The CQUIN Learning Network:

Differentiated Care for Patients at High Risk of HIV Disease Progression

Differentiated Care for TB/HIV

Felix Ndagije, MD, MSc

ICAP at Columbia University

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Columbia University
Mailman School of Public Health

Background

- In 2015, ~1.2M who developed tuberculosis disease worldwide were HIV positive. [1]
  - TB accounted for ~ 1/3rd of HIV-related deaths. [1]
- With "Treat All", HIV-associated TB epidemic will be mitigated, but alone will not be sufficient to eliminate preventable TB among PLHIV. [2]
- Data from high-burden countries indicate suboptimal uptake of ART among TB/HIV patients, and a few TB/HIV patients initiate ART within the recommended timeframe. [3, 4]

[1] WHO Global TB Report 2015; [2] Chui C, CROI 2016; [3] Lawn 2011; [4] Murphy 2011

Why Differentiated Care of TB/HIV patients? Diversity of Care Needs for PLHIV

PATIENTS PRESENTING WELL

- Initiation of ART
- Adherence and retention support

PATIENTS PRESENTING WITH ADVANCED DISEASE

- Initiation of ART
- Clinical package to reduce morbidity and mortality
- Opportunistic infection screening and management. TB screening, diagnosis and treatment, co-trimoxazole prophylaxis and IPT[2]

STABLE PATIENTS

- Differentiated care within the community (out of the facility)
- ARV delivery models

UNSTABLE PATIENTS

- Adherence and retention support
- Viral load testing
- Switch to second- or third-line ART if indicated
- HIV drug resistance testing
- Opportunistic infection screening and management. TB screening, diagnosis and treatment, co-trimoxazole prophylaxis and IPT[2]

[5] WHO, 2015

Why Differentiated Care of TB/HIV patients?

- Compared to the general population, PLHIV have a significantly higher risk of TB even if they are stable on treatment and have high CD4+ count. [6]

- A number of clinical trials have demonstrated that initiating ART early during TB treatment (< 4 weeks) greatly increases AIDS-free survival by 34-68% among individuals with advanced HIV disease. [7, 8]

- However, even with ART, patients with TB/HIV are at a greater risk of dying than those without TB. [6]

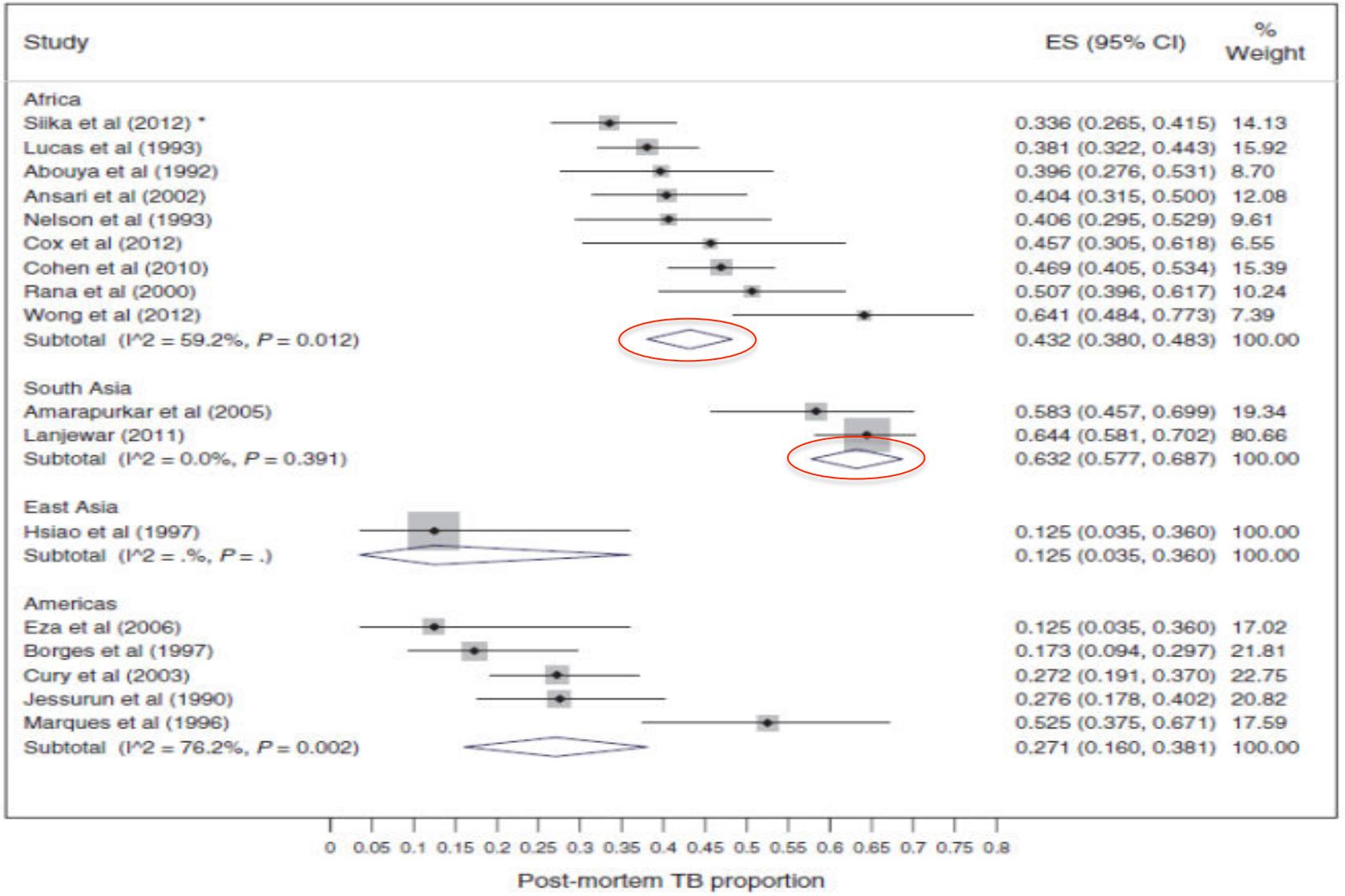
[6] Gupta 2014; [7] Havlir 2011; [8] Blanc 2011

Proportion of hospitalizations among HIV-positive patients due to TB

Region	Proportion (95% CI)	# Studies	# Patients
Adults			
Africa	23.90 (18.40, 29.40)	15	6264
South East Asia	27.00 (16.90, 37.00)	3	1922
Western Pacific	33.10 (14.40, 51.80)	6	1035
Eastern Mediterranean	27.80 (21.90, 33.70)	3	696
Europe	6.90 (3.50, 10.50)	14	21578
North America	20.00 (3.17, 36.83)	2	220
South and Central America	12.00 (8.50, 15.50)	8	4129
Overall	**17.70 (16.00, 20.20)**	**51**	**35845**
Children			
Africa	15.10 (8.30, 21.90)	8	1206
South East Asia	4.40 (1.40, 7.50)	4	853
South and Central America	6.70 (2.80, 10.70)	3	733
Overall	**10.80 (7.60, 13.90)**	**15**	**2792**

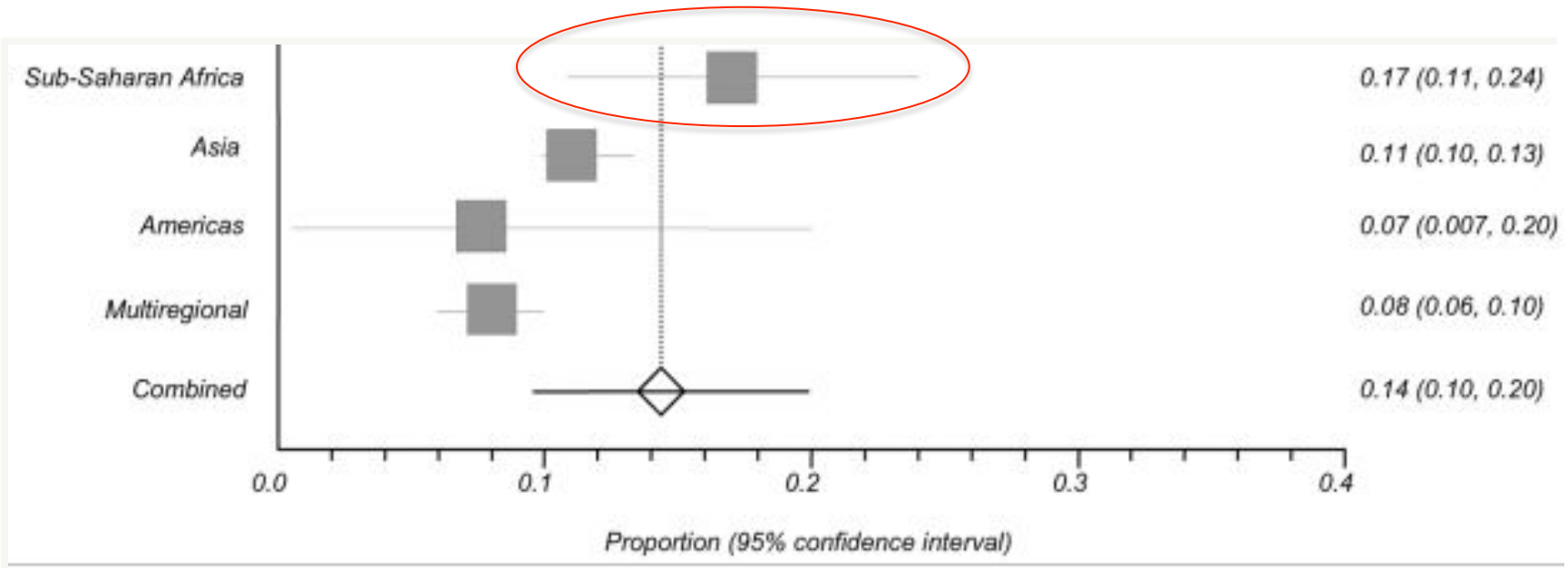
[9] Ford N et al. JIAS 2016

Prevalence of TB in post-mortem studies of HIV-infected adults and children in RLS



[10] Gupta et al. AIDS 2015

TB as a Cause of Early Mortality among Adults Initiating ART in Low and Middle Income Countries (LMIC)



TB was a cause of 5% - 44% early mortality in Sub-Saharan Africa

[11] Gupta A, 2011

Start TB Patients on ART and Retain on Treatment (START) Study

- Cluster randomized trial in Lesotho
- Evaluated combination intervention package (CIP) aimed at improving treatment outcomes among TB/HIV patients
- Standard of care for TB/HIV patients: monthly visits with nurse at health facility
- With CIP, all TB/HIV patients initiating ART received:
  - Ongoing health education and adherence counseling from facility-based village health worker
  - Weekly follow-up by phone or home visits from community-based village health worker
  - SMS medication adherence messages and appointment reminders
  - Transportation reimbursement and airtime vouchers

[12] Howard et al., Global Health Action 2016;9:3154

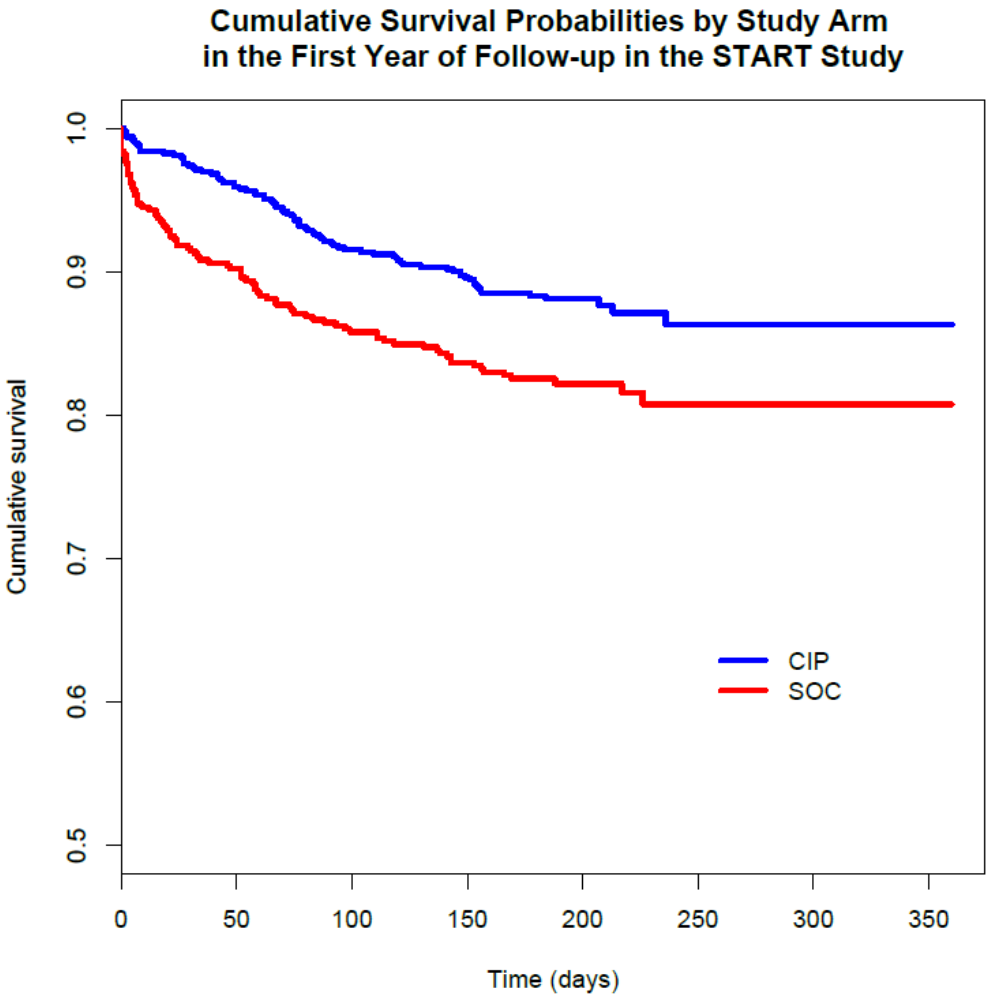
TB Treatment Outcomes (N=1233)

Study Arm	N (%)	TB treatment success N (%)	Unadjusted Risk Ratio (95% CI)	p-value
CIP	713 (58)	577 (**81%**)	1.11 (0.98, 1.26)	0.11
SOC	520 (42)	379 (**73%**)	Ref	

Treatment Category	Total N (%)	Cure N (%)	Treatment completed N (%)	Treatment failure N (%)	LTFU N (%)	Transfer out N (%)	Death N (%)
CIP	713 (58)	189 (**27**)	388 (**54**)	15 (2)	20 (3)	16 (2)	85 (**12**)
SOC	520 (42)	89 (**17**)	290 (**56**)	7 (1)	20 (4)	18 (3)	96 (**18**)
Total	1233 (100)	278 **(23)**	678 **(55)**	22 (2)	40 (3)	34 (3)	180 **(15)**

[13] Howard et al., Union World Conference on Lung Health, 2016
Abstract OA-2981

Survival Probability



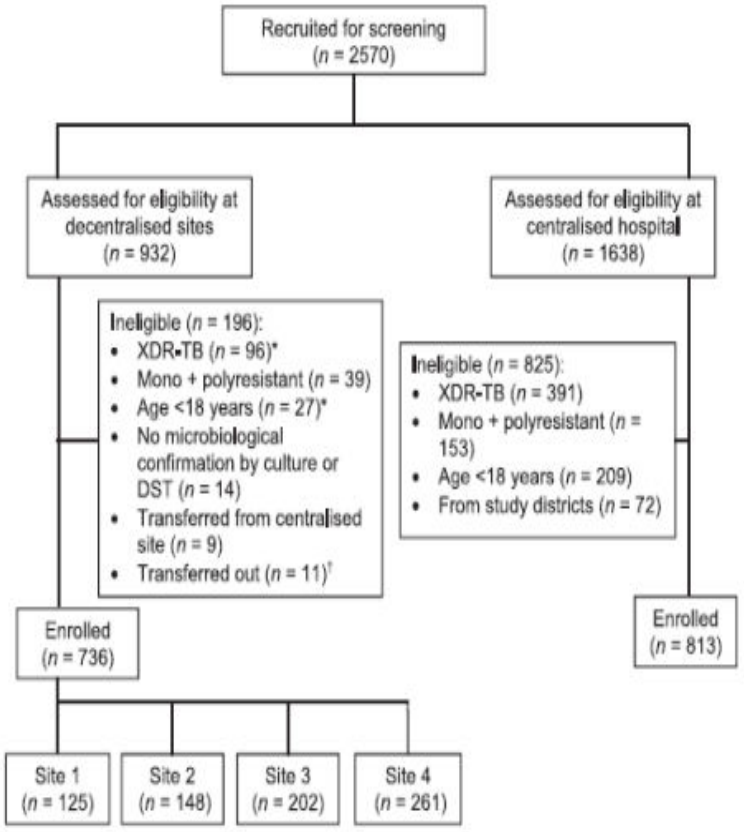
HR 0.64 (95% CI 0.47, 0.86) p=0.003

[13] Howard et al., Union World Conference on Lung Health, 2016 Abstract OA-2981

Differentiated Models of Care for MDR-TB

- MDR-TB treatment is more difficult for patients to tolerate than 1st line anti TB
  - Long duration of treatment (18–24 months)
  - Frequent medication toxicities
  - Daily administration of an injectable drug for at least 6 months
- Most countries have therefore adopted in-patient models of care at centralized, specialized hospitals and outcomes are suboptimal.
- An alternative community-based model of care could improve MDR-TB treatment outcomes and access closer to patients' homes.

Community-Based Care vs. Centralized Hospitalization for MDR-TB patients, KZN, South Africa



- Patients diagnosed with MDR-TB were referred to:
  1. Community-based site
  2. Centralized hospital
- All received standardized MDR-TB treatment and ART per national guidelines

[14] Loveday et al., 2014

Treatment outcomes stratified by HIV status in patients with MDR-TB

Table 5 Treatment outcomes stratified by HIV status in patients with MDR-TB in KwaZulu-Natal, South Africa*

	HIV-positive			HIV-negative		
	Centralised hospital ($n = 576$) n (%)	All community-based sites ($n = 528$) n (%)	P value	Centralised hospital ($n = 212$) n (%)	All community-based sites ($n = 164$) n (%)	P value
Cured	200 (34.7)	286 (54.2)	<0.001	71 (33.5)	79 (48.2)	<0.001
Treatment completed	109 (18.9)	35 (6.6)	<0.001	46 (21.7)	16 (9.8)	<0.001
Treatment success	309 (53.6)	321 (60.8)	0.013	117 (55.2)	95 (57.9)	0.372
Died	82 (14.2)	98 (18.6)	0.114	24 (11.3)	19 (11.6)	0.970
Failed	23 (4.0)	32 (6.1)	<0.001	5 (2.4)	14 (8.5)	0.008
Default	160 (27.8)	65 (12.3)	<0.001	66 (31.1)	32 (19.5)	0.025
Transferred out	2 (0.4)	12 (2.3)	†	0	4 (2.4)	†

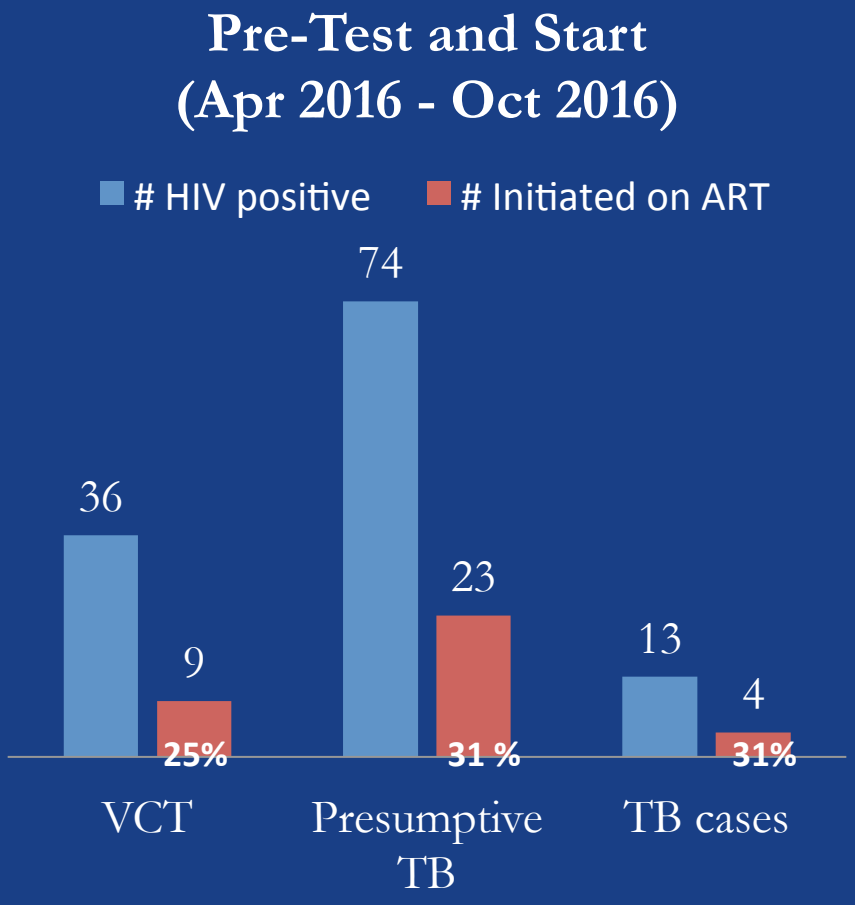
* Treatment outcome definitions used are WHO definitions for the management of MDR-TB (see Table 2).[17,18]
† Not included in multivariate model; too many missing values.
HIV = human immunodeficiency virus; MDR-TB = multidrug-resistant tuberculosis; WHO = World Health Organization.

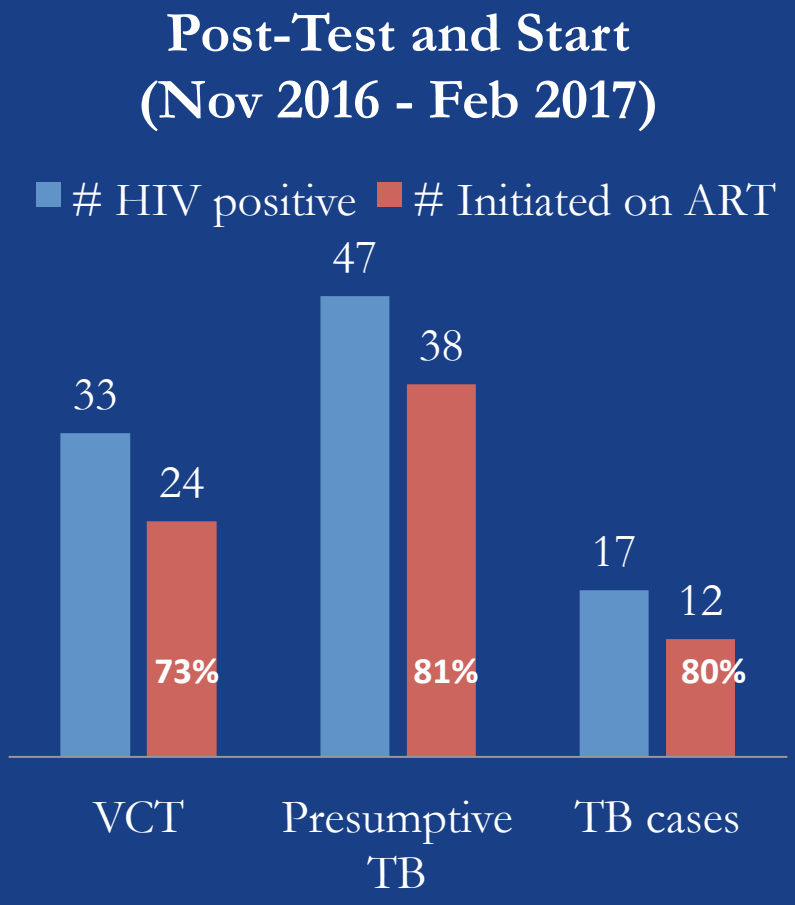
[14] Loveday et al., 2014

Provision of TB/HIV Services for Migrant Miners in Lesotho at Employment Office

- TB/HIV services provided 6 days/week at TEBA offices that dispense pay to miners and their family members
- Lay counselors provide TB screening, HIV testing
- Xpert MTB/RIF testing on-site
- Nurses provide same-day TB treatment or ART initiation
- Care supporters provide education, adherence counseling
- Medications dispensed when clients collect pay

Change in ART Initiation with On-Site Test and Start at TEBA Offices





Impact and Lessons Learned

- Differentiation considers *Clinical, Social* and *Contextual* needs of TB/HIV clients
- START shows that even with sick patients managed in facilities, community follow up in between clinic visits is beneficial for patients
- As stable patients are managed more in communities, and facilities increasingly focus on advanced disease, non-traditional delivery approaches need to be brought to scale to address high mortality and treatment outcomes for patients with TB/HIV

Thank you!

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