



World Health  
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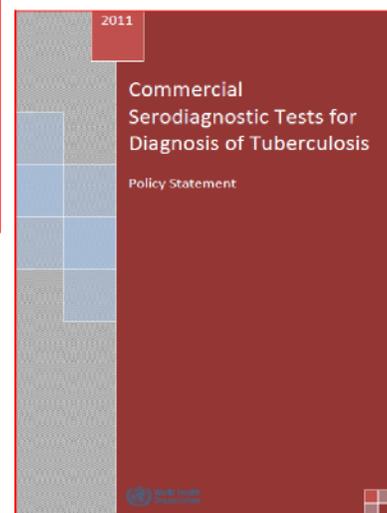
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# TUBERCULOSIS

## Serodiagnostic Tests

### Policy Statement 2011

#### COMMERCIAL SERO DIAGNOSTIC TESTS FOR DIAGNOSIS OF ACTIVE TUBERCULOSIS



#### CONCLUSION

- It is strongly recommended that **these commercial tests not be used** for the diagnosis of pulmonary and extra-pulmonary TB.
- Currently available commercial serodiagnostic tests (also referred to as serological tests) provide inconsistent and imprecise findings.
- There is no evidence that existing commercial serological assays improve patient outcomes, and high proportions of false-positive and false-negative results may have an adverse impact on the health of patients.

#### EVIDENCE INTO POLICY AND PRACTICE

#### RESULTS

##### **Pulmonary tuberculosis:**

67 studies were reviewed, including 32 studies from low- and middle-income countries. The results demonstrated that sensitivity and specificity from individual studies were highly variable. Pooled results of the most widely used tests showed sensitivity at 76% and 59% and specificity at 92% and 91% in smear-positive and smear-negative patients respectively. An evaluation by the TDR programme of 19 rapid commercial tests, in comparison with culture plus clinical follow-up, showed similar variability with sensitivity values of 1% to 60% and specificity of 53% to 99%.

##### **Extrapulmonary tuberculosis:**

27 studies were reviewed, including 10 studies from low- and middle-income countries. The results demonstrated that sensitivity and specificity values from individual studies were highly variable. Pooled sensitivity was 64% for lymph node TB and 46% for pleural tuberculosis. Pooled sensitivity and specificity for the most widely used tests were 81% and 85% respectively. In a single study involving HIV-infected patients, the sensitivity of the test was 33%.

#### **Sensitivity**

Low sensitivity results in an unacceptably high number of patients being wrongly given the 'all clear' (i.e. a false-negative). This can lead to them dying from untreated tuberculosis, and the disease also being transmitted to others.

#### **Specificity**

Low specificity leads to an unacceptably high number of patients being wrongly diagnosed with TB (i.e. a false-positive). This can lead to them undergoing a six month course of unnecessary treatment, while the real cause of their illness remains uninvestigated and undiagnosed.

- This is the first 'negative' policy recommendation on TB issued by WHO and was developed in compliance with the GRADE process for evidence synthesis and formulation of recommendations. It was approved by the WHO Guidelines Review Committee having satisfied the requirements for guideline development and issued in July 2011.
- This recommendation does not apply to serological tests for latent TB infection, currently under review by WHO.

# THE NEGATIVE IMPACT OF COMMERCIAL SEROLOGICAL TESTS IN COUNTRIES

- A blood test can cost up to \$30 per patient
- More than a million commercial serological tests are carried out every year
- Most serological tests available in low- and middle- income countries have no published evidence to support their claims of accuracy
- The blood tests are often performed in countries where diagnostic regulatory mechanisms are weak or absent
- There are perverse financial incentives that may encourage the blood tests to be used by doctors, laboratories, diagnostic companies and other stakeholders.
- Compared to appropriate diagnosis of TB through WHO-endorsed tests in a country like India, it is estimated that serological testing would result in 121,000 additional false-positive diagnoses. Research also suggest that for each additional smear-negative TB case found by serology, more than six additional false-positive cases would be inappropriately diagnosed (Cost-effectiveness of TB Serology in India, by Dowdy et al, in press in PLoS Medicine 2011)

## WHAT THE EXPERTS SAY:

*"In the best interests of patients and care-givers in the private and public health sectors, WHO is calling for an end to the use of these serological tests to diagnose tuberculosis. A blood test for diagnosing TB disease is bad practice. Test results are inconsistent, imprecise and put patients' lives in danger,"*  
**Dr Mario Raviglione, Director of WHO Global TB Programme**

*"For more than one thousand years, the notion of 'first do no harm' has been a fundamental health principle. As the evidence points out, reliance on a blood test to identify TB can have harmful consequences and therefore it has no place in TB patient care, either here in India, or elsewhere,"*  
**Blessina Kumar, leading advocate for TB care**

*"Blood tests for TB are targeted at countries with weak regulatory mechanisms for diagnostics, where questionable market incentives can override the welfare of patients. It's a multimillion dollar business centred on selling substandard tests with unreliable results,"*  
**Dr Karin Weyer, Coordinator, TB Diagnostics and Laboratory Strengthening, WHO Global TB Programme**

## WHY IS TB DIFFICULT TO DIAGNOSE?

- The most widely used method to detect TB is the 125 year-old sputum smear microscopy test, which has a number of drawbacks, including low sensitivity (especially in HIV-positive individuals and children) and inability to determine drug-resistance.
- Conventional diagnosis of drug resistant TB relies on bacterial culture and drug susceptibility testing, a slow and cumbersome process. During this time patients may be inappropriately treated, drug-resistant strains may continue to spread, and resistance may become amplified.
- In contrast, a new DNA-based TB test (Xpert MTB/RIF) endorsed by WHO in December 2010, is rapid, fully-automated and therefore not as susceptible to human error. It provides a highly accurate diagnosis in a single test that identifies both the presence of TB and drug-resistant TB. This means patients can be offered the proper treatment immediately.