

INTENSIFIED TUBERCULOSIS CASE FINDING AMONG HIV-INFECTED INDIVIDUALS

The HIV-TB co-epidemic requires increased surveillance and case finding.

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An estimated 9.4 million new cases of tuberculosis (TB) occurred worldwide in 2009. Approximately 1 million incident TB cases were HIV-positive, resulting in 0.38 million deaths.¹ South Africa is one of the 22 high-burden countries that account for 80% of all new TB cases globally and has the second highest TB incidence rate (970/100 000) worldwide. In 2009 an estimated 60% of all TB patients diagnosed in South Africa were HIV-positive.

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The risk of developing TB disease in HIV-infected individuals with latent or recent TB infection is more than 20 times higher compared with uninfected individuals.² HIV-infected individuals are at higher risk of TB at any stage of HIV disease.^{3,4} Without antiretroviral therapy case fatality rates are as high as 50% in co-infected individuals.^{5,6} ART greatly reduces TB risk and mortality in HIV-infected individuals;⁷ however, HIV-infected individuals on ART remain at higher risk for TB disease and death compared with individuals without HIV.

The World Health Organization (WHO) and the Stop TB Partnership developed several policies and guidelines to reduce TB-associated morbidity and mortality in people living with HIV. Within these policies the four core prevention strategies are intensified case finding; isoniazid preventive therapy; infection control (also known as the three Is); and antiretroviral therapy.^{8,9}

What do we mean by intensified case finding?

The terms intensive case finding or active case finding refer to strategies to identify and treat people with TB who have not presented to health care facilities on their own initiative. The WHO defined intensified TB case finding for HIV-infected individuals as 'the regular screening of all people with HIV or at high risk of HIV or in congregate settings (such as mines, prisons, military barracks) for symptoms and signs of TB followed promptly with diagnosis and treatment and doing the same for household contacts'.¹⁰

Why is intensified case finding important?

The prevalence of previously undiagnosed TB depends on TB incidence in the general population, health care infrastructure and degree of immune suppression. Several studies from South Africa reported a high burden of previously undiagnosed TB in people living with HIV.¹¹⁻¹⁴ Thus, strategies to reduce the burden of undiagnosed and therefore untreated TB among individuals living with HIV are important for South Africa. Intensified TB case finding and prompt treatment aim to interrupt disease transmission and reduce TB-associated morbidity and mortality. It is the central intervention of the three Is strategy, because its aim is to identify patients as either having active TB (and in need of treatment) or being free of TB disease (and warranting preventive therapy). Infection control measures are more effective when individuals with and without TB disease are separated and TB treatment is initiated.

How many patients do we need to screen to diagnose one TB case?

The yield of intensified TB case finding and therefore the number needed to screen to diagnose one new TB case is variable and depends on TB incidence in the general population, the setting (e.g. prison, ART clinics, HIV counselling and testing) and the diagnostic algorithm.¹⁵ HIV-infected patients with TB disease are often less symptomatic than patients without HIV.^{16,17} The presence of HIV decreases the sensitivity of smear microscopy (especially in patients with low CD4 counts) and chest radiographs often show atypical or normal chest radiographic appearances (pulmonary infiltrates with no cavities, lower-lobe involvement, intrathoracic lymphadenopathy, and even normal appearance).^{16,18-20} Therefore the appropriate screening algorithm is important.

How should we screen HIV-infected individuals for TB?

The WHO recommends in their most recent guidelines on intensified TB case finding for people living with HIV in resource-constrained settings that 'All adolescent and adults living with HIV, wherever they receive care, should be regularly screened for TB using a clinical symptom-based algorithm at every visit to a health facility or contact with a health worker'.²¹ Individuals who do not report any of the following symptoms – current cough, fever, weight loss or night sweats (CFWS) – are unlikely to have active TB. Those individuals do not need any further investigations and should be offered isoniazid preventive therapy. Individuals who screen positive for CFWS should be evaluated for TB according to the national guidelines. The South African National TB guidelines recommend performing smear microscopy on two specimens taken on consecutive days.²² The first specimen should be a spot specimen and the second one an early morning specimen. If these two specimens are negative for acid-fast bacilli a third specimen should be sent for smear and culture and a 5-day course of amoxicillin should be started. The national guidelines are being updated with the roll-out of molecular testing.

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Intensified TB case finding in children is complicated by the fact that there are limited data regarding the best approach to screening infants and children for TB. The WHO guidelines recommend that HIV-infected children with poor weight gain, fever, current cough or contact history with a TB case should be evaluated for TB. The prerequisite for regular screening of HIV-infected children is access to early diagnosis of HIV in children.

How sensitive and specific is symptom screening?

The CFWS screening rule was found to have a sensitivity of 78.9% (95% confidence interval (CI) 58.3 - 90.9%) and specificity was 49.6% (95% CI 29.2 - 70.1%) in a meta-analysis using data from more than

8 000 HIV-infected adults and adolescents.²³ The sensitivity was increased to 90.6% (95% CI 66.7 - 97.9%) and specificity decreased to 38.9% (95% CI 12.8 - 73.3%) when adding abnormal chest radiographic findings into the symptom screening rule.

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The meta-analysis investigated study-level and individual-level predictors for sensitivity and specificity of the screening tool. The screening tool was more sensitive and more specific in individuals with CD4 counts less than 200 cells/ μ l, but less sensitive and less specific in individuals who had previously been screened for TB. The WHO guidelines recommend regular repeated screening for TB at every contact with a health care worker. Therefore, HIV-infected individuals attending ART clinics or HIV wellness clinics will be screened repeatedly. This might result in an overall reduction of the sensitivity and specificity of the CFWS symptom screening. The effect of repeated screening on sensitivity and specificity is currently unknown.

With the right referral system and procedures in place it should be feasible for HIV and adherence counsellors, lay health care workers and administrative staff to perform symptom screening.

Data on the validity of clinical screening algorithms in HIV-infected children are lacking. A study from Rwanda showed that the presence of cough for more than two weeks, failure to thrive, or fever had a sensitivity of 90% and specificity of 65%.²¹ However, a study from South Africa reported a sensitivity of only 56% and a specificity of 62% for weight loss or cough for more than 2 weeks or fatigue.²⁴

What is the negative and positive predictive value of the symptom screen?

Both negative (NPV) and positive predictive values (PPV) depend on the prevalence of TB in the screened population. With the low specificity of symptom screening the PPV is only 7.6% in a population with a TB prevalence of 5%; it rises to 28.1% in a population with a TB prevalence of 20%. The low PPV is of concern with regard to costs and resource, as it means that the majority of

Table I. Negative predictive value for symptom screen alone and chest radiograph in addition to symptom screen

TB prevalence	Symptom screening alone	Symptom screening plus CXR
5%	97.8	98.7
10%	95.5	97.4
20%	90.4	94.3

individuals investigated for TB actually do not have TB. However, the situation is similar in HIV-negative TB suspects.

The NPV is high both for symptom screening alone (97.8%) (Table I) and symptom screening with chest radiography (98.7%) when the prevalence of TB is 5% in the screened population. This high NPV ensures that those who are negative on screening are unlikely to have TB and hence can reliably start isoniazid preventive therapy. The situation is different in populations with a high TB prevalence, as is the case in many South African settings. The NPV is only 90.4% when using the symptom screen alone in populations for a setting where TB prevalence is 20%. If TB prevalence is high (>10%) one should consider including chest radiography in the screening algorithm.

Implementation

The CFWS symptom screening requires that you ask four questions. Despite this simple screening tool only 1.7 million (5%) of the estimated 33 million people living with HIV were screened for TB in 2009.¹ Scale-up of intensified TB case finding will require increased awareness among clinicians, task shifting and expansion of screening outside the traditional clinic setting. With the right referral system and procedures in place it should be feasible for HIV and adherence counsellors, lay health care workers and administrative staff to perform symptom screening. Patient files should prompt health care staff to ask those four questions at every visit. Intensified TB case finding should not be restricted to ART clinics and HIV wellness clinics, but should also be a fixed component of antenatal care and sexual transmitted infection services. Implementation of intensified TB case finding should also take place outside the health care service – in prisons, schools, work places, mobile services and stand-alone HIV testing services.

The WHO guidelines concentrate on pulmonary TB. Guidance and data on intensified case finding for extrapulmonary TB are scarce. A combination of symptom screening and physical examination for lymphadenopathy will be a reasonable screening tool. As the screening for extrapulmonary TB includes a physical examination, screening for extrapulmonary TB will need to be conducted by health care staff.

References available at www.cmej.org.za

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- People living with HIV have a 20-fold increased risk for TB disease compared with people not infected with HIV.
- The risk for TB disease is high at any stage of HIV disease.
- Adults and adolescents living with HIV should be screened for TB with a clinical algorithm at every visit to a health facility or contact with a health worker.
- Anybody who does not report any one of the symptoms of current cough, fever, weight loss or night sweats is unlikely to have active TB and should be offered isoniazid preventive therapy.
- Anybody who does report current cough, fever, weight loss or night sweats should be investigated for TB according to the national guidelines.
- HIV-infected children with poor weight gain, fever, current cough or contact history with a TB case should be evaluated for TB.