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PATHOLOGY MATTERS
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FROM HUMBLE BEGINNINGS to a Full-Fledged TB Laboratory:

Innoquest's Journey from 2019 to Today.

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Tuberculosis (TB) remains a major global health concern, and accurate diagnosis is key to control its spread. The diagnosis of TB has evolved dramatically with a growing arsenal of tools which caters for every clinical setting. From the simplicity of conventional microscopy to the precision of molecular methods, each technique offers unique insights into TB detection and its susceptibility profile, meeting the diverse clinical needs of patients.

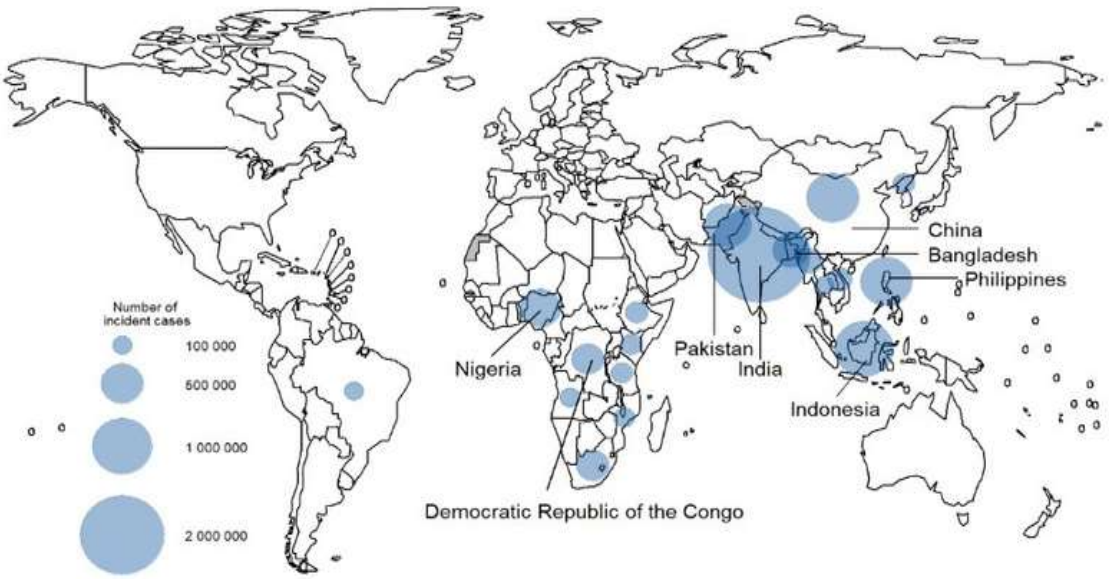

Figure 1: Estimated TB incidence in 2021, for countries with at least 100 000 incident cases. The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2021, are labelled.1

The Evolution of TB Diagnostics: From Microscopy to Molecular Methods

Microscopy remains one of the key tools for TB screening, offering a widely used and cost-effective method for detecting acid fast bacilli. Fluorescence microscopy (FM) is the current screening approach rather than the conventional Ziehl- Neelsen (ZN) staining. FM offers greater sensitivity (10 -13% more), provides faster results with more efficient screening of TB samples, especially in a high-volume setting. The strength of FM lies in its ability to detect early TB cases and paucibacillary TB, where the bacterial load is low and can be missed with conventional staining methods. This shift also aligns with the need for rapid and reliable screening tools in the fight against TB.

Culture remains the gold standard approach for TB diagnosis and both solid Lowenstein-Jensen medium and liquid Mycobacterial Growth Indicator Tube (MGIT) media is used to isolate Mycobacterium tuberculosis (MTB) complex from clinical samples. The liquid culture medium has appreciably reduced the time required for detecting growth (7 to 14 days) and facilitates antimicrobial susceptibility testing.

Innoquest Pathology integrates an endorsed rapid molecular diagnostic platform into our routine TB diagnostic algorithm. This test confirms the presence of MTB DNA and Rifampicin (Rif) resistance which is an important marker for multidrug resistant TB (MDR-TB) with speed and accuracy. The World Health Organization (WHO) strongly advocates the use of molecular techniques as a frontline diagnostic tool as it helps mitigate the inevitable delays associated with conventional culture methods.

However, molecular tests are recommended to be used alongside conventional culture methods. While molecular tests provide the speed of diagnosis, conventional cultures remain essential for confirming diagnosis, identifying a wider range of drug resistances and monitoring treatment efficacy over time.

Drug Susceptibility Testing: Addressing the Challenge of Drug Resistance

In keeping with WHO's goals to track drug resistant TB, we routinely carry out Drug Susceptibility Testing (DST) for first line anti TB drugs namely rifampicin (RIF), isoniazid (INH), ethambutol, pyrazinamide and streptomycin. A two-tier susceptibility testing for INH is provided to detect low level/partial resistance at a concentration of 0.1ug/ml and high-level resistance at a concentration of 0.4ug/ml. Low level INH resistance may still be manageable with higher INH doses while high level resistance requires a shift to alternative drugs. Thus, DST together with precise detection of resistance spectrum, provides the basis for clinicians to individualized treatment plans thus improving patient outcomes and reducing unnecessary exposure to more toxic drugs.

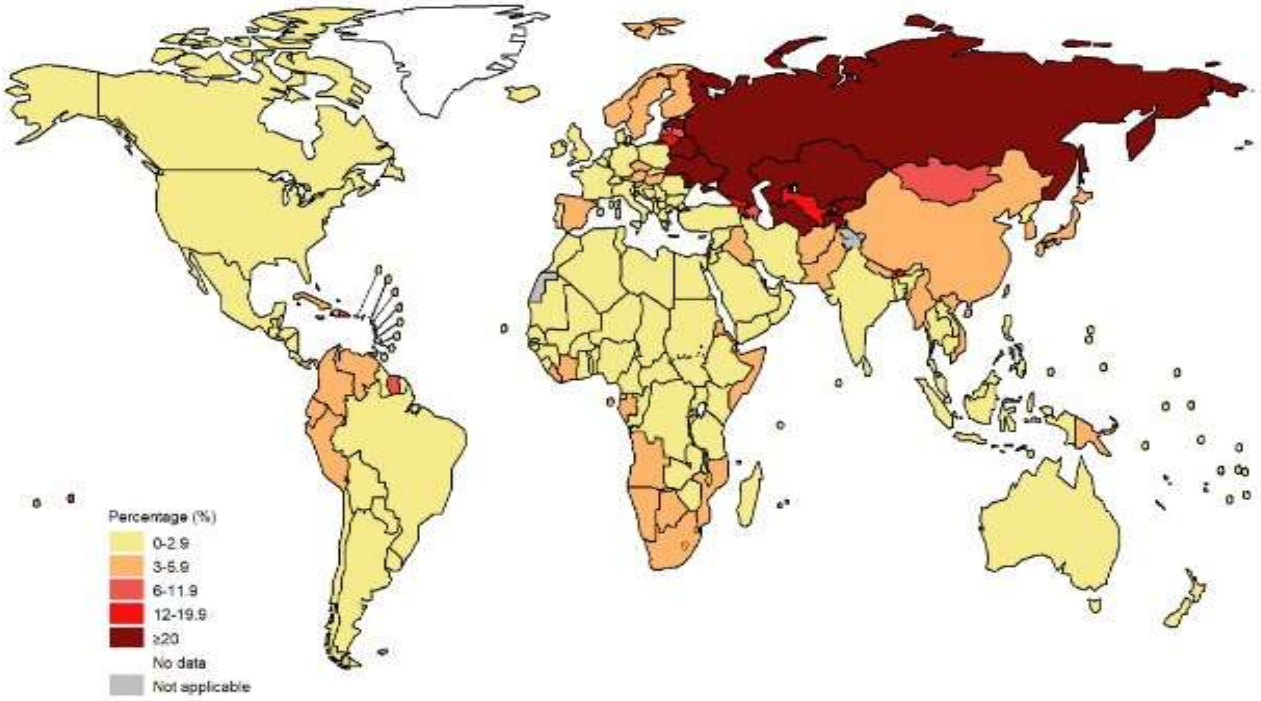

Figure 2: Percentage of new TB cases with MDM/RR-TB, 2021. Rifampicin-resistant or multidrugresistant TB (defined as resistance to both rifampicin and isoniazid), collectively referred to as MDR/RRTB.1

Susceptibility data over the years has revealed an increasing trend of monoresistance to Isoniazid (INH) compared to Rifampicin (RIF), based on our de-identified data. In 2022, out of 361 isolates, 0.6% were resistant to RIF, while 2.8% showed resistance to INH. In 2023, 1.1% of 285 isolates tested showed monoresistance to RIF while 3.4% to INH. 0.7% of the isolates were MDR-TB. For 2024, of the 324 isolates, none demonstrated RIF monoresistance, but INH monoresistance remained at 3.4%. MDR –TB accounted for 0.9% of the isolates. In comparison, Atiya et al (2023) reported INH resistance at 3.6%, rifampicin resistance at 1.5% and MDR-TB at 0.9% in Malaysia.[4] Our findings are largely consistent with their MDR TB rates, and our INH resistance closely mirrors their reported data. We however observed a lower rifampicin resistance rate.

Rising INH Monoresistance: A Diagnostic and Treatment Gap

Our findings highlight a key gap in the current approach to molecular TB diagnosis. Currently, the first line molecular test focuses on detecting RIF resistance alone as a marker for MDR-TB. This approach falls short without screening for INH resistance. With a consistently higher rate of INH monoresistance over the last three years, relying solely on detection of RIF resistance can result in incomplete diagnostics, leading to suboptimal treatment regimens which can further promote drug resistance and add to the health burden. Our findings warrant further comparison with national data to determine if this trend reflects a broader pattern in our clinical setting or is occurring in isolation. By understanding this context, we can take proactive steps to prioritize the detection of both RIF and INH resistance through frontline molecular diagnostics. This proactive approach is key to strengthening TB control efforts while aligning with WHO's End TB Strategy, which aims to eliminate TB as a public health concern by 2035.

Delivering Accurate and Timely TB Diagnoses: Our Commitment to WHO Standards

In addition to offering a full range of TB diagnostic tests, Innoquest Pathology maintains compliance to WHO guidelines which recommend that laboratories report at least 80% of Mycobacterium tuberculosis culture and DST results within 28 days, a global standard for quality assurance. Our laboratory has achieved a notable milestone in that 86% of our TB culture and DST are delivered during this timeframe, surpassing the international benchmark and underscoring our dedication to prompt and reliable patient care.

As we approach **World TB Day** on March 2025, themed "**Yes! We Can End TB: Commit, Invest, Deliver**", our laboratory reaffirms its dedication to this cause. Through continuous investment in diagnostic advancements and a steadfast commitment to timely and precise testing, we strive to play a pivotal role in the fight against TB, supporting national and global efforts to reduce TB prevalence and its related complications.

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