Does a Universal Test and Treat strategy impact ART adherence in rural South Africa?
ANRS 12249 TasP cluster randomized trial

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Antiretroviral Treatment as Prevention • ANRS 12249
Ukuphila kwami, ukuphila kwethu (my health for our health)

- Increasing number of guidelines are recommending ART regardless of CD4 count
  - To decrease HIV transmission
  - To maximise individual health benefit *(START, TEMPRANO)*

- Programmatic data on adherence suggest adherence is better in those initiating ART at lower CD4 counts
  (Chi BH, IJE 2009; Maqutu D, Afr J AIDS Res. 2010)

- Few studies have documented adherence in individuals starting ART outside of national treatment guidelines *(Vivek J, AIDS 2014, Safren S, JAIDS 2015)*

Objective & hypothesis

- Objectives
  - To investigate whether CD4 count at ART initiation has an impact on treatment adherence in the first six months of ART
  - To explore whether CD4 count at initiation has an impact on viral load suppression at 6 months

- Hypothesis:
  - Patients with higher CD4 counts at ART initiation have poorer adherence
  - As a result of poorer adherence, patients with higher CD4 counts at ART initiation have poorer virological suppression

Study design

- Cluster randomized trial[1]

Home-based HIV-testing

- Adult aged 16+ years
- Member of household in cluster
- Written informed consent

INTERVENTION
ART initiated
regardless of CD4 count
and clinical stage

CONTROL
ART initiated according to
South African guidelines
(<=350 CD4,WHO stage 3 or 4)

Cohort analysis

HIV positive and initiated on ART within the trial

[1]Iwuji C et al. Trials 2013

Study procedures

- Baseline clinic visit
  - PIMA point of care CD4 count
  - Safety bloods – FBC, U/E & LFTs
  - HIV RNA viral load (VL)

- Follow up visit
  - ART start within 2 weeks in intervention arm & if eligible in control arm
  - ART dispensed monthly
  - Adherence measured monthly using self-report (4-day recall visual analogue scale *(VAS)* and pill count *(PC)*
  - CD4 count 6-monthly & VL at 3 months and 6-monthly thereafter

Statistical analysis

- Outcome 1: adherence at each visit during first 6 months after ART start
  - VAS and PC
  - Categorised as <95% vs. ≥ 95%
- Primary exposure of interest: CD4 count at initiation

- Outcome 2: Virological suppression at 6 months
  - VL at 6-months using +/- 3 months window
  - < 400 copies/mL (suppressed) vs. ≥ 400 copies/mL (not suppressed)
- Primary exposure of interest: CD4 count at initiation
- Secondary exposure: Adherence (VAS and PC)

Statistical methods

- Outcome 1 (adherence <95% at each visit):
  - Random effects logistic regression
  - CD4 at initiation fit as continuous covariate
    - Shape of association with outcome examined using fractional polynomials
  - Age and gender were included a priori in models
  - Potential confounders assessed and included if changed OR for CD4 initiation by >10%

- Outcome 2 (VL suppression at 6m):
  - Logistic regression
  - CD4 at initiation fit as continuous covariate
  - Overall adherence at 6 months, categorised as <95% vs. ≥ 95%
  - Age and gender included a priori in models
  - Potential confounders assessed in same way as for Outcome 1

Cohort analysis (irrespective of arm)

Initiated ART within Trial
382

ART initiation CD4≤350
N=230

ART initiation CD4>350
N=152

On ART ≥ 6 months
N=252
72% female
median age 35 y (IQR=28-46)

ART initiation CD4≤350
N=150
median CD4 count 219
(IQR=150-286)

ART initiation CD4>350
N=102
median CD4 count 555
(IQR=421-697)

Adherence

- 208/252 (83%) had overall adherence at 6 months ≥ 95% when measured by VAS

  - CD4<=350: 122/150 (81%)

  - CD4>350: 86/102 (84%)

- 221/251 (88%) had overall adherence at 6 months ≥ 95% when measured by PC

  - CD4 <=350: 133/149 (89%)

  - CD4>350: 88/102 (86%)

Outcome 1: adherence <95% at each visit

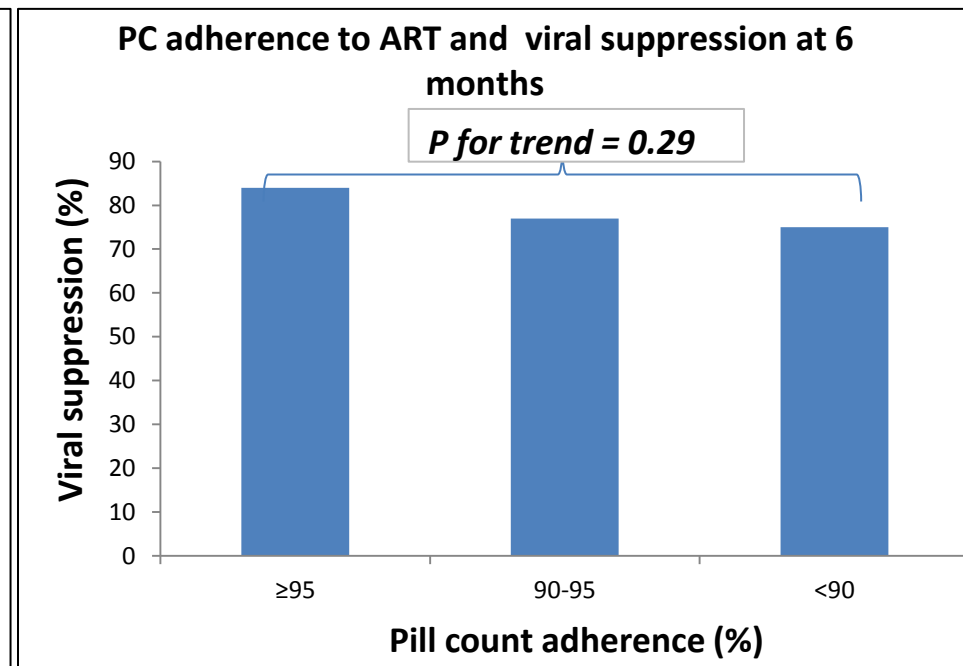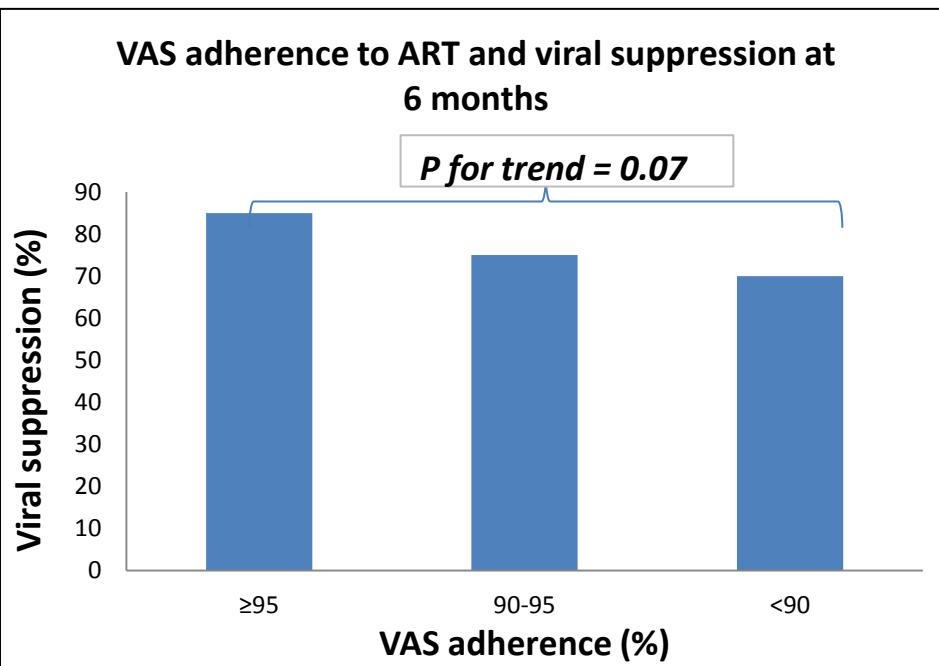|	Adherence<95% n visits/ total visits (%)	Crude OR (95% CI)	Adjusted OR[1] (95% CI)
VAS adherence (N = 1884 visits)			
CD4 at initiation			
≤350	200/1,112 (18)	*P = 0.598*	*P = 0.983*
351-500	48/302 (16)	0.97 (0.88–1.08)[2]	1.00 (0.90–1.11)[2]
>500	76/470 (16)		
Pill count adherence (N = 1707 visits)			
CD4 at initiation			
≤350	131/1,021 (13)	*P = 0.866*	*P = 0.331*
351-500	31/271 (11)	1.01 (0.93–1.10)[2]	1.04 (0.96–1.13)[2]
>500	54/415 (13)		

[1]adjusted for sex and age.

[2] OR for linear trend in odds of adherence <95% for each 100 unit increase in CD4 count.   Modelled as linear association with continuous CD4 count

Outcome 2: viral suppression at 6 months

- 229/252 (91%) have 6 months VL data available
  - 190/229 (83%) have VL < 400 copies/mL at 6 months
- Trend of decreasing VL suppression with decreasing adherence

VAS adherence to ART and viral suppression at 6 months

P for trend = 0.07

Viral suppression (%) (y-axis: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90)

VAS adherence (%) (x-axis: ≥95, 90-95, <90)

PC adherence to ART and viral suppression at 6 months

P for trend = 0.29

Viral suppression (%) (y-axis: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90)

Pill count adherence (%) (x-axis: ≥95, 90-95, <90)

Outcome 2: viral suppression at 6 months

Characteristics	Virological suppression n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
N = 229 participants **CD4 at initiation** ≤350 351-500 >500	109/136 (80) 32/36 (89) 49/57 (86)	P = 0.125 1.13 (0.97–1.33) [1]	P = 0.159 1.12 (0.96–1.32)[1, 2]
VAS adherence		P= 0.07	P=0.06
≥ 95%	156/183 (84)	1	1
<95%	34/46 (74)	0.49 (0.23–1.06)	0.46 (0.20 – 1.03)[3]

[1]OR for linear trend in odds of viral suppression, for each 100 unit increase in CD4 count.   Modelled as linear association with continuous CD4 count

[2]adjusted for sex and age

[3]adjusted for CD4 count, age, sex and marital status

Outcome 2: viral suppression at 6 months

Characteristics	Virological suppression n (%)	Crude OR (95% CI)	Adjusted OR[1] (95% CI)

N = 229
CD4 at initiation
   ≤350
   351-500
   >500
	109/136 (80)
	32/36 (89)
	49/57 (86)
		P = 0.125
		1.13 (0.97–1.33) [1]
			P = 0.159
			1.12 (0.96–1.32) [1,2]

Pill count adherence		*P = 0.278*	*P = 0.398*
≥ 95%	164/195 (84)	1	1
<95%	26/34 (76)	0.61 (0.25–1.48)	0.66 (0.26 – 1.72)[3]

[1]OR for linear trend in odds of viral suppression, with every 100 unit increase in CD4 count. Modelled as linear association with continuous CD4 count

[2]adjusted for sex and age

[3]adjusted for CD4 count, age, sex and quality of life

Conclusions/Discussion

- No evidence that higher CD4 counts at ART initiation was associated with reduced adherence or poorer virological suppression in the short-term

- Weak evidence of a decreasing trend in virological suppression with lower adherence, especially as measured by VAS

- This preliminary data add to the emerging evidence on adherence in individuals initiating ART at higher CD4 counts

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