# DetecTB

Tuberculosis : Overview & Significance

- Tuberculosis (TB) is a bacterial disease cause by the bacteria Mycobacterium tuberculosis.
- Spread by indirect contact by breathing in droplets coughed by an infected individual.
- 2 types of Tuberculosis: **latent** & **active**. If the patient has latent tuberculosis, they do not experience symptoms and they do with active Tuberculosis.
- Tuberculosis is a disease that affects the whole world with nearly **1/4** of the **global population** being estimated to have been infected with disease.
- It is the **world's top infectious killer**: **1.5 million** people die from TB per annum, despite being a preventable and curable disease.

Mycobacterium tuberculosis

Alveoli
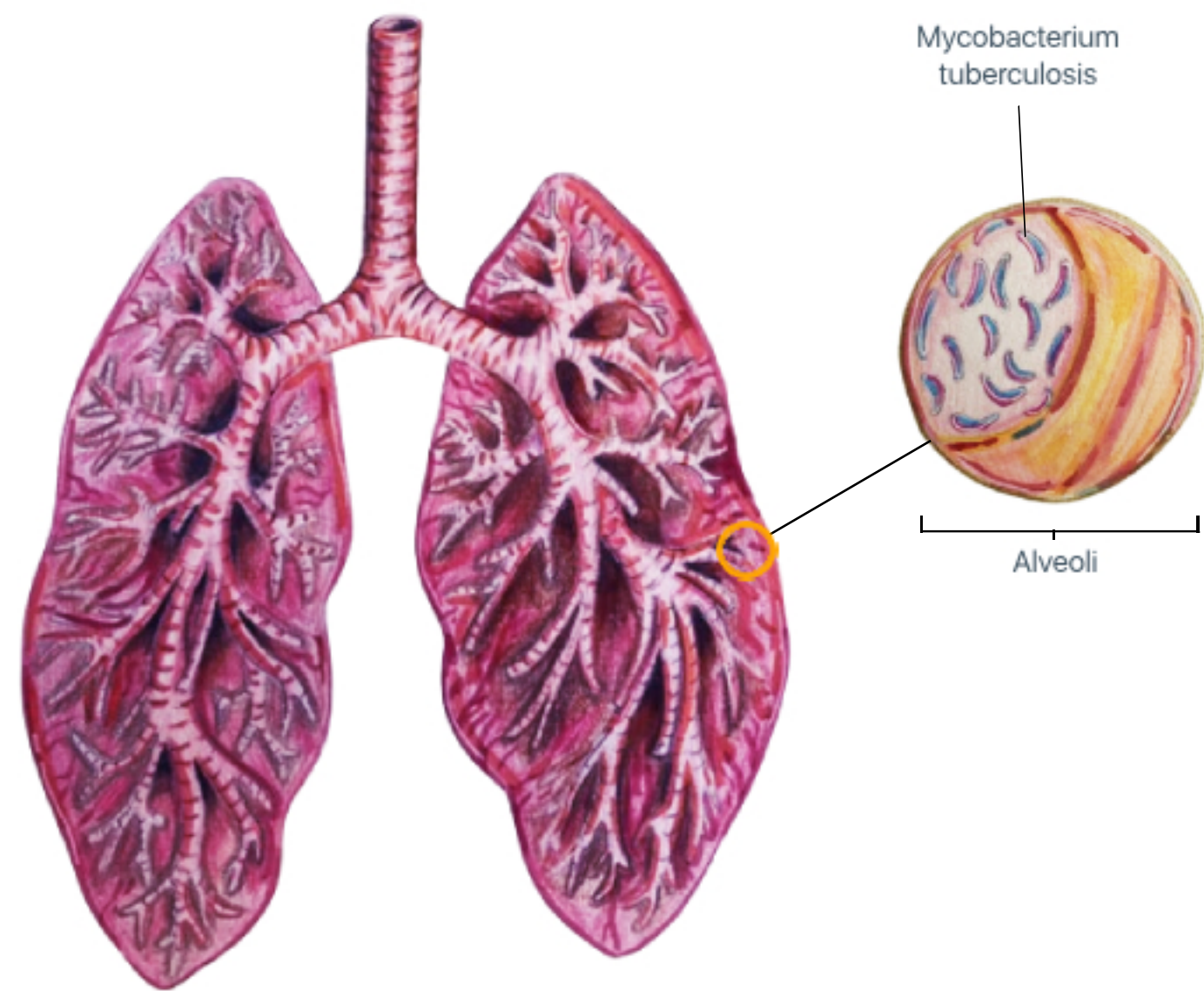
Why is Tuberculosis on the rise?

Global Mobility
Increased migration and international travel means that Tuberculosis can spread between countries. This can happen when people move from areas of high Tuberculosis prevalence (e.g. South Asia) to low prevalence (e.g. USA).

Poor Healthcare Infrastructure
This leads to **poor infection control** due to late diagnosis so less preventative measures such as **isolation** can be undertaken for other people which increases the spread of Tuberculosis.

Urbanisation
Tuberculosis is a **communicable** disease that is transmitted via airborne particles called droplet nuclei, therefore higher rates of Tuberculosis are found in areas of high population density due to overcrowding.

Resistant strains
Multidrug-resistant Tuberculosis (MDR TB) develops due to improper use of antibiotics and incomplete treatment courses, due to random DNA mutations.

Social acceptablility

We aim for everyone to feel confident to use detecTB. We believe that through thorough clinical testing, we will be able to assure the public that detecTB is **100% safe**. As well as this, we plan to launch many advertisement and educational campaigns, which will increase the public's awareness of the severity of Tuberculosis and the impact of detecting the disease early. We also plan to have regular clinical testing even after the launch of our product to ensure that detecTB continues to work in the long term and this will also help us to identify when new resistant strands of antibiotic resistant Mycobacterium tuberculosis emerge, detecTB will no longer show a positive result despite the patient having Tuberculosis as the **LAM** antigens will no longer be complementary to the **SMITB14** monoclonal antibodies in detecTB.

Manufacturing & affordability

We aim to make the TB tester extremely cheap, especially compared to the current methods of detection with the cheapest testing being £75 for children under 11 years.
To manufacture detecTB we will need many key components, such as sample swabs, extraction buffer solution, extraction tube, sample pads, conjugate pads, nitrocellulose membrane coated with immobilised SMITB14 monoclonal antibodies, absorbant pads, casing material and packaging. The sample swabs will be made from a sythetic fiber tip and an aluminium shaft to balance cost and environmental impact and will cost £0.85 per swab The extraction buffer solution will be made up of saline solution with detergents and stabilisers and will cost £0.10 per test. The extration buffer tubes will be made of starch-based plastics so they are more environmentally friendly compared to normal plastic tubing and will cost £ $0.00033 per test and £1.50 per pound. The sample pads will be made up of absorbant cellulose rather than fiberglass as its environmentally friendly and will cost £0.02-0.03 per pad The conjugate pads will be made of cellulose fibers dye-labelled with monoclonal antibodies will cost £0.20-0.30 per pad. The nitrocellulose membrane will cost £0.25-0.50 per pad. The absorbant pads will be made of Cellulose and will cost £0.01-0.02 per pad. The casing material will be made of PLA and will cost £0.014 per 10 tests. The packaging will be made of biodegradble plastic film and will cost £0.03 per test If bulk discounts, quality control, labour, reasearch and development, regulations and intellectual property is factored in would increase the price 1-2 pounds.

Our proposal: detecTB

Aims & Objectives
○ Provide a test that is **quick** and **easy** to use for **everyone**
○ To provide a much **earlier diagnosis** of Tuberculosis than what other methods currently offer
○ Reduce **financial stress** on the NHS due to Tuberculosis
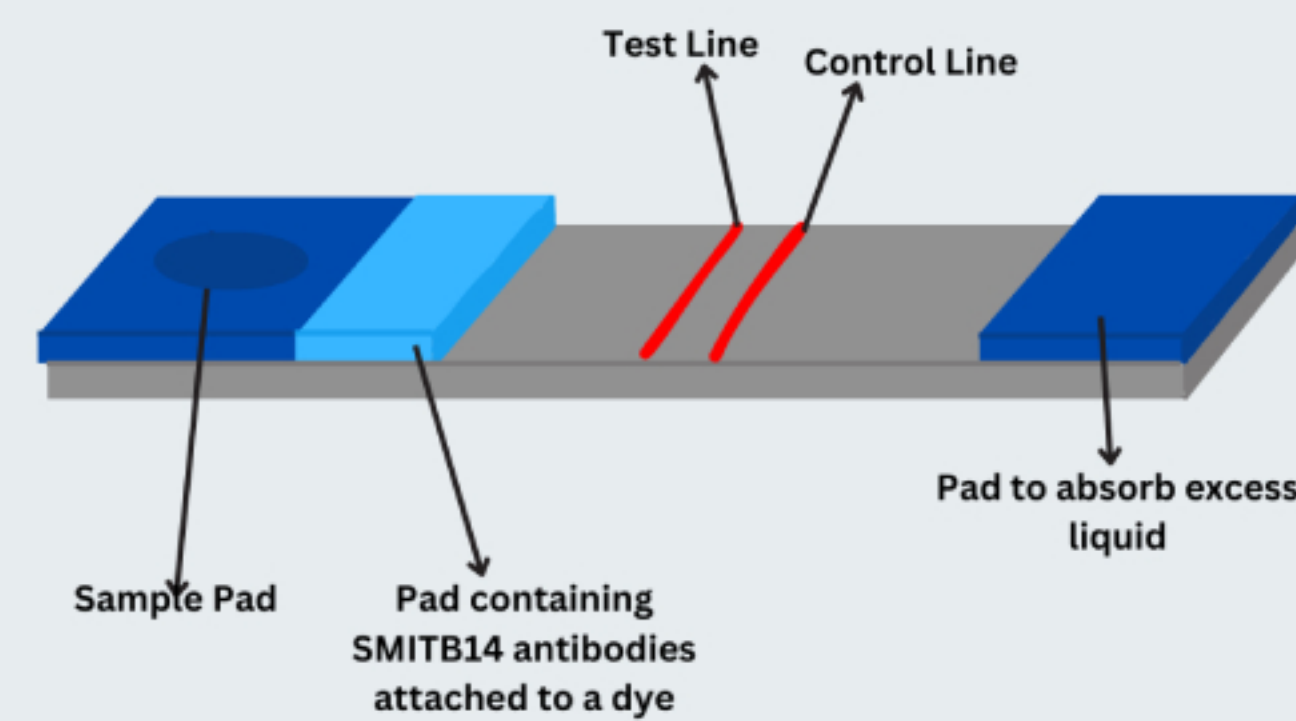
How to use detecTB
- A throat/nasal swab will be taken by rotating the swab at least five times on the tonsils and in both nostrils. It shall then be placed into an extraction buffer tube. While the buffer tube is squeezed, the swab is stirred again, at least five times.
- The swab is then removed and the sides of the tube are squeezed tightly to ensure that all the liquid has been extracted and the cap is then pressed tightly onto the tube.
- Three drops are added to the sample pad and the liquid will travel up the test.
- After an approximate **half an hour** waiting period, a result will appear.
- A single line on the **'Control' site** indicates a negative result. A line on the 'Control' site and a line on the 'test' section indicates a positive result. A line on the 'test' section alone suggests that the test has not been effective and will have to be redone.

Test Line   Control Line

Sample Pad   Pad containing SMITB14 antibodies attached to a dye   Pad to absorb excess liquid

The Science behind detecTB
- The nasal/throat mucus swab of an infected person will contain the Mycobacterium tuberculosis bacteria (with the **LAM** antigen on the outer cell wall of the bacterial cells).
- The swab sample will be then mixed with a liquid buffer solution (which should consist predominantly of saline solution).
- Once three drops of the solution are placed onto the sample pad and the liquid will then travel up the test strip.
- A line of **SMITB14 monoclonal antibodies**, specific to the **'AM' fragment** of the **LAM** antigen. The antibodies will be attached to a dye of distinct colouration – such as **fluorescein**.
- In the presence of the Mycobacterium pathogen, the antibody will bind to the antigens and the dye will become prominent- an **orange/red** line should appear on the 'test' area.
- A line of colouration should also appear on the **'control' site** which will contain control/ general antibodies.

5 Major current methods:

- Tuberculin Skin test
- Molecular tests
- Sputum microscopy
- Interferon-gamma release assays (IGRA)
- Chest X-Rays/ Complete Tomography (CT Scans)

Pros & Cons of current methods

✓
- Our test will have an easy to determine positive or negative system similar to the **IGRA test** without the blood sample, and it will be able to detect between active and latent tuberculosis
- We looked at the **Rapid Covid Test** statistics and due to the similarities between the two tests we believe there will be a high social acceptation of the tests.
- It will be more sensitive to the **Lipoarabinomannan antigen** (LAM) so it will be able to detect tuberculosis in both immunocompromised individuals and people with other types of tuberculosis.

✗
- Tuberculin skin test takes **48-72 hours** so it would not be useful in a rapid test: in that time there can be further progression of Tuberculosis where the severity would only increase further.
- The **IGRA test** require a blood sample and a sample of the Tuberculosis bacteria which is not feasible for a home rapid test and it cannot differ between active and latent Tuberculosis.
- Some are not comfortable to urinate on an absorbent strip for the **LAM tests**.

Impact of current TB screening and diagnosis methods on the NHS

It is estimated that **1.8 million people** are killed worldwide by Tuberculosis each year. Early detection is key to preventing this spread.
- Current methods of screening and diagnosis for Tuberculosis require specialist training and equipment, which have a substantial financial impact on the NHS.
- Screening for latent Tuberculosis is often required for people with poor living conditions, substance and alcohol abuse, poor health, close contacts to active people or recent migrants from high incident countries.
- Common methods to detect for active Tuberculosis are **chest X-Rays** (each one costing the NHS £75), **ultrasounds** (£109- 179) and **CT scans** (with more complex scans costing the NHS over £1000). These procedures require equipment, staff time, administrative processes and complex technology that the NHS has to provide.
- The **HPA** (Health protection agency) and NHS are jointly responsible for screening new arrivals into the UK. This includes X-Ray facilities and medically qualified staff at Heathrow and Gatwick.
- The cost of these operations is estimated to be **~£2.5 million per annum**.
- It has been found that X-Rays do not produce conclusive evidence of active Tuberculosis, and due to changes in passenger flows over the past two decades each X-Ray now costs thousands of pounds. The screening cost may be higher than treating the disease, meaning it is no longer considered effective either clinically or financially.

We believe detecTB will provide a much cheaper, faster and easier way to detect TB, whilse saving the NHS millions of pounds every year.

TB: Clinical Testing

Why?
- Testing for **efficacy** of detecTB.
- Testing for **optimum concentration** of **SMITB14 Monoclonal antibodies** in detecTB.
- Identify any **practical problems** with the use of our detecTB.

How?
- Mucus of volunteer patients will be taken and passed through detecTB to see if it shows a positive result or not.
- We will use a **large sample size** (1000 infected patients etc.) to ensure that detecTB is fully functional.
- Testing will be divided into distinct categories: **sex**, **age**, **weight** & **ethnicity**. Results within each category will be compared to results of other categories to ensure our test works on everyone: the aim is for the results to be the same regardless of these factors.

Control
- Healthy volunteers will also be sampled as a **control** measure to ensure that detecTB shows a positive result based from the mucus samples alone.
- Placebos will also be used to help make sure positive results are based from mucus samples alone.
- Double blind test will be carried out where neither the patient nor doctor know who is receiving the placebo to **remove bias** in the research results.

Why is it important to stop the spread of Tuberculosis through early diagnosis?

According to the World Health Organisation, the number of people diagnosed with Tuberculosis went from: 7.1 million in 2019 -> 5.8 million in 2020

The importance of early diagnosis has been seen in the past few years after Covid-19:
- During these years, reduced access to medical care has led to delayed diagnoses, which in somecases led to a latent infection progressing into an active disease.
- Treatment of Multidrug-resistant Tuberculosis (MDR TB) is accompanied by many challenges.
  > Firstly, second line drugs must be used in treatment, and these have many **side effects** (e.g hearing loss and gastritis).
  > Treatment is very **expensive** and requires a strong health infrastructure that many 3rd world countries do not have.
  > The course of antibiotic treatment for Tuberculosis is also vey long, spanning from **6-12 months**, and in countries where there is not a strong health infrastucture, this can often be a big problem as people can not easily access a pharmacy with the correct antibiotics, or the antibiotics may be too expensive to consume over such a long period of time.
- Early diagnosis can reduce this problem, where if the bacteria is detected in its latent form, the course of antibiotics is much shorter (around 3-6) months.

DetecTB will help with earlier diagnosis of Tuberculosis as we aim to make it as cheap and easy to use as possible. The test will be able to be used by everyone at home meaning a trip to the hospital will not be needed to test for Tuberculosis, which will also reduce the stress on the NHS as less appointments will be booked to test for Tuberculosis, especially when a person does not have Tuberculosis.

Meet our team!

Trisha - Lung drawing, How to use & science behind detecTB
Penuel - Current methods of detection & their pros & cons, Affordability
Kiana - Why is TB on the rise, Importance of early diagnosis of TB
Ihan - Graphic design, Overview, Clinical trials, Social acceptability, Aims
Beth - Impact of TB on the NHS
Avni - Website, Diagram of detecTB

Abreviations & definitions

TB - Tuberculosis
LAM - Lipoarabinomannan (Antigen on TB bacteria)
MDR - Multidrug-resistant
SMITB14 - Monoclonal antibody we are using in detecTB
PLA - Polylactic acid

Scan to access our website!