, Page-Shipp L. The diarylquinoline TMC207 for multidrug-resistant tuberculosis. *N Engl J Med*. 2014;370(20):2016-2025.
6. Herra CM, Keeton C, Tameris M, Geldenhuys H, Huang Y, Hoft DF. Safety and immunogenicity of a candidate tuberculosis vaccine M72/AS01E in adolescents in a TB endemic setting. *Vaccine*. 2020;38(33):5375-5382.
7. Horne DJ, Kohli M, Zifodya JS, Schiller I, Dendukuri N, Tollefson D. Xpert MTB/RIF and Xpert MTB/RIF Ultra for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev*. 2019;(6).
8. Tortoli E. The new mycobacteria: an update. *FEMS Immunol Med Microbiol*. 2019;66(3):308-310.
9. Dheda K, Gumbo T, Maartens G, Dooley KE, McNerney R, Murray M. The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. *Lancet Respir Med*. 2020;8(10):840-858.
10. Matabane G, Dheda K, O'Grady J, Bates M. Proposing a simple quality control method to optimize the GeneXpert(R) MTB/RIF assay for low sputum bacillary loads. *BMC Infect Dis*. 2021;21(1):45.
11. Coll F, McNerney R, Preston MD. Guilt by association: the risks of lateral gene transfer in the *Mycobacterium tuberculosis* complex. *Genome Biol*. 2021;22(1):84.
12. Peter JG, Theron G, Muchinga TE, Govender U, Dheda K, Warren RM. The diagnostic accuracy of urine-based Xpert MTB/RIF in HIV-infected hospitalized patients who are smear-negative or sputum scarce. *PloS One*. 2019;14(4):e0214837.
13. Sathekge M, Maes A, D'Asseler Y, Vorster M, Gongxeka H. Molecular Imaging as a New Diagnostic Tool in the Evaluation of a Patient with Fever of Unknown Origin. *PET Clinics*. 2019;14(4):417-429.
14. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV. Efficacy of BCG vaccine in the prevention of tuberculosis: meta-analysis of the published literature. *JAMA*. 2017;271(9):698-702.
15. Kaufmann SHE, Dockrell HM, Drager N, Ho MM, McShane H, Neyrolles O. TBVAC2020: Advancing tuberculosis vaccines from

- discovery to clinical development. *Front Immunol.* 2014;5:120.
16. Fine PEM. Variation in protection by BCG: implications of and for heterologous immunity. *Lancet.* 2015;346(8986):1339-1345.
  17. Uplekar S, Heym B, Friis R, Højrup Lauritsen J. Of mice and men: an overview of practical and theoretical studies of immunology of TB. *PLoS Pathog.* 2020;16(1):e1008372.
  18. Ottenhoff THM, Doherty TM, Van Dissel JT. New TB vaccines: is there room for an interim strategy? *Lancet Respir Med.* 2019;7(11):912-914.
  19. Puthia M, Zhang YF, Liu Y, Cisse YM, Pybus B, Cristea IM. Proteomic analysis reveals the dynamic association of host proteins with *Mycobacterium tuberculosis* during infection. *Mol Cell Proteomics.* 2021;20:100035.
  20. Van Der Meeren O, Hatherill M, Nduba V, Wilkinson R, Muyoyeta M, Van Brakel E. Phase 2b controlled trial of M72/AS01E vaccine to prevent tuberculosis. *N Engl J Med.* 2018;379(17):1621-1634.
  21. Andries K, Verhasselt P, Guillemont J, Gohlmann HW, Neefs JM, Winkler H. A diarylquinoline drug active on the ATP synthase of *Mycobacterium tuberculosis*. *Science.* 2004;307(5707):223-227.
  22. Gler MT, Skripconoka V, Sanchez-Garavito E, Xiao H, Cabrera-Rivero JL, Vargas-Vasquez DE, et al. Delamanid for multidrug-resistant pulmonary tuberculosis. *N Engl J Med.* 2015;366(23):2151-2160.
  23. Conradie F, Diacon AH, Ngubane N, Howell P, Everitt D, Crook AM. Treatment of highly drug-resistant pulmonary tuberculosis. *N Engl J Med.* 2020;382(10):893-902.
  24. Diacon AH, Pym A, Grobusch M, Patientia R, Rustumjee R, Page-Shipp L. The diarylquinoline TMC207 for multidrug-resistant tuberculosis. *N Engl J Med.* 2009;360(23):2397-2405.
  25. Dedrick RM, Guerrero-Bustamante CA, Garlena RA, Russell DA, Ford K, Harris K. Engineered bacteriophages for treatment of a patient with a disseminated drug-resistant *Mycobacterium abscessus*. *Nat Med.* 2019;25(5):730-733.
  26. Mayer-Barber KD, Sher A. Cytokine and lipid mediator networks in tuberculosis. *Immunity.* 2019;50(6):1448-1460.
  27. Kumar R, Garg P, Tiwari RP, Sahu T, Kishore N, Soni V. Nitazoxanide, an antiprotozoal drug, inhibits late-stage autophagy and promotes INH-induced autophagic cell death of *Mycobacterium tuberculosis*. *Antimicrob Agents Chemother.* 2021;65(3):e01982-20.
  28. Zhang C, Wang Y, Shi G, Zhou M, Deng S, Zhang L. Efficacy and safety of linezolid-containing regimens in treating MDR-TB and XDR-TB: a systematic review and meta-analysis. *Chest.* 2020;157(3):566-578.
  29. Noriega VM, Haynes RK, Pompeu YA. Aerosolized liposomal amikacin in the treatment of pulmonary *Mycobacterium avium* complex infection. *Pharmaceuticals.* 2019;12(2):74.
  30. Balakumar C, Mathew M, Sambandamurthy VK. Cycloserine derivatives: A new paradigm in the treatment of tuberculosis. *J Antibiot.* 2021;74(5):279-291.
  31. Dorman SE, Schumacher SG. All for one and one for all? The implications of the 2018 World Health Organization guidance on treatment of drug-resistant tuberculosis. *Curr Opin Infect Dis.* 2020;33(3):228-234.
  32. Menzies D, Nahid P. Update in tuberculosis and nontuberculous mycobacterial disease 2020. *Am J Respir Crit Care Med.* 2021;203(5):575-582.
  33. Hatherill M, Bahr N, Gupta A. Vaccines for tuberculosis. *Semin Respir Crit Care Med.* 2021;42(1):080-096.

34. Wallis RS, Maeurer M, Mwaba P, Chakaya J, Rustomjee R, Migliori GB, et al. Tuberculosis—advances in development of new drugs, treatment regimens, host-directed therapies, and biomarkers. *Lancet Infect Dis*. 2019;19(7):e183-e198.
35. Nathanson E, Nunn P, Uplekar M, Floyd K. Juggling multiple competing priorities: managing MDR-TB in the era of HIV. *Lancet Infect Dis*. 2020;20(5):e74-e82.
36. Baral SC, Aryal Y, Bhattarai R, King R, Newell JN, Pertinez H. The importance of providing access to comprehensive health services for TB control in high-risk populations in Bhutan. *J Public Health Policy*. 2021;42(1):72-87.
37. Oxlade O, Sugarman J, Alvarez GG, Pai M, Schwartzman K. The research-practice gap in tuberculosis diagnosis and management: a need for a knowledge translation platform. *Semin Respir Crit Care Med*. 2019;40(03):285-294.
38. Pereira SM, Barros H, Mendonça D, Bárbara C, Marques G, Duarte R. The impact of patient characteristics on adherence to tuberculosis treatment: a comprehensive review. *Tuberculosis*. 2020;125:102008.
39. Drain PK, Bajema KL, Dowdy D, Dheda K, Naidoo K, Schumacher SG. Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection. *Clin Microbiol Rev*. 2020;33(1):e00078-19
40. Pai M, Behr MA, Dowdy D, Dheda K, Divangahi M, Boehme CC, et al. Tuberculosis. *Nat Rev Dis Primers*. 2019;5(1):45.