TB or Not TB?

Communicable Diseases in Global Health.

Global health focuses on improving healthcare worldwide and emphasises the need for medical support for displaced populations, whose health needs are often multiple and complex. In particular, communicable diseases, are common, frequent and often fatal due to the overpopulated living conditions in refugee camps, and lack of immediately available healthcare. This constitutes a global health threat.

Why we chose to focus on TB:

Tuberculosis (TB) is one of the most widespread communicable diseases with 1.3 million deaths in 2022, according to WHO, as it can be easily transmitted. Over 90% of TB infections and deaths occur in developing countries, in 2006 there were over 32 million displaced people and refugees with 85% of them originating from countries with high TB burdens. Meaning it increases the risk and the proportion of people affected in the camps.

The WHO has formed an 'End TB strategy' with the goal to reduce TB incidence by 80% and decrease TB deaths by 90%. This is partly in response to the high TB burden among refugees and migrants ranging from 19 to 754 cases within a population of 100,000 individuals in a disaster setting.

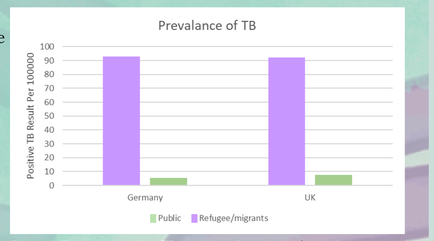


Figure 1: Graph comparing TB cases in migrants/ refugees in comparison to average diagnosis.

In disaster scenarios, health systems collapse exacerbating the need for targeted resources that limit the spread of communicable diseases. Inadequate TB detection and diagnosis in these areas means that TB remains a global health concern.

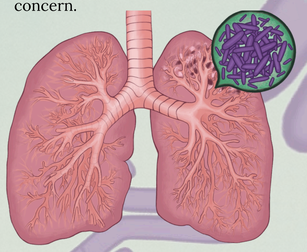


Figure 2: Original diagram of TB lung

What is TB?

TB is an infectious disease that most often affects the lungs. It is caused by Mycobacterium TB. It spreads through the air when infected people cough, sneeze or spit. TB is preventable and curable.

5–10% of people infected with TB eventually get symptoms and develop TB disease. Those who are infected but do not display symptoms aren't contagious and are known as latent. Certain conditions can increase a person's risk for TB disease: Such as diabetes, human immunodeficiency virus (HIV), Acquired immunodeficiency syndrome (AIDS), being malnourished or tobacco use.

Prevention

Seeking out medical attention for symptoms such as a prolonged cough, a fever and unexplained weight loss.
All high risk individuals getting tested for TB.
If prescribed treatment to prevent TB, complete the full course.
Anyone who has TB should practise good hand hygiene such as, wearing a mask, covering your mouth and nose when coughing or sneezing, and disposing of used tissues properly.

Treatment:

TB is treated with antibiotics. Treatment is recommended for both TB infection and disease. To be effective, these medications need to be taken daily for 4–6 months.

Methods of diagnosis already used

A symptomatic patient will be assessed with respiratory and lymph node examinations.

Currently, due to the lack of access to X-rays in refugee camps, sputum samples are analysed microscopically for acid-fast bacilli (AFB)12. The smears are stained using the Ziehl-Neelsen method. Any TB suspect with two positive smears is a TB patient.

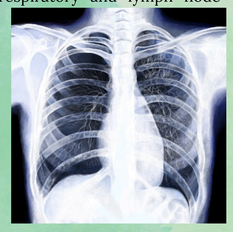


Figure 3: Drawing of TB lungs in X-ray test.

This differs from the methods used on the general population where tests like X-rays, Computed tomography (CT) scans and Ultra Sounds (US) are used along with mucus samples and biopsies of the infected tissue.
A method to diagnose latent TB is tuberculin skin testing where tuberculin is injected into patients forearm. A red lump indicates a positive test.

Advantages of the diagnosis methods in use:

- Accurate results - 80% of pulmonary TB cases are sputum positive.
- Can be implemented into disaster scenarios.
- Light microscopes are easily transported.
- Less training needed to implement tests.

Disadvantages of the diagnosis method already used:

- Accurate results take several days.
- There may not be room for isolation tents or suitable lab bench space.
- Examination via microscopy is not always possible and requires trained staff.

Our Proposal: TB Self Test Kits

We have designed self-testing TB kits, which will test for both latent and active TB, this slots into priority 3 (diagnosis) of the WHO plan.

This model has been inspired by COVID-19 kits.

The test will be found in kits named 'TB Self Test Kits' for clarity and recognition.

These kits will be given to refugee camps, and used in on-camp test centres. These kits will also be used by refugees and migrants coming into the UK.

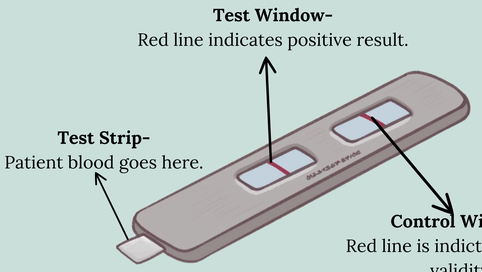


Figure 4: Shows a diagram of our prototype

The Science Behind Our Proposal:

Key features:
Antigen: ESAT-6. This protein is highly immunogenic, it can provoke an immune response.
Monoclonal Antibody: A single clone of B cells which would bind to a specific part of the ESAT-6 protein and can be easily synthesised.
Antibody: The ESAT-6 antibody would be able to recognise the multiple epitopes on the ESAT-6 antigen.

ESAT-6 is injected into the mouse. Mouse produces ESAT- 6 antibodies. These are combined with myeloma cells forming hybridoma cells. Hybridoma cells divide to produce monoclonal antibodies specific to ESAT-6.

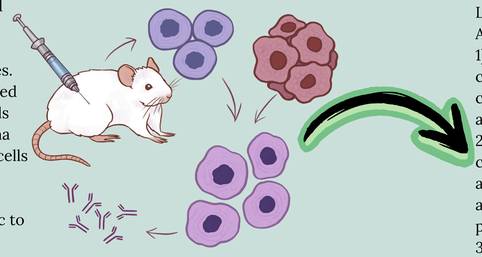


Figure 5: The process used to form monoclonal antibodies for our testing kits

Lateral Flow Assay (LFA) using Monoclonal Antibodies:
1) The blood is washed over the strip and moved by capillary action to the test window where if the complementary antibody is present it will bind to the antigens bound to the strip.
2) A monoclonal antibody in the test region binds to a complementary antibody that is already bound to the antigen on the strip that has the fluorescent dye attached, causing a line to appear. Indicating a positive result.
3) The control window has the antibody-antigen complex bound to the dye. The monoclonal antibody bound to the control strip forms a positive test line, if not the test is invalid and another will be sent out to the refugee.

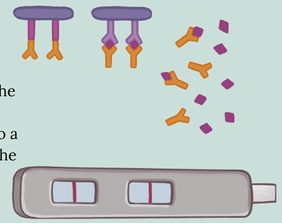


Figure 6: Original diagram showing the mechanism of the LFA.

Diagnostic trials

Before clinical trials, diagnostic trials take place. This is when you study or compare procedures, therefore our LFA test would be analysed in a labratory for its specificity and sensitivity in comparison to the gold standard tests currently being used to diagnose active and latent TB. Diagnostic trials is one of the three pillars of the WHO established end TB strategy.

Figure 7: Syringe indicating Diagnostic Trialling.

Clinical trials

After this concludes, clinical trials are conducted in a series of phases. Each phase has a different purpose and helps researchers answer different questions. Such as the accuracy or optimum wait time for our test. There is no phase I or II as there is no need for anything to be tested on tissues or animals. The trials will not exceed 18 months.

Phase III trials:
Researchers will test the kit on a small group of people (20–80). The purpose is to study the treatment's safety. A feasibility study is also conducted to ensure self testing can be done.

Phase III
2 months

Phase IV trials:
Testing begins on a larger group of people (100–300) some infected with TB and some not. Someone who is infected with TB should show a positive result. The test's safety will be further monitored.

Phase IV
4 months

Phase V trials:
Testing continues on large groups of people (1,000–3,000) confirming its effectiveness on a mass scale and make sure the 15 minute waiting time found in phase IV is accurate.

Phase V
6 months

Phase VI trials:
After it is approved by the MHRA and made available to all, researchers track its safety and effectiveness in the general population.

Phase VI
6 months

Figure 8: Infographic describing clinical trials

Triage system

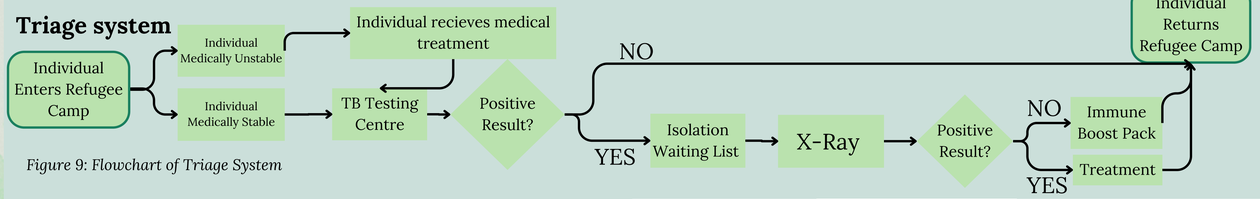


Figure 9: Flowchart of Triage System

How will it be accessed?

"Disasters reduce the delivery of health services by negatively affecting the infrastructure of health facilities in the affected areas."

Transport:

With factories placed strategically, kits should be mass transported to refugee camps and airports in the UK with ease.

Manufacturing:

Our test will be manufactured under the same umbrella of second party companies the NHS uses for equipment. There will be a factory within the UK alongside factories acquired in areas with proximity to refugee camps with TB prevelance. Such as Germany and Turkey.

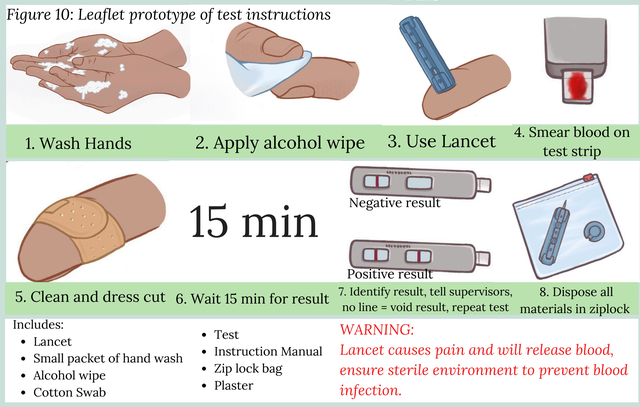
In Camp Patient Access:

- 'Testing centre' set up in camps, its size determined by camp population.
- 1 medical volunteer per 20 patients, for support with kit use and to record results.

In UK Patient Access:

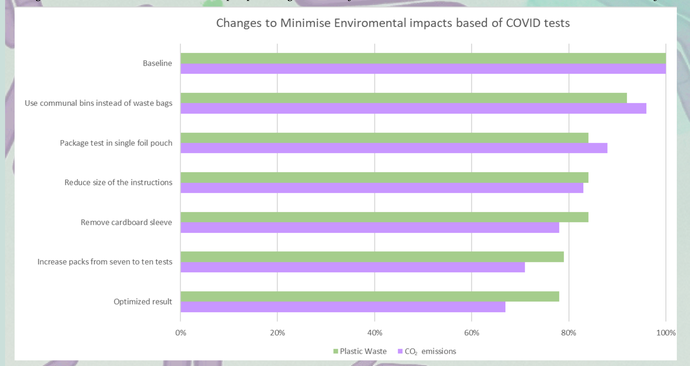
- Kits handed to individual alongside regular facilities provided.

Figure 10: Leaflet prototype of test instructions



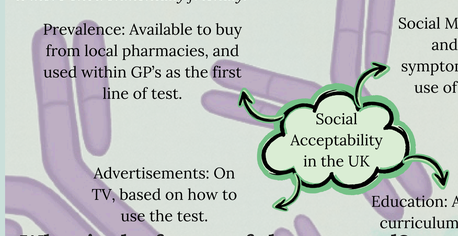
Factors:	Pros of our Proposal	Cons of our Proposal
Enviromental	Can be reduced through methods depicted in '*Figure 6*'	Our idea is similar to a COVID test which produced 61g of CO_2 and 17g of plastic in total.
Ethical	• Pamflet in kit are universal. • Our product is not intrusive. • Treatment provided to upset individuals.	• Refugees may have a language barrier. • Traumatized individuals might find the test overwhelming and refuse.
Health and medical	• Streamline TB treatment. • Test works with pre-existing TB diagnostic techniques • Medical devices are easily stored at room temperature.	• Tests for both latent and active TB. • Risk of blood infection.
Economic	• Lightweight and more cost effective compared to other tests. • X-Ray tests are of greater cost than our proposal. • Reduced healthcare professional involvement.	• Monoclonal antibodies are quite costly to manufacture. • Transporting kits may be costly.

Figure 11: This table evaluates our proposal against the factors listed to understand its limitations and benefits.



This graph shows the environmental impact of COVID tests and how different protocols reduced the plastic waste and carbon dioxide emissions. We would aim to use these findings against our proposal design to minimise the environmental impact of our kits.

Figure 12: This graph shows different alternatives to how the test is currently desiged, to make it more environmentally friendly.



What is the future of the proposal?

1. Implemented into one refugee camp.
2. Implemented to refugee camps on a national scale
3. Given to those at high risk e.g immunosuppressed, asthmatics and the elderly.
4. Further development of the science behind this test so the Mycobacterium TB bacillary Load can be detected, indicating if the patient has latent or active TB.
5. Used in hospitals as the first test for TB as a quick diagnosis.
6. App to self-report the results, so the data feeds directly into a central patient medical record system to support treatment and surveillance.

Key features of our long term solution:

- Simple to use with reduced patient-doctor interactions.
- Prevents in-person contact with other patients.
- Can work alongside/within already formed TB protocols.
- Easy to transport and store in a disaster scenario.

Meet The Team:

Sabaa Qaisar (Biology, Chemistry, English):
--> Team Leader, Organisation and support.
Anvi O'Shaughnessy (Biology, Mathematics, Music):
--> Researcher, poster layout.
Keira Williams (Biology, Chemistry, Mathematics):
--> Science Researcher, poster layout.
Gracie Davies (Biology, Mathematics, Geography):
--> Biology Researcher.
Lara Robinson (Chemistry, Further Maths, Physics):
--> Team Statiscition and Researcher, Title credit.
Leila Soderback (Art, Mathematics, Chemistry):
--> Artist, all drawings and design.

References:

Waldegrave School