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Beyond the BCG vaccine: Novel approaches to tuberculosis prevention and control in Africa

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ABSTRACT

Tuberculosis (TB) continues to be a predominant cause of illness and death across Africa, intensified by HIV co-infection, poverty, and weak health systems. The Bacillus Calmette-Guérin (BCG) vaccination has traditionally reduced severe pediatric TB, although its restricted effectiveness against adult pulmonary TB and diminishing immunity highlight the need for novel techniques. This study examines innovative strategies for TB prevention and control beyond the BCG vaccination, specifically within African settings. A thorough narrative review was performed using peer-reviewed literature from sources such as PubMed, Google Scholar, and EBSCOhost. The study consolidates results on TB vaccine development, diagnostic advancements, treatment protocols, and comprehensive public health measures. Novel vaccine candidates, including M72/AS01E and VPM1002, have potential in augmenting immunity and alleviating the TB burden. Innovations in diagnostics, such as GeneXpert, point-of-care instruments, and AI-enhanced screening, are enhancing early detection. Concise preventative regimes (e.g., 3 HP, 1 HP), innovative pharmacological combinations (e.g., BPaL), and community-oriented care models are revolutionizing treatment results. Socio-economic approaches, One Health (OH) frameworks, and digital monitoring technologies enhance TB control initiatives. This review adopts a systems-based framework, integrating biomedical, diagnostic, therapeutic, socio-economic, and OH strategies to evaluate TB prevention and control beyond BCG in African settings. By situating biomedical innovations within broader health system and societal contexts, the review highlights how TB control requires multi-layered approaches rather than reliance on a single intervention. Advancing beyond BCG requires a comprehensive strategy that incorporates biomedical innovation, enhancement of health systems, and interdisciplinary cooperation. The results advocate for policy change, investment in African-led research, and equal access to innovative TB technologies to attain sustained control and ultimate eradication.

Keywords: Africa, BCG vaccine, Diagnostics, One health, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a major infectious cause of death worldwide, with Africa being disproportionately affected by the overall burden.[1] The World Health Organization (WHO) reported that Africa accounts for approximately 25% of global TB cases,[2,3], with countries such as South Africa, Nigeria, and the Democratic Republic of the Congo exhibiting a relatively high prevalence of the disease.[4] The HIV epidemic, pervasive poverty, malnutrition, and inadequately supported healthcare systems exacerbate the morbidity and mortality rates of TB. In addition to its health implications, TB significantly affects the economy by reducing productivity, exacerbating poverty, and hindering sustainable development in numerous African nations.[5,6]

The Bacillus Calmette-Guérin (BCG) vaccine has played an important role in preventing TB for more than a century.[5,7]

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BCG is primarily administered to infants to prevent severe manifestations of pediatric TB, including miliary and meningeal TB.[8] However, its efficacy against pulmonary tuberculosis in adolescents and adults, the predominant and most transmissible type of the disease, remains markedly inconsistent.[9] This disparity arises from genetic variations among populations, environmental exposure to *Mycobacterium spp.,* and a decline in immunity with time.[10] Additionally, BCG does not inhibit the reactivation of latent TB infection; hence, it perpetuates transmission cycles in high-burden settings.[11] While BCG provides strong protection against severe pediatric TB forms such as miliary and meningeal disease, its efficacy against adult pulmonary TB, the predominant and most transmissible form, remains inconsistent, ranging from 0-50% depending on population and setting.[12,13] This review therefore emphasizes adult pulmonary TB outcomes, aligning the stated objective with age-specific evidence. In 2022, Africa reported an estimated TB incidence of 212 per 100,000 population, with South Africa (468/100,000), Nigeria (219/100,000), and the Democratic Republic of Congo (321/100,000) among the highest contributors.[14] Collectively, these countries account for nearly half of Africa's TB burden, underscoring the scale of the challenge. The aforementioned limits indicate that exclusive reliance on BCG is insufficient for controlling TB in Africa, where the disease proliferates rapidly in areas with fragile health systems, overcrowded living conditions, and restricted access to excellent healthcare. Owing to these issues, there is an urgent need to explore alternative preventive measures and treatments that exceed the limitations of current immunizations.

This narrative review seeks to critically evaluate novel strategies for the prevention and management of TB in African contexts. This study aims to comprehensively evaluate new strategies for the management and prevention of TB in Africa.

METHODS

Study design

This study was conducted as a structured narrative review to synthesize evidence on TB prevention and control strategies beyond the BCG vaccine in African contexts. The approach combined narrative synthesis with systematic transparency to enhance reproducibility.

Sources of evidence

Peer-reviewed journal articles, global health reports, and case-based evidence published between 2005 and 2025 were considered. Databases searched included PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, along with official reports from the WHO, Centers for Disease Control and Prevention, Global Fund, and national TB programs in Africa.

Search strategy

Keywords and MeSH terms were combined using Boolean operators (AND/OR). Search strings included: "Tuberculosis" OR "TB," "BCG vaccine" OR "BCG efficacy," "novel TB vaccines" OR "M72/AS01E" OR "VPM1002," "diagnostics" OR "GeneXpert" OR "AI screening" OR "LAM test," "preventive therapy" OR "3HP" OR "1HP," "drug-resistant TB" OR "BPaL regimen" OR "BPaLM," "community-based TB care" OR "digital adherence," "One Health" OR "zoonotic tuberculosis," and "Africa" OR "sub-Saharan Africa."

Eligibility criteria

Inclusion

- Studies focusing on TB prevention, diagnosis, or treatment in African populations and relevant studies from low- and middle-income countries (LMICs).
- Reports on vaccine candidates, diagnostic innovations, or therapeutic regimens.
- Policy, socio-economic, or OH interventions relevant to TB control.

Exclusion

- Non-English publications.
- Studies outside the 2005-2025 time frame.
- Articles lacking relevance to TB in African contexts.

Data extraction

Key data extracted included

- Vaccine candidate characteristics, trial phases, and efficacy outcomes.
- Diagnostic innovations and performance metrics (sensitivity, specificity, turnaround time).
- Preventive and therapeutic regimens, adherence rates, and WHO recommendation status.
- Socio-economic and health system interventions (nutrition, housing, digital tools).
- One Health approaches and zoonotic TB burden estimates.

Data synthesis

Findings were synthesized thematically into five domains: (i) biomedical innovations, (ii) diagnostic advancements, (iii) therapeutic regimens, (iv) socio-economic/structural interventions, and (v) OH frameworks. Contradictions and uncertainties across studies were highlighted, and African-specific constraints (e.g., HIV prevalence, health system fragility, resource limitations) were integrated into the analysis. Where available, quantitative estimates (incidence, prevalence, efficacy percentages, completion rates, cost-effectiveness ratios) were incorporated to strengthen analytical depth.

The shortcomings of the BCG vaccine

BCG vaccine, which was first made available in 1921, is still the only vaccine that is approved for use against TB. However, even though it has been important in the past, its effectiveness varies greatly across age groups, populations, and geographic areas. Studies have shown strong protection against severe pediatric forms of TB, such as miliary and meningeal disease, but limited or inconsistent efficacy against pulmonary TB in adults, the most common and transmissible form of the disease.[15,16] Several factors, including host genetics, exposure to environmental mycobacteria, and regional differences in immune priming, influence this variable efficacy. The reported efficacy of BCG varies widely: approximately 60-80% protection against severe pediatric TB, but only 0-50% against adult pulmonary TB, depending on geography and population.[13,17] This variability highlights the need for age-specific interpretation and underscores the limited utility of BCG in reducing adult transmission.

The masking and blocking hypotheses suggest that previous exposure to environmental mycobacteria may diminish the immune response elicited by BCG, a phenomenon observed in tropical regions of Africa.[18] Another major problem is that immunity does not last long; it starts to fade after 10-15 years, leaving most teens and adults unprotected.[19] Since BCG is given mostly at birth, this decline in long-term protection undermines its ability to reduce transmission in adult populations. Furthermore, the ineffectiveness of BCG against pulmonary TB in adults is a significant limitation. Clinical trials conducted in Africa and Asia have consistently indicated negligible protection among adults.[20] Attempts at re-vaccination have not significantly increased immunity, with a New England Journal of Medicine trial showing no major protective effect of BCG revaccination against M. tuberculosis infection [Table 1].[20]

Novel TB vaccine candidates

M72/AS01E vaccine: *Promising results from clinical trials and potential for widespread use.*

In one trial of the M72/AS01E-4 vaccine in people living with HIV, a two-dose regimen of the M72/AS01E-4 vaccine, which was administered 1 month apart, was well tolerated, with an acceptable safety profile, and was immunogenic in antiretroviral-treated participants aged 16-35 years with well-controlled HIV. The M72/AS01E-4 vaccine reactogenicity profile, as assessed by solicited adverse events, was consistent with previous M72 trials in people living with or without HIV, including the phase 2b efficacy trial of 3500 adults without HIV. In summary, a two-dose regimen of the M72/AS01E-4 vaccine, which was administered 1 month apart, was well tolerated, had an acceptable safety profile, and was immunogenic in virally suppressed, ART-treated people living with HIV aged 16-35 years. The timely completion of this trial supported the decision to include a larger number of people living with HIV in the M72/AS01E-4 global registration phase 3 trial.[21]

In another trial, it was found that the M72/AS01E scenarios could avert approximately 12.7 (11.0-14.6) million cases and 2.0 (1.8-2.4) million deaths, and the BCG re vaccination scenarios could avert approximately 9.0 (7.8-10.4) million cases and 1.5 (1.3-1.8) million deaths among the 72.2 (63.3-79.7) million cases and 13.8 (6.1-13.2) million deaths predicted by the Status Quo baseline between 2025 and 2050. Although modeling studies from India suggest that M72/AS01E vaccination could avert millions of TB cases, extrapolation to African contexts requires caution. The epidemiological landscape in Africa is characterized by high HIV prevalence, diverse genetic backgrounds, and fragile health systems, all of which may influence vaccine performance. Current evidence is limited to phase IIb data in HIV-negative adults, with Africa-specific phase III trials only now underway in South Africa and other sub-Saharan countries.[22] Similarly, VPM1002 has demonstrated safety and immunogenicity in African neonates, including HIV-exposed infants, but adult efficacy data remain inconclusive.[23] Therefore, while these candidates are promising, definitive conclusions about their capacity to substantially reduce TB burden in Africa await region-specific phase III outcomes.

Table 1: Summary of BCG vaccine limitations in selected African regions

S/N	Region	Observed Limitation	Supporting Evidence	References
1	Southern Africa	Poor adult protection, waning immunity	Despite the presence of neonatal BCG, adult pulmonary TB rates remain high in Southern Africa.	[14,15]
2	East Africa (Malawi)	No benefit from revaccination	Revaccination trial found no significant protection.	[20]
3	West Africa (Nigeria, Ghana)	Environmental interference from mycobacteria.	High exposure may reduce vaccine “take”.	[18]
4	Central Africa	Spatial heterogeneity in efficacy	Environmental and host factors influence outcomes.	[14]

TB: Tuberculosis, BCG: The Bacillus Calmette-Guérin

The cost-effectiveness ratios for the base case M72/AS01E scenario were approximately seven times higher than those for the base case BCG revaccination scenario, but regardless of the realized product characteristics, nearly all vaccine characteristics and coverage scenarios were cost-effective at the most conservative country-level threshold compared to the new vaccine baseline. The average annual cost of M72/AS01E vaccination was four times greater than that of BCG revaccination. Introducing the vaccine could lead to an annual incremental program cost of US$190 million for M72/AS01E and US$23 million for BCG revaccination, accounting for vaccination costs as well as savings in diagnostic and treatment costs. Our modeling demonstrated a 40% greater health impact from M72/AS01E than from BCG revaccination. The difference in impact was due to assumptions about vaccine characteristics and delivery. On the basis of clinical trial data and expert opinions, we assumed that the base case, the M72/AS01E vaccine, would prevent disease and be efficacious in everyone without active disease at vaccination. M72/AS01E and BCG revaccination may substantially reduce the TB burden in India over future decades and would be cost-effective regardless of the assumed product characteristics. Using clinical trial data to assess vaccine characteristics, researchers identified variability in the vaccine profile as a significant source of uncertainty.[24,25]

VPM1002: *A genetically modified BCG with improved safety and efficacy.*

One study showed that VPM1002 was less likely to cause reactions than the BCG vaccine. Both vaccines were able to make the body immune, but the immune responses caused by BCG were stronger than those caused by VPM1002 starting at week six. This study revealed the non-inferiority of VPM1002 to the BCG vaccine in terms of the incidence of grade 3 or higher local adverse reactions or vaccine-related ipsilateral or generalized lymphadenopathy of 10 mm or greater. This finding is important because of the difference in the local percentage of multifunctional CD4+ T cells (95% CI), p-value, and percentage of multifunctional CD8+ T cells (95% CI), p-value. The statistical analysis demonstrated a substantial improvement in the functionality of both CD4+ and CD8+ T cells within the VPM1002 group. These findings indicate that VPM1002 not only aligns with the safety profile of the BCG vaccine but also has the potential to generate a more vigorous immune response, necessitating further exploration of its clinical applications. BCG VPM1002 Day 0: $n=37$. VPM1002 and BCG elicited similar immunological responses in both HIV-unexposed and HIV-exposed infants, as assessed by variations in IFNγ concentrations in whole blood assays and cytokine expression in CD4+ and CD8+ T cells.[26,27]

Other vaccine candidates in development: *Current pipeline of TB vaccines.*

There are currently 19 types of new TB vaccines in different stages of clinical trials. Four are in phase I (AdHu5Ag85A, GX-70, TB/FLU-01 L, and TB/FLU-04 L), three are in phase IIa (ID93+GLA-SE, AEC/BC02, and ChAdOx1.85A), five are in phase IIb (RUTI, DAR-901, H56:IC31, H4:IC31, and MVA85A), and five are in phase III (MIP, SRL172, MTBVAC, VPM1002, and M72/AS01E). While advancements have occurred in the investigation of novel TB vaccines, the integration of innovative technologies has introduced new avenues for research, including the use of mRNA vaccines and deep learning methodologies. Despite the numerous challenges facing the field of TB vaccine development, including economic, policy, and social constraints, it is essential to recognize that the development of novel TB vaccines is a public health endeavor that promotes the well-being of humanity. Governments and international organizations should provide robust support and actively promote international collaboration and exchange in this endeavor.[28] Future TB vaccine adoption in Africa should be guided by a structured decision framework that balances evidence strength, feasibility in HIV-endemic contexts, and equity of access. Comparative analysis highlights distinct profiles: M72/AS01E targets adolescents and adults with latent TB infection, demonstrating robust T-cell responses but with unresolved questions regarding durability and generalizability beyond trial populations.[22] VPM1002, a recombinant BCG, shows a favorable safety profile and potential for neonatal use, including HIV-exposed infants, but its adult efficacy remains uncertain.[23] Kaufmann *et al.* emphasize that African health systems must weigh these differences against infrastructural realities, cost-effectiveness, and integration into existing immunization platforms.[29] Such a framework ensures that vaccine adoption is evidence-based, context-appropriate, and equitable [Table 2].[30-34]

Table 2: Comparison of emerging TB vaccines and their trial outcomes.

S/N	Vaccine	The latest phase of clinical trials is underway	Outcomes of the earlier phases	References
1	M72/AS01E	III	Phase I: The LTBI population vaccinated with M72/AS01E can prevent latent infections from developing into TB; the vaccine efficacy in the 36th month was 49.7%; Phase II: M72/AS01E induced strong T-cell and antibody responses, including NK cells and IFN-generation.	[22,30]

(Contd...)

Table 2: *(Continued)*

2	Gam TBvac	III	Phase I: Different doses of vaccines were evaluated for immunogenicity, with a half dose (0.5 mL) having the best effect; Phase II: The vaccine is well-tolerated and induces specific and persistent Th1 and humoral immunity responses.	[31,32]
3	VPM 1002	III	Phase I: VPM1002 has safety and immunogenicity in response to B and T cells; Phase II: Inoculation with VPM1002 can induce multifunctional CD4+ and CD8+ T cells, and it is safe for both HIV-exposed and HIV-unexposed infants. Both VPM1002 and BCG are immunogenic, but from the 6th week onward, the intensity of the immune response is primarily induced by BCG. The effectiveness of BCG surpasses that of VPM1002.	[33-34]

LTBI: Latent tuberculosis infection, NK: Natural killer (cells), IFN: Interferon (commonly IFN-γ = Interferon gamma), BCG: Bacillus Calmette-Guérin (vaccine).

Improvements in TB diagnosis and early detection

Early detection of TB is essential to prevent its spread and reduce mortality, particularly in high-burden regions of Africa.[35] Conventional diagnostic methods, such as sputum smear microscopy, are cost-effective; however, they exhibit limited efficacy and frequently overlook numerous cases, particularly individuals with HIV and pediatric patients.[36,37] Recent technological advancements have greatly improved the speed and accuracy of testing, which has led to new ways to manage The GeneXpert Mycobacterium tuberculosis/rifampicin resistance (MTB/RIF) assay is a highly useful diagnostic tool that can detect M. tuberculosis and rifampicin resistance within two hours using molecular techniques.[38,39] In several African countries, it has reduced the time required to obtain test results and initiate treatment.[40] However, the high cost of equipment, the need for regular maintenance, and the need for a reliable power supply have made it difficult for people in areas with few resources to access them.

Researchers are developing cost-effective, portable, and user-friendly point-of-care diagnostics to address these issues in rural and remote regions.[41] Lateral flow urine lipoarabinomannan (LAM) tests have demonstrated efficacy in HIV-positive patients with advanced disease, in which traditional sputum-based testing is less dependable.[42] Emerging technologies include the utilization of artificial intelligence (AI) and digital health platforms to enhance TB screening. AI-enhanced interpretation of chest X-rays and mobile applications for contact tracing are improving surveillance and broadening diagnostic capabilities.[43,44] These enhancements represent significant advancements in ensuring prompt TB diagnosis for all individuals. To reduce diagnostic delays and enhance TB control in African nations, ensuring the equitable utilization of these devices is crucial. Despite encouraging advances, AI-based TB screening is constrained by several limitations. False positives remain common, particularly in populations with a high prevalence of non-TB lung disease. Algorithmic bias is a concern when models are trained predominantly on non-African datasets, potentially reducing accuracy in local contexts. Regulatory uncertainty regarding clinical validation and integration into national TB programs further complicates adoption.[45] These challenges underscore the need for rigorous African-specific validation before large-scale deployment [Figure 1].

Preventive therapy and treatment innovations

The problems with BCG indicate that more preventive and therapeutic measures are needed. Recent advances include shorter regimens for latent TB infection, new drug combinations, and community-based care models. Low adherence has long been a problem with traditional preventive therapy (6-9 months of isoniazid monotherapy). The 3 HP regimen (once weekly isoniazid + rifapentine for 3 months) has the same effectiveness and higher completion rates, especially among HIV-positive individuals.[46] The 1 HP regimen (one month of daily isoniazid + rifapentine) also showed similar effectiveness and better adherence.[47] These shorter, safer regimens are critical for large-scale preventive therapy programs in Africa.

New drug combinations for active TB, such as innovative multidrug regimens, such as BPaL (bedaquiline, pretomanid, linezolid) and BPaLM (adding moxifloxacin), have revolutionized the treatment of drug-resistant TB. The BPaL regimen has achieved approximately 90% favorable outcomes in clinical trials and has proven cost-effective in South African modeling studies.[48] The reduced linezolid doses in the ZeNIX trial further minimized adverse effects. However, vigilance is necessary to prevent the emergence of resistance.[49,50] Similarly, while the BPaL regimen has demonstrated ~90% success in controlled trials, real-world rollout in Africa has been hindered by linezolid-associated toxicity, including peripheral neuropathy and myelosuppression, as well

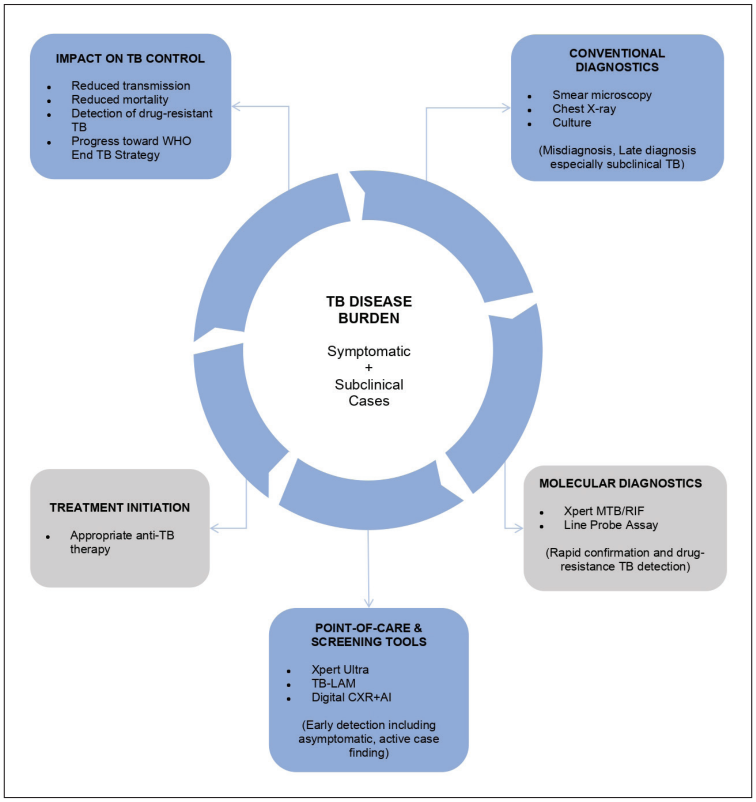

Figure 1: Flowchart of diagnostic advancements and their impact on TB control. TB: Tuberculosis, WHO: World Health Organization, MTB/RIF: *Mycobacterium tuberculosis*/Rifampicin resistance (MTB/RIF) assay, TB-LAM: Tuberculosis lipoarabinomannan.

as emerging resistance.[51,52] Limited pharmacovigilance infrastructure and constrained laboratory capacity exacerbate these risks. Thus, although BPaL represents a major advance in MDR/XDR-TB therapy, its implementation in resource-limited African settings requires careful monitoring, dose optimization, and strengthened safety surveillance.

Treatment in community-decentralized, community-led TB care models improves access and adherence. Interventions such as home-based DOT, digital adherence technologies (e.g., SMS reminders, video DOT), and the integration of TB services within primary and HIV care platforms have improved outcomes in multiple African contexts.[53] [Table 3].

Table 3: Innovative treatment and preventive regimens

S/N	Regimen /Model	Target Population	Outcome	Challenges	References
1	3 HP	Latent TB (including HIV positive)	High completion, good efficacy.	Drug interactions, scale-up.	[46]
2	1HP	Latent TB (HIV positive)	Comparable efficacy, better adherence.	There is a scarcity of data on HIV-negative individuals.	[47]
3	BPaL	MDR/XDR TB	≈ 90% success, cost-effective.	Linezolid is known for its toxicity and, resistance.	[48,50]
4	BPaLM	MDR/pre-XDR TB	Under evaluation.	The evaluation is focused on safety and regulatory issues.	[49]
5	Community -based care	All TB patients	Improved access, retention.	Lack of proper supervision and quality control.	[53]

TB: Tuberculosis, HIV: Human immunodeficiency virus, MDR: Multidrug-resistant (tuberculosis), XDR: Extensively drug-resistant (tuberculosis), HP: Isoniazid plus Rifapentine preventive therapy regimen, 3HP: Once-weekly isoniazid + rifapentine for 3 months, 1HP: Daily isoniazid + rifapentine for 1 month, BPaL: Bedaquiline, Pretomanid, and Linezolid regimen, BPaLM: Bedaquiline, Pretomanid, Linezolid, and Moxifloxacin regimen.

Socio-economic and structural methodologies

Controlling TB effectively requires more than just medical tools. It is important for all African countries to address social determinants, gaps in the health system, and long-term policy frameworks. Poverty, malnutrition, overcrowding, and poor housing conditions constitute some of the factors that perpetuate high TB vulnerability. Malnutrition and food insecurity weaken host immunity and increase the likelihood of disease progression.[54] Settlements that are too crowded cause diseases to spread through the air faster. Socio-economic interventions, cash transfers, nutritional assistance, and housing improvements have proven effective in lowering the risk of TB and improving treatment adherence.[55]

To meet TB control goals, African health systems need better infrastructure, diagnostics (such as GeneXpert), supply chains, and people.[56] Integrating TB care with HIV and primary-care services improves efficiency and continuity. Digital tools and e-health registries can strengthen surveillance and accountability. Achieving the End TB targets depends on political commitment and sustainable financing. Governments must prioritize domestic funding for TB research, training, and drug procurement while leveraging support from partners such as the Global Fund and WHO.[57] To determine what causes TB, policies that encourage public-private partnerships (PPPs) and cooperation between different areas of housing, nutrition, and education are needed [Figure 2].

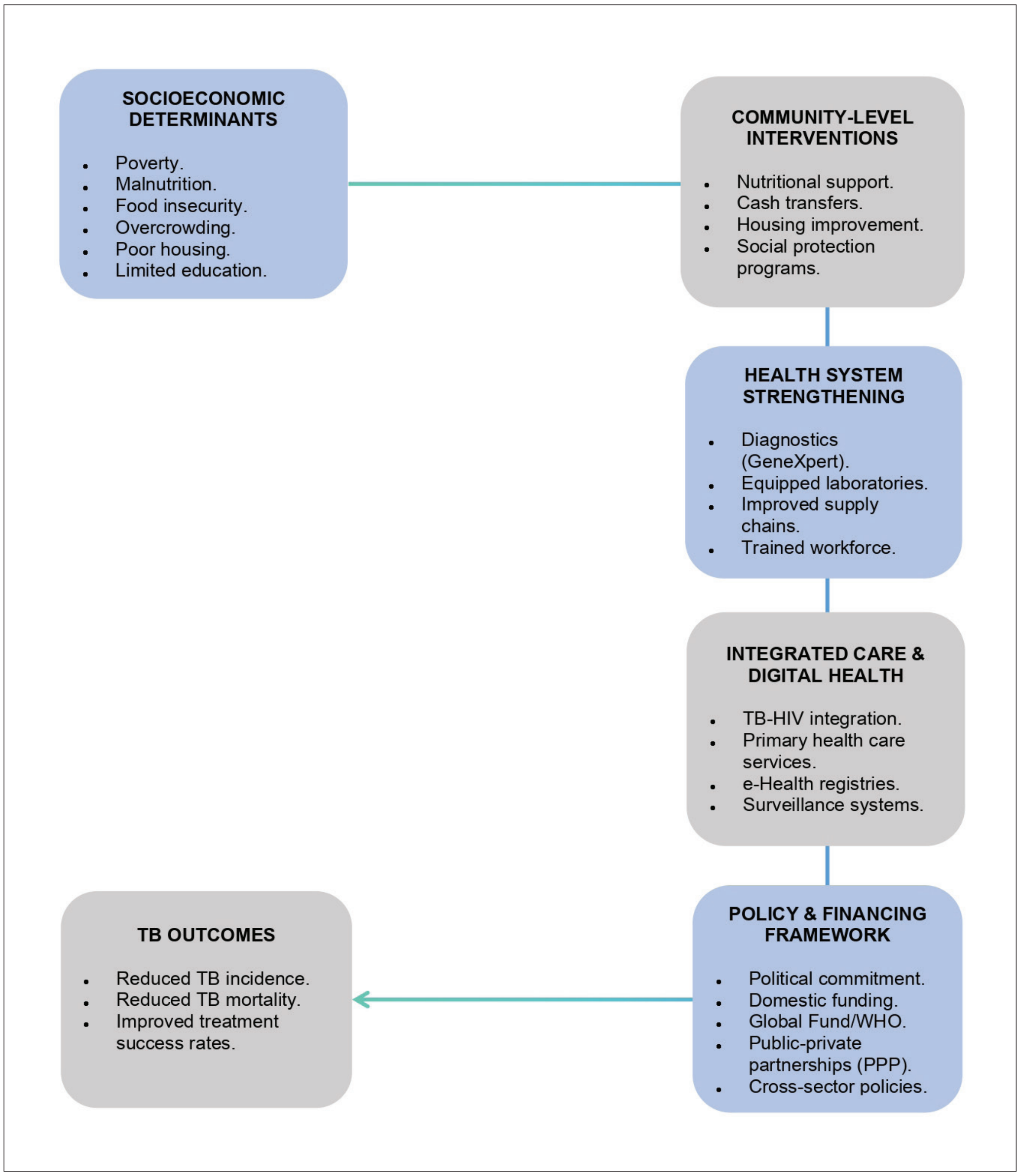

Figure 2: The impact of social factors on TB outcomes. TB: Tuberculosis, WHO: World Health Organization.

One health and holistic approaches

OH is a broad, cross-disciplinary approach to public health that recognizes the health issues that affect people, animals, and ecosystems and promotes cooperation between the fields of human, animal, and environmental health.[58] In Africa, effective TB control necessitates strategies that extend beyond human health, acknowledging its significant connections with animals and the environment. Zoonotic TB, which is caused mainly by *Mycobacterium bovis*, is a major public health concern at the human-animal interface in West Africa.[59] M. tuberculosis is the bacterium that causes most cases of human TB. Zoonotic TB, on the other hand, shows how human, animal, and environmental health are linked.[59] Zoonotic TB caused by *Mycobacterium bovis* contributes a minority of human TB cases in Africa, with prevalence estimates generally ranging from 1-2% depending on region and diagnostic methodology.[60,61] While this burden is non-negligible in pastoralists and cattle-farming communities, it remains small compared to the overwhelming dominance of *M. TB*. Consequently, OH approaches should be framed as context-specific adjuncts that strengthen surveillance and control in high-risk populations, rather than as central pillars of TB control strategies continent-wide. This re-framing ensures proportional allocation of resources while acknowledging the importance of integrated human-animal-environmental health interventions. The OH framework emphasizes this interconnection, stating that zoonotic TB affects all three sectors simultaneously.[62] Epidemiologists, veterinarians, ecologists, and public health officials must collaborate to identify disease hotspots and implement targeted interventions.[63] Such integrated collaboration enhances surveillance, promotes data sharing, and increases collective preparedness for zoonotic threats.

TB is still most common in 30 countries with a high burden, and it affects more people who are at risk, such as refugees and migrants. This is because they have less access to healthcare and live in bad conditions.[64] The National OH Strategic Plan for Rwanda is an example of working together across borders and sectors. It brings together the Ministries of Health, Agriculture, and Environment to improve surveillance and emergency response.[63] This partnership has raised awareness in the community and lowered the spread of zoonotic diseases such as rabies and brucellosis. This shows how combining policy-driven initiatives can strengthen TB control efforts.

To make OH work, we need new technologies and rules. Digital health tools, such as electronic surveillance systems and mobile health (mHealth) apps, are changing the way TB services are provided and monitored.[65,66] DOT is still the most common way to ensure that patients stick to their treatment, but video-observed therapy and digital adherence technologies make it even easier for patients to stay in touch and follow up.[67] These actions show how technology, coordinated policies, and cross-sectoral collaboration can all work together to lower the spread of TB and improve health outcomes in Africa.

The framework shows how health systems for people, animals, and the environment work together to stop and control TB. It emphasizes the importance of collaboration and information sharing among health ministries, veterinary services, and environmental sectors. This is all about integrated surveillance, which is made possible by digital health platforms. It guides joint responses, policy harmonization, and community involvement to achieve long-term TB control [Figure 3].

Implications for clinical and public health

To turn TB research into real-world action, we need strong clinical and public health systems supported by good surveillance and response systems. Surveillance systems are very important in the OH framework because they help keep track of disease trends, find cases early, and ensure that data are always available for making smart decisions to lessen the effects of zoonotic outbreaks.[65] These systems produce essential data that inform strategic measures designed to safeguard at-risk human and animal populations. An efficient early warning system must deliver prompt, precise, and sensitive data capable of identifying anomalous patterns in human, animal, or environmental health occurrences, thereby facilitating swift epidemiological response and containment strategies.[68]

TB remains a significant global public health issue, prompting its inclusion in the Sustainable Development Goals (SDGs) for eradication by 2030.[69] Nigeria has the sixth-highest number of people with TB in the world and the highest number in Africa. It is still a major focus for disease control.[69,70] The National Tuberculosis Program (NTP) and its partners have worked hard, but there is still a large difference between the number of TB cases reported and the number that actually occur in the country. In 2020, there were an estimated 9.9 million cases of TB worldwide, but only 5.8 million cases were reported. Nigeria is a major part of this problem.[69,71] These gaps are caused by poor diagnosis, weak reporting systems, and insufficient access to care.

New and creative ways to solve these problems have been developed. KNCV Nigeria has rolled out the TB-LAMP diagnostic tool and made changes to the Early Warning Outbreak Recognition System to make it easier for people in the community to find case.[69,72,73]. Strengthening laboratory networks, making GeneXpert analyzers more widely available, and ensuring that people can access important diagnostic tools are still top priorities. Similarly, strategies that improve health education, use

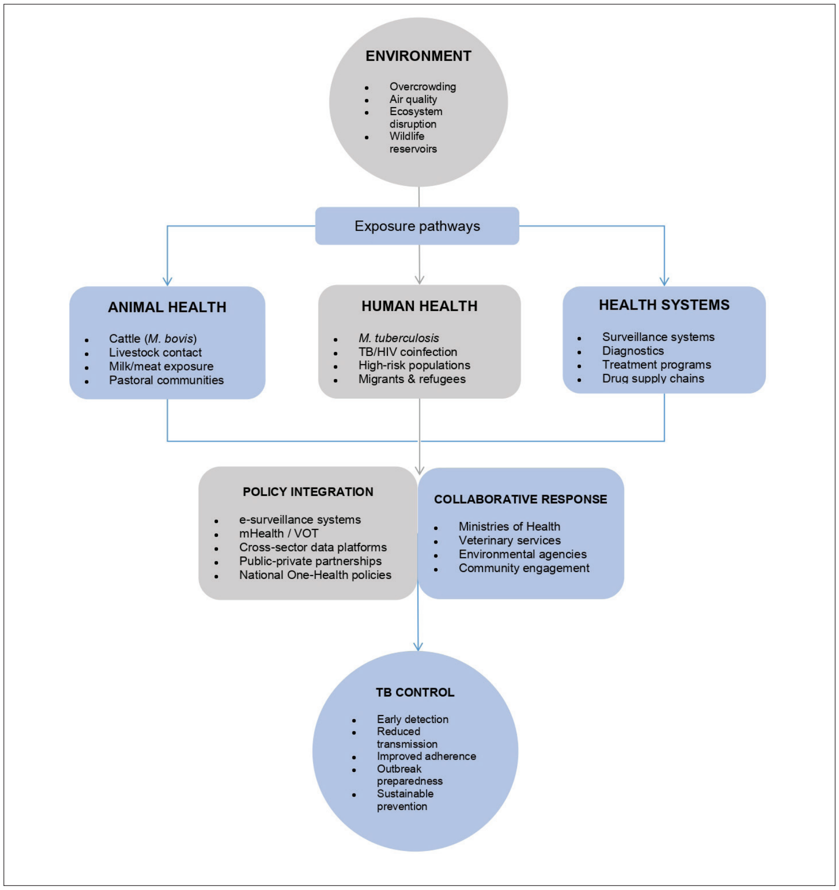

Figure 3: Conceptual framework for One Health in TB prevention and control.

social and local media to spread the word, and involve community leaders in advocacy are essential. Policy changes need to ensure that national TB strategies are in line with global goals by making funding better, encouraging PPPs, and addressing social factors such as poor nutrition and access to healthcare. The inclusion of gender-sensitive approaches will help close care gaps even more and bring us closer to ending TB by 2030 [Table 4].

Table 4: A list of successful public health programs.

S/N	Intervention Area	Key Actions	Expected Outcomes	References
1	Surveillance Systems.	Real-time data collection, cross-sector integration.	Identifying challenges early and maintaining a watch on trends.	[68]
2	Early Warning and Intervention.	Make EWORS better and look into outbreaks promptly.	Rapidly halting TB outbreaks.	[69]
3	Networks for Diagnostics and Laboratories.	Expand GeneXpert and TB-LAMP use.	Improved diagnostic accuracy and reporting.	[70]
4	Community Engagement.	Leverage media and local leaders for TB awareness.	Increased case detection and treatment adherence.	[71]
5	Policy and Partnerships.	Align NTP with Sustainable Development Goal (SDG) 3, expand public-private collaboration.	Sustainable TB control and reduced treatment gaps.	[72]
6	Socio-economic Support.	Address undernutrition, expand health insurance access.	Enhanced prevention and equitable TB care.	[73]

TB: Tuberculosis, EWORS: Early warning outbreak recognition system, LAMP: Loop-mediated Isothermal amplification, NTP: National tuberculosis program.

Challenges in research and future prospects

Despite considerable progress in TB research, challenges remain that impede the eradication and management of the disease in African countries.[74] A notable deficiency is the absence of adequate long-term evidence regarding new vaccine candidates.[16] Even though clinical trials with M72/AS01E and VPM1002 show promise, there are still concerns about how well they will work in the long run, how well they will work in different African populations, and how easy they will be to use in places with few resources.[22] Current research is often limited by its limited scope and geographic range, hindering the generalization of findings to regions with diverse epidemiological and genetic characteristics.[75]

The subsequent challenges pertain to the factors that complicate execution, such as political instability, inadequate healthcare institutions, and disrupted supply chains, which persist in complicating the prevention and treatment of TB.[76,77] Despite the availability of novel tests and treatments, accessibility remains limited owing to prohibitive costs, insufficient laboratory facilities, and the challenges associated with traveling to remote or difficult-to-reach locations.[77-79] Health disparities resulting from poverty, malnutrition, and HIV co-infection hinder TB control initiatives and foster conditions conducive to continuous transmission.[80]

Money problems also make it harder for people to get ahead in life. Research on TB does not yield enough money compared with the number of people who have the disease around the world, and most of the money is allocated to rich countries.[81] This difference makes it harder for Africa to lead in innovation, makes it take longer to test new medicines in local settings, and keeps people dependent on research goals set by others. Additionally, regulatory hurdles and slow policy implementation may lead to delays in the integration of innovative technologies from clinical trials into the national program.[81]

Moving forward, we need a clear plan for our research. Our top priorities should be to conduct large, multi-center vaccine trials among African populations, look at long-term effects, and add new vaccines to current immunization schedules. Research must concentrate on abbreviated and safer preventive protocols, innovative treatment combinations for multi-drug-resistant TB, and the integration of digital health tools into standard surveillance practice.[82] Improving implementation research will be crucial for converting insights into practice, especially in rural areas and settings with limited resources.[83,84] We need to ensure that people from different fields work together in the end. The OH Initiative focuses on the health of people, animals, and the environment. This approach offers ways to address zoonotic reservoirs and the spread of TB across borders.[85] Policymakers, researchers, and communities must collaboratively formulate policies that reconcile innovation with accessibility, ensuring that scientific progress provides equitable benefits for the African population.[86]

To solve problems with TB research in Africa, we need long-term funding, political will, and new ways of doing things that fit the situation. Africa can eliminate TB as a public health threat and surpass the limitations of the BCG vaccine through collaborative efforts [Figure 4].

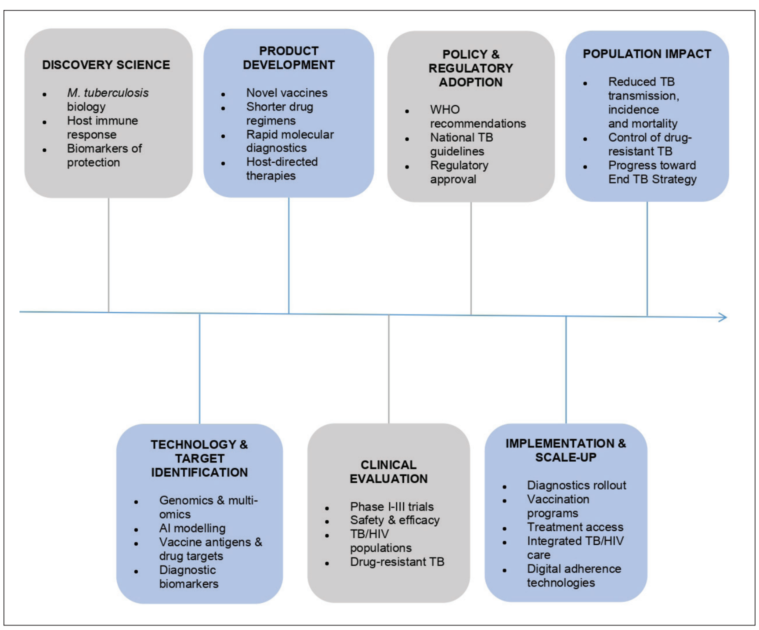

Figure 4: Research and innovation road-map for TB elimination

CONCLUSION

TB continues to pose a significant public health concern across Africa, exacerbated by socio-economic inequalities, vulnerable health systems, and elevated rates of HIV co-infection. The BCG vaccination has traditionally contributed to the reduction of severe pediatric TB; nevertheless, its limited effectiveness against adult pulmonary TB and diminishing immunity over time highlight the pressing need for more comprehensive and effective measures. This assessment underscores the essential need to transcend BCG and adopt a comprehensive strategy for TB prevention and control.

Novel vaccine candidates, including M72/AS01E and VPM1002, provide intriguing alternatives, exhibiting enhanced immunogenicity and safety characteristics in clinical studies. Their incorporation into national immunization programs requires meticulous evaluation of cost-effectiveness, delivery logistics, and population-specific efficacy. Innovations in diagnostics, especially molecular technologies like GeneXpert and AI-augmented screening, are transforming early detection; yet, achieving equal access continues to be a problem in resource-constrained environments.

Novel treatment procedures, such as abbreviated preventative therapy and multi-drug-resistant TB regimens like BPaL and BPaLM, are enhancing adherence and clinical results. Community-based care approaches significantly improve accessibility and retention, particularly in underprivileged areas. In addition to medicinal therapies, it is crucial to address the socio-economic determinants of TB, poverty, malnutrition, and overcrowding for effective and sustained control. Investments in housing, nutrition, and healthcare infrastructure must parallel clinical breakthroughs.

The OH concept provides a robust perspective for comprehensive TB control, acknowledging the interrelation of human, animal, and environmental health. Intersectoral coordination, digital monitoring instruments, and regional alliances are essential for addressing zoonotic TB and improving readiness.

African states must prioritize domestic financing, promote multidisciplinary research, and integrate national policies with global objectives to meet the End TB Goals by 2030. Policymakers, researchers, and communities must collaborate to guarantee that scientific advancements result in accessible, equitable, and culturally relevant treatments. By adopting innovation and tackling structural obstacles, Africa can spearhead the redefinition of TB control and finally eradicate it as a public health menace**.**

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