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The effect of antiretroviral therapy on chest radiograph appearance in HIV-associated pulmonary tuberculosis

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19th BHIVA, Manchester, April 2013

Background

- Clinical features of tuberculosis (TB) vary with the degree of HIV-associated immunosuppression (CD4 count)
- Positive sputum smears and lung cavitation are associated with TB transmission
- We have previously shown that combination antiretroviral therapy (cART) does not affect the proportion smear positive, independently of CD4 count[1]
- The effect of cART on lung cavitation, independent of CD4 count, is unknown and relevant to TB control

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[1]van Halsema *et al,* CROI 2010, abstract P-126

Aim

- To examine the effect of cART on chest radiograph (CXR) appearance, particularly cavitation, as a marker of TB infectiousness

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Setting

- TB case notification rates
  2450 – 3000/100,000/year in 2008[1]
- High HIV prevalence (around 29%[2]) on background of high TB incidence due to silicosis
- Thibela TB was a cluster-randomised trial of a mass TB prevention intervention
- TB screening and community-wide isoniazid preventive therapy were delivered in intervention clusters

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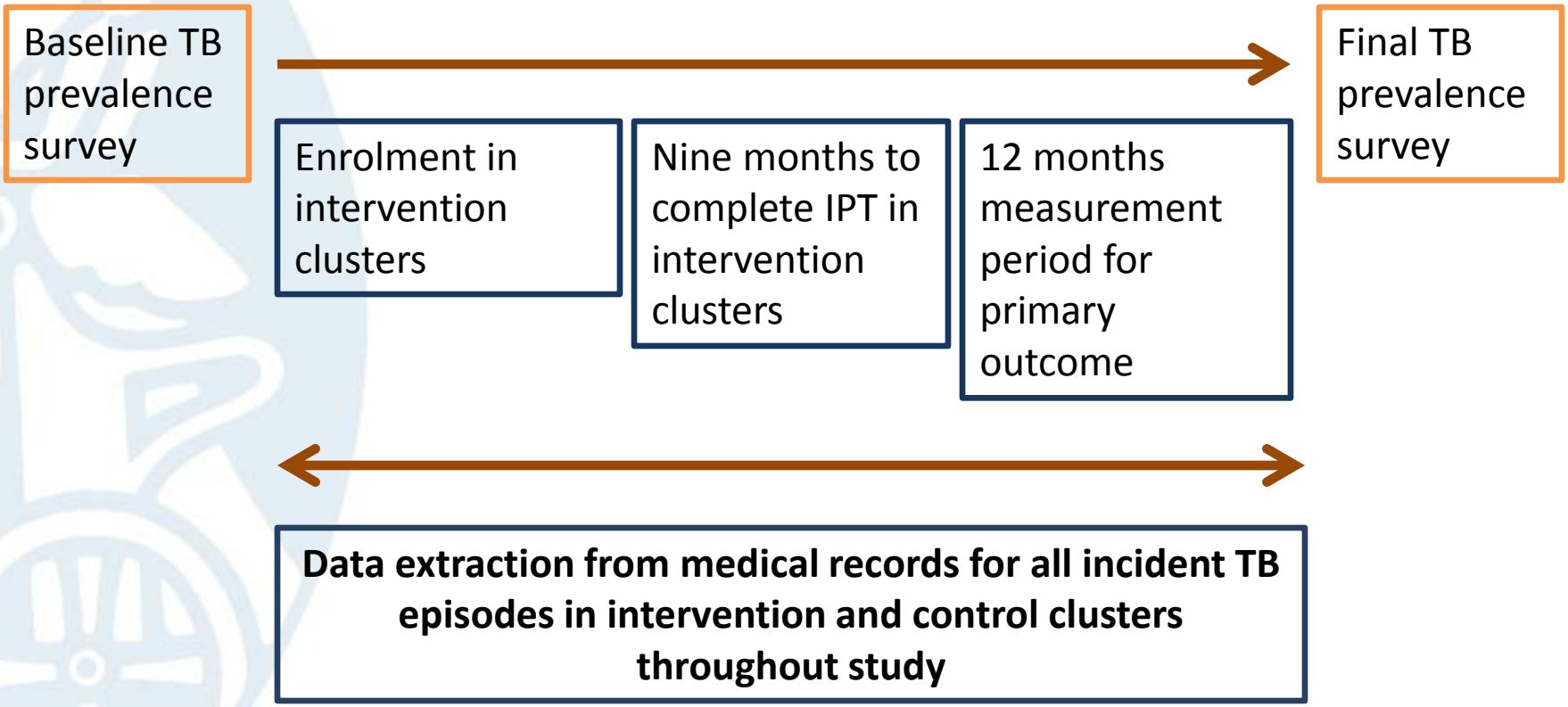
[1]van Halsema *et al*, Int J Tuberc Lung Dis 2012 [2]Lewis *et al*, Am J Resp Crit Care Med 2009

Thibela TB study design



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Adapted from Fielding *et al*, Contemp Clin Trials 2011

Methods

- Cross-sectional analysis of TB episodes from 2004-9
- CXRs read by investigators masked to HIV and cART status
- Analysis included individuals with:
  - Known HIV and cART status
  - Pulmonary +/- disseminated or extrapulmonary disease
  - Sputum smear and/or *M. tuberculosis* culture positive
  - Available CXR within 2 months of TB treatment start
- Those on cART <=90 days analysed separately in view of possible immune reconstitution inflammatory syndrome

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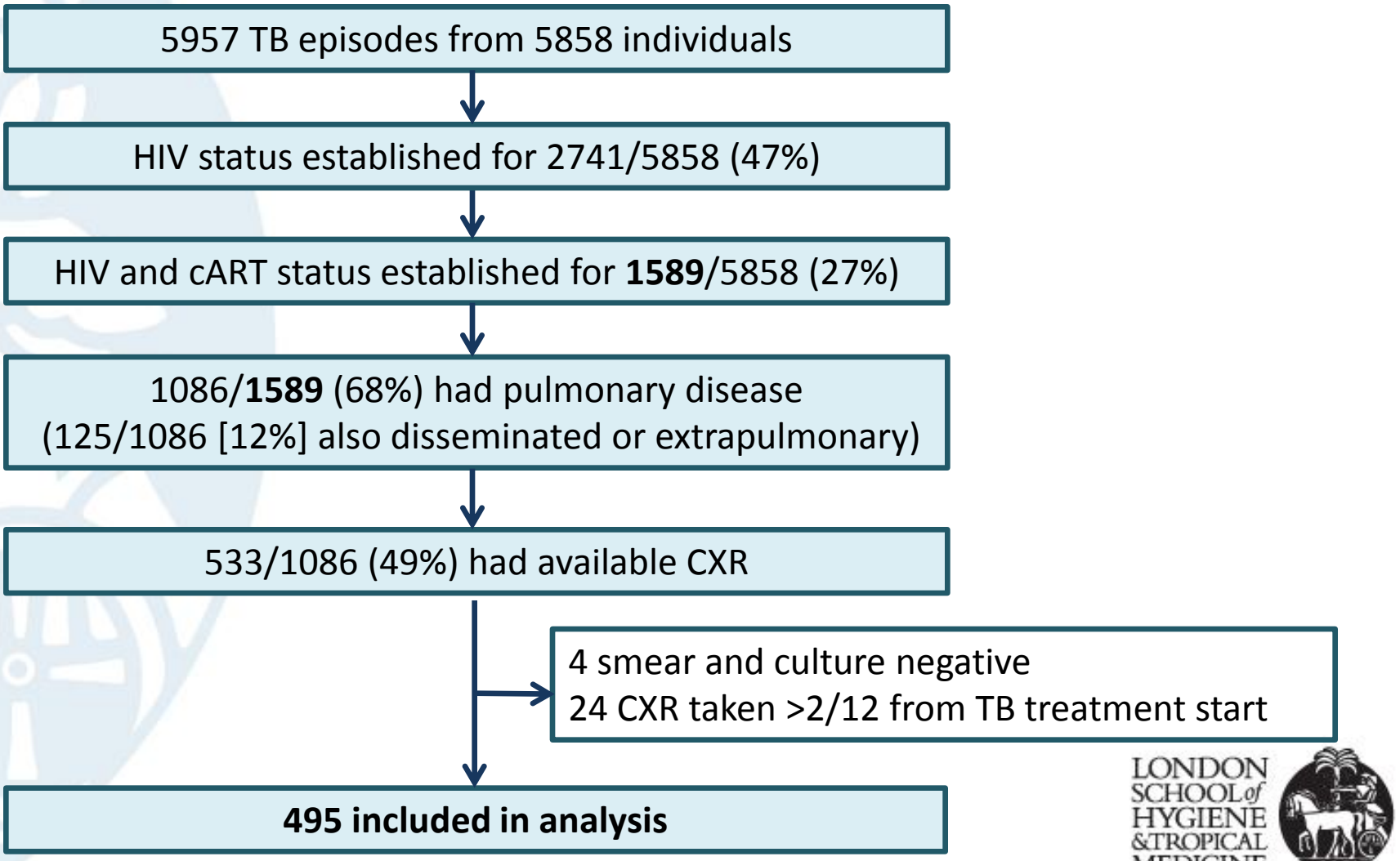
Results: numbers included



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Results: study group characteristics

Variable	Number[1] (% of 495)
Male gender	481/494 (97%)
Median age	43 years (IQR 38, 48)
Living in hostel/informal housing	343/492 (71%)
First TB episode	318/487 (65%)
Sputum smear positive	370 (75%)
M. tuberculosis culture positive	385/423 (91%)

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[1]Denominator given where some data missing [2]IQR = interquartile range

Results: HIV and cART status

Group	Number	Median CD4 count (cells/µl; IQR[1]; number with known CD4 count)
HIV-negative	156	-
HIV-positive not on cART	224	139* (76, 220; n=201)
HIV-positive on cART <=90 days	28	187 (90, 339; n=26)
HIV-positive on cART >90 days	87	219* (125, 333; n=80)
Total	495	149 (86, 263; n=307)

*Difference in CD4 distribution between those on cART >90 days versus not on cART: p<0.002 by Kruskal-Wallis test

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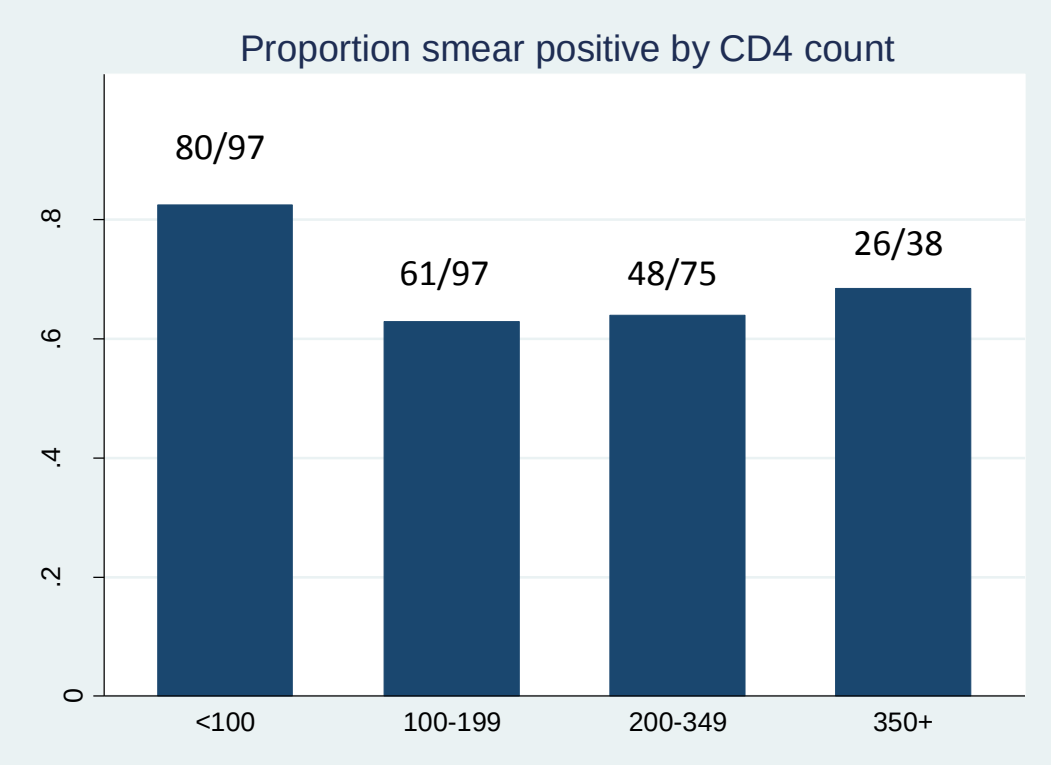
[1]IQR = interquartile range

Results: sputum smear status



- Proportions smear-positive, regardless of cART status, varied non-linearly with CD4 count among HIV-positive individuals (chi^2 p=0.01)

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Results: Bacillary density and cavitation

Cavitation	Smear grade: number (% of row total)					
	Negative	Scanty+	1+	2+	3+	Total
No	85 (31)	4 (2)	96 (35)	39 (14)	48 (18)	272 (100)
Yes	35 (16)	3 (1)	63 (29)	37 (17)	80 (37)	218 (100)
Total	120 (25)	7 (1)	159 (33)	76 (16)	128 (26)	490 (100)

- Cavitation is associated with higher sputum bacillary density (chi^2 $p<0.001$)

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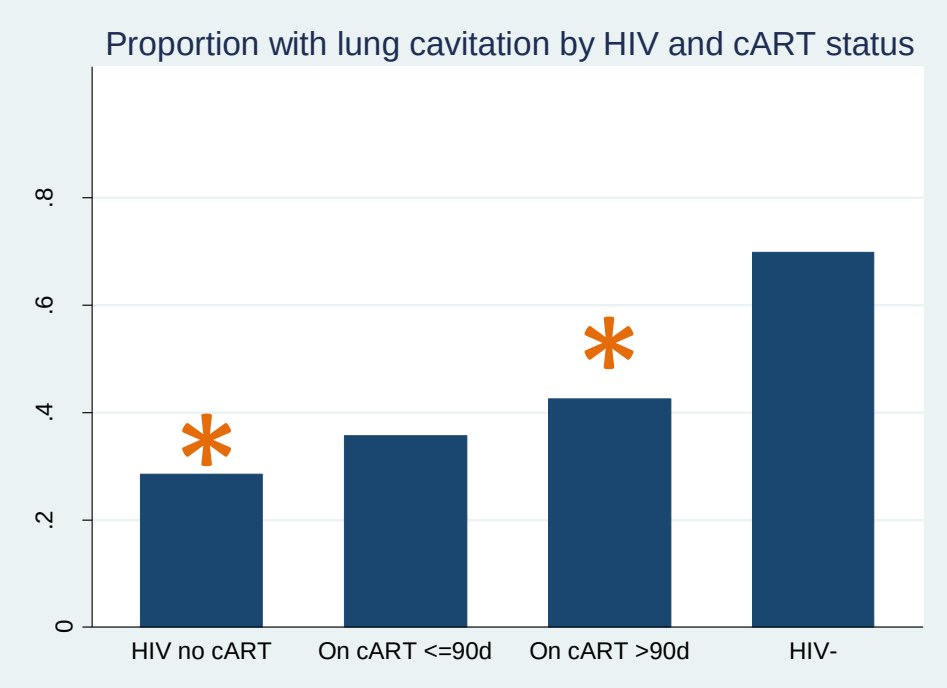
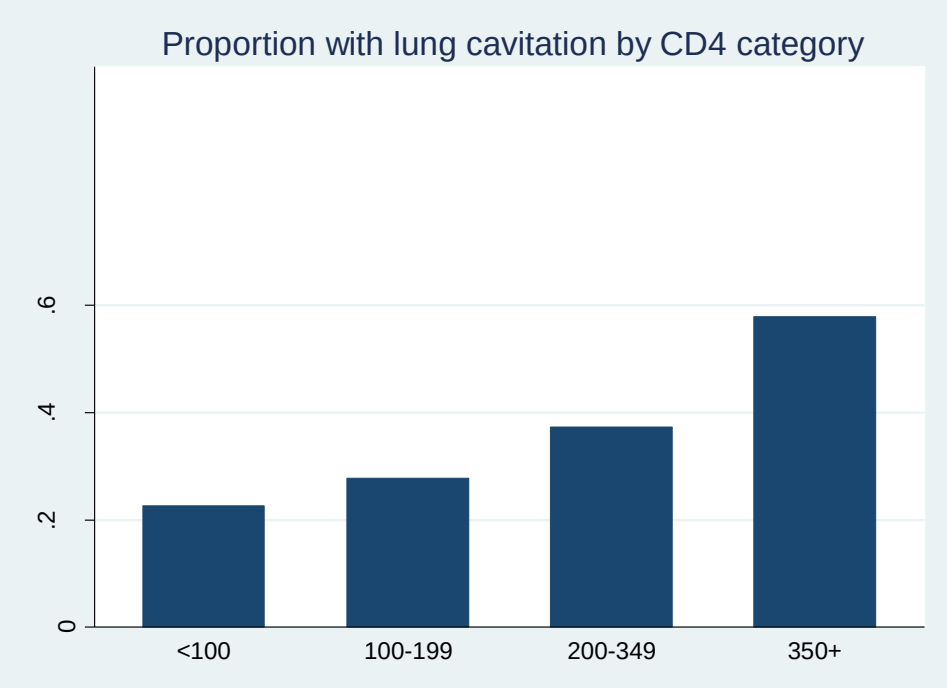
Results: lung cavitation





Comparing HIV-positive on cART >90 days vs. not on cART, odds ratio (OR) for cavitation 1.85 (1.11-3.09); p=0.02

Cavitation linearly associated with CD4 count: OR for cavitation 1.61 (1.27-2.06) for each increase in CD4 category (p<0.001)

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Results: multivariable analysis

Model	Number of TB episodes included	OR for lung cavitation On cART >90 days vs. off cART	p-value[2]
cART status (unadjusted)	311	1.85 (1.11-3.09)	0.02
cART status, adjusted for CD4	281	1.66 (0.95-2.91)	0.08
cART status, adjusted for CD4, age, episode type[1]	**259**	**1.50 (0.82-2.72)**	**0.19**

- cART not associated with lung cavitation after adjustment in multivariable model

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[1]Episode type = First or subsequent TB episode for that individual [2]p-values from Wald test in multivariable model

Study limitations

- Observational study with possible bias
  - HIV testing in those with more severe disease
  - cART used in group with specific characteristics
  - Missing data possibly associated with HIV-related outcomes

- Gold mining workforce with particular characteristics, eg silicosis, but internal comparisons still valid and relevant to other settings

- Some variation in timing of CD4, CXR, smear measurement could affect estimation of ORs

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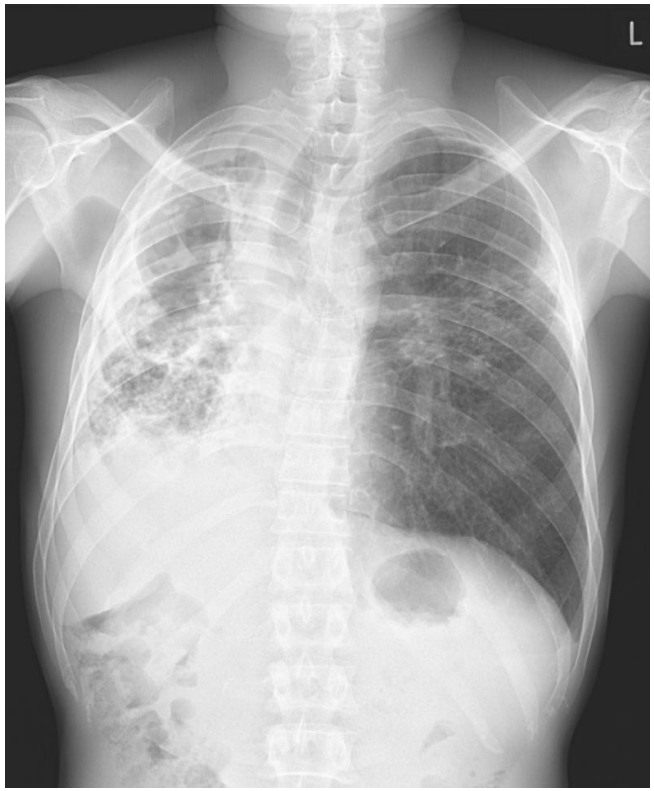
Conclusions

- High proportions smear positive in lowest CD4 stratum
- cART use was not associated with lung cavitation after adjustment for CD4 count
- Overall, cART is likely to increase infectiousness of TB through CD4 recovery
- This has implications for TB control in high HIV-prevalence areas, including nosocomial settings
- Data may be of use in modelling the impact of widespread cART use on TB transmission



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British HIV Association

BHIVA

19th Annual Conference of the British HIV Association (BHIVA)

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