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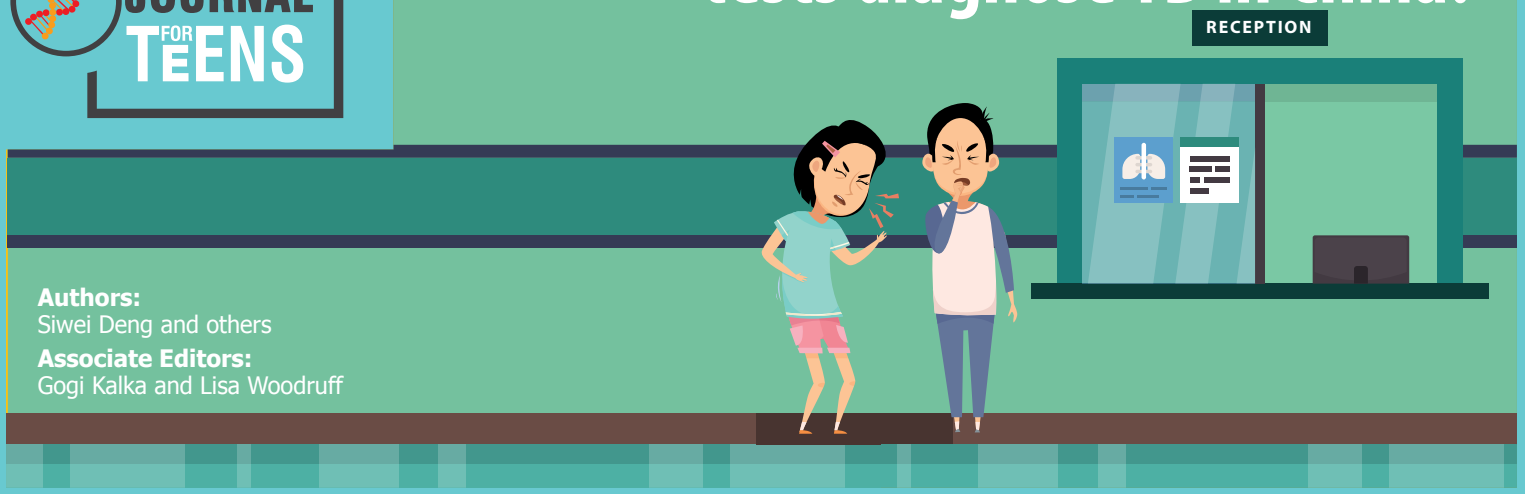
How accurately can molecular tests diagnose TB in China?



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Abstract

Tuberculosis (TB) is a global health concern, especially in China where about 1 million people are diagnosed with TB each year. Early treatment is key to combating the spread of the disease, so the faster it is diagnosed, the better. Many of the traditional tests for TB take a long time to yield results. A new method, called *molecular diagnosis*, produces results more quickly, but is it as accurate as traditional methods in diagnosing TB? To find out, we conducted a literature review and a *meta-analysis* of relevant Chinese studies looking at the accuracy of six molecular diagnostic TB tests that the Chinese Food and Drug Administration has approved. We found that molecular diagnostic TB tests are simple, fast, and accurate.

Introduction

Tuberculosis is one of the deadliest *infectious diseases* in the world. It kills over 1 million people each year and has infected a quarter of the world's population. It is caused by the bacterium *Mycobacterium tuberculosis* (Fig. 1), and you can catch it from someone sick with TB who coughs, sneezes or even just talks to you. If you inhale the bacteria, they may begin to multiply inside you and can spread throughout your body, harm your lungs and potentially other organs.

Luckily, not everybody who gets infected with TB actually gets sick. In fact, if your immune system is strong, it can help you fight off the bacteria and keep them in an inactive state. If that happens, your TB is *latent*, you don't have any symptoms and are not contagious. If you have a weaker immune system however, you can develop *active TB*. People with active TB can have symptoms such as coughing (sometimes with blood), fever, and weight loss. TB can affect other organs as well, and if not treated, can be fatal.

But here is some good news: many cases of TB can be treated relatively easily with antibiotics if detected early. Traditional diagnostic tests for TB, such as *culturing* bacteria from sputum samples, take a long time. This is not good, as bacteria grow exponentially in the body over time. Fortunately, newer molecular tests detect TB bacteria much faster by looking for bacterial DNA or RNA in the body. We wanted to know how accurate these new tests are in China, where tuberculosis is a major public health problem, infecting millions of people each year.

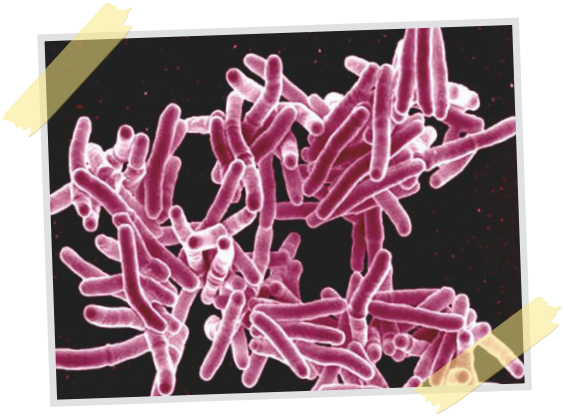

Figure 1:
Mycobacterium tuberculosis, the bacterium that causes TB.

Credit:
NIAID on flickr under 2.0 Generic (CC BY 2.0)

Methods

To answer our question, we did a literature review and looked for scientific articles published between 2000 and 2017 that assessed the accuracy of six molecular TB tests approved by the Chinese Food and Drug Administration. We set criteria for the studies so that we would be able to compare their results. Based on these criteria, we eliminated studies that included diseases other than TB, had non-Chinese participants, were duplicates, showed *bias*, or lacked necessary information. In the end, 41 studies met our criteria. We then did what is called a *meta-analysis* of these studies: we extracted their data, pooled their information, and used statistical analysis to assess the effectiveness of the six different molecular TB tests.

As measures of effectiveness, we looked at *sensitivity* and *specificity* for each molecular test. Sensitivity tells us how correctly a test identifies people with a disease. It gives us the rate of 'true positives'. The higher the sensitivity, the better the diagnostic test.

Specificity is the ability of the test to correctly identify people without the disease. No diagnostic tests are perfect, so sometimes a person is diagnosed with a disease but does not actually have it. This is called a "false positive". Specificity gives us the rate of "true negatives", which is the percentage of people correctly diagnosed as healthy.

Molecular diagnostic test	Sensitivity (%)	Specificity (%)
Xpert MTB/RIF	91	92
LAMP	90	93
LPA	87	94
CPA	87	97
(SAT)-TB	79	72
PCR	90	93

Table 1:
Measures of effectiveness (sensitivity and specificity) of the six molecular tests we studied.

Which of the analyzed molecular tests was the most accurate in diagnosing TB? Which one was the least accurate?

Results

- Overall, we found that most molecular tests were accurate: five out of six tests diagnosed the presence or absence of TB well. (Table 1)
- Three out of six tests had rates of sensitivity and specificity of 90% or above.
- The Xpert MTB/RIF test had the highest sensitivity.
- The CPA test had the highest specificity.
- The (SAT)-TB test had the lowest sensitivity and the lowest specificity.

Discussion

Overall, the values for effectiveness we assessed for the six molecular TB tests were comparable to what other researchers found, but in some cases, we got different results. We believe this is due to the differences in the individual studies, or simply the fact that they were hard to compare because they lacked important details. Overall, we noticed the need for stricter standards for all these studies so that they can be more easily compared.

Because we had to omit so many studies to start with, our sample size was fairly small, so our results should be viewed with caution. However, it is encouraging to have further indication that these tests are accurate.

Why do we care about these tests? Other TB tests, like viewing sputum under a microscope, are much cheaper and easier to do, but they are not always reliable in diagnosing TB. Another traditional test, bacterial culture, takes a long time to yield results. Molecular tests are more accurate and they diagnose TB effectively in a very short time. Some require more sophisticated equipment, but our analysis shows that the Xpert MTB/RIF test is accurate, fast, and easy to perform.

Conclusion

This study focused on China, but tuberculosis (TB) is a global problem. There were more than 10 million new cases of TB in 2017 alone. Luckily, many cases of TB are easily treatable. Early and accurate diagnosis is crucial for treatment and to keep the disease from spreading. Our analysis shows that new molecular tests offer accuracy, speed, and efficiency in detecting TB.

Glossary of Key Terms

Active TB – the form of TB in which a person is infected with *Mycobacterium tuberculosis* and has symptoms. Active TB is contagious.

Bias – In science, a factor in a study or experiment design that can cause results to be incorrectly interpreted.

Culturing bacteria – growing bacteria in a laboratory (such as on a petri dish or in a test tube).

Infectious disease – a disease that is caused by a microorganism and can be spread from one person to another.

Latent TB – an inactive form of tuberculosis. People with latent TB are infected with *Mycobacterium tuberculosis*, but show no symptoms, and are not contagious. However, latent TB can turn into active TB under certain circumstances, so it is still important to diagnose and treat it.

Meta-analysis – examining data and results from multiple studies to get an overarching result.

Sensitivity – (also called the "true positive rate") measures the proportion of sick people who are correctly identified as sick with a specific disease out of all people tested and diagnosed with a disease.

Specificity – (also called the "true negative rate") – measures the percentage of healthy people who are correctly identified as not having a specific disease, in our case, tuberculosis.

Sputum – a mixture of saliva and mucus. People with active TB cough sputum up from their lungs. It can be examined under a microscope for *M. tuberculosis*, the organism that causes TB.

Check your understanding

1 Why is it important to quickly and accurately diagnose TB?

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2 What benefit does molecular TB testing have over more traditional tests?

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3 What is the difference between latent TB and active TB?

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4 Which factors play a role in whether you have latent or active TB?

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5 What is the difference between sensitivity and specificity, and why do we need both?

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