Comparing Adherence Methods: Which Best Predicts Virological and Resistance Outcome?

POSTER 1029

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INTRODUCTION

Consistent ART adherence is critical to realising the clinical and prevention benefits of ART. As there is no gold standard, a variety of methods have been used to monitor ART adherence, including:

- **Self-report (SR)** -most frequently used method, but imprecise and overestimates adherence;
- **Clinic-based pill counts /tablet return (TR)** – usually overestimates adherence;
- **Pharmacy refill (PR) data** - also overestimates adherence, but more consistently associated with virological failure;
- **Electronic drug monitoring (EAMD)**- most closely associated with virological failure, though may underestimate adherence ; and
- **Therapeutic drug monitoring (TDM)** - associated with virological outcomes, though its precision relative to other adherence monitoring approaches is poorly understood.

OBJECTIVES: to compare multiple methods of quantifying adherence within one cohort: and to determine whether electronic adherence monitoring using Wisepill® better predicts virological and resistance outcomes than standard adherence measures, including self-report, pill counts, iDART pharmacy refill data and spot EFV concentrations.

METHODS

STUDY DESIGN and SETTING

A sub-study of a 48-week randomised controlled study at large community outpatient ART clinic in Cape Town, South Africa.

PARTICIPANTS

ART-naïve adults consecutively commencing ART and willing to sign informed consent. All received pre-treatment ART education and an EAMD (Figure 1).

DATA COLLECTION & ANALYSIS

3-day **SR** pill counts, viral load (VL) and mid-dose efavirenz (EFV) concentrations **(TDM)** were collected at week 48. **PR** and **EAMD** data were assessed cumulatively .



Figure 1: EAMD

METHODS continued

Primary outcome: VL >40 copies/ml at week 48.

Secondary outcome: IAS-USA HIV-1 drug resistance mutation.

Univariate and multivariate logistic regression models were used to explore each adherence measure's relationship to virological failure and genotypic resistance at weeks 16 and 48. Receiver Operator Characteristics (ROC) were generated to view the overall predictive power of the univariate and multivariate models. The area under the curve derived from the ROC, with 95% confidence intervals, was used to compare the prediction of virological failure or resistance by each adherence measure.

RESULTS

230 participants commenced the study, between July 2012 and March 2013, with 180 having viral loads at week 48.

Table 1: Baseline demographic and clinical characteristics.

Variable	Full cohort	With VL at week 48
Number: n	230	180
Female sex: n(%)	150 (65.2)	121 (67.2)
Age in years: mean (sd)	34.5 (9.1)	35.0 (9.4)
Height (cm): mean (sd)	164.0 (8.6)	164.0 (8.1)
Weight (kg): median (IQR)	67.3 (57.8-79.6)	68.1 (58.7-80.4)
BMI: median (IQR)	24.3 (21.3-29.8)	24.6 (21.5-30.7)
WHO stage: n(%) 1	84 (36.5)	73 (40.6)
2	47 (20.4)	39 (21.7)
3	75 (32.6)	51 (28.3)
4	24 (10.4)	17 (9.4)
CD4 count (cells/mm³): median (IQR)	225 (133-287)	233 (144-287)
Log HIV-RNA (copies/ml): median (IQR)	4.9 (4.4-5.4)	4.8 (4.4-5.4)
NNRTI at start: n(%) Efavirenz	228 (99.1)	178 (98.9)
Nevirapine	2 (0.9)	2 (1.1)
NRTI at start*: n(%) Tenofovir	225 (97.8)	177 (98.3)
Zidovudine	4 (1.7)	3 (1.7)
Stavudine	1 (0.4)	-
HADS depression score of 8 or above (borderline or case): n(%)	74 (32.1)	58 (32.2)
HADS anxiety score of 8 or above (borderline or case): n(%)	89 (38.7)	70 (38.9)
Non-disclosure: n(%)	11 (4.7)	7 (3.9)
CAGE score ≥2: n(%)	35 (15.2)	25 (13.9)

Table 2: Median adherence percentage with inter-quartile range at each study visit, by adherence measure.

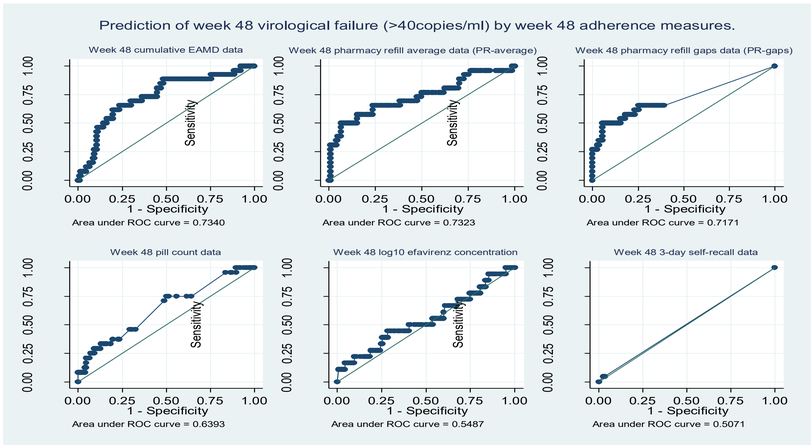
SR and **EFV** concentrations: measured on the date of the visit;
TR over 60 days before week 48 visit;
PR and **EAMD** adherence: cumulative data from baseline to week 48.

	n	Week 48
Self-report (%): median (IQR)	169	100 (100-100)
Pill count (%): median (IQR)	178	100 (95-107)
Average pharmacy refill (%): median (IQR)*	178	103 (95-105)
Gaps pharmacy refill (%): median(IQR)*	178	100 (95-100)
EAMD adherence (%): median (IQR)*	180	86 (59-94)
EFV concentration (mg/L): median(IQR)	156	2.1 (1.5-3.4)
Viral suppression: n(%)	180	154 (85.6)

RESULTS continued

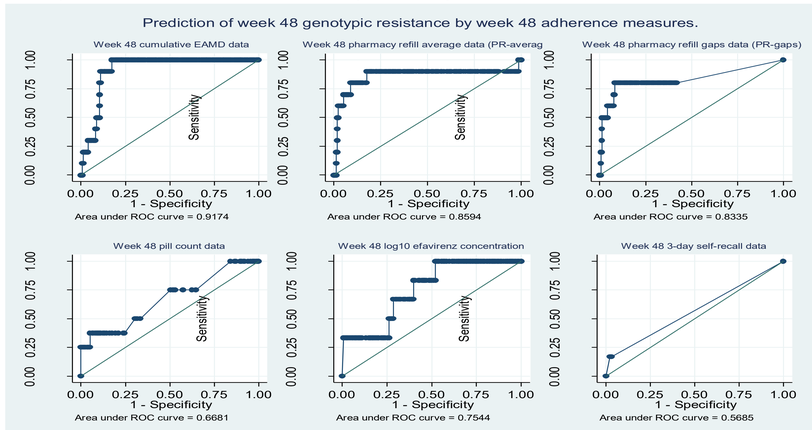
Figure 2: Receiver Operating Characteristic (ROC) curves showing prediction of virological failure (>40 copies/ml) and resistance at week 48 by six adherence measures. Univariate model data are shown.

2a - prediction of virological failure (>40 c/ml)



AUC ROC (95%CI):	
EAMD:	0.74 (0.63-0.84)
PR-ave:	0.73 (0.61-0.85)
PR-gap:	0.72 (0.59-0.85)
TR:	0.64 (0.52-0.76)
EFV:	0.55 (0.40-0.70)
SR:	0.51 (0.46-0.56)

2b - prediction of resistance (any IAS major mutation)



AUC ROC (95%CI):	
EAMD:	92 (0.87-0.96)
PR-ave:	0.82 (0.60-1.0)
PR-gap:	0.85 (0.67-1.0)
TR:	0.67 (0.45-0.88)
EFV:	0.77 (0.58-0.93)
SR:	0.57 (0.40-0.73)

CONCLUSION

Adherence levels were high.

- **EAMD** adherence data and **PR** measures best predicted virological failure and development of resistance at week 48.
- **TR** performed reasonably well.
- **SR** adherence measures are unreliable for research purposes or clinical monitoring.
- Log values of mid-dose **EFV** concentration were predictive of resistance at week 48, but not failure.

PR data is available and more immediately implementable option in a resource poor setting, but **EAMD** should be considered.

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