Abstract # **830**

Decreased TB Recurrence After Introduction of ART in Durban, South Africa

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Background

- **Recurrent tuberculosis (TB) threatens TB control**
- **Late recurrence is usually due to reinfection**
- **HIV-infected persons are at increased risk of reinfection, which could be due at least in part to immune compromise**

Hypothesis

The introduction of antiretroviral therapy (ART) in a setting with high TB incidence and HIV co-infection would be associated with decreased TB recurrence risk.

Methods

Study design:
- Retrospective cohort study

Study site:
- Prince Cyril Zulu Communicable Diseases Clinic (PCZCDC)
  - Durban, KwaZulu Natal, South Africa
  - Large, urban setting near transport hub
  - Focused TB care with ART gradually implemented starting in 2005

Institutional Review Board / Ethics Approvals:
- Approval from all sites and institutions involved

Study population:
- Adult (≥ 18 years) TB patients
- Seen at clinic from January 2000 through December 2012
- Follow-up through December 2013

Definitions:
- **TB recurrence:** A TB episode occurring after cure or treatment completion of a prior TB episode. Eligibility started 180 days after first episode treatment start date.
- **Days to TB recurrence:** Number of days from 1st episode treatment start date to 1st recurrence treatment start date
- **Early TB recurrence:** TB recurrence ≤ 365 days from first episode treatment start date
- **Late TB recurrence:** TB recurrence > 365 days from first episode treatment start date

Results

Table 1 TB recurrence among 71,235 adult TB patients seen at PCZCDC from January 2000 to December 2013

TB Recurrence	n (%)
Total recurrences (multiple possible)	5,996
Days to TB recurrence, median (IQR)	917 (533, 1,530)
Patients with at least 1 recurrence	5,366 (8)
Early recurrence	573/5,366 (11)
Late recurrence	4,793/5,366 (89)

IQR: interquartile range

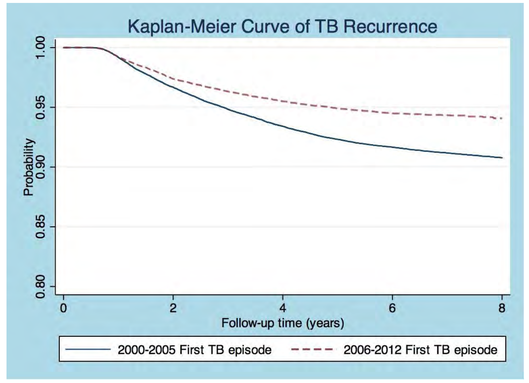

Figure 1 Kaplan-Meier survival curve of first TB recurrence by time period of first TB episode (HR 0.65, 95% CI 0.61-0.70, P<0.001, unadjusted Cox proportional hazards)

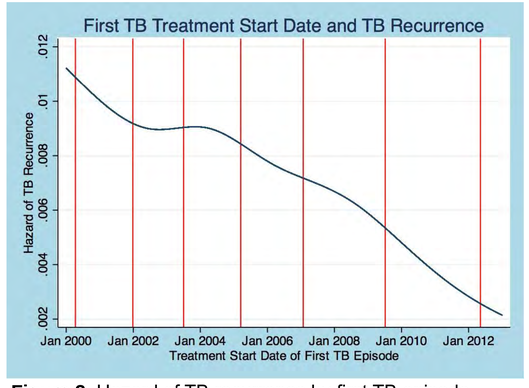

Figure 2 Hazard of TB recurrence by first TB episode treatment start date (continuous variable with restricted cubic spline knots denoted by red lines)

Table 2 Characteristics of 13,085 adult TB patients seen at PCZCDC from January 2009 to December 2013 based on HIV serostatus (the most complete HIV data were available during this period)

Demographic & Clinical	HIV seropositive n = 9,764	HIV negative n = 3,321	P value
Age, median (IQR), years	35 (30, 41)	31 (25, 43)	<0.001
Male sex	4,904 (50)	2,038 (61)	<0.001
Race*			<0.001
Black	9,631 (99)	3,113 (94)	
Asian	41 (0)	108 (3)	
Coloured	84 (1)	72 (2)	
White	8 (0)	28 (1)	
Culture status			<0.001
Culture-confirmed	3,691 (38)	1,271 (38)	
Culture-negative	1,500 (15)	367 (11)	
Unknown	4,573 (47)	1,683 (51)	
Smear status			<0.001
Smear-positive	3,507 (36)	1,649 (50)	
Smear-negative	4,943 (51)	1,316 (39)	
Unknown	1,314 (13)	356 (11)	
Multidrug-resistant TB	395 (4)	101 (3)	0.01
Outcomes			<0.001
Cured	2,350 (24)	1,051 (31)	
Treatment completed	2,502 (26)	654 (20)	
Died	327 (3)	50 (2)	
Defaulted treatment	1,031 (11)	326 (10)	
Treatment failure	9 (0)	0 (0)	
Moved	3,302 (34)	1,151 (35)	
Other	13 (0)	14 (0)	
Unknown	230 (2)	75 (2)	
TB Recurrence	**HIV seropositive**	**HIV negative**	**P value**
Days to TB recurrence, median (IQR)	572 (385, 839)	638 (417, 1,006)	0.13
Patients with at least 1 recurrence	402 (4)	69 (2)	<0.001
Early recurrence	85/402 (21)	16/69 (23)	0.70
Late recurrence	317/402 (79)	53/69 (77)	

IQR: interquartile range
* Race categories as recorded in clinic medical record

Table 3 Risk of TB recurrence among adult TB patients with known HIV status, Cox proportional hazards model

	Adjusted HR (95% CI)	P value
HIV seropositive	2.00 (1.54-2.59)	<0.001
Age (per 1-year increase)	1.03 (1.02-1.04)	<0.001
Male sex	1.44 (1.19-1.74)	<0.001
Race*		
Asian vs Black	0.78 (0.29-2.13)	0.64
Coloured vs Black	0.43 (0.14-1.34)	0.15
White vs Black	1.37 (0.34-5.55)	0.66

IQR: interquartile range, HR: hazard ratio, CI: confidence interval
* Race categories as recorded in clinic medical record

Limitations

- **Retrospective cohort; no isolates available for testing**
- **Clinical electronic medical record not originally designed for research purposes**
- **Limited HIV data prior to 2009**
- **Loss to follow-up, transient population**

Conclusions

- **Most episodes of TB recurrence occurred late**
  - **Suggests exogenous reinfection rather than relapse**
- **TB recurrence risk decreased after ART implemented**
- **Despite the improvements noted after the uptake of ARVs for HIV care, TB recurrence risk remains high**

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