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ANIMATION SCRIPT

HOW CAN WE TREAT MULTIDRUG-RESISTANT TUBERCULOSIS?

PROFESSOR ANDREW NUNN

TO MAKE THE MOST OUT OF THIS SCRIPT, YOU COULD:

- Stick it in your book as a record of watching Andrew's animation
- Pause the animation and make notes as you go
- Add your own illustrations to the sheet
- Create your own animation to accompany it
- Add notes from classroom discussions
- Make notes of areas you will investigate further
- Make notes of key words and definitions
- Add questions you would like answered – you can message Andrew through the comments box at the bottom of his article: **futurumcareers.com/how-can-we-treat-multidrug-resistant-tuberculosis**

SCRIPT:

Approximately 10 million people currently have tuberculosis (TB) worldwide, with more patients dying from TB each year than from any other infectious disease.

Based at University College London, Professor Andrew Nunn is developing an effective regimen to treat patients with multidrug-resistant tuberculosis (MDR-TB).

MDR-TB is the form of the disease that is resistant to the two most effective anti-TB drugs, rifampicin and isoniazid. 95% of patients with TB have drug-susceptible disease, so little research has focused on patients with MDR-TB. Outcomes for patients with drug-resistant TB have been very poor. Those treated unsuccessfully have infected other people with drug-resistant TB, and many have died from the disease.

Until recently, the regimen recommended by the World Health Organization involved treatment for 20 or more months. This long time period means that adherence can be poor and the drugs often have unpleasant side effects. Andrew is working on a large-scale, multi-country clinical trial called the STREAM trial. The STREAM trial started in 2012, when there were an estimated 450,000 cases of MDR-TB worldwide. The objective was to evaluate a nine-month regimen which had been developed from promising studies in Bangladesh. In STREAM, patients were randomised to receive the nine-month regimen or the longer WHO regimen.

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Clinical trials can take a long time due to the length of the treatment regimen and the need to follow patients after treatment to check they remain disease free. To assess whether results are generalisable, they need to be conducted in a variety of settings.

The nine-month regimen used in the STREAM trial targets maximum effectiveness rather than efficacy because some drugs considered to have reasonable efficacy may not be effective in real world settings. 424 patients from four countries – Ethiopia, Mongolia, Vietnam and South Africa – took part in the first stage of the trial.

Patients had to attend the study clinic every four weeks for two and a half years for treatment and follow-up appointments. Sputum samples were collected on each occasion to assess for possible treatment failure or relapse. The outcome of treatment was classed as unfavourable if they were not cured, they relapsed, had to change their allocated regimen, were lost to follow-up or died from any cause.

STREAM was a non-inferiority trial, meaning that the aim was to check that the new regimen was not much worse than the existing treatment. The difference in the proportion of favourable outcomes between the control regimen (the 20 month WHO-recommended regimen) and the nine-month study regimen was calculated.

The long WHO regimen had a 1% higher success rate. This difference was small enough for the new regimen to be considered non-inferior. These results confirmed that the regimen originally studied in Bangladesh is effective in a variety of settings.

Following this, the majority of TB programmes are moving away from the long WHO regimen. The second stage of STREAM is evaluating a fully oral regimen (where there is no need for injections) and a six-month regimen. Ultimately, it is hoped that regimens of less than six months will be available for all patients with TB.

Andrew, and researchers like him in the field of epidemiology, have shown that life-changing progress can be made through well-conducted clinical trials.

How will you contribute to this progress?

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