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Groundbreaking: new study shows TB diagnosis and drug resistance testing can be reduced to just 23 hours

From 15 days to just 23 hours — that's the median turnaround time for full tuberculosis (TB) diagnosis that includes resistance testing to the most important TB drugs, according to a groundbreaking study published in *Open Forum Infectious Diseases* journal on Wednesday, 31 July 2024. This advance represents a significant leap forward in the fight against TB.

The study, titled "Reflex Xpert MTB/XDR testing of residual rifampicin-resistant specimens: a clinical laboratory-based diagnostic accuracy and feasibility study in South Africa," was co-led by Helen Cox, a professor in the Division of Medical Microbiology at the University of Cape Town (UCT). The study is part of the TB-CAPT Consortium, funded by the European and Developing Countries Clinical Trials Partnership.

Globally, the largest barrier to providing effective treatment for the 410 000 individuals estimated to develop multidrug or rifampicin-resistant tuberculosis (MDR/RR-TB) annually is rapid and effective diagnosis; only two in five are diagnosed with rifampicin resistance and receive any second-line TB treatment. Additionally, providing the most effective second-line treatment for MDR/RR-TB and preventing the emergence of further drug resistance requires knowledge of resistance to isoniazid and key second-line TB drugs included in currently recommended regimens.

South Africa has a high burden of MDR/RR-TB, with 11 000 individuals estimated to develop MDR/RR-TB in 2022 and approximately 7 000 of these diagnosed. The World Health Organization (WHO)-endorsed Xpert MTB/RIF and Xpert MTB/RIF Ultra (Cepheid, Sunnyvale, CA) low-complexity automated nucleic acid amplification tests have been rolled out widely in South Africa and elsewhere, providing rapid Mycobacterium tuberculosis complex (MTBC) detection as well as rifampicin resistance mutation detection for all individuals investigated for TB. However, current testing for resistance to isoniazid and second-line TB drugs has relied on line probe assays (LPAs) and phenotypic drug susceptibility testing (DST), resulting in incomplete results and delays in diagnosis.

At the time of the study, the National Health Laboratory Service (NHLS) used (and still uses in low throughput laboratories) WHO-approved Xpert MTB/RIF Ultra for detecting TB and rifampicin resistance from sputum samples. A second sputum sample is usually collected (from patients) and kept for culturing and other tests to determine further TB drug resistance (routine testing). This study used leftover samples processed on Xpert MTB/RIF Ultra that were then tested using the Xpert MTB/XDR platform. This approach eliminated the

need for a second sputum sample and significantly reduced the time required to determine drug resistance.

"The new Xpert MTB/XDR test was much faster, providing results in 23 hours compared to 15 days with routine testing. This method increased the availability of results and drastically cut down the turnaround time," said Dr Widaad Zemanay, the study's co-author and research coordinator in UCT's Faculty of Health Sciences.

Zemanay said faster diagnosis of TB drug resistance allows for the more rapid initiation of effective treatment and, therefore, improves patient outcomes while reducing further transmission of drug-resistant TB.

The study formed part of one arm of the TB-CAPT that aimed to provide evidence for impactful implementation of TB and TB/HIV co-infection diagnostic strategies, including drug-susceptibility testing through a series of trials in Tanzania, Mozambique and South Africa.

The study in South Africa focused on diagnosing resistance to TB drugs in two separate NHLS laboratories (Greenpoint, Cape Town and Gqeberha). It was a laboratory-based study assessing the diagnostic accuracy and feasibility of a reflex testing approach, where Xpert MTB/XDR was performed on residual specimens previously processed for Xpert MTB/RIF Ultra and found to have resistance to the most important TB drug, rifampicin.

This data has the potential to greatly impact national TB programs globally, said Professor Cox. "Additionally, data collected through this study has allowed ongoing investigation around resistance to the new TB drugs currently used in South Africa (e.g., bedaquiline)."

She commented: "The multinational collaboration within the TB-CAPT initiative produced groundbreaking research on TB drug resistance diagnostics in South Africa. The study's local findings wield global significance by validating a novel reflex testing method, offering a blueprint for improved TB management worldwide. This collaborative effort exemplifies the power of international partnerships in advancing public health initiatives."

ENDS

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