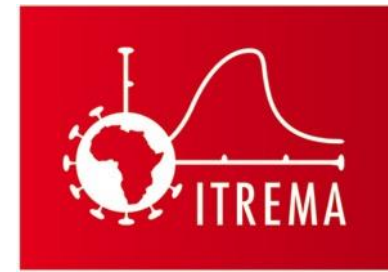# Barriers to adherence: predictors and markers of treatment response

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Acknowledgements

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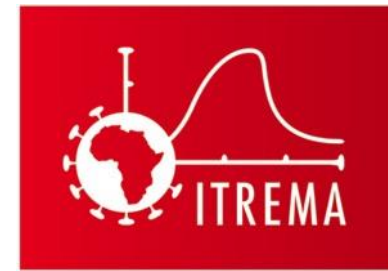
Pill count and patient-reported adherence do not predict antiretroviral treatment response in rural South Africa
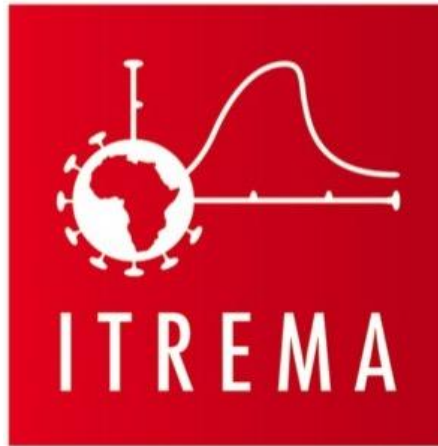
# Patient adherence is a key factor in successful combination antiretroviral therapy for HIV infection

'Adherence is Achilles' heel of cART

Critical questions

- How much adherence is needed?
  - 95% 'gold standard' (Paterson et al. 2000)
  - More forgiveness of newer drugs/regimens?

- How much adherence is achieved?
  - On average 62% report ≥90% adherence (Ortego et al. 2011)
  - ~70% of adults in Africa are (95%) adherent (Soomro et al. 2018)

- What factors influence adherence?
  - Reported barriers by age group (Shubber et al. 2016)
  - Predictors and correlates of adherence (Langebeek et al. 2014)

- How can adherence be enhanced?
  - Peer counseling, adherence clubs, SMS (Haberer et al. 2017)
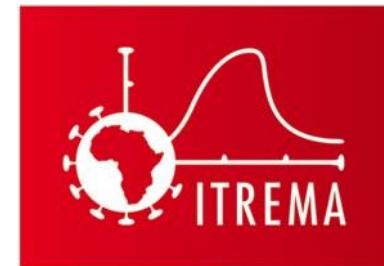 - Enhanced care, SMS, counseling + SMS, supporters (Mills et al. 2014)

Measuring adherence
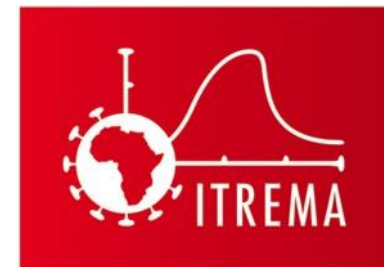
- Self-reported use
- Clinic pill count
- Pharmacy refill
- Electronic monitoring
- Blood drug levels

Electronic monitoring and pharmacy refill better predictors of viral response than clinic pill count; self-report use poor predictor (Orrell et al. 2017)
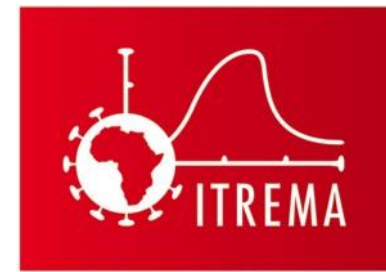
Research questions

In a resource constrained, rural, clinical setting:

- What sociodemographic, psychosocial and clinical characteristics predict viral load?

- What is the diagnostic value of poor patient-reported adherence and/or pill count <95%?

Methods

- Adults with HIV; ART-naïve or experienced
- Outcome measure defined as a viral load of ≥1000 copies per mL over one year follow-up
- Sociodemographic, clinical and psychosocial characteristics assessed by proven measures
- Adherence assessed as poor patient-reported adherence (AIDS Clinical Trial Group) and/or pill count <95%, over one year follow-up

Sample at study start
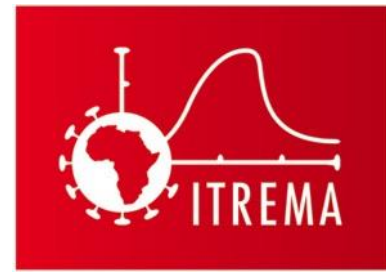
- 501 people with HIV, 207 newly initiating ART

- 70.1% (351/501) female

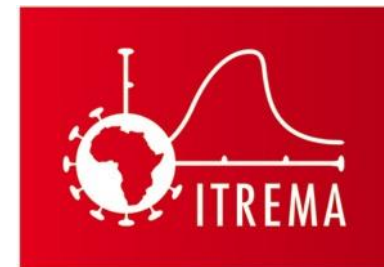- Average age 42.6 years (35.6 – 49.1)

Outcome and markers
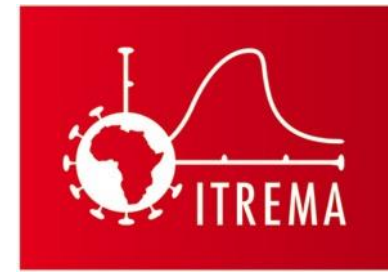
12.7% (52/411) VL ≥1000

36.2% (160/442) poor self-reported adherence
14.7% (61/414) pill count <95%

Predictors of VL (1)

| Sociodemographic characteristics	VL ≥1000 (n=52)	VL <1000 (n=359)	OR	aOR†
Age	40.6 (36.1-47.4)	42.9 (36.4-49.6)	0.98 (0.96-1.01)	
Male gender	**23 (44.2%)**	**103 (28.7%)**	**1.97 (1.08-3.56)***	
Education				
Low (none to level 12)	48 (92.3%)	334 (93.0%)	0.90 (0.33-3.15)	
High (college or university)	4 (7.7%)	25 (7.0%)	1.11 (0.32-3.02)	
Number of household members	4.0 (3.0-7.0)	4.0 (3.0-7.0)	0.99 (0.89-1.10)	
In a relationship	30 (57.7%)	224 (62.4%)	0.82 (0.46-1.50)	
Unemployed	28 (53.8%)	175 (48.7%)	1.23 (0.69-2.21)	
Household income/person (ZAR)	329 (92-1208)	400 (139-907)	0.83 (0.44-1.56)	
Food insecurity last month	7 (13.5%)	26 (7.2%)	1.99 (0.76-4.64)	

Predictors of VL (2)
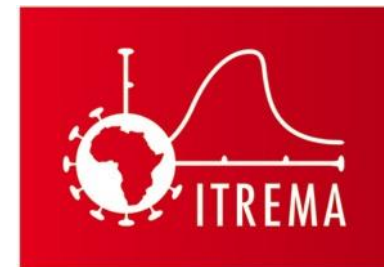
Clinical characteristics	VL ≥1000 (n=52)	VL <1000 (n=359)	OR	aOR†
Frequent use of alcohol	2 (3.8%)	7 (1.8%)	2.01 (0.29-8.60)	
Symptoms of depression (PHQ-9)				
Minimal	44 (84.6%)	336 (93.6%)	ref	ref
Mild to severe	8 (15.4%)	23 (6.4%)	2.66 (1.06-6.09)*	1.97 (0.75-4.83)
TB co-infection	4 (7.7%)	8 (2.2%)	3.61 (0.94-11.94)	
WHO stage				
I/II	41 (78.8%)	334 (93.0%)	ref	ref
III/IV	11 (21.2%)	21 (5.8%)	4.27 (1.87-9.35)**	2.68 (1.10-6.38)*
CD4+ count				
<50	10 (19.2%)	76 (21.2%)	0.92 (0.42-1,87)	
<200	36 (69.2%)	206 (57.4%)	1.98 (1.02-4.10)*	2.65 (1.28-5.95)*
200-500	12 (23.1%)	116 (32.3%)	0.65 (0.31-1.26)	
>500	0	20 (5.6%)		
HIV-related quality of life score (%)	69.8 (63.8-80.6)	75.0 (69.0-83.6)	0.97 (0.94-1.00)	

Predictors of VL (3)
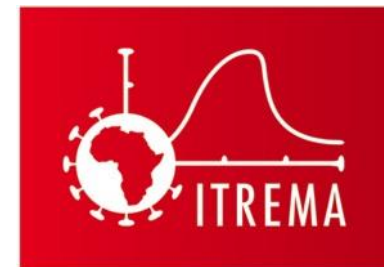
| Psychosocial characteristics	VL ≥1000 (n=52)	VL <1000 (n=359)	OR	aOR†
Adherence self-efficacy (ACTG)	4.0 (3.0-4.0)	4.0 (3.0-4.0)	0.81 (0.45-1.40)	
Household support (NKPS)	4.0 (3.2-4.0)	4.0 (3.4-4.0)	0.81 (0.58-1.17)	
Non-household family support	4.0 (3.2-4.0)	4.0 (3.4-4.0)	0.83 (0.65-1.06)	
Coping strategy scores (CISS-21)				
Task orientated	25.0 (21.0-32.3)	26.0 (21.0-33.0)	0.99 (0.95-1.04)	
Emotion orientated	18.0 (13.8-21.0)	18.0 (14.0-22.0)	0.98 (0.92-1.03)	
Avoidance orientated	13.0 (10.0-17.0)	16.0 (21.0-20.0)	0.93 (0.88-0.98)*	0.46 (0.24-0.85)*
Caregiver trust (HAQII)	5.6 (5.0-6.0)	5.6 (5.0-6.0)	0.68 (0.39-1.23)	
HIV-related (internalized) stigma	1.2 (1.0-2.0)	1.2 (1.0-1.6)	1.92 (0.96-3.76)	

Diagnostic accuracy
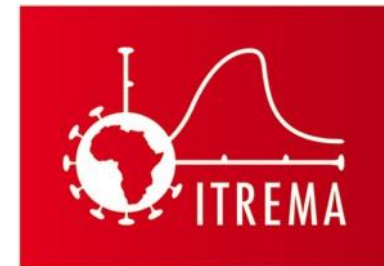
Combined marker of poor patient-reported adherence and/or pill count <95% at week 48

Not associated with VL ≥1000 (p=0.348)

- Low sensitivity (0.32, 0.17-0.51)
- Low specificity (0.75, 0.71-0.80)
- Low positive predictive value (0.11, 0.05-0.19)
- High negative predictive value (0.93, 0.89-0.95)

Conclusions
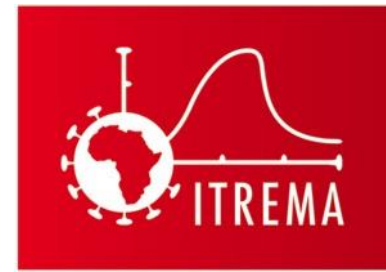
- Substantial (12.7%) poor treatment response (VL≥1000) in people with HIV in rural setting
- WHO stage, CD4 count, depression and avoidance coping associated with viral load
- Adherence markers (patient-reported and/or pill count) not diagnostic of viral load

Discussion - predictors
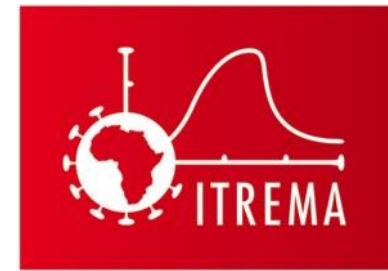
- Sociodemographics not independently related
  - Targeting men for prevention of treatment failure?
- Clinical characteristics and mental health
  - Initial worse health or reflection of worse response?
- Avoidance coping mostly thought maladaptive
  - Procrastination or denial
  - Distraction and containment?

Discussion – markers
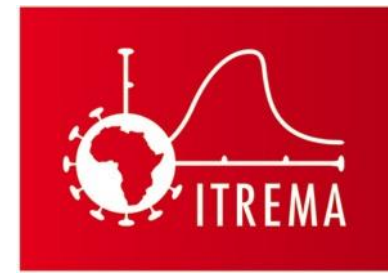
- Lack of diagnostic value of behavioral markers
  - Practical issues: understanding adherence questions, bringing pills for counting
  - Validity issues: memory constraints, socially desirable responding
- Reconsidering adherence measures
  - Appropriateness for setting and context: standard of care, resources, (health) literacy, alliance
  - Formative qualitative research: interviews, focus groups, observations; support & trust