TUBERCULOSIS

A THEORETICAL NANO FLEX TARGET

"1.4 MILLION PEOPLE DIED FROM TB IN 2019" -WHO

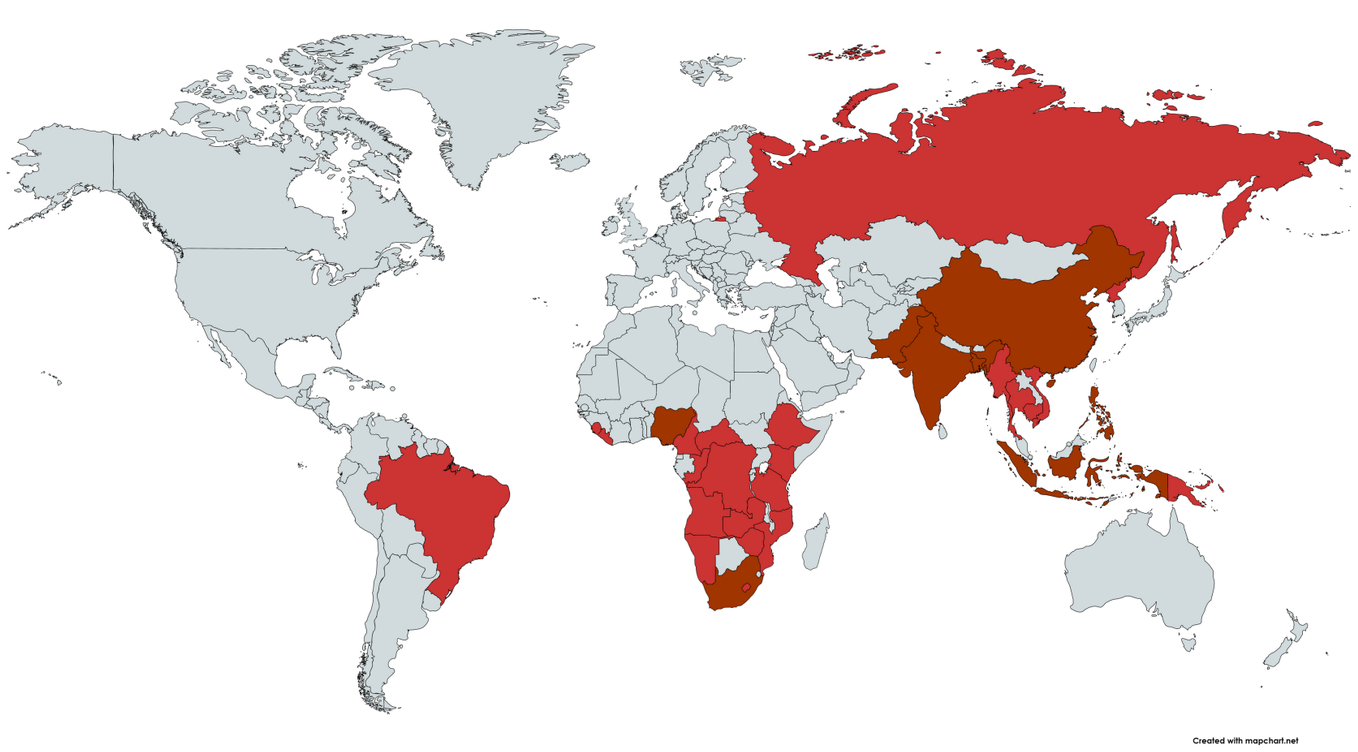
WHAT IS TUBERCULOSIS?

Tuberculosis disease (TB) is a highly infectious pulmonary disease characterized by a prolonged cough, chest pain, weakness or fatigue, weight loss, fever and night sweats (1). The disease is mainly caused by the bacterium *Mycobacterium tuberculosis (M. tuberculosis)* in humans and can be lethal if left untreated. Most people which are infected are asymptomatic and have what is referred to as Latent-Tuberculosis Infection (LTBI). However, LTBI has a high chance of becoming active later in life, causing TB (2).

WHO CAN GET TUBERCULOSIS?

Anyone who is in close contact with an infected individual has an increased risk of contracting the disease. Risk groups involve immunocompromised individuals and those living or working within areas of high TB incidence, such as homeless people, drug users or HIV-infected individuals (2).

SEVERELY AFFECTED COUNTRIES WORLDWIDE



The 30 high TB burden countries according to WHO

"AN ESTIMATED 10 MILLION PEOPLE FELL ILL WITH TB WORLDWIDE IN 2019" -WHO

87% of new TB cases occured in these 30 high TB burden countries, in 2019, whereby eight countries accounted for more than 60% of cases; Bangladesh, China, India, Indonesia, Nigeria, Pakistan and the Philippines.

WHAT DO THE EXPERTS SAY?

"...IT ENDS UP BECOMING A NEGLECTED DISEASE, A DISEASE THAT HAS NEVER LEFT HISTORY." - Marlucia Garrido

Amazonas state has the highest incident rate among the states of Brazil with 76.1 cases per 100 000 inhabitants in 2019. Marlucia Garrido, a state coordinator of the Tuberculosis Control Program in Amazonas, describes the difficulties with treatment and adverse effects correlated to them. Also, how malnutrition or **lack of food may cause patients to stop taking medications correctly** and even abandon the treatment, leading to a very high dropout rate as seen in Manaus, the capital of Amazonas having up to 15% dropout rate.

1. CDCTB (2020) Tuberculosis (TB). Centers for Disease Control and Prevention. [online] https://www.cdc.gov/tb/default.htm (Accessed October 20, 2020)
2. Tuberculosis (TB) [online] https://www.who.int/news-room/fact-sheets/detail/tuberculosis (Accessed October 20, 2020)

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"IT'S A PANDEMIC, EVEN THOUGH PEOPLE DON'T USUALLY TALK ABOUT IT IN THAT WAY." - Nuno Rufino de Sousa

Having 46 TB cases per 100 000 inhabitants in 2019 (1), Brazil is among the highest burden countries in the world (2). In an interview Nuno Rufino de Sousa, a laboratory technician at Karolinska Institutet in Stockholm, describes the needs, difficulties and improvements required in Brazil. According to Nuno, "most of the transmission today can be traced back to specific hotspots such as schools or prisons where people agglomerate, which, in combination with poorer ventilation help the spreading". He says that something as simple as **better ventilation can minimize the spread by up to 70%.**

Read more about what Nuno and Marlucia had to say about the situation in Brazil in the Interviews Section!

DIAGNOSIS

TB and LTBI diagnosis is challenging due to that multiple tests are required to confirm that *M. tuberculosis* is the cause of disease or present in a patient. Sputum tests may be hard to acquire, culturing is slow, and present tests may not be able to differentiate between active or latent TB; an important distinction for proper treatment. One of the main challenges with TB is that there is a possibility of developing drug or multi-drug resistance, which can make treatment more difficult. Below is a table comparing common tests and our vision of what NANOFLEX will provide as a specific, cost-effective, point-of-care cellular biosensor for TB or LTBI (3-6).

Method	Cost	Time	Benefits	Drawbacks
Automated real time PCR: Xpert MTB/RIF	$$	2h	✓ Simple procedure ✓ Can detect drug resistance	✗ Requires special equipment ✗ Risk for false positive if previous exposure to TB
Cell Culture with DNA Analysis	$$	2-6w	✓ Detect presence of bacilli ✓ Can identify drug resistance	✗ Slow culture growth ✗ Requires specialized laboratory
Interferon-gamma Release Assay (IGRA) from Blood Sample	$$$	24h	✓ No cross-reactivity to prior vaccination or by other *Mycobacterium spp.*	✗ Not useful for early detection ✗ May be less sensitive if individual is HIV-infected
Nucleic Acid Amplification Test (NAAT)	$$$	1d	✓ Can identify strain and drug resistance	✗ Need specialized laboratory ✗ Lower sensitivity than culturing ✗ Labor intensive
NANOFLEX	$	6-9h	✓ Specific to *M. tuberculosis* ✓ No special equipment required ✓ Both active and latent TB can be detected	✗ Refrigerated storage conditions
Sputum Smear with Acid-fast Bacilli (AFB) Staining	$	2h	✓ High specificity for presence of bacilli	✗ Cannot differentiate type of *Mycobacterium* ✗ Need experienced staff
Tuberculin Skin Test (TST)	$	1-2d	✓ No special equipment required	✗ Cannot differentiate active of latent TB ✗ Cannot differentiate type of *Mycobacterium* ✗ False positive can occur if individual is vaccinated ✗ May not be able to detect early infection

1. Reis-Santos, B., Shete, P., Bertolde, A., Sales, C. M., Sanchez, M. N., Arakaki-Sanchez, D., Andrade, K. B., Gomes, M. G. M., Boccia, D., Lienhardt, C., and Maciel, E. L. (2019) Tuberculosis in Brazil and cash transfer programs: A longitudinal database study of the effect of cash transfer on cure rates. PLOS ONE. 14, e0212617
2. TB profile [online] https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&lan=%22EN%22&iso2=%22BR%22 (Accessed October 22, 2020)
3. CDCTB (2020) Tuberculosis (TB). Centers for Disease Control and Prevention. [online] https://www.cdc.gov/tb/default.htm (Accessed October 20, 2020)
4. Tuberculosis (TB) [online] https://www.who.int/news-room/fact-sheets/detail/tuberculosis (Accessed October 20, 2020)
5. Médecins Sans Frontières and Partners in Health. Tuberculosis Practical guide for clinicians, nurses, laboratory technicians and medical auxiliaries. 2017 Edition.
6. Tuberculosis | Lab Tests Online [online] https://labtestsonline.org/conditions/tuberculosis (Accessed October 20, 2020)