

Missed opportunities for accessing HIV care among Tshwane tuberculosis patients under different models of care

Running head: Antiretroviral treatment access for TB patients

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SUMMARY

Background: This study aimed to compare access to HIV care for tuberculosis patients in settings with Antiretroviral Treatment (ART) and tuberculosis care under one roof (“semi-integrated sites”) and settings with geographically separately rendered care, in Tshwane, South Africa.

Methods: Historical cohort study of patients registered with tuberculosis at 46 TB treatment points, with follow-up until the end of TB treatment. ART initiation for HIV-positive TB patients was established through linkage of TB register patient identifiers to the electronic ART register. Data analysis entailed univariate and multivariate competing risk analysis.

Results: Records of 636 and 1297 patients for semi-integrated and separate facilities respectively were reviewed. Co-trimoxazole prophylactic therapy and CD4 count recording were lower in semi-integrated than separate facilities, but the reverse was true for referral to HIV-related care.

A higher percentage of patients started ART in semi-integrated than in separate facilities (70.5% vs. 44.6%, $P < 0.001$). In competing risk analysis (with death and LTFU as competing risks), attending a semi-integrated facility (SHR 2.49, 95%CI 1.06-5.88) and TB case load > 401 (SHR 1.45, 95%CI 1.04-2.03) were associated with increased ART initiation.

Conclusions: ART and TB treatment under one roof appears to facilitate ART initiation for HIV-positive TB patients.

Key words: tuberculosis, antiretroviral treatment, integration

South Africa has the 3rd highest number of incident TB cases in the world. Seventy three percent of the patients with TB were estimated to be HIV-positive in 2008.¹ Case-fatality in TB is substantially increased in the presence of HIV infection, even when patients receive optimal TB chemotherapy.² Provision of Co-trimoxazole Prophylactic Therapy (CPT) and early ART initiation are critical interventions to improve outcomes in HIV-positive TB patients.³⁻⁶ Nevertheless, only 51% of TB patients were tested for HIV in South Africa in 2009. Of the HIV-positive patients detected, 71% started or continued CPT and 42% received ART.⁷

One of the possible explanations for this poor performance is insufficient integration of TB and HIV/AIDS care. Proponents of integrated care argue that integrated care may increase HIV Counselling and Testing (HCT), reduce loss to follow-up and waiting time, improve staff efficiency and record keeping and reduce TB case fatality rates.^{6,8-10} Integration may also increase cure rates for patients with TB if patient-centered ART adherence approaches are employed.¹¹

Different models of HIV/TB service delivery from no integration, to several degrees of partial integration and full integration have been tried out in a variety of clinical settings in the world.^{8,11,12} In the South African public service context, TB and HIV/AIDS care have traditionally been rendered separately and within their own distinct cultures.⁸ Most primary care facilities in the public health system are nurse driven and render TB diagnostic and treatment services. They also offer TB patients HIV and CD4 count testing, CPT and referral for ART on or off-site. In the municipality where our study was undertaken, ART was initially only provided at hospitals where doctors and pharmacists are available. Later on - in an attempt to improve access to ART treatment and integrate care - ART was also introduced at some primary care facilities, albeit in a vertical fashion.

This study aimed to compare access to HIV-related care, in particular ART initiation between non-integrated or “separate facilities” (patients receiving TB and ART care at two geographically separate facilities) and “semi-integrated facilities” (TB and ART provided under the same roof, but at different consultation rooms by different health care providers) in Tshwane, the executive capital of South Africa.

MATERIALS AND METHODS

Study setting and study participants

This was a historical cohort study. The patient population comprised of all patients diagnosed with TB and registered in the TB registers at all Tshwane public facilities from October 2008 to March 2009. All patients were followed up until the end of their TB treatment to determine ART initiation.

At the time of the study, ART initiation took place at seven hospitals and four Community Health Centres (CHCs) - all of which were supported by the Foundation for Professional Development (FPD), a private funding and teaching organization. These four CHCs were the only sites in Tshwane where both TB treatment and full ART treatment were provided at the same facility and are classified as “semi-integrated facilities” for the purpose of this study. TB patients at all other TB clinics (classified as “separate facilities”) had to travel to the ART sites at the above mentioned hospitals or CHCs to start ART.

Sampling size

Sample sizes were calculated to have 80% power to detect a 10% difference in outcome proportions in semi-integrated vs. separate facilities, using single-sample z-tests, since complete sampling was used for the semi-integrated facilities. After allowing for a possible 20% missing records, the required sample size could be achieved by including all records from the semi-integrated facilities and every third record from separate facilities, over a 6-month period. TB registers were used as the sampling frame from which individual TB records were drawn.

Measurements

HIV and TB care received by patients was obtained from the standardized individual TB treatment records. Information regarding ART treatment initiation was obtained primarily from the electronic ART patient management system. This data warehouse was introduced at all public sector ART facilities in Tshwane by the FPD, with the exception of one hospital (for which the records were retrieved manually).

The ID numbers - if available - or names, place of residence and date of birth on the TB records were linked with patient identifiers on the ART registers on a one by one

basis. Demographic, TB episode, TB case load, HCT, CD4 count at the time of TB diagnosis, referral for HIV care and CPT were obtained from the individual TB records. ART start dates were obtained from the ART database.

Eligibility for ART treatment was defined as having a CD4 count of 200 cells/ μ l or less and did not include WHO staging. Although the guidelines enforced at the time of the study also made provision for ART initiation in Stage IV disease,¹³ our study assessed the practice of nurses - who were not trained to do clinical staging of ART patients and did not capture staging on TB records. Data collection and linkage were piloted at two clinics.

Data analysis and management

Data were single entered in Epi-Info by full-time data capturers under the supervision of an experienced data manager. Check files built into Epi Info and a programme written in Stata version 11 were used to reduce capturing errors.¹⁴ Data analysis was performed using Stata version 11.¹⁴ Descriptive summary statistics were calculated as means with their standard deviations, as proportions, and as medians with inter-quartile ranges, as appropriate. Comparisons of unadjusted proportions were carried out using a single sample two-sided z-test.

The study subjects for the competing risk survival analysis were all those who met the criteria for ART eligibility but excluding those who transferred in or out. Our outcome of interest was having started ART, as recorded in the ART data base. TB treatment outcomes “death” or “defaulted” were classed as a “competing risk”. Patients who did not start ART, or neither died nor defaulted were censored at the recorded TB treatment outcome date.

The following explanatory co-variables were considered for inclusion in the competing risks regression model: semi-integrated vs. separate facilities; yearly number of TB cases seen in the clinic; type of health care facility; new or retreatment TB case; sex; age; CD4 count; type of TB and whether the patient received directly observed treatment or not. Co-variables with P-values of less than 0.25 were then retained - following recommendations for multiple binary logistic regression - for inclusion in the competing risks regression model.¹⁵ Interaction terms were generated between the semi-integrated vs. separate variable and each of the other retained co-variables and eliminated using backwards hierarchical

regression.¹⁶ Results were adjusted for clustering on TB facilities using robust standard errors.

Ethical approval

The study was approved by the Ethics committees of the University of Pretoria and the South African Medical Research Council.

RESULTS

TB data were collected for 46 TB treatment points. Eighty two percent of TB patient records could be traced for the time period of the study: of these 636 records for the four semi-integrated sites and 1298 for the 42 separate sites were sampled. The record of one outlier with an implausible long TB treatment duration was excluded from the analysis. Only 933 (48.2%) of the TB records had an ID number, but most ART records did. TB records were linked on a one to one basis to over close to 73000 records on the ART database.

Baseline characteristics of registered TB patients by facility type

The median age of patients was 35 for semi-integrated and 34 years for separate facilities and nearly half were female. Over 93.3% of the patients presented with their first episode of TB. A higher percentage of patients presented with Pulmonary Tuberculosis at semi-integrated facilities than at the separate facilities (86.2% vs. 80.6%). DOT supervision in the intensive phase was higher in separate facilities than in semi-integrated facilities (86.7% vs. 72.3%). Median CD4 counts were very similar in both types of facilities, a finding to be interpreted with some caution since values were available for less than half of the HIV-positive patients (Table 1).

HIV counselling, testing and non-ART HIV-related care by facility type

At both semi-integrated and separate facilities a high percentage of patients knew that they were HIV sero-positive by the time they registered for TB treatment (39.8% and 32.8%). For the remainder, 78.6% and 81.8% were counselled at semi-integrated and separate facilities respectively. Most counselled patients were subsequently tested at both facility types (90.7% and 89.1%). Overall 70.3% of

Table 1 Tuberculosis records: characteristics of study subjects*

	Semi-integrated facility (N=636: complete sampling)		ART at separate facility (N=1297: sampling 1 in 3)	
	Age (Median [IQR])	N=632	35 (27-44)	N=1288
Female	310/629	49.3%	618/1281	48.2%
First episode of TB	598/629	95.1%	1203/1290	93.3%
PTB (including PTB + EPTB)	531/616	86.2%	990/1229	80.6%
Newly registered [†]	593/634	93.5%	1125/1266	88.9%
DOT intensive phase	460/636	72.3%	1124/1297	86.7%
HIV sero-status Known +ve	253/636	39.8%	425/1297	32.8%
New +ve	194/636	30.5%	411/1297	31.7%
Negative	74/636	11.6%	212/1297	16.4%
Unknown	115/636	18.1%	249/1297	19.2%
CD4 count (Median [IQR])				
All HIV +ve	N=171	123 (57-195)	N=450	120.5 (51-226.3)
New HIV +ve	N=85	106 (59-216.5)	N=244	108 (52.3-203.5)

*All information obtained from TB registers and individual TB patient records

[†]i.e. not transferred in or moved in

HIV = human immunodeficiency virus; TB = tuberculosis; N = sample size; SD = standard deviation; PTB = pulmonary tuberculosis; EPTB = extra-pulmonary tuberculosis; DOT = directly observed treatment; +ve = positive; CD4 = CD4 count in cells/μl of blood; IQR = inter-quartile range.

Table 2 HIV counselling, testing and care by type of facility*

Variable	Semi-integrated facility (N=636)		ART at separate facility (N=1297)		P [†]
	Counselled if not known +ve	301/383	78.6%	713/872	
Tested if counselled [‡]	273/301	90.7%	635/713	89.1%	0.172
CPT if HIV +ve	289/447	64.7%	573/836	68.5%	0.018
CCMT referral	194/447	43.4%	132/836	15.8%	<0.001
Recorded CD4 count					
Known +ve not on prior ART	43/215	20.0%	63/363	16.8%	0.104
Known +ve on prior ART	9/38	23.7%	23/62	37.1%	0.033
New HIV +ve	85/194	43.8%	244/411	59.4%	<0.001

*All information obtained from TB registers and individual TB patient records

[†]P-values for single sample, 2-tail z-tests

[‡]No patients were tested without counselling at either facility type

HIV = human immunodeficiency virus; N = sample size; +ve = positive; CCMT = HIV comprehensive care, management and treatment programme; CD4 = CD4 cell count/μl of blood.

patients were HIV-positive, 11.6% HIV-negative and 18.1% had an unknown status for the semi-integrated facilities. At separate facilities 64.5% of patients were HIV-positive, 16.3% HIV-negative and 19.2% had an unknown HIV status. Separate facilities performed considerably better in terms of CPT and more often recorded CD4 counts for newly diagnosed HIV positive patients and for patients on prior ART. Conversely, semi-integrated facilities much more often recorded referring patients for HIV care (Figure 1, Table 1 and Table 2).

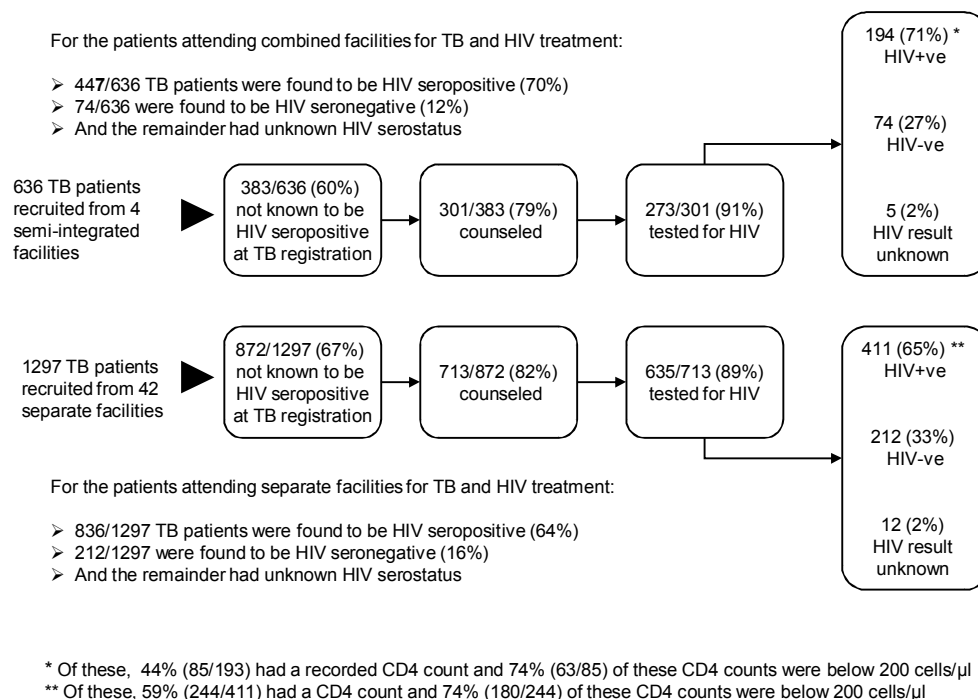


Figure 1 HIV counselling, testing and HIV-positivity rates at semi-integrated vs. separate facilities

ART initiation by facility type

Table 3 presents the unadjusted results for ART initiation for both types of facilities. After excluding TB patients who were already on ART prior to being diagnosed with TB, patients with a CD4 count \geq 200 cells/μl or a missing CD4 count and patients transferred in or out, 105 and 233 patients were available for analysis in the semi-

Table 3 ART initiation by type of facility for HIV-positive patients

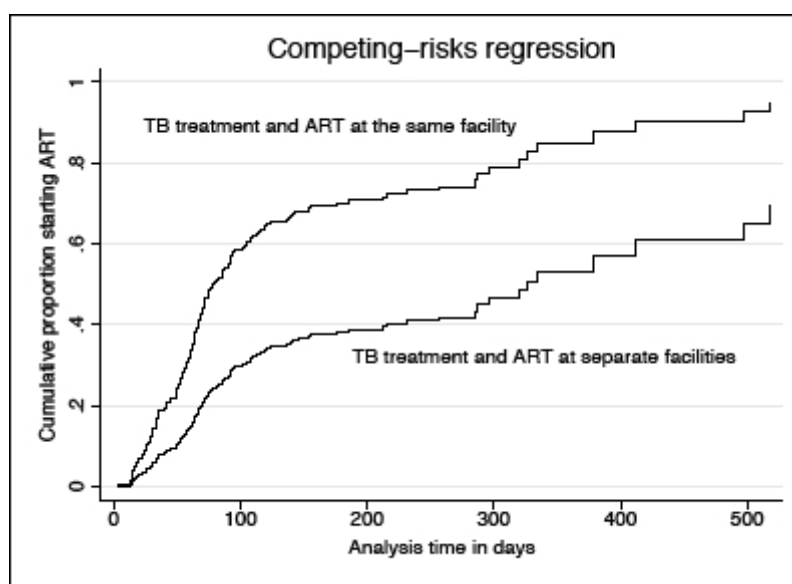
Variable	Semi-integrated facility (N=447)		ART at separate facility (N=836)		P*
Not on ART prior to TB treatment	409/447	91.5%	774/836	92.6%	
No CD4 count recorded	281/409	68.7%	469/774	60.6%	
With CD4 count <200	117/409	28.6%	284/774	36.7%	
Not transferred/moved in/out	105/117	89.7%	233/284	82.0%	
% of these patients starting ART [†]	74/105	70.5%	104/233	44.6%	<0.001* [†]
Time to ART initiation (Median [IQR])	67.5 (53-92)		67 (35-109.5)		0.995**

*P-value for single sample 2-tail z-test, **Wilcoxon ranksum test

[†]Crude (unadjusted) Risk Ratio = 1.58 (95% Confidence interval: 1.31-1.91: chi square P <0.001)

ART = antiretroviral treatment; HIV = human immunodeficiency virus; TB = tuberculosis; CD4 = CD4 cells/ μ l blood.

integrated and separate facilities respectively. Although there was no difference in median time to ART initiation, a significantly higher percentage initiated ART at semi-integrated facilities than at separate facilities (70.5% vs. 44.6%, $P < 0.001$). The difference in the cumulative proportion of patients initiating ART at different time points is presented in Figure 2.

**Figure 2** Cumulative proportion of patients starting on ART in semi-integrated vs. separate facilities

Note: P-value for subhazard ratio comparing semi-integrated with separate facilities=0.0006

Table 4 Tuberculosis records: subjects considered for competing risks regression*

	Semi-integrated facility (N=105)		ART at separate facility (N=233)	
Age (Mean [SD])	N=104	37.3 (8.5)	N=232	36.8 (10.2)
Female	63/105	60.0%	106/229	46.3%
First episode of TB	102/105	97.1%	218/233	93.6%
PTB (incl. PTB + EPTB)	85/101	84.2%	185/226	81.9%
DOT intensive phase	85/105	81.0%	199/233	85.4%
Newly diagnosed HIV +ve	53/105	50.5%	145/233	62.2%
CD4(Median [IQR]) All HIV +ve	N=105	78 (44.5-135.5)	N=233	77 (36.5-123)
New HIV +ve	N=53	74 (46-118)	N=145	78 (44-124)

*All information obtained from TB registers and individual patient records: all subjects neither transferred/moved in/out and with CD4 counts <200 cells/ μ l
HIV = human immunodeficiency virus; TB = tuberculosis; N = sample size; SD = standard deviation; PTB = pulmonary tuberculosis; EPTB = extra-pulmonary tuberculosis; DOT = directly observed treatment; +ve = positive; CD4 = CD4 count in cells/ μ l of blood; IQR = inter-quartile range.

Table 5 Competing risks regression results*

	Univariate analysis		Multivariate analysis			
	CSHR	P > z	ASHR	95% RCI for ASHR		
				Lower	Upper	P > z
Semi-integrated vs. separate facility [†]	1.97	0.006	2.49	1.06	5.88	0.037
>401 vs. <402 TB patients/year	1.85	0.039	1.45	1.04	2.03	0.029
TB treating facility type [§]						
Provincial community health centre	Reference		Reference			
Municipal clinic	0.54	0.019	1.37	0.57	3.27	0.476
Provincial clinic	0.67	0.148	1.79	0.72	4.41	0.209

* 338 Subjects were neither transferred in or out and were eligible to start on ART; 336 of these study subjects had full data available for multivariate competing risks regression. [†] Only variables with a P-value <0.25 in the univariate analysis are presented here. [§] Some facilities are managed by provincial authorities and others by the municipality.
RCI = robust confidence interval; ASHR = adjusted subhazard ratio; CSHR = crude subhazard ratio; TB = tuberculosis

The baseline characteristics of the patients considered for inclusion in the competing risk analysis are compared in Table 4. Age distribution, type of TB and median CD4 counts were similar, but there appeared to be some differences for percentage of females, DOT in the intensive phase and having a first episode of TB vs. retreatment TB. In multivariate competing risk regression analysis patients attending semi-integrated services were significantly more likely to initiate ART than

patients who had to travel to another facility to receive ART (Sub Hazard Ratio [SHR] 2.49, 95%CI 1.06-5.88). Patients attending facilities with a TB caseload of over 401 new patients per year (3 separate and 2 semi-integrated facilities fell in this category) were also more likely to initiate ART (SHR 1.45, 95% CI 1.04-2.03) (Table 5).

DISCUSSION

Eligible HIV-positive TB patients attending semi-integrated facilities were more likely to initiate ART than patients who had to travel to another facility to receive ART (SHR 2.49, P=0.037). This confirms our hypothesis that providing TB and ART care at different facilities poses barriers to patients that may prevent them from accessing life saving treatment. Reduced access to HIV care for TB patients in a non-integrated system was also demonstrated in two studies that compared off- and on-site voluntary counselling and testing in the Democratic Republic of Congo and Cambodia.^{17,18} Okot-Chono et al. found that only 66% of 333 adult TB patients were tested for HIV in Uganda, and that only 12% of the HIV-positive patients were on both ART and CPT and about a third had not received any HIV care, mostly due to limited TB-HIV inter-clinic referral and poor service integration.¹⁹ Similar findings came out of India where only between 30% and 38% of HIV-infected TB patients started ART during treatment.^{20,21} Our findings support the call of many researchers to integrate HIV and TB services.^{9,22,23} The beneficial effect of integrating ART and TB services in one facility (whether fully or partially) has been demonstrated in a variety of settings.^{11,24-26}

In this study, a high percentage of patients knew their HIV status by the time they registered for TB treatment at both types of facilities and HIV counselling and testing rates were high. CPT was somewhat less well recorded and may point towards either poor recording or poor provision of this essential prophylactic medication. Separate facilities recorded CPT and CD4 counts more often than semi-integrated facilities. This may be explained by the fact that information about CPT and CD4 results is kept in ART files and not in the TB files at semi-integrated facilities, for those patients who have enrolled for ART. This calls for having only one file per patient, a system already successfully introduced at ART sites in Khayelitsha, South

Africa.¹¹ Referral for HIV care was recorded more often at semi-integrated facilities: this appears logical since referral is easier if ART is provided at the same facility.

In terms of other predictors of ART initiation, patients attending facilities with a larger TB caseload were more likely to initiate ART independent of whether the facility had ART on site or not. The reasons for this are not clear but it may be that professional nurses who see more TB patients are also more experienced in HIV-related care and the need for referral for ART initiation.

Our study has several limitations. Missing records and patients linked to the wrong patients in the ART database (due to spelling and recording errors) may have introduced bias. This is a retrospective record review: it is therefore difficult to distinguish between a service “not rendered” and a service “rendered, but not recorded”. Some underestimation of ART initiation is possible. Our figures regarding ART initiation are solely based on the ART data collected for the Tshwane public sector facilities. Some patients may have received ART outside Tshwane, at the workplace or from private practitioners. There is however no reason to believe that patients’ health seeking behaviour outside the public sector would differ for patients attending the two types of facilities. Our finding of differential ART initiation is therefore likely to remain valid. Conversely, we may have over-estimated ART initiation. Some of the patients who did not have a CD4 count test result recorded on their TB records may have been eligible for ART. A sensitivity analysis was carried out involving all HIV-positive TB patients, irrespective of CD4 count results, who were not on prior ART, and were not transferred in or out. Among these subjects, 47.5% (158/333) started on ART before the end of their TB treatment at semi-integrated facilities vs. 30.4% (186/612) at separate facilities ($P < 0.0001$) with a crude risk ratio of 1.56 (95%CI 1.32 to 1.84). It is important to note that under these assumptions, ART initiation is low even at semi-integrated facilities. This may mean that vertical organization of TB and HIV care creates hurdles for patients to access care even within the same facility. Furthermore, our study results may not be generalisable to settings without external funding support.

CONCLUSION AND RECOMMENDATIONS

To our knowledge, this study was the first of its kind to compare semi-integrated with non-integrated facilities for ART initiation. The electronic data made it possible

to link TB and HIV information from the TB sites to all public sector ART sites, something which would have been extremely cumbersome with manual ART records.

HIV counselling and testing of TB patients is well established in both types of facilities. However, recording and/or provision of CPT and CD4 testing needs improvement, particularly in semi-integrated sites. ART initiation for eligible HIV-positive TB patients was higher in semi-integrated facilities than in separate facilities. This finding supports the call for wider provision of ART care at primary care facilities.

We recommend the introduction of a “one patient, one file, one appointment” principle at all facilities that provide TB and ART services. This will facilitate a shift away from functions and tasks to ‘patient-centered care’,²⁷ integrated monitoring systems and earlier ART initiation in HIV-positive TB patients with subsequent reduced mortality.⁴⁻⁶

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