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TB-HIV SUPPLEMENT

Cross-referral between voluntary HIV counselling and testing centres and TB services, Maharashtra, India, 2003–2004

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SUMMARY

SETTING: India has a high tuberculosis (TB) burden, with 1.8 million new cases per year. Although an estimated 2.5 million people are infected with human immunodeficiency virus (HIV), the national HIV prevalence is <1%. India's size and diverse TB-HIV epidemiology pose a major challenge to the implementation of links between TB and HIV/AIDS programme services.

METHODS: A pilot cross-referral initiative was instituted between voluntary counselling and testing centres (VCT) and the diagnostic and treatment facilities of the Revised National TB Control Programme (RNTCP) in four districts of Maharashtra, India.

OBJECTIVE: To detect TB disease among VCT patients and selectively screen TB patients for referral to VCT services.

RESULTS: Between July 2003 and June 2004, 336 (3%) of 9921 VCT patients were identified as TB suspects and 83 (29%) were diagnosed with TB disease. Of the 765 selectively referred TB cases, 181 (24%) were found to be HIV-positive, representing 11% of the newly detected persons living with HIV in the four districts.

CONCLUSIONS: The pilot cross-referral initiative yielded significant numbers of active TB cases among VCT patients and HIV-positive persons among TB patients. Collaborative activities between HIV/AIDS and TB programmes need to be rapidly scaled up to other states in India.

KEY WORDS: tuberculosis; HIV; AIDS; voluntary counselling and testing; cross-referral

HUMAN IMMUNODEFICIENCY VIRUS (HIV) infection is the strongest risk factor for progression from *Mycobacterium tuberculosis* infection to tuberculosis (TB) disease, and poses a serious threat to TB control. India has an estimated 2.5 million people living with HIV/acquired immune-deficiency syndrome (AIDS) (PLWHA), the second highest total globally.[1] There is considerable geographic variability in HIV prevalence in India,[2] and six states have been identified as high HIV prevalence (>1% among women attending antenatal clinics).[1] India has the largest number of dually infected persons, with approximately 40% of PLWHAs co-infected with *M. tuberculosis*.[3] Co-infected PLWHAs may rapidly progress to active TB, and have a 5–10% annual risk of developing TB.[4–7] Studies in India suggest that 50–60% of PLWHAs have had TB disease in the course of their illness.[8]

With an estimated 1.8 million new cases annually, India ranks first among the world's 22 highest TB burden countries.[9] By March 2006, DOTS was expanded nationwide to all 35 states (population 1.14 billion), and case detection reached 66% in 2005.[3] DOTS regimens for TB have been shown to significantly prolong the life of PLWHAs, prevent drug resistance, and, by rendering the patient non-infectious, reduce the transmission of *M. tuberculosis*.[10] Close collaboration between the Revised National TB Control Programme (RNTCP) and the National AIDS Control Programme (NACP) could decrease TB morbidity and mortality among PLWHAs, ensure that TB patients have access to HIV/AIDS prevention, care and treatment and dampen the potentially negative impact the HIV/AIDS epidemic may have on TB control.[2]

In 2001, the RNTCP and NACP developed a joint TB-HIV action plan, which is currently being implemented in 14 states.[3] As recommended by the World Health Organization (WHO),[11] the plan includes establishing routine screening for symptoms of TB at voluntary counselling and testing (VCT) sites and referral to RNTCP services. Early referral should ensure the prompt detection and initiation of TB treatment. Selective referral of TB patients with symptoms of other

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opportunistic infections and/or high risk behaviour to VCTs should ensure early detection of HIV/AIDS and access to prevention, care and treatment services.[12]

One of the largest Indian states, Maharashtra has 35 districts and a population of around 100 million.* HIV prevalence rates vary across the state, with 14 districts reporting high HIV prevalence.[1] We report the first year's results for a pilot TB-HIV cross-referral programme in four districts of Maharashtra.

MATERIALS AND METHODS

The pilot was implemented between July 2003 and June 2004 as part of routine services. Pilot sites (districts) were selected based on HIV prevalence, availability of RNTCP services and VCT locations. Two high HIV prevalence districts (Nashik and Sangli) and two low HIV prevalence districts (Bhandara and Nanded) were selected. Nashik (population 5 million) had two VCTs, one in a district hospital and the other in a sub-district hospital; Sangli (2.6 million), and Nanded (2.8 million) had one VCT each in a government medical college; and Bhandara (1.1 million) had one VCT in a district hospital. All five VCTs were located in the same campus as a microscopy centre (MC).

A 2-day modular training on TB-HIV and the operationalisation of the cross-referral mechanism was conducted for VCT counsellors and RNTCP senior TB treatment supervisors (STS). The training included basic information on TB and HIV (e.g., signs and symptoms, diagnosis, treatment options, risk factors, etc.) and the record keeping and reporting system. RNTCP and VCT personnel were trained in identifying suspected TB cases as per RNTCP guidelines.[13] There is one STS per 500 000 population, who ensures that directly observed treatment (DOT) providers are in place and all TB patients are on DOT.† The Medical Officer, VCT and District TB Officer also received 2 days of TB-HIV training and were given detailed written information about the pilot project. Quarterly regional review meetings with VCT and RNTCP staff held by the state-level Programme Officers, District TB-HIV Co-ordination Committee Meetings and district-level weekly/fortnightly/monthly meetings between the VCT and RNTCP personnel were instrumental in monitoring and trouble-shooting implementation. Although there was discussion of cross-referral between programmes, emphasis was laid on referrals from the VCTs to the TB diagnostic services, as the aim of the first phase of the pilot was to increase early diagnosis and treatment of TB disease among VCT patients.

The VCT has two types of patient: those who come for the first time to a VCT ('new patients'), and those who come for further counselling after learning about their HIV status ('follow-up patients'). Counsellors screened all VCT patients for symptoms suggestive of TB disease. Patients with cough $\geq$3 weeks were referred directly to an MC using the standard sputum examination request form.[13] Persons with lymph node swellings or symptoms of TB (e.g., fever, weight loss, etc.), were referred to the Medical Officer of the MC. Referrals from VCT to TB services were made irrespective of HIV status. The counsellor recorded the information about the patient's referral to TB services in the VCT register. Monitoring and evaluation relied on cross-checking line-lists from standard TB and VCT registers, i.e., no additional registers were introduced.

Although no written questionnaire or screening checklist was used, TB patients were screened by medical officers providing TB services, and those reporting multiple sexual partners or a partner with HIV, oral/oesophageal candidiasis, diarrhoea for >1 month and/or sexually transmitted infections were referred to the VCT. The referrals received from TB services were documented in the VCT register, but by design the TB service sites did not maintain documentation of the referrals of TB patients to VCTs.

Using the VCT and TB registers, a line-list of persons successfully referred from VCT to MCs was jointly prepared by the VCT counsellor and the RNTCP STS at the end of each month. To help maintain confidentiality, the line-list did not include the HIV status of individuals referred. HIV status was matched later by the VCT counsellor for the purpose of monthly reporting of aggregated outcomes of referral by HIV status. TB patients referred to VCTs were also recorded only in the VCT register. The final aggregate TB-HIV report was prepared by the VCT counsellor and sent to the State AIDS Control Society, with a copy to the respective District TB Officer. To allow for the time taken during referral, TB diagnosis and treatment initiation, the monthly reports were prepared approximately 30 days after close of the reporting period.

An Excel (Microsoft, Redmond, WA, USA) database was used for statistical analyses (e.g., χ^2 test) of data collected on cross-referrals. A $P < 0.05$ was considered statistically significant.

RESULTS

Patients attending VCT

During the 1-year period, 9921 patients (new and follow-up) attended the five VCTs. The median monthly VCT attendance was 118 (range 18–435). New patients comprised 6826 (69%) of the total, with 99% (6729) consenting to HIV testing. Of the 6826 new patients, 772 (11%) were selectively referred from facilities providing TB services.

Overall HIV seroprevalence among new patients was 25% (range among VCTs 18–29%). Among the

* http://www.censusindia.net Accessed 29 April 2005.
† http://www.tbcindia.org Accessed 12 April 2006.

772 selectively referred TB patients from the five VCTs, 765 (99%) consented to HIV testing; 181 (181/765, 24%) tested positive for HIV (range among VCTs 12–45%). These 181 TB patients with HIV contributed 11% (181/1684) of the total persons found to have HIV at the VCTs.

Referral from VCTs to MCs

Of 9921 VCT patients, 336 (3%) were identified as having TB symptoms and referred to an MC (Figure and Table 1), with 4% identified among new patients and 1.4% in follow-up patients ($P < 0.001$). The percentage of referrals to MCs varied by VCT (range 1.8–9.5%). Most referrals occurred during the pre-test counselling visit. Analysis showed that 192 (57%) of the referred patients were HIV-positive.

Follow-up from VCT to MCs

Of 336 referrals, 287 (85%) reported to an MC (Tables 2 and 3), of whom four persons had only symptoms of extra-pulmonary TB (EPTB) and did not undergo sputum examination. Of the 283 persons undergoing sputum examination, 222 (78%) reported to an MC on the same day as their referral and another 48 (17%) within 7 days. The remaining 13 patients reported after 7 days. There was no difference in the proportion of referrals reaching the MCs by sex (data not shown) or by HIV status (Table 3). Of the 287 (85%) successful VCT-to-MC referrals, 83 (29%) were diagnosed as having TB disease: 51 (61%) were sputum smear-positive pulmonary TB (PTB), 20 (24%) smear-negative PTB and 12 (15%) EPTB.

Of the 168 referrals with TB symptoms and HIV infection who were actually evaluated at an MC, 36 (21%) were diagnosed with TB disease: 16 (44%) had sputum-positive PTB, 11 (31%) sputum-negative PTB and 9 (25%) EPTB (Table 3). Among the 119 HIV-negative referrals evaluated at an MC, 47 (40%) were diagnosed with TB: 35 (75%) had sputum-positive PTB, 9 (19%) sputum-negative PTB and 3 (6%) EPTB (Table 3). The proportion of TB cases diagnosed among the HIV-negative referrals (40%) was significantly higher than among the HIV-positive (21%) referrals ($P < 0.001$).

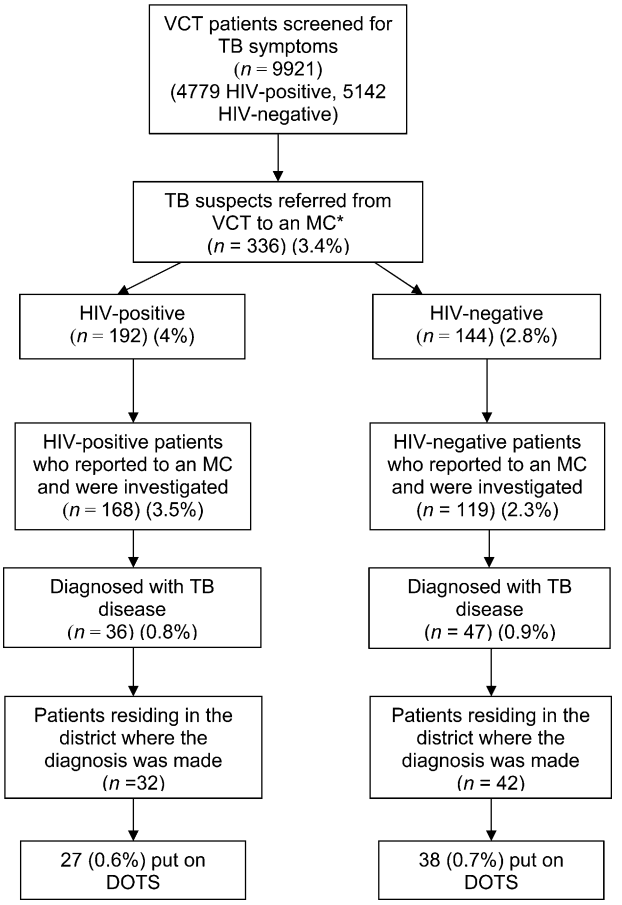

Figure Referral of TB suspects from VCT to RNTCP TB Services. * Three other persons referred to an MC did not consent to HIV testing and were excluded from the analyses. VCT = voluntary counselling and treatment centre; TB = tuberculosis; MC = microscopy centre; HIV = human immunodeficiency virus.

Table 1 Characteristics of VCT patients in Bhandara, Malegaon, Nanded, Nashik and Sangli Districts, India, June 2003–July 2004

	Bhandara *n/N* (%)	Malegaon *n/N* (%)	Nanded *n/N* (%)	Nashik *n/N* (%)	Sangli *n/N* (%)	Total *n/N* (%)
Profile of patients at VCT						
New patients attending VCT services	1060	616	1551	1222	2377	6826
New patients tested for HIV	1055	616	1459	1222	2377	6729
HIV-positive patients among new patients	191 (18)	177 (29)	348 (24)	326 (27)	642 (27)	1684 (25)
Follow-up patients at VCT	155	112	223	502	2103	3095
Referral of patients from VCT to TB services						
VCT patients identified and referred as TB suspects	69/1215 (6)	69/728 (10)	50/1774 (3)	68/1724 (4)	80/4480 (2)	336/9921 (3)
Referred patients who reported to an RNTCP microscopy centre	58/69 (84)	61/69 (89)	41/50 (82)	61/68 (90)	66/80 (83)	287/336 (85)
Patients diagnosed with TB	8/58 (13.8)	26/61 (43)	11/41 (27)	12/61 (20)	26/66 (39)	83/287 (29)
Diagnosed TB patients put on DOTS in the district where diagnosed*	6/6 (100)	21/24 (88)	6/10 (60)	11/12 (91)	21/22 (96)	65/74 (88)

* Of those diagnosed TB patients residing in the district where the diagnosis was made.
VCT = voluntary counselling and treatment centre; HIV = human immunodeficiency virus; TB = tuberculosis; RNTCP = Revised National TB Control Programme.

Table 2 Referral of patients from VCT to MC in Bhandara, Malegaon, Nanded, Nashik and Sangli Districts, India, by HIV status, July 2003–June 2004

	Bhandara *n/N* (%)	Malegaon *n/N* (%)	Nanded *n/N* (%)	Nashik *n/N* (%)	Sangli *n/N* (%)	Total *n/N* (%)
HIV-positive patients						
Patients who reported to an RNTCP MC	32/38 (84)	22/26 (85)	33/38 (87)	46/49 (94)	35/41 (85)	168/192 (88)
Patients diagnosed with TB	4/32 (13)	8/22 (36)	9/33 (27)	8/46 (17)	7/35 (20)	36/168 (21)
TB patients put on DOTS*	3/3 (100)	8/8 (100)	5/8 (63)	7/8 (88)	4/5 (80)	27/32 (84)
HIV-negative patients						
Patients who reported to an RNTCP MC	26/31 (84)	39/43 (91)	8/12 (67)	15/19 (79)	31/39 (80)	119/144 (83)
Patients diagnosed with TB	4/26 (15)	18/39 (46)	2/8 (25)	4/15 (27)	19/31 (61)	47/119 (40)
TB patients put on DOTS*	3/4 (75)	13/18 (72)	1/2 (50)	4/4 (100)	17/19 (90)	38/47 (81)

* Of those diagnosed TB patients residing in the district where the diagnosis was made.
VCT = voluntary counselling and treatment centre; MC = microscopy centre; HIV = human immunodeficiency virus; RNTCP = Revised National TB Control Programme; TB = tuberculosis.

Contribution of VCT to the TB programme

During the study period, VCTs referred 65 (1%) of the 15 835 TB patients registered for treatment in the respective four districts. Annual TB case notification rates for the 9921 VCT patients were 363 and 655 per 100 000 for smear-positive and all cases, respectively, compared with 73 and 138/100 000 for the district.

DISCUSSION

Over the 1-year period, 3% of VCT attendees were identified as TB suspects and 1% were diagnosed with TB disease by implementing a routine screening and cross-referral mechanism. Although at the time of referral HIV status was not known, the difference in proportion of TB suspects identified among HIV positives (4%) and HIV negatives (3%) was statistically significant.

The majority of TB suspect referrals from the VCTs were successfully screened at the TB services; however, staff felt that the 15% that were lost could be reduced by co-locating VCT and MC services, and if possible, by having a health worker or volunteer accompany patients through the referral process.

Of the 287 (85%) successful VCT-to-MC referrals, 29% were diagnosed with TB. However, significantly less TB disease was diagnosed among HIV-positive (21%) than HIV-negative referrals (40%). A high community TB prevalence could explain the high percentages of TB cases diagnosed among both HIV-positive and -negative VCT patients. As respiratory infections other than TB are common in PLWHAs, this may also partly account for the higher proportion of HIV-positive individuals identified with TB symptoms and the subsequent lower proportion diagnosed with TB as compared to HIV-negative persons. Difficulties in diagnosing smear-negative PTB in HIV-infected TB suspects could also have played a role. However, data from subsequent wider implementation of the TB-HIV cross-referral mechanism show almost equivalent proportions diagnosed amongst HIV-positive and -negative persons, but with higher proportions of smear-negative PTB and EPTB seen among PLWHAs.[3]

The diagnosis of a significant number of TB cases among HIV-negative persons, particularly sputum-positive PTB patients, emphasises the need to screen for symptoms of TB among all VCT patients, irrespective of their HIV status. The diagnosis of TB disease

Table 3 Referral and diagnosis of TB in HIV-positive and HIV-negative patients in Bhandara, Malegaon, Nanded, Nashik and Sangli Districts, India, July 2003–June 2004

	HIV-positive *n/N* (%)	HIV-negative *n/N* (%)	Total *n/N* (%)	Statistical results
Referrals				
VCT patients with TB symptoms referred to an RNTCP microscopy centre	192/4779 (4)	144/5142 (3)	336/9921 (3)	$\chi^2 = 11.21$, $P = 0.00$
Referred patients who reported to an RNTCP microscopy centre	168/192 (88)	119/144 (83)	287/336 (85)	$\chi^2 = 1.56$, $P = 0.21$
Patients diagnosed with TB	36/168 (21.4)	47/119 (40)	83/287 (29)	$\chi^2 = 11.06$, $P = 0.00$
TB patients put on DOTS*	27/32 (84)	38/42 (91)	65/74 (88)	$\chi^2 = 0.63$, $P = 0.42$
Type of cases detected				
Sputum-positive pulmonary TB	16/36 (44)	35/47 (75)	51/83 (61.4)	$\chi^2 = 7.76$, $P = 0.00$
Sputum-negative pulmonary TB	11/36 (31)	9/47 (19)	20/83 (24)	$\chi^2 = 1.45$, $P = 0.23$
Extra-pulmonary TB	9/36 (25)	3/47 (6.4)	12/83 (154.5)	$\chi^2 = 5.71$, $P = 0.02$

* Of those diagnosed TB patients residing in the district where the diagnosis was made.
TB = tuberculosis; HIV = human immunodeficiency virus; VCT = voluntary counselling and treatment centre; RNTCP = Revised National TB Control Programme.

in nine (23%) follow-up VCT patients highlights the need for regular TB symptom screening also during follow-up counselling for PLWHAs.

The majority of the TB cases were placed on DOTS. It was, however, not possible to ascertain the treatment status of 30% of the sputum-positive cases (15/51). This highlights the urgent need to establish a 'referral for TB treatment' system for patients, with a feedback mechanism from the respective 'receiving' districts. In higher prevalence settings, the RNTCP may also need to consider following up treatment outcomes by HIV status.

The TB case detection rate of 655/100 000 among the VCT patients was nearly five times higher than that of the general population, which suggests that expanding access to VCT services and facilitating the referral of TB suspects could potentially improve the care of persons diagnosed with HIV and make a significant contribution towards TB case detection and control.

The total number of TB referrals to VCT was not documented, as it was operationally impossible within the existing capacity of the health services to collect the number of referrals from the hundreds of general health facilities that provide TB services. However, the information on the number of TB cases accessing VCTs was captured in the VCT records. Using the official country policy of selective referral of TB patients for VCT,[12] 24% HIV seropositivity was found in those TB patients referred to the VCT. This high prevalence level was most likely due to the selection of only those TB patients who were at higher HIV risk or who had obvious signs of HIV/AIDS. Representative data on HIV prevalence among TB cases in these districts are not yet available. It is important to ensure that patients detected through cross-referrals are linked to HIV/AIDS services such as for cotrimoxazole preventive treatment and anti-retroviral treatment (ART). However, at the time of the pilot, neither ART nor cotrimoxazole prophylaxis were available in the districts.

Our study had a number of limitations. The study was a field-level programme pilot conducted within the existing health care services. Although we were unable to keep a log of the total number of referrals of TB patients from the numerous general health facilities that provided TB services, we were able to evaluate the outcomes for those referred once they arrived at the VCT sites. The programme focused on the detection of TB disease among VCT patients, as there was wide-scale availability of diagnostic and treatment facilities for TB. The lack of a standardised screening tool in the health facilities that refer TB patients to VCT is another limitation of this early collaboration, which focused primarily on exchanging information between the two programmes. We also did not evaluate the treatment outcomes of the TB patients stratified by HIV status.

This simple screening and cross-referral system between the VCTs and MCs, with minimal additional logistical or financial input, demonstrated the feasibility and potential benefits for both the HIV/AIDS and TB programmes. The activity was accomplished through simple measures: joint training of health workers from both programmes, utilisation of the existing record keeping system and referral forms and maintenance of a simple line-list. The use of a line-list ensured accuracy of the data reported and placed the responsibility for reporting on both programmes. We found that regular meetings of counsellors, senior TB treatment supervisors and district TB-HIV coordination committees and VCT-RNTCP performance review by the state-level programme officers strengthened the referral linkages.

VCTs can serve as a potential entry point for TB services for all patients, regardless of HIV status. Similar VCT–MC service linkages are now established across 14 states (covering a population of 633 million) in India, and in 2006 nearly 60 000 VCT patients were referred for TB evaluation and 51 000 TB patients referred to VCT for counselling and testing.[14] Efforts are currently being made to ensure that those TB patients identified with HIV infection receive high quality care for their TB disease and are linked to life-saving HIV/AIDS prevention, care and support services.

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RÉSUMÉ

CONTEXTE : L'Inde connaît un fardeau élevé de tuberculose (TB), comportant 1,8 millions de nouveaux cas par an. Bien que les estimations d'infection par le virus de l'immunodéficience humaine (VIH) s'élèvent à 2,5 millions de personnes, la prévalence nationale du VIH est <1%. La taille de l'Inde et la discordance des épidémiologies de TB et de VIH/syndrome d'immunodéficience acquise (SIDA) constituent un défi majeur pour la mise en œuvre de liens entre les services des programmes TB et VIH/SIDA.

MÉTHODES : On a institué une initiative pilote de référence croisée entre les centres d'accompagnement et de tests librement consentis (VCT) et les services de diagnostic et de traitement du Programme National Révisé de Lutte contre la Tuberculose dans quatre districts de Maharashtra, Inde.

OBJECTIF : Détecter la maladie TB chez les clients des VCT et dépister de manière sélective les patients TB pour les référer aux services de VCT.

RÉSULTATS : Entre juillet 2003 et juin 2004, 336 (3%) des 9921 clients VCT ont été identifiés comme suspects de TB et 83 (29%) diagnostiqués comme atteints d'une maladie TB. Sur les 765 cas TB sélectivement référés, 181 (24%) se sont avérés séropositifs pour le VIH, ce qui représente 11% des nouvelles personnes détectées comme atteintes du VIH dans les quatre districts.

CONCLUSIONS : L'initiative pilote de référence croisée a recueilli des nombres significatifs de cas de TB active parmi les clients de VCT et de sujets séropositifs pour le VIH parmi les patients TB. Les activités de collaboration entre les programmes VIH/SIDA et TB doivent être rapidement étendues à d'autres états de l'Inde.

RESUMEN

MARCO DE REFERENCIA: La India presenta una alta carga de morbilidad por tuberculosis (TB), con 1,8 millones de casos nuevos por año. Aunque se calcula que 2,5 millones de personas están infectadas por el virus de la inmunodeficiencia humana (VIH), la prevalencia a escala nacional es <1%. La gran superficie de la India y la diversidad de las características epidemiológicas de la TB y el VIH plantean un gran reto al establecimiento de vínculos entre los servicios de los programas contra la TB y contra la infección por el VIH y síndrome de inmunodeficiencia adquirida (SIDA).

MÉTODOS: Se realizó un programa experimental de remisión cruzada entre los centros de orientación y prueba diagnóstica voluntarias del VIH (VCT) y los centros de diagnóstico y tratamiento del Programa Nacional Revisado de Lucha contra la Tuberculosis en cuatro distritos de Maharashtra, India.

OBJECTIVO: Detectar la enfermedad TB en los usuarios de los centros de VCT y practicar una selección de pacientes TB con el fin de remitirlos a los servicios de VCT.

RESULTADOS: Entre julio de 2003 y junio de 2004, de los 9921 usuarios del centro de VCT, en 336 (3%) hubo presunción clínica de TB, de los cuales 83 (29%) obtuvieron confirmación diagnóstica. De los 765 casos de TB remitidos selectivamente, 181 (24%) presentaron una serología positiva para el VIH, es decir el 11% de las personas recientemente diagnosticadas con infección por el VIH en los cuatro distritos.

CONCLUSIÓN: Con el programa experimental de remisión cruzada se detectó un número significativo de casos de TB activa en los usuarios del centro de VCT y de personas positivas para el VIH entre los pacientes con TB. Es importante ampliar rápidamente las iniciativas conjuntas entre los programas contra la infección por el VIH/SIDA y los programas contra la TB a otros estados de la India.