Cost-Disruptive Tools for Tuberculosis Screening and Diagnosis

Tuberculosis (TB) remains a leading cause of death from a single infectious agent worldwide. According to the World Health Organization (WHO) Global TB Report 2025, an estimated 10.7 million people developed TB in 2024, and 1.23 million died from the disease, despite the availability of effective treatment. Although global TB case notifications have continued to recover following disruptions during the COVID-19 pandemic, WHO estimates that only approximately 78% of incident TB cases were diagnosed and notified in 2024, leaving a persistent detection gap that contributes to ongoing transmission, delayed treatment, and avoidable morbidity and mortality.[1] WHO has therefore emphasized systematic TB screening as a critical strategy to identify people with TB earlier and to reach individuals who are missed by passive, symptom-based case detection.[2]

A growing body of evidence indicates that symptom-based screening alone is inherently insufficient to close the TB detection gap. Analyses of national TB prevalence surveys consistently show that a substantial proportion of bacteriologically confirmed TB is subclinical, meaning individuals have minimal or no symptoms at the time of detection.[3] As a result, symptom-gated approaches systematically miss large numbers of people with active TB. Importantly, screening-detected TB is not clinically trivial. A systematic review and meta-analysis demonstrated that individuals with radiographic evidence of TB but negative sputum cultures have a substantial risk of progression to culture-positive disease, and that treatment significantly reduces this risk.[4] Recent longitudinal evidence suggests that individuals with low-burden disease identified through molecular screening, such as Xpert Ultra “trace” results, have a meaningful risk of subsequent TB, even when baseline symptom assessments are uninformative.[5] These findings underscore the clinical and public health importance of detecting TB earlier in its course.

Despite the rationale for systematic screening, the modern evidence base for population-level impact remains heterogeneous, and current screening tools face important limitations. A systematic review found that community-based active case finding can increase TB detection and may reduce prevalence when implemented with sufficient coverage and intensity, but outcomes vary widely and depend heavily on the tools used and the screening strategy employed.[6] WHO’s consolidated guidance on TB screening reflects this uncertainty, issuing conditional recommendations and emphasizing appropriate triage and confirmatory pathways.[2] At the same time, recent modeling and empirical studies suggest that achieving meaningful population impact will require screening tools that are substantially more affordable, scalable, and operationally feasible than many existing options.[7,8]

To guide innovation, WHO and global stakeholders created target product profiles (TPPs) for TB screening and triage tools that describe complementary approaches.[9] One pathway prioritizes high sensitivity for symptom-agnostic population screening, accepting lower specificity with downstream confirmatory testing. A second pathway allows higher specificity and lower sensitivity, enabling tools that may function either within simplified two-step algorithms or as single-step tests. Notably, a sufficiently sensitive and specific $1-class diagnostic could function within a one-step screening algorithm if it meets WHO diagnostic TPP performance requirements.[10] Screening and diagnosis should not be viewed as mutually exclusive categories, but as performance-defined roles within a programmatic cascade.

Crucially, all approaches are constrained by economics at scale. To be viable replacements or complements to symptom screening, screening tools must be operationally feasible in low- and middle-income settings and have very low incremental cost per person screened, such that high population coverage and frequent screening are feasible. Similarly, diagnostic tools intended for decentralized confirmation must meet both performance and cost thresholds to enable same-visit decision-making without reverting to centralized laboratory pathways. The TPPs emphasize affordability, operational

simplicity, and minimal infrastructure requirements alongside performance, recognizing that even modest per-test costs can become prohibitive when applied to millions of people.

Recent global experience with diagnostic innovation has demonstrated how rapid technological advances can be achieved when clear performance targets and deployment constraints are defined.[11] Importantly, the TPPs are agnostic to underlying technology and emphasize functional requirements rather than modality, allowing for a wide range of innovations including novel devices, digital tools, and approaches based on previously unexplored biological or physiological signals. Technologies of interest are those capable of supporting high-coverage, low-cost, symptom-agnostic screening or diagnostic strategies while generating credible early evidence toward meeting minimal or optimal TPP performance targets, regardless of biomarker, form factor, or implementation pathway.

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