New tuberculosis technologies: challenges for retooling and scale-up

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The availability of new tools does not mean that they will be adopted, used correctly, scaled up or have public health impact. Experience to date with new diagnostics suggests that many national tuberculosis programmes (NTPs) in high-burden countries are reluctant to adopt and scale up new tools, even when these are backed by evidence and global policy recommendations. We suggest that there are several common barriers to effective national adoption and scale-up of new technologies: global policy recommendations that do not provide sufficient information for scale-up, complex decision-making processes and weak political commitment at the country level, limited engagement of and support to NTP managers, high cost of tools and poor fit with user needs, unregulated markets and inadequate business models, limited capacity for laboratory strengthening and implementation research, and insufficient advocacy and donor support. Overcoming these barriers will require enhanced country-level advocacy, resources, technical assistance and political commitment. Some of the BRICS (Brazil, Russia, India, China, South Africa) countries are emerging as early adopters of policies and technologies, and are increasing their investments in TB control. They may provide the first opportunities to fully assess the public health impact of new tools.

KEY WORDS: tuberculosis; new tools; diagnostics; scale-up; retooling

IMPLEMENTATION of the Stop TB Strategy has greatly expanded tuberculosis (TB) diagnostic and treatment services and saved millions of lives.[1] However, the slow decline of TB incidence remains a cause for concern.[2] TB elimination by 2050 looks impossible, unless substantially better tools are developed and deployed imaginatively to combat the TB problem.[3,4] Indeed, the development of new tools is a major component of the revised Global Plan to Stop TB (2011–2015),[5] and progress is being made in this area, as summarised in other articles in this State of the Art series.

Progress with new tools is most visible with the expanded portfolio of TB diagnostics that are now available and endorsed by the World Health Organization (WHO; Figure 1).[2] Intensive efforts in the area of TB drug development are likely to yield results in the near future, while new TB vaccine development is proving to be harder than expected.

The availability of new tools, however, does not mean that they will be adopted, used correctly, or scaled up, particularly in high TB burden countries. Experience to date with new diagnostics suggests that national TB programmes (NTPs) in high-burden countries do not necessarily adopt and scale up new technologies, even if the tools are backed by strong evidence and policies.[6–8] Why is this, and what are the biggest challenges for scaling up new technologies in countries?

Based on our experiences with diagnostics, we describe several common barriers, ranging from policy issues to advocacy. While our focus is on diagnostics, we believe many of the challenges we describe will also pose barriers to the scale-up of new TB drugs and vaccines as they come through the pipeline.

Previous articles in this series   Editorial: Yew W-W, Borgdorff M W, Enarson D A. New tools for global tuberculosis control: are we any closer? Int J Tuberc Lung Dis 2012; 16(7): 855–856. **No 1:** Drobniewski F, Nikolayevskyy V, Balabanova Y, Bang D, Papaventsis D. Diagnosis of tuberculosis and drug resistance: what can new tools bring us? Int J Tuberc Lung Dis 2012; 16(7): 860–870. **No 2:** Grosset J H, Singer T G, Bishai W R. New drugs for the treatment of tuberculosis: hope and reality. Int J Tuberc Lung Dis 2012; 16(8): 1005–1014. **No 3:** Maertzdorf J, Weiner J III, Kaufmann S H E. Enabling biomarkers for tuberculosis control. Int J Tuberc Lung Dis 2012; 16(9): 1140–1148.

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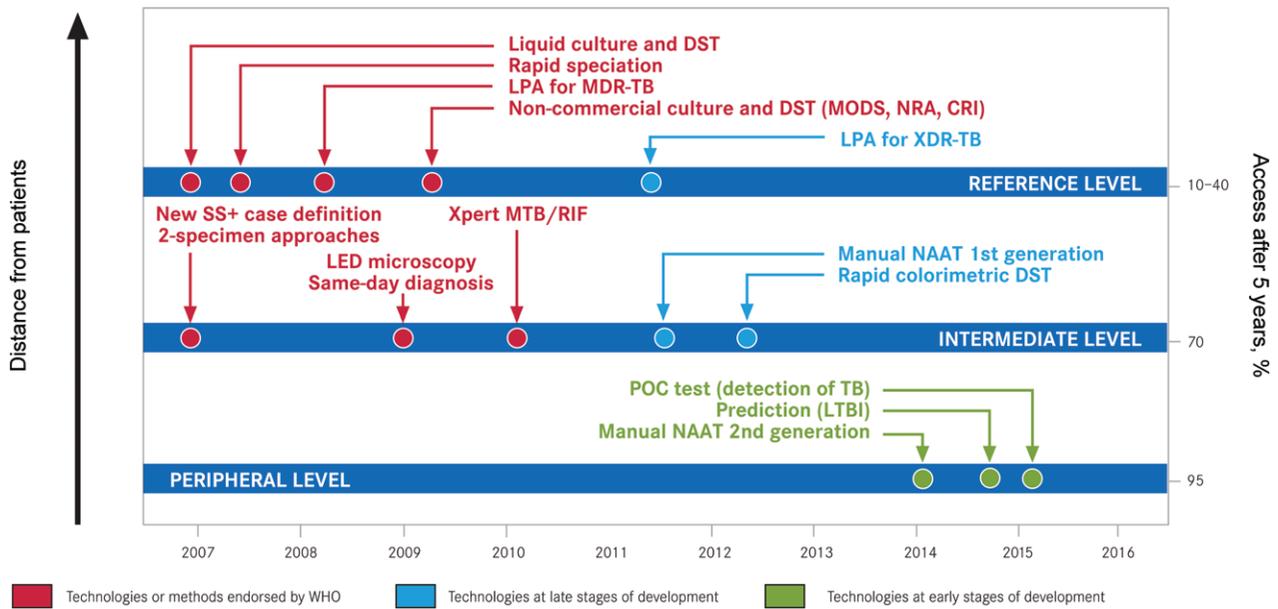
Figure 1 TB diagnostics pipeline in 2011. Reproduced with permission from the World Health Organization.[2] DST = drug susceptibility testing; LPA = line-probe assay; MDR-TB = multidrug-resistant TB; MODS = microscopic observation drug susceptibility; NRA = nitrate reductase assay; CRI = colorimetric redox indicator assay; SS+ = sputum smear-positive; LED = light emitting diode; NAAT = nucleic acid amplification test; POC = point-of-care; TB = tuberculosis; LTBI = latent TB infection. This image can be viewed online in colour at http://www.ingentaconnect.com/content/iuatld/ijtld/2012/00000016/00000010/art00003

GLOBAL POLICIES ARE HELPFUL BUT NOT SUFFICIENT FOR COUNTRY-LEVEL SCALE-UP

Since 2007, the WHO has reviewed and endorsed several TB diagnostics and approaches, ranging from liquid culture and optimised sputum smears, to molecular diagnostics such as line-probe assays and the Xpert® MTB/RIF assay (Cepheid Inc, Sunnyvale, CA, USA). The current WHO policy process is based on the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach to guideline development,[9] and is largely based on test accuracy data (i.e., sensitivity and specificity), technical feasibility and reagent costs.[7,10] This is a reflection of the fact that the majority of the published literature on TB diagnostics is focused on test accuracy.[10–13]

While WHO policies have credibility, and are often required by donors such as the Global Fund, World Bank and UNITAID, they are clearly not sufficient for scale-up, and often do not address the questions of country-level policy makers.[7] These policy makers (e.g., NTP managers) are often confused by the many tests and policies and unsure about how to integrate them into their existing algorithms and protocols.[6,7] Changes in existing protocols are not easy to make, especially with large and complex NTPs where even small changes require enormous effort to implement on a national scale. Furthermore, none of the new technologies are meant to be stand-alone tests: they need to be added to existing algorithms, and data on sensitivity and specificity do not capture these nuances. Policy makers are interested in cost-effectiveness analyses in their specific settings, and do not necessarily find global analyses helpful for decision making.[14] Countries are also hesitant to scale up new tests that might require substantially increased resources for multidrug-resistant TB (MDR-TB) treatment services, and this is of particular concern with the Xpert MTB/RIF assay.[15]

The original value chain or pathway for new TB diagnostics development, evaluation, policy, scale-up and impact was envisioned as a linear process,[16] where one step would naturally lead to the next. We now know that this linear process is too simplistic to capture the real world complexity of what evidence is needed to support scale-up at the country level.[7] The linear process also assumes that global evidence and policies will automatically inform local policies and decisions in countries where scale-up should occur.

A new, phased evaluation pathway has recently been proposed by a group of experts and representatives of NTPs, donors and international organizations.[7] To accelerate the adoption of new diagnostics, the proposed policy process is now envisioned as a two-step process: an initial technical recommendation, followed by a programmatic recommendation.[7] The technical recommendation would follow the current GRADE process and be based on test accuracy with limited costing and feasibility data, while programmatic recommendation would include patient-important outcomes, cost-effectiveness when implemented under routine conditions, and other factors (Table 1) critical to successful scale-up at the country level.[7]

Table 1 Description of the main research questions, designs, and outcomes per phase in the proposed revised pathway focused on the post-accuracy phase of tuberculosis diagnostics. Reproduced with permission from Cobelens et al.[7]

Stage in the new evaluation pathway	Global or local	Main questions to be answered (type of evidence)	Type of study designs	Outcomes evaluated
Before policy	Global	Does the test have the technical requirements and operational potential to improve the diagnosis of TB?	Controlled field validation and demonstration studies in a limited number of well-controlled settings	Test accuracy (sensitivity and specificity), surrogate patient-important outcomes (turnaround times, time to diagnosis and treatment, improvement of case detection in the study population), ease of use and basic cost comparisons
Before scale-up	Global and local	What are the test's effectiveness, cost-effectiveness and operational requirements when used in routine practice?	Pilot implementations under routine programmatic conditions at the level in the health care system at which the tool is intended to be used, focusing on diagnostic algorithms or scenarios in which the tool is incorporated, in a number of countries/settings selected for their representativeness for major epidemiological settings and resource levels; study designs include pragmatic, randomised or cluster-randomised trials, for example following a phased-implementation design	Effectiveness data to be collected would include improvement in case detection, time until treatment initiation, pre-treatment morbidity and mortality and treatment outcomes; cost and effectiveness of the entire process and include diagnostic as well as treatment costs, both for the health system and for the patient; operational data would include infrastructural and human resource requirements, and practical constraints to implementation
During and after scale-up	Local	Is the new diagnostic tool implemented to its optimum effect, what are the constraints in scale-up, cost and resource projections to reach and sustain full scale-up, what is the epidemiological impact?	Primarily monitoring and evaluation of data sets from routine recording and reporting systems. Targeted operational studies may be needed, as well as larger studies to estimate the epidemiological impact of the new diagnostic scenario, such as population surveys of TB disease or TB infection prevalence or representative drug resistance surveys	Utilisation of the test and associated resource utilisation; changes in case notifications of TB and drug-resistant TB, in TB incidence and prevalence, in proportions of patients who test positive, in treatment delay, and in treatment outcomes; changes in patient expenditures for TB diagnosis; and broader effects on the health system such as integration of diagnostic services for various disorders; these indicators would be monitored over time and between relevant segments of the population

TB = tuberculosis.

As shown in Figure 2, the new value chain separates activities at the global level from activities that need to occur at the country level.[7] It also involves multiple feedback loops whereby evidence at each level can inform subsequent decisions to scale up new technologies (or not), and decisions to modify or revise existing policies based on epidemiological impact (or lack thereof) at the country level.[17]

DECISION MAKING AT THE COUNTRY LEVEL IS COMPLEX AND POLITICAL COMMITMENT IS WEAK

While policies are mostly global, scale-up of technologies is a local issue that must occur at the country level. In countries, most NTPs and health ministries do not appear to have a clear process for evaluating and incorporating new tools into their programmes, and country-level decision making appears to be a complex and poorly understood process. As previously mentioned, the type of evidence needed for scale-up is not adequately addressed in current policies. Furthermore, as new tools for TB have emerged only recently, NTPs are just beginning to put together processes for their adoption and scale-up.

Lack of strong political will and commitment to TB is a challenge, especially as country-level decision makers have other, competing priorities. Poor commitment is often reflected in the low budgets allocated to TB within the overall national health expenditure (which may already be quite low).[18] For example, despite being the largest TB control programme in the world, the Revised National TB Control Programme (RNTCP) in India is reported to be under-funded, although evidence shows that the programme is cost-effective, with exceptional return on investment from a societal perspective.[19]

LIMITED ENGAGEMENT OF AND SUPPORT TO NTP MANAGERS

NTP managers are key decision makers at the programmatic level in most countries, and their engagement is a vital ingredient for success. Despite their obvious importance, they often work with limited staff capacity and tight budgets, reporting to superiors and politicians who may have a limited understanding of the complexities of TB control. Discussions with NTP managers in countries suggest some degree of confusion on how to deal with the large
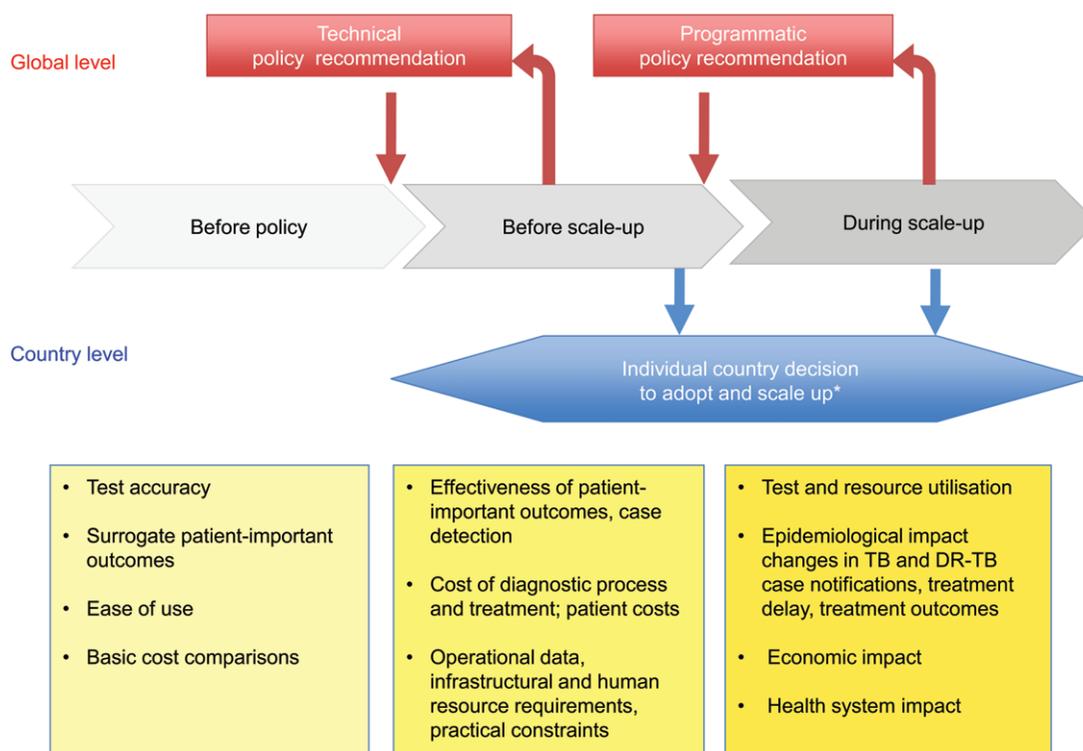
Figure 2 The proposed revised value chain for new diagnostic tests for tuberculosis. The grey arrows in the middle represent the stages in the evaluation pathway, the coloured boxes represent policy decisions at global (red, upper) and country (blue, lower) levels. Countries would adopt implementation at different points and should feed back their experiences (* in the blue box). In the *before scale-up* and *during and after scale-up* stages, evaluation data would be collected on diagnostic algorithms incorporating the new test. Reproduced with permission from Cobelens et al.[7] This image can be viewed online in colour at http://www.ingentaconnect.com/content/iuatld/ijtld/2012/00000016/00000010/art00003

number of diagnostics that have gone through the WHO policy process, especially when there are competing options for the same purpose.[6,7] For example, there are six WHO-endorsed tools for MDR-TB, and NTP managers struggle to choose between them. While NTP managers want simple, affordable tools that can be decentralised to the point of care, existing technologies often require laboratory capacity and infrastructure, and this dampens their enthusiasm for new tools.

NTP managers have promoted sputum smear microscopy for a long time, and it can be challenging for them to migrate to newer platforms. In countries such as India, a tool that replaces sputum smear microscopy in the public health sector would impact over 13 000 microscopy centres and even more end-users. With these sorts of volumes and limited budgets, it is clear that NTPs must prioritise where to place new tools within their existing health services. This sort of prioritisation is complex, especially when the ideal data to aid in making these decisions are limited. NTPs that have begun scaling up some technologies find it hard to suddenly shift to more recently approved tools ('new tool fatigue').[7] For example, NTPs that began scaling up liquid culture and line-probe assays only recently are now considering the adoption of Xpert MTB/RIF.

It is thus important to understand the perspectives of NTP managers, and engage them early in the process of product evaluation and policy development. After policies are made, it is important to continue the engagement with NTPs by providing them with technical support for the implementation of the policies. Technical agencies, such as the WHO and the International Union Against Tuberculosis and Lung Disease, can play a big role in this process. Indeed, the WHO's support to the RNTCP in India is a great example of on-the-ground technical assistance in programme management and implementation.[20]

HIGH COST AND POOR FIT WITH USER NEEDS

With diagnostics, we are now learning that technologies developed in the West cannot be passively imported into high-burden countries and easily scaled up. There is often a big gap between the manufacturer's price (even with special negotiated pricing) and the final price paid by NTPs, providers or patients. Shipping, import/customs duties, and distributor margins often inflate prices considerably. This is clearly seen with technologies such as liquid culture and Xpert MTB/RIF, where the actual costs in countries such as India are substantially higher than prices negotiated by the Foundation for Innovative New Diagnostics

(FIND). In some countries, imported technologies are viewed with suspicion due to their high costs, or regulations are made to favour domestic products. This raises the issue as to whether NTPs prefer to support domestic vs. imported technologies, and the importance of locally designed or manufactured products for country-level scale-up.

Diagnostic companies must understand that diagnostic testing in resource-limited settings occurs in a variety of settings, and critical requirements such as uninterrupted power, laboratory capacity, skilled expertise, temperature control and specimen transport cannot be taken for granted. While end users can handle a certain degree of complexity, having several moderately complex tests in a TB algorithm inflates training budgets and/or user error. Designing new tests that are simple for the end user requires on-site end-user observations throughout the product design process. To get around such issues, technologies may need to be designed in resource-limited settings ('frugal or reverse innovation'), from the ground up, to ensure that they are robust, rugged, field-tested in a variety of conditions and appropriately priced.[21]

Cost is a major barrier for the introduction of any new technology. Decision-makers in most countries tend to look at actual costs and immediate benefits rather than the cost-effectiveness or potential impact of technologies in reducing disease transmission and future health care costs.[14] Such short-term aspirations are often deeply rooted within political processes.

Previous efforts with drugs and vaccines suggest that a variety of cost reduction approaches are possible, including advanced market commitments, global access agreements by funders, direct negotiations by countries and donors, pooled funds, patent pools and buy-outs, equitable licensing, open source research and generic manufacturing.

Several approaches are currently being tried to reduce the costs of technologies such as Xpert MTB/RIF.[22] Special pricing negotiations between manufacturers and FIND have been important for ensuring lower prices for the public sector in high-burden countries.[23] Activists and civil society groups have played a role in raising awareness about the high cost of Xpert MTB/RIF. Donors such as UNITAID have supported market-based approaches to reduce costs,[24] and countries are also directly negotiating with diagnostic manufacturers.[25]

Despite these efforts, technologies such as liquid culture, line-probe assays and Xpert MTB/RIF continue to remain expensive, posing a major hurdle for scale-up of these otherwise very useful technologies.[15,22] The private sector is often an early adopter of new technologies in high-burden countries. However, the pricing of the Xpert MTB/RIF assay in the private sector in India and other developing countries is substantially higher than the pricing for the public sector, imposing additional barriers for scale-up.[22]

The private sector manages over half of all TB patients in India, and although TB disproportionately affects poor people, even poor patients seek care in this sector.[26] An estimated one third of the Indian population lives below the poverty line, and studies show that <10% of TB patients in India belong to the highest income category.[26–28] This has implications for ability and willingness to pay. Diagnostic companies and laboratories therefore need to consider mass-market pricing based on high volumes but low margins, rather than aiming at the premium segment of the TB market in high-burden countries. This requires a better assessment of the size of the TB diagnostics market, thorough analyses of various pricing strategies, and innovative business models that can support public health goals and yet remain financially viable for industries.

Measures need to be taken to ensure that poor patients are adequately served by the private health sector. Special pricing agreements for poor patients in the private sector may be the answer, as it is clear that their care cannot simply be left to market forces.

UNREGULATED MARKETS AND INADEQUATE BUSINESS MODELS

Scale-up of new technologies in private and public sectors is quite different, with distinct incentive structures and motives. In many high TB burden countries, the private sector is the dominant provider of health care.[29] In India, for example, 70–80% of first contact care happens in the private sector. The private sector in these countries is a heterogeneous mix of qualified and unqualified providers, modern and alternative health systems, and facilities that range from corporate to charitable institutions. Quality of care, therefore, is highly variable.[30]

TB diagnostic and treatment practices are known to be suboptimal, and mismanagement of TB is a concern.[31] Consequently, there are diagnostic delays, irrational or unsupervised treatment and unnecessary patient expenditures (mostly out-of-pocket).[31] TB patients in these settings are caught between two suboptimal options—an under-funded public programme with limited capacity, and an unregulated private sector where mismanagement is common.[18] Not surprisingly, patients often move between private and public sectors, and from one provider to another, while continuing to spread the infection.[32]

India offers two scenarios that are highly relevant for the scale-up of new TB diagnostics (now) and new TB drugs (future).

Diagnostics
Studies from India suggest that there is widespread use of serological, antibody tests for TB, although these tests have never been recommended by any

agency and are known to be inaccurate and not cost-effective.[33–35] An estimated 1.5 million tests are performed in the private sector every year, at a cost exceeding USD 15 million.[33,34]

Why are suboptimal diagnostics so widespread, and what factors can explain their market success? Based on our root cause analysis (Figure 3), there are many underlying reasons that explain the popularity of serological tests.[34] In terms of technical/medical causes, the RNTCP's current low budget does not allow scale-up of the newer, WHO-endorsed technologies. Thus, under the RNTCP, most patients have access only to smear microscopy—a test that is insensitive and underused in the private sector, while serological tests meet a *perceived* need among doctors and patients. In terms of economic causes, imported molecular or liquid culture tests are too expensive, leaving serological tests as the main alternative. Although

serological tests are inaccurate, various players along the value chain profit from their use, and this sustains a market for these tests. Finally, there are regulatory causes—TB tests are poorly regulated in India, and a large number of serological kits are on the market. Private health care in general is poorly regulated, and doctors in the private sector are outside the scope of the RNTCP and do not necessarily follow standard guidelines.

A big challenge for India is thus to wean doctors and laboratories away from inaccurate TB tests and introduce validated, WHO-endorsed products. This will require market-based business models that will actually work in the Indian private sector. The lessons learned from the serology story can also offer valuable clues for new product developers. Table 2 shows tests characteristics that are most likely to ensure success in the Indian market.[34]
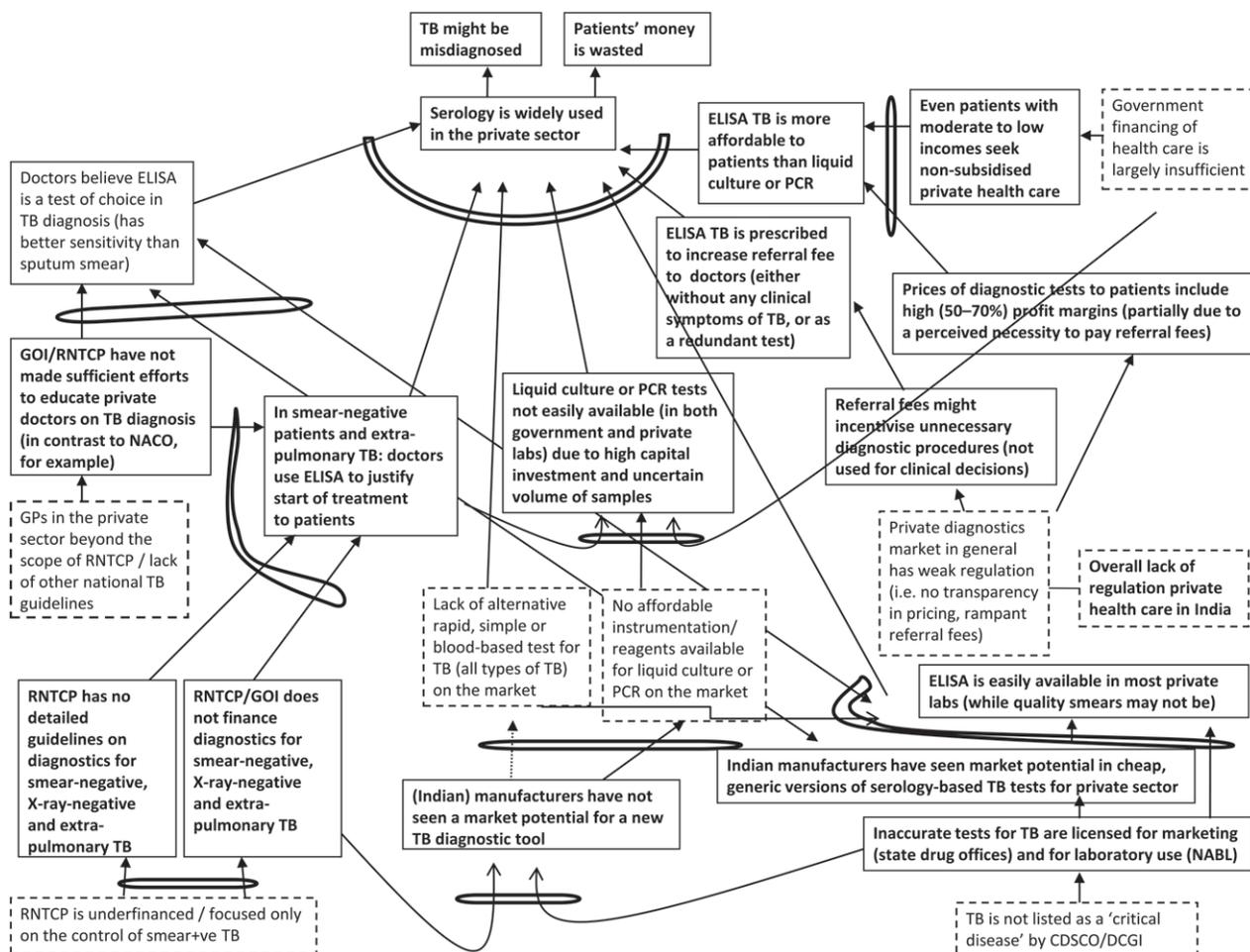

Figure 3   Root causes of the widespread use of TB serodiagnostics in the private sector in India. Dashed-line boxes show root causes. Arrows in the CRT signify relationships between the entities. In addition, the CRT uses a unique symbol, the oval or ellipse, to show relationships between interdependent causes. Lines with arrows on both ends indicate feedback loops (e.g., wide availability of TB ELISA in the laboratories might make some doctors believe that it is a good test). Reproduced with permission from Jarosławski and Pai.[34] TB = tuberculosis; ELISA = enzyme-linked immunosorbent assay; PCR = polymerase chain reaction; GOI = Government of India; RNTCP = Revised National Tuberculosis Control Programme; NACO = National AIDS Control Organization; GP = general practitioner; CDSCO = Central Drugs Standard Control Organization; DCGI = Drug Controller General of India; NABL = National Accreditation Board for Testing and Calibration Laboratories; CRT = current reality tree.

Table 2 If a new diagnostic is to succeed in the Indian private market, then the popularity of commercial serology tests in India suggests that it should have the following characteristics:*

Test characteristic	Rationale
Should be perceived by doctors as a more sensitive and sophisticated test than sputum smears	Doctors often fear under-diagnosis of TB. They don't want to miss a TB case for ethical as well as monetary reasons (the patient will be under their treatment for months). They fear that their reputation will suffer if they offer patients smear tests or refer them to an RNTCP centre.
Should be a rapid test—either a point-of-care test that can be performed in the clinic or a laboratory test that can produce results within the same day	Given the doctor-centric nature of private health care, doctors need to draw monetary benefit from the procedure. A rapid test result ensures that patients will stay with the doctors and will not drop-out. Tests such as cultures are very unpopular among doctors because of the lengthy time delays and because they rarely influence doctors' clinical decisions.
Should be performed on blood or urine sample and a single test should be sufficient for diagnosis	Stigma related to TB makes sputum a less desired sample. Also, patients with suspected TB or chronic fevers often give blood samples for other laboratory tests (e.g., complete blood counts) and this will make a test based on sputum disadvantaged compared to a test that can be performed on the same blood sample. Also, doctors might be afraid that patients will not show up for a second visit if more than one test is needed to make a diagnosis.
Should be suitable for the detection of extra-pulmonary TB	Neither sputum smears nor chest X-rays are suitable for detection of extra-pulmonary TB. There is a highly unmet need for a test for this type of TB.
Laboratories should not need to make big investments in capital/equipment	Laboratories might be reluctant to invest in equipment/facility if they are not certain of a good volume of samples. This applies also to reagent rental schemes which oblige laboratories to buy a certain amount of reagents in a given time.
It should not be too cheap or too expensive, but be in the middle range of about INR500† (price to the patient) in the private sector	The current private health care system is to a large extent driven by referral fees, which represent about 30% of the price patients pay for the test. To be successful in the current scenario any diagnostic test must assure a referral fee to doctors in a range of INR150–300 per patient. Affordability for patients dictates that the test should not significantly exceed INR500.†

*Adapted and reproduced with permission from Jarosławski and Pai.[34]
†Approximately US$10.
TB = tuberculosis; RNTCP = Revised National TB Control Programme.

Drugs

Prescription studies and drug market analyses in India show widespread use of irrational drug regimens, significant overuse of anti-tuberculosis drugs and easy over-the-counter access to anti-tuberculosis drugs.[36–38] This creates huge challenges for the introduction of new TB drugs (or any new antibiotic, for that matter) into such unregulated markets, especially if new TB drugs are not incorporated into multidrug regimens and fixed-dose combinations.

Clearly, new tools cannot be scaled up in such market-driven settings without successful engagement of the private health sector to address such irrational, profit-oriented diagnostic and treatment practices. Globally, attempts to engage private care providers in TB control on a large scale have yielded disappointing results. While small-scale, public-private mix (PPM) models have been shown to work in many studies,[39] there are no examples of large-scale, successful, sustained engagement of the private health sector in TB control.

Will new technologies provide the best approach to engaging the private sector and improving TB case detection? A recent study from Karachi, Pakistan, provides evidence that technological innovations alone may not be sufficient to engage the private sector.[40] This study engaged lay persons as well as private providers and hospitals, and combined communications, incentives, and referral services to dramatically increase TB case notifications.[40] These interventions, more than new diagnostics, played a major role in the success of this innovative PPM project. Process innovations with better business and service delivery models may thus be as important as, or more important than, product innovations.[41]

One reason for the lack of large-scale success of PPM models is that the best business models for engaging the private sector are poorly worked out. There are several obstacles to successful PPM models, and new business models are needed to overcome them. For example, governmental agencies are highly bureaucratic and inflexible, and payments for services are often delayed. This is a huge disincentive for the private sector. As the private sector is highly fragmented and heterogeneous, there is no easy mechanism to engage with this sector, even for contracting out services. Intermediary agencies and social franchising approaches may offer some solutions, and are indeed being attempted in various PPM models.

LIMITED CAPACITY FOR LABORATORY STRENGTHENING AND IMPLEMENTATION RESEARCH

Despite efforts by agencies such as UNITAID, the Global Laboratory Initiative, and the US President's Emergency Plan for AIDS Relief, laboratory capacity remains weak in many countries, and this means that technologies that require laboratory capacity will not be scaled up unless laboratory strengthening occurs.[42] The limited scale-up and impact of liquid culture is a good example of how insufficient laboratory capacity can be a major barrier for scale-up.

Even when innovative tools are backed by strong global policies, they cannot have an impact unless they are translated into national policies and practice in high-burden countries. Large-scale implementation research is necessary at the country level to make

scale-up decisions and to inform best practice; however, developing countries often lack the capacity to conduct such research.[8] This, in turn, can become a barrier for the scale-up of new technologies. On the other hand, the emergence of new tools provides wonderful opportunities for innovative and integrative implementation research.[43] As noted by Small and Katoch, the implementation of diagnostics, in particular, lends itself to this approach because the cycle time between product development, evaluation and implementation is relatively short.[43] Furthermore, diagnostics are well suited for integration into innovative business models which may include other components such as PPM and information and communications technologies.[41]

INSUFFICIENT ADVOCACY AND DONOR SUPPORT

We recently compared the human immunodeficiency virus (HIV) and TB diagnostics landscapes.[44] Our comparison showed that research and development (R&D) in TB has greatly lagged behind HIV. Patients, providers and activists have played a big role in advocating innovations in HIV diagnosis and treatment and in lobbying for affordable and generic products.[45] Funders, researchers, the industry and governments have responded to this pressure by supporting R&D efforts for drugs, diagnostics and vaccines.

In comparison to HIV, R&D advocacy for TB has been weak, and private industry and donor interest has always been low.[45] The revised Global Plan to Stop TB 2011–2015 estimates that at least US$9.8 billion is needed for TB R&D over the next 5 years to achieve 50% reduction in TB prevalence and mortality by 2015.[5] Nevertheless, according to analyses by Treatment Action Group and the Stop TB Partnership, TB research globally remains grossly underfunded—the total funding gap for the next 5 years (2011–2015) is estimated at US$6.4 billion (64%).[46]

This is worrying. Progress in the area of point-of-care test development will require major investments in biomarker and basic research. The Stop TB Partnership and WHO have set 2015 as the deadline for developing a simple, point-of-care test for TB. This goal is unlikely to be met without greater engagement of the industry, funders, governments and researchers. This, in turn, requires more intensive advocacy. Advocacy is also necessary to implement tools and policies, particularly for products that lack commercial value or industry support.[8] In particular, advocacy plans should be country-focused, funded, well-orchestrated, and aimed at policy makers and leaders within countries.

CONVERTING CHALLENGES INTO OPPORTUNITIES

Although we have discussed several major challenges for the scale-up of new tools, recent experiences

from the BRICS (Brazil, Russia, India, China, South Africa) countries give us several reasons for hope and optimism.

Data from the most recent Global TB Control report have shown dramatic reductions in TB cases and deaths in China, thanks to substantial investments made by the Chinese government.[2] Between 1990 and 2010, prevalence rates were halved, mortality rates were cut by almost 80% and incidence rates fell by 3.4% per year. The methods for measuring such trends in China are now being held up as a model for other countries.[2]

Brazil's leadership in advocating for and scaling up affordable HIV treatment is legendary. Brazil, one of the founding members of UNITAID, recently passed a law authorising an annual contribution to UNITAID based on the equivalent of US$2 for each passenger boarding an international flight on national soil.[24] UNITAID is a major donor for the roll-out of TB, HIV and malaria diagnostics, and Brazil's commitment is expected to reach $12 million a year.

In India, the RNTCP is beginning a new phase, the National Strategic Plan for the period 2012–2017. The programme has already shown great commitment by setting the ambitious goal of universal access to quality diagnosis and treatment for all TB patients in the country.[47] The RNTCP's vision recently received a much-needed lift from the government, which raised the allocation for the RNTCP by 80% over the last fiscal year's budget. In addition, the Indian health ministry recently issued an order that requires all health care providers to notify every TB case to local health authorities.[48] For the first time in India, the private health sector has to notify all TB cases; this is critically important both for monitoring the TB epidemic and for engaging the private sector. Furthermore, in June 2012, the Indian health ministry banned the use, sale and importation of serological tests for TB,[49] following the 2011 WHO negative policy against use of these tests.[50]

Considerable commitment from the South African health ministry has led to dramatic increases in the number of persons on antiretroviral treatment.[51] This commitment also led to the rapid introduction and scale-up of Xpert MTB/RIF via the National Health Laboratories Service. South Africa is the single largest purchaser of Xpert MTB/RIF, with over 300 000 specimens tested since scale-up began in 2011.[22] By becoming an early adopter of new technologies, South Africa is inspiring other countries, and is also helping to drive down the price of Xpert MTB/RIF, the price of which dropped to $9.98 per cartridge in August 2012, thanks to the investments by the United States President's Emergency Plan for AIDS Relief (PEPFAR), United States Agency for International Development (USAID), UNITAID, and the Bill & Melinda Gates Foundation.

Taken together, it is clear that the emerging econo-

mies are increasing their investments in public health, becoming less reliant on external aid and taking the lead in innovations and affordable health technologies.[52] Indeed, there is evidence that BRICS nations are contributing significant new resources to global health and development.[52] With the slowing down of the Western economies, BRICS may well represent the new hope for global TB control.

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RÉSUMÉ

La disponibilité de nouveaux outils ne signifie pas qu'ils seront adoptés, utilisés correctement, utilisés de manière plus étendue ou qu'ils auront un impact sur la santé publique. Les expériences jusqu'à ce jour au sujet des nouveaux moyens de diagnostic suggèrent que beaucoup de programmes nationaux de la tuberculose dans des pays à fardeau élevé hésitent à adopter et à utiliser plus largement de nouveaux outils même lorsque ceux-ci sont appuyés par les évidences et par les recommandations de politique au niveau mondial. Nous suggérons qu'il y a plusieurs barrières communes à l'adoption nationale effective et à l'extension de nouvelles technologies : les recommandations mondiales de politique qui ne fournissent pas suffisamment d'informations en vue de l'extension, les processus complexes des prises de décision et la faible implication politique au niveau des pays, un engagement limité des directeurs et un soutien limité à ceux-ci, le coût élevé des outils et leur adaptation médiocre aux besoins de l'utilisateur, le caractère non régulier des marchés et les modèles inadéquats d'affaires, la capacité limitée des laboratoires à renforcer et à mettre en œuvre la recherche, et un plaidoyer insuffisant comme un soutien insuffisant des donateurs. Surmonter ces barrières exigera un plaidoyer renforcé au niveau national, des ressources, de l'assistance technique et un engagement politique. Certains des pays BRICS (Brésil, Russie, Inde, Chine, Afrique du Sud) émergent en adoptant précocement les politiques et les technologies et augmentent leurs investissements dans la lutte contre la tuberculose. Ils peuvent offrir les premières opportunités pour évaluer complètement l'impact des nouveaux outils sur la santé publique.

RESUMEN

La disponibilidad de nuevos instrumentos no significa que serán adoptados, que se usarán en forma correcta, que se ampliará su escala de aplicación ni que tendrán un efecto en la salud pública. La experiencia hasta la fecha con los nuevos métodos diagnósticos indica que muchos de los programas nacionales contra la tuberculosis en los países con alta carga de morbilidad se muestran reticentes a adoptar y ampliar el uso de los nuevos instrumentos, incluso cuando existen pruebas científicas y recomendaciones de políticas mundiales que los respaldan. Se propone que existen los siguientes obstáculos comunes a la adopción nacional y a la ampliación de la escala de aplicación de las nuevas tecnologías: las recomendaciones de políticas mundiales no aportan información suficiente sobre la expansión; los complejos mecanismos de toma de decisiones y la falta de compromiso político a escala de los países; la limitada participación y el respaldo a los directores de los programas nacionales; el alto costo de los instrumentos y su deficiente adaptación a las necesidades de los usuarios; los mercados no reglamentados y los modelos empresariales inadecuados; la limitada capacidad de fortalecimiento de los laboratorios y de ejecución de las investigaciones y la insuficiencia de la promoción de la causa y de respaldo de los donantes. A fin de superar estos obstáculos es preciso reforzar la promoción de la causa a escala nacional, aumentar los recursos y la asistencia técnica y fomentar el compromiso político. Algunos de los países del grupo BRICS (Brasil, Rusia, India, China y Suráfrica) aparecen como adoptadores precoces de políticas y tecnologías y están aumentando sus inversiones en el control de la tuberculosis. Estos países podrían ofrecer las primeras ocasiones de evaluar de manera integral el impacto de salud pública de los nuevos instrumentos.