

Universal HIV testing in London TB clinics: cluster randomised controlled trial

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Abstract

Rationale: We assessed whether implementation of a combination of interventions in London tuberculosis clinics raised the levels of HIV test offers, acceptance and coverage.

Methods: A stepped-wedge cluster randomised controlled trial was conducted across 24 clinics. Interventions were training of clinical staff and provision of tailor-made information resources with or without a change in clinic policy from selective to universal HIV testing. Primary outcome: HIV test acceptance amongst those offered a test, before and after the intervention; Secondary outcome - offer of HIV testing. Additionally, the number and proportion of HIV tests among all clinic attendees (coverage) was assessed.

Results: 1315 patients were seen in 24 clinics. The offer and coverage of testing rose significantly in clinics without ($p=0.002$ and $p=0.004$ respectively) and with existing universal testing ($p=0.02$ and $p=0.04$ respectively) of policy. However, the level of HIV test acceptance did not increase in 18 clinics without routine universal testing ($p=0.76$) or the 6 clinics with existing universal testing ($p=0.40$).

Conclusion: The intervention significantly increased the number of HIV tests offered and proportion of participants tested, although acceptance did not change significantly. However, the magnitude of increase is modest due to the high baseline coverage.

Keywords: HIV, implementation of policy, information resources, raising awareness

Introduction

Tuberculosis (TB) is a leading cause of illness and death in people living with HIV.¹

Almost a quarter of the world's two million HIV-related deaths each year are associated with TB². Early identification of HIV infection in those with TB is essential, given the overlapping risk groups, consequences of co-infection and the improved prognosis of TB in HIV positive individuals once antiretrovirals have been commenced.

Internationally, there is an increasing move from 'opting in' testing, where individuals are tested who have specifically come to a service to find out their HIV status towards 'opt-out' or universal testing where people are tested routinely unless they specifically request not to be tested.^{3, 4} To our knowledge the only reports of universal HIV testing of TB patients is from retrospective analysis of surveillance data, which demonstrates that universal HIV testing of TB patients may be achievable through 'opt – out' HIV testing.⁵

In 2008, HIV status was known for 22% of all notified TB cases globally.⁶ There is wide variation in the extent to which universal HIV testing is implemented in TB clinics between countries. In the United States, national guidelines take a proactive approach to normalise the diagnosis of HIV infection⁷ and it is recommended that all patients commencing treatment for TB are screened for HIV infection. By contrast, many European countries, have failed to take this proactive approach, and still have variable policies for different groups: France, Germany and Spain routinely test TB patients for HIV⁸, while in Poland there is no similar recommendation.⁸ In the UK the

recommendations are less clear. The British HIV Association advocate an approach supported by the Chief Medical Officer (CMO) for England of an universal policy for HIV testing in all high risk groups, including those with TB^{4, 9, 10}. However, the UK National Institute for Health and Clinical Excellence recommends that all TB patients should have a risk assessment and, if appropriate, testing for HIV.¹¹ The offer of HIV tests in TB clinics remains variable¹²; half of individuals are not offered tests despite high levels of TB-HIV co-infection in London.¹³

Previous work in antenatal clinics demonstrated a change in policy from a selective opt-in to universal opt-out HIV test.¹⁴ The provision of supporting information and training to healthcare professionals has led to an increase in the uptake of HIV testing.¹⁵ This has led to universal HIV testing of expectant mothers in antenatal care.^{15, 16} Based on a systematic search of the literature, we found no randomised controlled trials investigating 'universal HIV testing' in TB clinics. In view of this and the recommendation to normalise HIV testing of TB patients, a universal HIV testing policy^{9, 10} was implemented in London.

We report the results of a stepped-wedge cluster randomised controlled trial of the impact of implementing universal HIV testing, the provision of training and of tailored information materials on the offer, acceptance and coverage of HIV testing among TB patients.

Methods

Study design

All TB clinics in London (31) were invited to participate in the study. Four clinics declined. The intervention was introduced sequentially using a step-wedge design in 27 TB clinics; two clinics subsequently merged and two dropped out. Therefore the trial was completed in 24 centres (Figure 1).

Eligible participants included all patients seen and diagnosed with TB in participating centres between September 2009 and March 2010 who were not already known to be HIV infected. Participants seen at each clinic prior to the intervention served as the control group; once the interventions were implemented they were considered as the intervention group (Figure 2).

Interventions

The trial was designed to evaluate a complex intervention. Two types of centres were eligible for participation: group A consisted of clinics using a selective HIV testing policy and group B comprised clinics where universal testing had already been initiated. The intervention consisted of three elements for group A: (i) a change in HIV testing from a risk-based selective approach to a universal offer of testing without detailed pre-test discussion (opt-out), (ii) training of TB clinic staff and (iii) the provision of tailor-made information material for patients and healthcare workers in English, Farsi, French, Polish, Gujarati, Hindi, Punjabi, Somali, Tamil, Turkish and Urdu (Supplementary Material). The languages for translation were chosen based on a survey of the ethnic

background of patients attending the participating clinics. Group B had the latter two measures only. Identical information materials were used in all centres.

The implementation of a universal policy implies that HIV testing is a standard part of medical care with all patients offered the test irrespective of age, ethnicity, religion or risk of infection. Written consent is not required. Patients were informed that they would be tested for HIV at the same time as other baseline blood tests. This was recorded as an 'offer'; however participants still had the right to opt-out. The date the HIV test was conducted was recorded and these patients were classified as having "accepted" the test. This information was sent on a monthly basis from the TB clinics to the study centre.

Information resources included a multilingual information card for a patient, which was specifically designed to address all routine tests conducted in TB clinics. An information leaflet for nurses and other healthcare workers provided guidance on the universal policy. All clinics were also provided with a multilingual table top information display (Supplementary Material).

Training involved providing members of the clinical team with a short didactic session delivered by one of the study investigators, followed by a question and answer period. The session lasted approximately 45 minutes in each centre and was undertaken in the month coinciding with the initiation of other elements of the intervention. Clinicians were requested to offer the test at the first opportunity during the diagnostic process.

Outcome measures

The primary outcome measure was acceptance of testing, defined as the proportion of eligible individuals tested amongst those who were offered a test (Figure 3 Supplementary Material). This was assessed before (control arm) and after the intervention. The main, pre-specified, secondary outcome measure was the proportion of eligible individuals offered a test. In addition, we assessed “coverage” before and after the intervention, which we defined as the proportion of individuals who were tested, amongst all the study participants (whether offered a test or not). In this analysis, patients who had not been offered a test and those who opted out were both considered not having taken up the test.

Exclusion criteria

Individuals subsequently found not to have TB, patients diagnosed with TB at the post-mortem, those admitted to hospital at the time of study (study included TB clinics only), and those managed by non-TB units were excluded from the study (Figure 1).

Randomisation, masking and step wedge design

As the intervention would eventually be implemented in all clinics, a stepped-wedge design allowed randomisation. A cluster design with the clinic as the unit of intervention was used. The intervention was sequentially rolled out to clusters of clinics over the study period. The order was determined using a computer generated random sequence (Figure 2). The persons randomising the clinics were blinded to their identity and selected three clinics every month from group A to receive the intervention (18

clinics) and one in group B (6 clinics) at time point zero. By the end of the study all participating TB clinics received the intervention.

Data collection

We collected individual level data on the offer of an HIV test for each TB case, as well as whether they were tested, from all participating clinics over the study period (September 2009 - March 2010). The control group comprised patients from clinics who had not received the intervention (Figure 2). In addition information on age, gender, place of birth, time of arrival in the UK (if foreign born) and episode start date were collected from the London TB Register. Data on the characteristics of clinics and anonymised information on patients/staff (staffing levels) were also obtained.

Statistical methods

Group A and group B clinics were analysed separately. HIV test acceptance was compared in the control and intervention groups using χ^2 tests, with adjustment for cluster sampling.¹⁷ Possible confounding was assessed using mixed effects logistic regression models, with intervention/control status, age, sex, country of birth, whether seen in a TB clinic which also ran an HIV clinic, and the patient to : staff ratio (this was coded as a four-level categorical variable; 0-19, 20-39, 40-79 and 80+ patients per : staff member). These groupings roughly corresponded to the quartiles of the distribution of patient: to staff ratios among group A clinics and were used as the fixed effects with clinic as the random effect, to adjust for the cluster-randomisation. All covariates which were significantly associated (χ^2 test adjusted for cluster sampling $p < 0.01$) with the outcome (acceptance of HIV test) were included in the final model,

along with the pre-intervention/post-intervention variable to calculate adjusted odds ratios and 95% confidence intervals. The adjusted proportions of individuals who accepted HIV testing were estimated from this model. For group B clinics, the prevalence of the outcome was near 100%, resulting in small cell sizes (or cell sizes equal to zero), therefore exact, rather than mixed effect, logistic regression models (including clinic as a fixed linear predictor) was implemented to obtain more reasonable estimates for the odds ratios.

Similar models for all analyses were also constructed to examine whether the secondary outcome, offer of a HIV test, was associated with the intervention. We also estimated the effect of the intervention on the coverage of testing using similar models.

The sample size calculation was based on preliminary data obtained from clinics in the East London sector. In order to detect a 40% increase in HIV testing acceptance, with 80% power and a type I error probability of 5%, a total of eight clinics would be required, assuming 100 attendees per clinic and a coefficient of variation (an indicator of between clinic variations) of 0.1.

Results

A total of 1315 participants, 963 patients from 18 group A clinics and 352 in 6 group B clinics, were included in this study (Figure 1). Table 1 shows the demographic characteristics of the participants. The two groups were similar in terms of age, gender and country of birth.

Overall, at baseline group A test acceptance was 84% (183/217), offer 76% (235/308), and coverage 72% (221/308). Following the intervention these increased to 86% (462/534), 87% (568/655) and 81% (534/655) respectively. Group B acceptance was 81% (91/112), offer 89% (125/141) and coverage 76% (107/141). Following the intervention these increased to 87% (172/197), 96% (202/211) and 85% (180/211) respectively.

Acceptance of testing

Group A: Age group and country of birth were significantly associated with acceptance of HIV tests (χ^2 test $p < 0.001$ and 0.03 respectively) and were included in the adjusted model (Table 2). Acceptance of HIV tests was 73% in those over 65 and 100% in patients under 16 years. Non-UK born patients had a higher acceptance compared to the UK born. Receiving the intervention did not appear to be significantly associated with a higher acceptance of HIV tests in the multivariable analysis (adjusted odds ratio 1.53 (95% CI 0.84, 2.81) χ^2 test $p = 0.76$) (Table 3).

Group B: No covariates were significantly associated with the outcome, and consequently only the pre- and post-intervention variables were included in the final model. There was no increase in the acceptance of HIV tests with the intervention: adjusted odds ratio 1.40 (95% CI 0.67, 2.91) χ^2 test $p=0.4$ (Table 3).

Offer of testing

Group A: Age group was the only covariate which was significantly associated (χ^2 test $p<0.001$) with an offer of a test (Table 2) and thus was included in the final model for this group, along with the intervention variable. Fifty three percent of persons under 16 years old were offered the test, compared to 81% in those over 65 years. The intervention significantly increased test offer (1.67 (95% CI 1.07-2.60) χ^2 test $p=0.002$) (Table 3).

Group B: After univariate analysis, three variables were considered significantly associated with offer of HIV test, these were age-group (χ^2 test $p<0.001$), patient load/clinician (χ^2 test $p<0.008$) and whether a joint TB-HIV clinic was held (χ^2 test $p=0.01$). The two clinic-level variables were co-linear. Due to the small number of units (6), the adjusted odds ratio was estimated with only age and intervention effects as covariates and cluster as a fixed effect. In this group there was evidence of an association between the intervention and the offer of an HIV test (3.76 (95% CI 1.31-12.25) χ^2 test $p=0.02$) (Table 3).

Coverage of testing

Group A: Younger (> 16 years) and older age groups (< 65⁺), when compared with young adults (25 - 34), and UK born individuals (compared to non-UK born) were less likely to be tested. Therefore these two variables were included in the model. The adjusted odds ratio for testing was 1.83 (95% CI 1.3 - 2.71, Wald test $p=0.004$) (Table 3). In the fully adjusted model younger persons (>16 years) and older persons (65⁺) were significantly less likely to be tested compared to 25 - 34 years, while the association with being born in the UK was no longer significant.

Group B: For consistency, the model included age group and country of birth as linear predictors. This gave an odds ratio for coverage in the intervention compared to the control group of 1.84 (95% CI 1.03, 3.29, Wald test $p=0.04$) (Table 3).

Discussion

In this evaluation of a pragmatic public health intervention to improve HIV testing in TB clinics in London, we found an increase in the proportion of people tested, and offered testing, but not in the proportion that accepted the test when it was offered. Offers and coverage increased from 76% to 87% and 72% to 82% in centres without pre-trial universal testing, respectively. In clinics with pre-existing universal testing policies, offer and coverage rose from 89% to 96% and 76% to 85%, respectively. The demonstrated increase in coverage, even in a setting with a reasonably high baseline level of offer, suggests that the intervention increased the proportion of individuals tested but did not change the acceptance rate.

Previous research suggests that HIV co-infection is more likely to be missed with selective testing¹⁸, compared to a universal approach to HIV testing in TB patients and other settings^{19, 20}. HIV testing in TB clinics in the past 10 years has made significant progress in London and attempts are underway to integrate this into the routine clinical management of TB. Nearly 50% patients with TB in 2003 - 2004 in London^{21, 22} were not offered HIV testing. In 2007 the UK CMO²² issued a letter to public health professionals highlighting high rates of late diagnosis and poor outcomes in those diagnosed late. Attempts to implement this recommendation appear to raise the baseline for coverage by selective HIV testing in TB services from 50% to greater than 70%.

Within at group A where there was selective testing and subsequent universal testing as result of this study, we successfully increased the offers and coverage of HIV tests, but failed to increase acceptance among those offered a test. The lack of an increase in acceptance was disappointing, but may reflect the reasonably high level of acceptance at baseline (84% and 81% for groups A and B, respectively) and the complex nature of measures required to change patient behaviour. Another potential explanation for the lack of acceptance is ineffective dissemination of the informative material presented. Qualitative information collected during the trial suggests that many health care professionals did not always give the relevant materials to patients. Even with

increased coverage of 10%, 15% individuals remain to be tested, so there is still room to improve test acceptance.

In preparation for this study, we undertook a systematic review to identify the main barriers to HIV testing plus interventions with proven efficacy in TB clinics. Barriers can be broadly grouped into: (i) poor access to comprehensive services; (ii) lack of staff training for offering or normalising testing; (iii) lack of awareness among providers and patients regarding the benefits of early diagnosis of HIV; (iv) non-implementation of national TB programme policies and the (v) stigma associated with both HIV and TB.

There was little *a priori* evidence that any particular single measure would alter behaviour and it is unlikely that a single measure will be used in practice. This informed our choice of educational interventions to raise awareness, as well as to normalise testing, thereby reducing stigma.

This study was not powered to compare the effect of universal testing versus educational intervention; nevertheless a comparison of group A and B clinics shows a similar magnitude and direction of effect. This suggests additional benefit of the educational intervention beyond that due to implementation of universal testing.

Further, research in setting with low baseline coverage to confirm or refute our finding would be useful.

Age was particularly associated with low acceptance; most patients in this study accepted the test offered, except those in the over 65 year category.^{23, 24} Patients often declined testing because they believed they were not at risk of HIV. Recent reports in the UK suggest that there has been a three-fold increase in the number of older individuals accessing HIV care since 2000.²⁵ New diagnoses among older adults more

than doubled between 2000 and 2009, and accounted for 13% of all diagnoses in 2009²⁵. The disconnection between perceived and actual risk may reflect a patient's choice not to acknowledge their personal risk and a lack of knowledge about HIV transmission.²⁶

Although HIV testing is recommended for all children who are TB suspects or patients²⁷, this study showed that those under 16 years had the lowest offers of HIV testing. This is consistent with the observation that most paediatricians were not keen to join the study, reporting that they would conduct their own risk assessment to determine whether the child should have a HIV test. Many children with TB disease have parents who originate from high TB and HIV burden countries²⁸, highlighting the need to normalise HIV testing in this population. Therefore, further policy changes are required to specifically ensure that all healthcare workers and patients are more aware of the need for the HIV testing in all age groups. These results add to the argument for universal HIV testing in all TB patients, rather than taking a selective approach based on a potentially imperfect risk assessment.²⁹ The cost effectiveness of universal testing in TB settings should be investigated. Other research has shown that routine voluntary testing, as recommended by the US Centres for Disease Control, is a cost-effective intervention³⁰.

The limitations of our study include the allocation of the intervention at a cluster level that potentially provided a chance of contamination between centres. The effect is likely to be small due to minimal movement of patients between centres. A further limitation is the high baseline level of offer and acceptance of testing, limiting the

power of the study to detect the effect of the intervention. Nevertheless, we have been able to show a significant increase in offers and therefore coverage of testing using a randomised controlled trial. We were not able to mask allocation to staff members or patients due to the nature of the intervention. Changes in centres, patient population group and staff numbers over time may also affect the results of this study. Characteristics of the clinics assessed over the study period suggest that these were relatively stable. Finally, our study was investigating whether coverage of HIV testing could be increased; we did not determine whether they had an impact on HIV diagnosis. Nevertheless, wider testing would be expected to improve detection.

Conclusion:

This study has provided a pragmatic assessment of the efficacy of a combination of interventions to improve HIV testing in TB clinics. The intervention led to an increase in the number of offers of HIV tests and therefore the number and proportion of patients tested, despite the lack of a significant effect on acceptance among those offered a test. The implementation of a policy of universal testing, combined with supportive information, has the potential to positively impact on the levels of testing in TB clinics, thus increasing the health benefits associated with an earlier diagnosis of HIV infection. Our findings provide a framework for improving testing in other settings^{31, 32} and therefore to improve clinical outcomes.

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Reference List

- (1) Lawn SD, Churchyard G. Epidemiology of HIV-associated tuberculosis. *Curr Opin HIV AIDS* 2009;4(4):325-333.
- (2) World Health Organization. Priority Interventions. 2010.
- (3) CDC. *Reported Tuberculosis in the United States, 2010*. Atlanta, GA. U S Department of Health and Human Services, CDC, October 2011 2011.
- (4) BHIVA. *UK National Guidelines for HIV Testing 2008* 2008.
- (5) Sturtevant D, Preiksaitis J, Singh A et al. The feasibility of using an 'opt-out' approach to achieve universal HIV testing of tuberculosis patients in Alberta. *Can J Public Health* 2009;100(2):116-120.
- (6) Lonroth K, Castro KG, Chakaya JM et al. Tuberculosis control and elimination 2010-50: cure, care, and social development. *Lancet* 2010;375(9728):1814-1829.
- (7) Branson BM, Handsfield HH, Lampe MA et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006;55(RR-14):1-17.
- (8) ECDC. **Survey on Tuberculosis and HIV Co-infection Surveillance in EU and EEA Countries**. 2010.
Ref Type: Personal Communication
- (9) Sir Liam Donalson C&CB, CNO. Improving the detection and diagnosis of HIV in non-HIV specialties including primary care. 2009 Sep 1.
- (10) BHIVA B&B. *UK National Guidelines for HIV Testing 2008*. 2008.
- (11) National Collaborating Centre for Chronic Conditions. Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control. 2006. 2011. London, Royal College of Physicians.
Ref Type: Generic

- (12) Rodger AJ, Story A, Fox Z, Hayward A. HIV prevalence and testing practices among tuberculosis cases in London: a missed opportunity for HIV diagnosis? *Thorax* 2010;65(1):63-69.
- (13) Ahmed AB, Abubakar I, Delpech V et al. The growing impact of HIV infection on the epidemiology of tuberculosis in England and Wales: 1999-2003. *Thorax* 2007;62(8):672-676.
- (14) Hamill M, Burgoine K, Farrell F et al. Time to move towards opt-out testing for HIV in the UK. *BMJ* 2007;334(7608):1352-1354.
- (15) Simpson WM, Johnstone FD, Boyd FM et al. A randomised controlled trial of different approaches to universal antenatal HIV testing: uptake and acceptability and Annex: Antenatal HIV testing - assessment of a routine voluntary approach. *Health Technol Assess* 1999;3(4):1-112.
- (16) Townsend CL, Cortina-Borja M, Peckham CS, de RA, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS* 2008;22(8):973-981.
- (17) Rao JSA. On Chi-squared Tests For Multiway Contingency Tables with Proportions Estimated From Survey Data". *Annals of Statistics* 12, 46-60. 1984.
Ref Type: Generic
- (18) Sturtevant D, Preiksaitis J, Singh A et al. The feasibility of using an 'opt-out' approach to achieve universal HIV testing of tuberculosis patients in Alberta. *Can J Public Health* 2009;100(2):116-120.
- (19) Wang FL, Larke B, Gabos S, Hanrahan A, Schopflocher D. Potential factors that may affect acceptance of routine prenatal HIV testing. *Can J Public Health* 2005;96(1):60-64.
- (20) Jayaraman GC, Preiksaitis JK, Larke B. Mandatory reporting of HIV infection and opt-out prenatal screening for HIV infection: effect on testing rates. *CMAJ* 2003;168(6):679-682.
- (21) Rodger AJ, Story A, Fox Z, Hayward A. HIV prevalence and testing practices among tuberculosis cases in London: a missed opportunity for HIV diagnosis? *Thorax* 2010;65(1):63-69.
- (22) Donaldson Liam CMO BCC. Improving the detection and diagnosis of HIV in non-HIV specialties including primary care. 13 September 2007. *Letter* 2012.
- (23) Merchant RC, Seage GR, Mayer KH, Clark MA, DeGruttola VG, Becker BM. Emergency department patient acceptance of opt-in, universal, rapid HIV screening. *Public Health Rep* 2008;123 Suppl 3:27-40.

- (24) Lyss SB, Branson BM, Kroc KA, Couture EF, Newman DR, Weinstein RA. Detecting unsuspected HIV infection with a rapid whole-blood HIV test in an urban emergency department. *J Acquir Immune Defic Syndr* 2007;44(4):435-442.
- (25) 2010 Report. HIV in the United Kingdom: 2010 Report. 2011. Health Protection Agency, Health Protection Report 2010 4(47).

Ref Type: Generic

- (26) Merchant RC, Waxman MJ. HIV screening in health care settings: some progress, even more questions. *JAMA* 2010;304(3):348-349.
- (27) World Health Organisation. Guidance for National Tuberculosis and HIV Programmes on the management of Tuberculosis in HIV-infected children: recommendations for a public health approach. 2011. WHO , Geneva 2010.

Ref Type: Generic

- (28) Abubakar I, Laundry MT, French CE, Shingadia D. Epidemiology and treatment outcome of childhood tuberculosis in England and Wales: 1999-2006. *Arch Dis Child* 2008;93(12):1017-1021.
- (29) Long R, Boffa J. High HIV-TB co-infection rates in marginalized populations: evidence from Alberta in support of screening TB patients for HIV. *Can J Public Health* 2010;101(3):202-204.
- (30) Walensky RP, Freedberg KA, Weinstein MC, Paltiel AD. Cost-effectiveness of HIV testing and treatment in the United States. *Clin Infect Dis* 2007;45 Suppl 4:S248-S254.
- (31) Batey DS, Hogan VL, Cantor R et al. Routine HIV Testing in the Emergency Department: Assessment of Patient Perceptions. *AIDS Res Hum Retroviruses* 2011.
- (32) Chiao EY, Dezube BJ, Krown SE et al. Time for oncologists to opt in for routine opt-out HIV testing? *JAMA* 2010;304(3):334-339.

Table 1: Distribution of key variables in the dataset among pre-intervention and post-intervention groups

Variable	Post-intervention(%)	Pre-intervention (%)	χ^2 test for equality of proportions *	Post-intervention(%)	Pre-intervention (%)	χ^2 test for equality of proportions *
	Group A : Clinics introducing opt out testing and resources (total N=963)			Group B: Clinics introducing resources only (total N=352)		
Age group			0.45			0.45
<16	29 (4.4)	12 (3.9)		12 (5.7)	10 (7.1)	
16-24	93 (14.2)	54 (17.5)		46 (21.8)	26 (18.4)	
25-34	203 (31.0)	85 (27.6)		68 (32.2)	37 (26.2)	
35-44	123 (18.8)	51 (16.6)		43 (20.4)	40 (28.4)	
45-64	125 (19.1)	71 (23.1)		26 (12.3)	18 (12.8)	
65+	79 (12.1)	33 (10.7)		16 (7.6)	10 (7.1)	
Missing	3 (0.5)	2 (0.6)		0 (0)	0 (0)	
Country of birth			0.6			0.62
Outside UK	461 (70.4)	206 (66.9)		181 (85.8)	120 (85.1)	
UK	141 (21.5)	70 (22.7)		21(10.0)	17 (12.1)	
Missing	53 (8.1)	32 (10.4)		9 (4.3)	4 (2.8)	
Gender			0.1			0.46
Male	380 (58.1)	164 (53.2)		124 (58.8)	77 (54.6)	
Female	274 (41.8)	144 (46.8)		87 (41.2)	64 (45.4)	
Missing	1 (0.2)	0 (0)		0 (0)	0 (0)	
Seen in clinic with joint HIV/TB clinic			0.41			0.06
Yes	324 (49.5)	120 (39.0)		129 (61.1)	38 (27.0)	
No	331 (50.5)	188 (61.0)		82 (38.9)	103 (73.0)	
Missing	0 (0)	0 (0)		0 (0)	0 (0)	
Patient load in clinic						
Median	39.9	75.3	Wilcoxon Signed Rank test p<0.001	35.1	17.7	Wilcoxon Signed Rank test p<0.001
Inter-quartile range	68.9	95.4		25	16.3	

*Excluding missing category. Standard errors have been adjusted for cluster sampling using method by Rao & Scott. **This category excludes those individuals who refused a HIV test. And those who have had an HIV test prior to start of study (n=200 for clinics introducing opt-out testing , n=43 for those introducing resources only).

Table 2: Factors associated with acceptance and offer of HIV tests to all participants (TB patients registered) included in the study

Characteristics		Group A				Group B			
		HIV test acceptance		HIV test offered		HIV test acceptance		HIV test offered	
		Those accepted test/total number of participants offered the test (%)	p* value	Those who were offered HIV test/total number of participants in category (%)	p*value	Those accepted test/total number of participants offered the test (%)	p*value	Those who were offered HIV test/total number of participants in category (%)	p* - value
Country of birth	UK	~126/155 (81)	0.03	~168/210 (80)	0.07	~29/32 (91)	0.35	~34/37 (92)	0.36
	non-UK	470/549 (86)		568/667 (85)		223/259 (86)		281/297 (95)	
Gender	Male	376/424 (89)	0.17	461/544 (85)	0.21	152/180 (84)	0.17	187/198 (94)	0.83
	Female	269/315 (85)		341/417 (82)		111/122 (91)		140/149 (94)	
Patient load	1st quartile	148/175 (85)	0.14	195/238 (82)		107/125 (86)		141/143 (99)	0.008
	2nd quartile	171/200 (86)		216/256 (84)	0.55	91/97 (94)	0.08	101/116 (87)	
	3rd quartile	111/137 (81)		150/160 (94)		40/43 (93)		46/48 (96)	
	4th quartile	215/227 (95)		242/308 (79)		25/37 (68)		39/40 (98)	
Joint TB- HIV clinic	Yes	372/413 (90)	0.21	456/519 (88)	0.22	132/162 (81)	0.12	180/183 (98)	0.01
	No	273/326 (84)		347/443 (78)		131/140 (94)		147/164 (90)	
Age-group	<16	9/9(100)	<0.001	21/40 (53)		7/12 (58)		13/19 (68)	<0.001
	16-24	115/124 (93)		131/147 (89)		8/68 (12)		71/72 (99)	
	25-34	211/228 (93)		254/288 (88)		87/95 (92)		102/105 (97)	
	35-44	120/130 (92)		142/174 (82)	<0.001	61/71 (86)	0.08	77/82 (94)	
	45-64	128/155 (83)		161/196 (82)		31/37 (84)		41/43 (95)	
	65+	59/81 (73)		91/112 (81)		17/19 (89)		23/26 (88)	

^LTBR = London TB Register; *Value calculated with correction for cluster sampling; ~difference in offered and acceptance in table is different as the study considers 'prior test' as 'offer' as health care professionals did investigate the HIV status of patient.

Table 3. Outcome analysis of acceptance, offer and coverage of HIV testing among tuberculosis clinics in London from September 2009 - March 2010

Outcome	Control/intervention	Outcome	N for multivariable analysis(%)	x ² test for equality of proportions	Adjusted OR	
Group A: Clinics introducing opt out testing, training and resources						
Test accepted	Intervention n=534	Test accepted	462(86.5)	0.76	1.53 (0.84, 2.81) ^{†*}	
		Test not accepted	69(12.9)			
		Test information missing	3(0.6)			
	Control n =217	Test accepted	183(84.3)			1
		Test not accepted	25(11.5)			
		Test information missing	9(4.1)			
Test offered	Intervention n =655	Test offered	568 (86.7)	0.002	1.67 (1.07, 2.60) ^{†Δ}	
		Test not offered	86 (13.1)			
		Offer information missing	1 (0.2)			
	Control n =308	Test offered	235 (76.3)			1
		Test not offered	73 (23.7)			
		Offer information missing	0 (0)			
Coverage	Intervention n = 655	Test coverage yes	534 (81.5)	0.004	1.83(1.3, 2.7) ^{†Δ}	
		Test coverage no	121 (12.1)			
		Test coverage information missing	0 (0)			
	Control n = 308	Test coverage yes	221 (71.7)			1
		Test coverage no	87 (28.2)			
		Test coverage information missing	0(0)			

Table 3. (contd.) Outcome analysis of acceptance, offer and coverage of HIV testing among tuberculosis clinics in London from September 2009 - March 2010

Outcome	Control/intervention	Outcome	N for multivariable analysis(%)	χ^2 test for equality of proportions	Adjusted OR	
Group B : Clinics introducing training and resources only						
Test accepted	Intervention <i>n</i> =197	Test accepted	172(87.3)	0.4	1.40 (0.67, 2.91) ^{†*}	
		Test not accepted	21(10.7)			
		Test information missing	4(1.5)			
	Control <i>n</i> =112	Test accepted	91(81.3)			1
		Test not accepted	18(16.1)			
		Test information missing	3(2.7)			
Test offered	Intervention <i>n</i> =211	Yes	202(95.7)	0.02	3.76 (1.31, 12.25) ^{†Δα}	
		No	6(2.8)			
		Missing	3(1.4)			
	Control <i>n</i> =141	Yes	125(88.7)			1
		No	14(9.9)			
		Missing	2(1.4)			
Test coverage	Intervention <i>n</i> =211	Test coverage yes	180(85.3)	0.04	1.84(1.03, 3.29) ^{†Δ}	
		Test coverage no	31(14.7)			
		Test coverage missing	0(0)			
	Control <i>n</i> =141	Test coverage yes	107(75.9)			1
		Test coverage no	34(24.1)			
		Test coverage missing	0(0)			

†Adjusted for age group; *Model included only persons who had a test offered to them and who had not previously had a test; Δ model included all persons with prior test; α adjusted odds ration obtained from exact logistic regression

Figure 1 : Trial Profile

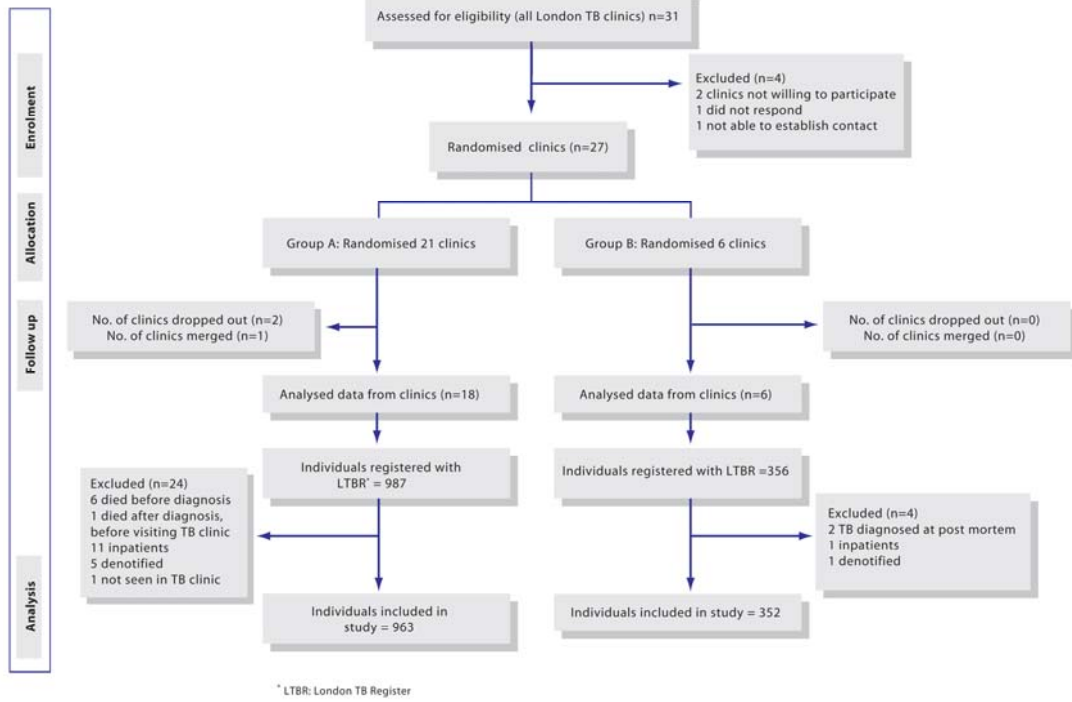
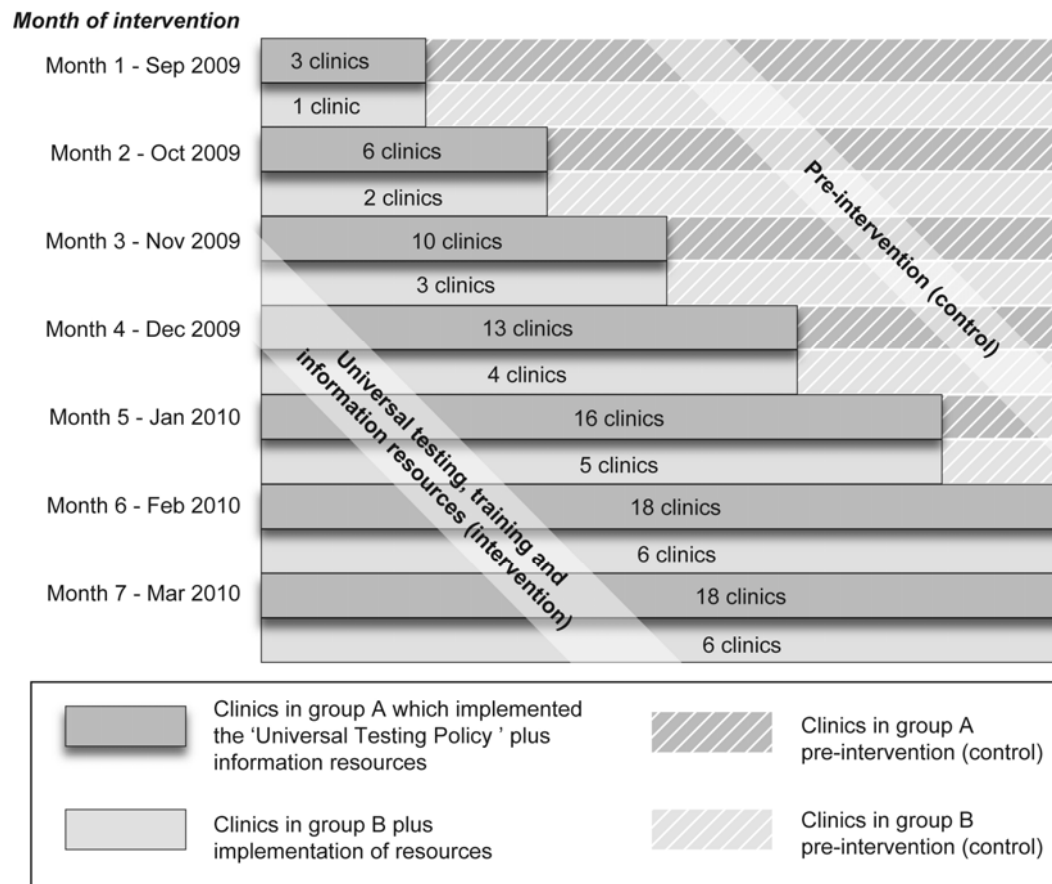


Figure 2: Step wedge design: schematic representation of the interventions among the TB clinics in London over a 7 month period



Group A pre-intervention (control) median number of patients per clinic: 17 (IQR 12.5 – 49.0); intervention 39.5 (IQR 20.8 – 95.0). Group B pre-intervention (control) median number of patients: 21.5 (IQR 13.25 – 47); intervention: 40 (IQR 28.5 – 50).