

**NOTES FROM THE FIELD****The role of technical assistance in expanding access to Xpert® MTB/RIF: experience in sub-Saharan Africa**A. N. Umubyeyi,¹ F. Bonsu,² R. Chimzizi,³ S. Jemal,⁴ M. Melese,⁴ E. Ruttoh,⁵ C. Mundy⁶<http://dx.doi.org/10.5588/pha.15.0069>

To improve tuberculosis (TB) diagnosis, many national TB programmes have committed to deploying Xpert® MTB/RIF. Implementation of this relatively new technology has suffered from a lack of comprehensive technical assistance, however, including the formulation of policies and plans to address operational issues. While providing technical assistance, we observed numerous operational challenges in the implementation and scale-up of Xpert in five sub-Saharan African countries: low coverage, poor laboratory infrastructure, limited access, poor linkages to treatment, inadequate data on outcomes, problems with specimen transport, diagnostic algorithms that are not aligned with updated World Health Organization recommendations on target patient groups and financing challenges. We recommend better country preparedness and training, laboratory information and quality systems, supply management and referral mechanisms.

An estimated 9.6 million people worldwide develop tuberculosis (TB) each year, yet only 6.3 million cases are reported and treated.^{1,2} Limited availability of sensitive, rapid TB diagnostics impedes case detection for both drug-susceptible and drug-resistant (DR) TB.

In 2010, the World Health Organization (WHO) endorsed the use of Xpert® MTB/RIF (Cepheid, Inc, Sunnyvale, CA, USA), a rapid diagnostic assay that can identify *Mycobacterium tuberculosis* and resistance to rifampicin (RMP).³ Its availability at lower-level health facilities is an added benefit to improving access to testing. The WHO recommends using Xpert as a primary diagnostic test for adults with suspected DR-TB, for children and adults with human immunodeficiency virus (HIV) with suspected TB in settings with high HIV prevalence, for children with suspected TB and for the detection of extra-pulmonary TB. Resources permitting, Xpert may also be used as an initial diagnostic test for all patients with suspected TB or as a follow-on test to microscopy for adults with smear-negative results. Such an algorithm may require additional screening, using either chest X-ray or further clinical assessment as a pre-test screening tool, to reduce the numbers of individuals to be tested.^{4,5}

Globally, the scale-up of Xpert remains the most important change in the TB diagnostics landscape, with over 4.8 million Xpert cartridges procured in the public sector in 116 of the 145 countries eligible for concessional pricing in 2014.⁶ Studies have docu-

mented the effectiveness of Xpert for detecting *M. tuberculosis* in clinical specimens⁷⁻¹² and for detecting RMP resistance.⁸ Commentaries, studies and models have presented potential uses and impacts of the test,⁴ but few results have been published on the programmatic implementation of large Xpert networks.

Implementers, policy makers and donors need information about real-world implementation. This paper presents the challenges, lessons and recommendations from our experiences in providing technical assistance in five countries.

INTERVENTION

National policy reform and strengthened laboratory capacity are vital for country uptake of new TB diagnostic technologies. The WHO has established a process to rapidly review the evidence base for new TB diagnostics and ensure that new tools meet performance standards. In parallel, the environment in which new diagnostic devices are being implemented is important. All the essential elements of laboratory services must be addressed, including laboratory infrastructure, biosafety measures and maintenance, equipment validation and maintenance, specimen transport and referral mechanisms, management of laboratory commodities and supplies, information and data management systems, quality management systems, strategies and funding for development of laboratory human resources and integration of diagnostic algorithms into laboratory strengthening plans.

To fulfil these requirements, countries must coordinate the support of donors and partners and propose a budget and plan that covers technical assistance needs, the development of a TB laboratory strategic plan—including the roll-out of Xpert—and the coordination of support from donors and partners.

Specific intervention

Management Sciences for Health (Arlington, VA, USA) has provided south-to-south technical assistance for the implementation of Xpert in five sub-Saharan African countries—the Republic of Congo, Eritrea, Ethiopia, Ghana and Kenya—in collaboration with the US Agency for International Development, the African Society of Laboratory Medicine, the WHO and the Global Fund to Fight AIDS, Tuberculosis and Malaria. This assistance has included support to develop scale-up plans, increase awareness of global policy guidance, train hundreds of technicians and clinicians

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KEY WORDS

TB diagnostic technology; Xpert; TB laboratory services; technical assistance; implementation of innovations

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and install 55 Xpert GX4 machines in collaboration with Cepheid between July 2013 and March 2015.

The technical assistance provided to countries included, to varying extents, the following interventions:

- Inform countries about the availability of the WHO checklist to assess the readiness and appropriateness of sites. Recommendations relate to optimising the placement and use of machines, aligning clinicians' case-finding practices to the recommended use of Xpert and supporting supply and specimen referral systems.
- Improve coordination between donors and partners to ensure that the purchase of equipment and reagents is in alignment with a national implementation plan and budget that follows WHO policies.
- Improve the linkage between Xpert test results and the comprehensive management of patients, including confirmatory testing and linkages to care and patient outcomes.

Results from two countries illustrate the direct impact of these interventions: in Kenya, 8221 Xpert tests were conducted during the first quarter of 2015, of which 1830 (22.3%) were positive for *M. tuberculosis* and 81 (4.4%) were RMP-resistant. In Ethiopia, an evaluation after the first year of implementation (July 2013–December 2014) showed a 22% increase in the number of DR-TB cases detected, while total TB cases detected rose from 58 802 to 63 168 (7.5%). The contribution of Xpert to TB case detection was 2% (source: Ethiopia National TB Programme, 2015).

RESULTS

Integration of Xpert as a point-of-care test into national policies

In most countries, Xpert is not used as a point-of-care test, and the status of integration of this novel diagnostic tool into national algorithms varies among countries.

Impact of Xpert on case notification

In all countries, we observed an increased number of bacteriologically confirmed cases. This observation was counterbalanced by an irregular impact on the total number of cases notified. Generally, Xpert allowed more rapid diagnosis for HIV-TB co-infected patients and notification of RMP-resistant cases.

Impact of Xpert on patient care

There were no significant or systematic improvements in the linkage of diagnosed patients to treatment or in terms of mortality. Empirical treatment generally remains the rule, despite the availability of additional information about drug resistance, for example, with Xpert testing. The utilisation of the Xpert machines is at 15% of full capacity overall, representing a missed opportunity to diagnose potential TB and DR-TB cases due to poor referral and transport systems.

Linkages between Xpert assay results and other technologies and treatment are weak. Follow-up cultures and drug susceptibility testing (DST) may not be undertaken, mainly due to a lack of capacity for DST.

LESSONS LEARNT

Although Xpert is a diagnostic device with demonstrated performance in research environments, the literature is equivocal about

its impact in programmatic conditions. Impacts on case notification or measurable patient outcomes should be considered the main indicators of success.

To increase the chances of achieving these results, the introduction of Xpert or any novel tool requires not only funding but also technical support for the revision of diagnostic and treatment guidelines. Furthermore, monitoring the progress and constantly evaluating the impact of new policies on indicators such as case detection, programmatic management of DR-TB and integration of TB-HIV activities are essential.

CONCLUSION

Realising the potential of WHO-recommended technologies such as Xpert to reduce the burden of TB depends on the behaviour of patients and providers, access to new tools, and the quality of TB treatment following diagnosis. Any Xpert roll-out strategy must balance the need to accelerate implementation with overall health systems strengthening. To achieve the maximum impact from novel diagnostics, countries should improve the quality of health care, commit the resources needed to develop and implement a strategic plan for laboratory services and involve laboratory experts to guide implementation.

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De nombreux programmes nationaux tuberculose (TB) se sont engagés à déployer le Xpert® MTB/RIF afin d'améliorer le diagnostic de la TB. La mise en oeuvre de cette technique relativement nouvelle a cependant souffert d'un manque d'assistance technique d'ensemble, notamment la formulation de politiques et de plans destinés à prendre en compte les problèmes opérationnels. Lorsque nous avons fourni cette assistance technique, nous avons observé de nombreux défis opérationnels dans la mise en oeuvre et l'expansion du Xpert dans cinq pays d'Afrique sub-saharienne : une faible

couverture, une infrastructure de laboratoire limitée, un accès limité, des liens médiocres avec la prise en charge thérapeutique, des données insuffisantes sur les résultats, des problèmes de transport des échantillons, des algorithmes de diagnostic qui ne sont pas en accord avec les dernières recommandations de l'Organisation Mondiale de la Santé relatives aux groupes cibles de patients et des défis financiers. Nous recommandons une meilleure préparation et formation des pays, une information des laboratoires et des systèmes de contrôle de qualité, une gestion des stocks et des mécanismes de référence.

Con el propósito de mejorar el diagnóstico de la tuberculosis, muchos programas nacionales han decidido generalizar la práctica de la prueba Xpert® MTB/RIF. Sin embargo, la introducción de esta técnica relativamente nueva se ha dificultado debido a una falta de asistencia técnica integral, que comprenda la formulación de normas y de planes que aborden los aspectos operativos. Durante la experiencia de prestación de asistencia técnica, se observaron múltiples dificultades operativas en la ejecución y en la ampliación de escala de la técnica Xpert en cinco países de África subsahariana, a saber: la baja cobertura, la insuficiencia de las infraestructuras de laboratorio, el

acceso limitado, la escasa vinculación con el tratamiento, la deficiencia de los datos sobre los desenlaces, los problemas relacionados con el transporte de las muestras, los algoritmos diagnósticos que no corresponden a las recomendaciones actualizadas de la Organización Mundial de la Salud en materia de grupos destinatarios de pacientes y las dificultades de financiamiento. Se recomienda procurar una mejor preparación y una mayor capacitación en el país, perfeccionar los sistemas de información y control de calidad de los laboratorios y poner en práctica procedimientos de gestión de los suministros y mecanismos de remisión.