Is testing for latent tuberculosis infection in an UK HIV clinic cost effective?

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Background:

HIV infection is the single strongest risk factor for reactivation of tuberculosis – increasing risk by approximately 20 times the background rate (1). Effective antiretroviral therapy reduces this by up to 80% and isoniazid preventive therapy by around 60% (2)(3).

Both BHIVA and NICE published guidance in 2011 on screening people living with HIV for latent tuberculosis infection (LTBI). BHIVA suggests using interferon gamma release assays (IGRA) in all persons depending on country of origin, time on ART and blood CD4 cell count (Table 1), whilst NICE recommends testing all those with blood CD4 <200 cells/μL with an IGRA and tuberculin skin test (TST) and those with blood CD4 between 200-500 cells/μL using an IGRA with or without TST.

Cost effectiveness has not been formally assessed for either strategy.

Table 1: BHIVA latent TB screening strategy

	Sub-Saharan Africa	Medium TB incidence country	Low TB incidence country
Blood IGRA	+	+	+
Blood CD4 count	Any	<500	<350
Duration of ART use	<24 months	<24 months	<6 months

Aim: To evaluate the cost effectiveness of both NICE and BHIVA latent TB testing strategies using HIV clinic data.

Methods:

We modeled both screening strategies using our centre's HIV clinical and demographic data obtained between 2000-2010. The Royal Free HIV database compiles prospective data for all those undergoing care in the department, including medication use, CD4 cell count and episodes of acute illness (including active TB disease).

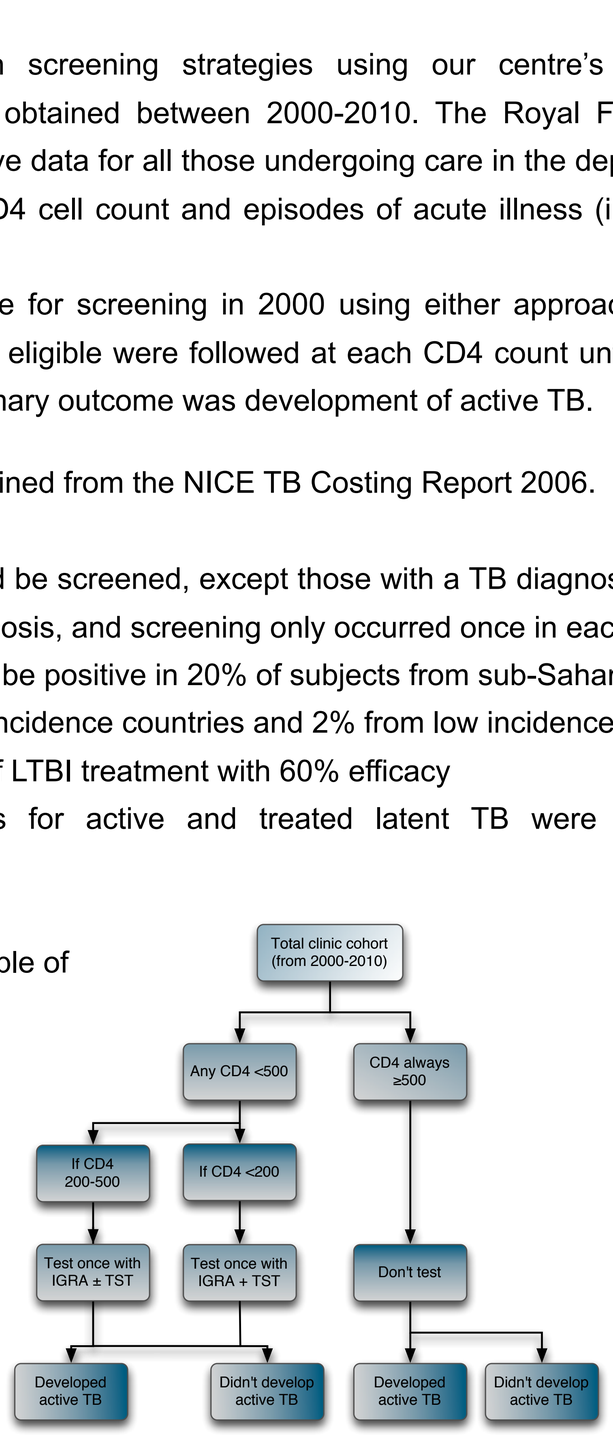
The number eligible for screening in 2000 using either approach was calculated. Those subjects not eligible were followed at each CD4 count until they met criteria for testing. The primary outcome was development of active TB.

Costings were obtained from the NICE TB Costing Report 2006.

We assumed:

- all subjects would be screened, except those with a TB diagnosis within 3 months of their HIV diagnosis, and screening only occurred once in each subject
- IGRA/TST would be positive in 20% of subjects from sub-Saharan Africa, 8% from middle incidence countries and 2% from low incidence countries
- a 100% uptake of LTBI treatment with 60% efficacy
- QALY reductions for active and treated latent TB were 0.676 and 0.007 respectively

Flowchart 1: Example of modeling using NICE criteria



References:

1. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med 1989;320(9):545.
2. Girardi E, Antonucci G, Vanacore P, Libanore M, Errante I, Matteelli A, Ippolito G. Impact of combination antiretroviral therapy on the risk of tuberculosis among persons with HIV infection. AIDS 2000;14(13):1985.
3. Akolo C, Adetifa I, Shepperd S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. Cochrane Database Syst Rev 2010(1):CD000171.

Results:

Between 2000 and 2010, 212 cases of TB disease were diagnosed in people with HIV at the Royal Free Hospital. 72 (34%) had a TB diagnosis greater than 3 months after their HIV diagnosis.

Table 2 indicates that whilst both strategies prevented cases of TB disease, the NICE strategy prevented more cases and had greater gain in QALYs at a lower cost.

Table 3 shows the characteristics of patients that developed TB disease and would have been missed using NICE and BHIVA screening strategies. The BHIVA guidelines predominantly missed patients with TB on ART interruptions or in those originally from the UK.

Table 2: Results and costings of each screening strategy, and of no screening

	No screening	NICE	BHIVA
Number in cohort	3306	3306	3306
Eligible for screening	0	2778	1478
Number needing LTBI treatment following screening	0	183	141
Number developed active TB in cohort	72	72	72
Number developed active TB, eligible for screening/LTBI treatment	0	66	42
Number of cases potentially prevented by screening	0	39	25
Cost of IGRA/TST (£)	0	79,062	37,940
Cost of LTBI treatment (£)	0	88,524	68,207
Cost of treating active TB cases developed despite screening (£)	367,200	168,300	239,700
Total cost of strategy (£)	367,200	335,886	345,848
QALYs gained by screening	0	25	16
Cost saving gained by screening (£)	-	31,314	21,352

Table 3:Characteristics of subjects missed by NICE and BHIVA testing criteria

	Developed TB, not eligible for screening under NICE	Developed TB, not eligible for screening under BHIVA
Number	6	30
CD4 count (cells/mm^3):		
Unknown	1 (17%)	1 (3%)
0-49	0 (0%)	3 (10%)
50-99	0 (0%)	1 (3%)
100-199	1 (17%)	6 (20%)
200-349	1 (17%)	8 (27%)
350-499	2 (33%)	8 (27%)
500+	1 (17%)	3 (10%)
Current ART status:		
Never on ART	1 (17%)	2 (7%)
Currently on ART	2 (33%)	17 (57%)
On ART interruption	3 (50%)	11 (37%)
Country of Origin:		
Sub-Saharan Africa	4 (67%)	14 (47%)
Medium incidence	0 (0%)	0 (0%)
Low incidence	2 (33%)	16 (53%)

Conclusions:

- Using data from 2000-10, our model suggests that either strategy is cost saving.
- The BHIVA strategy would have prevented fewer cases of active TB than NICE.
- The majority of cases of TB in people with HIV are in those with a new HIV diagnosis and these would not be prevented by systematic HIV clinic screening.
- A formal, prospective evaluation in a contemporary population is needed.