

## Living with HIV: Analysis of Data from the BREATHER Trial

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### Background

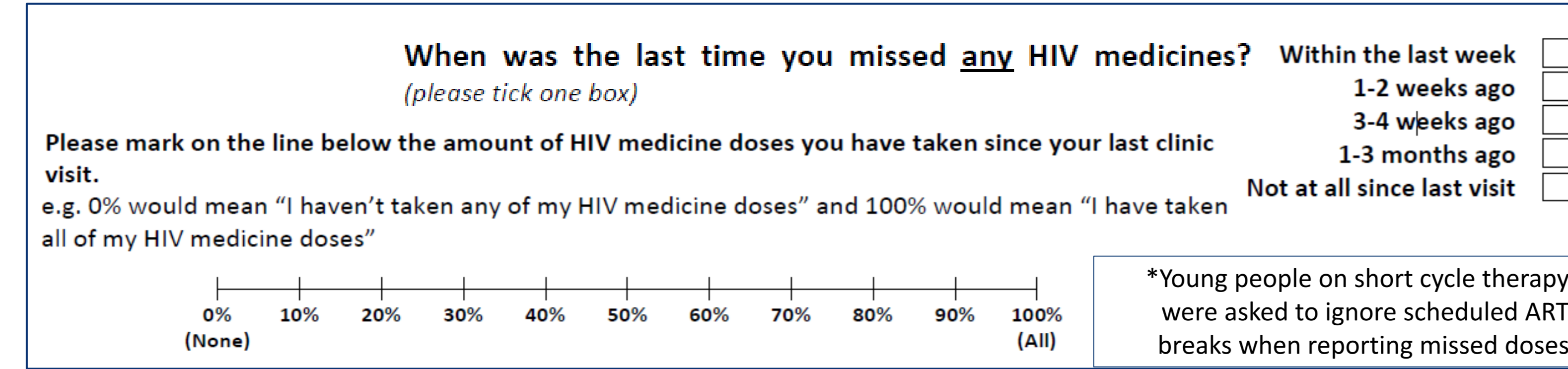
- Adherence to anti-retroviral therapy (ART) is critical to achieve successful clinical outcomes; it is known to be problematic during adolescence
- Measurement of adherence is challenging and better understanding of the validity of adherence tools may improve adherence assessment
- The BREATHER trial (ISRCTN97755073) randomised participants, age 8-24 years, to continuous ART versus short cycle therapy (5 days on, 2 days off) Young people had to be virologically suppressed on an efavirenz (EFV) based regimen to be eligible for BREATHER
- Our aim was to compare and evaluate the 6 different measures of adherence used in the BREATHER trial. The measures were evaluated against the outcome of viral rebound

### Methods

#### Adherence Measures

- Viral load (VL) and 6 measures of adherence; any missed doses in the last week; any missed doses since last visit; visual analogue scale (VAS) (excluding scheduled days off in short cycle therapy group) each reported by participant and caregiver were collected at weeks 4, 12, then 12 weekly up to week 204 (Figure 1)

Figure 1. Adherence questions for young people on continuous therapy\*



#### Statistical Methods

- The trial's primary outcome was confirmed viral rebound (2 consecutive VL $\geq$ 50c/ml) and was used in this analysis as a proxy for "true" adherence. Trial arms were pooled as there were no significant differences between arms for any adherence measure or viral rebound
- The association between viral rebound and each adherence measure/ baseline characteristics were analysed using random effects logistic regression, adjusting for visit week and trial arm

### Results

#### Baseline characteristics

- There were 199 participants, median age was 13.9 [IQR 11.9,17.4] years and median duration of ART was 6.0 [4.1,8.3] years (Table 1)

#### Follow-up and young person/caregiver reported adherence

- Median follow-up was 188 [IQR 155,203] weeks
- At 2438/3157 (77%) follow-up visits young people completed questionnaires; at 1461/3157 (46%) follow-up visits caregivers completed questionnaires. Completion by young person/caregiver was driven by age

Figure 2. Missed doses reported by young people (YP) over trial follow-up

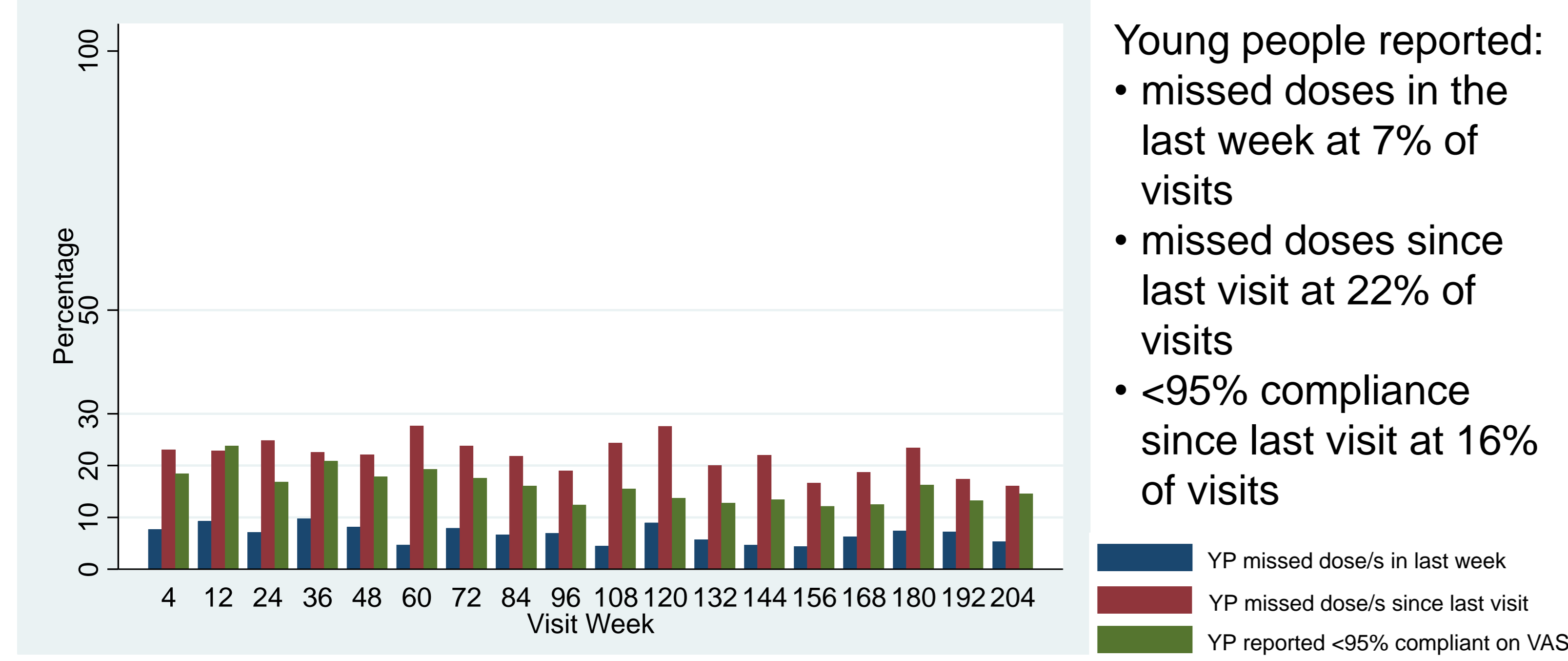
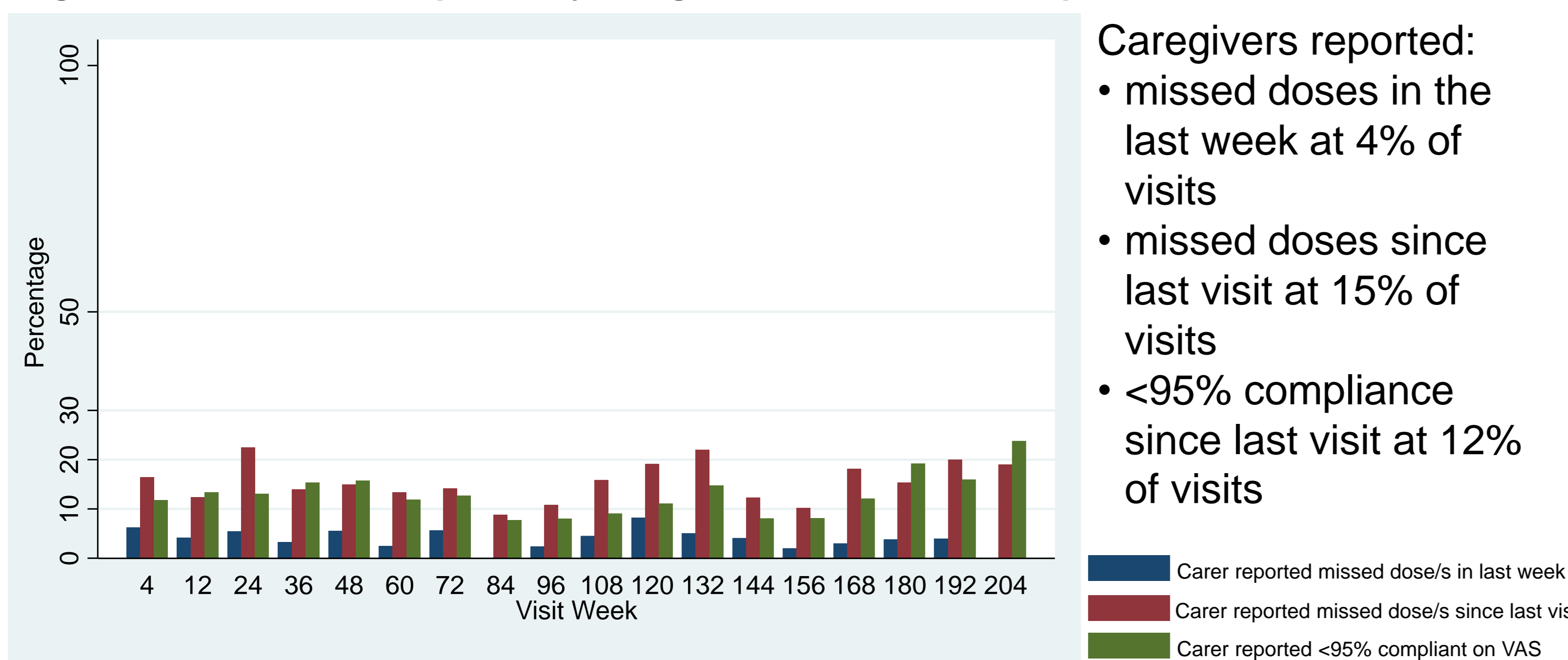


Figure 3. Missed doses reported by caregivers over trial follow-up



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### Results

#### Viral Rebound

- 32 (16%) participants had confirmed viral rebound (2 consecutive VL $\geq$ 50c/ml)
- Confirmed viral rebound occurred at 118/2812 (4%) visits
- None of the baseline characteristics were associated with viral rebound (Table 1)

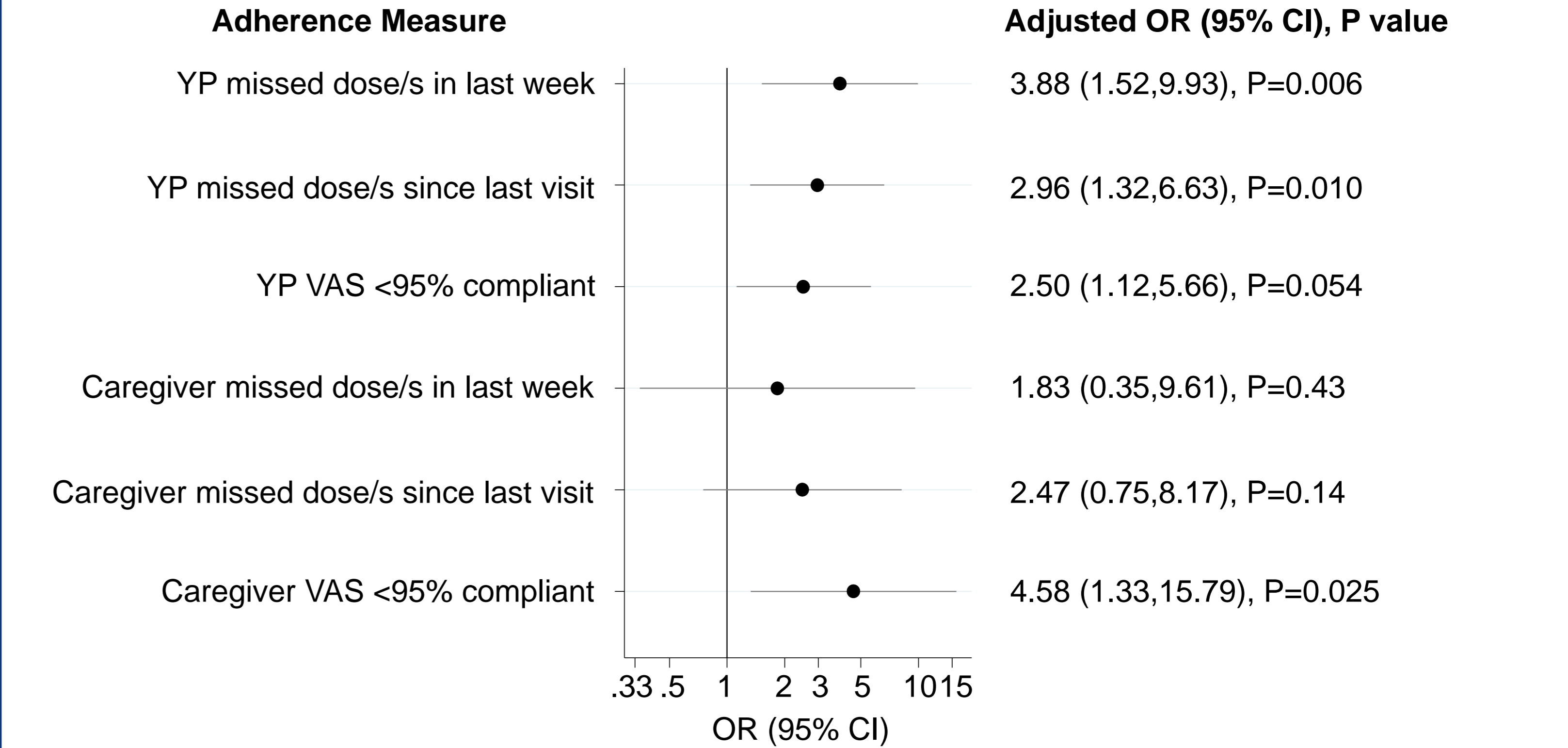
Table 1: Baseline characteristics of BREATHER participants and association with confirmed VL  $\geq$  50 c/ml

Baseline characteristic	n=199 (%)	Confirmed VL $\geq$ 50c/ml		P-value*	
		n (% with viral rebound)	Adjusted OR (95% CI) ‡		
Age (years)	8-12	77 (39)	15 (19)	1.00	0.88
	13-17	80 (40)	10 (13)	0.74 (0.17,3.22)	
	18-24	42 (21)	7 (17)	0.90 (0.16,5.10)	
Sex	Male	105 (53)	16 (15)	1.00	0.64
	Female	94 (47)	16 (17)	1.22 (0.33,4.48)	
Ethnicity	White	41 (21)	6 (15)	1.00	0.60
	Black African	112 (56)	17 (15)	1.32 (0.20,8.63)	
	Asian	37 (19)	7 (19)	4.00 (0.16,98.37)	
	Other	9 (5)	2 (22)	1.73 (0.19,15.43)	
Clinic location	Africa	70 (35)	11 (16)	1.00	0.13
	Non-Africa	129 (65)	21 (16)	1.35 (0.35,5.27)	
Mode of infection	Other†	19 (10)	4 (21)	1.00	0.66
	Vertical	180 (90)	28 (16)	0.37 (0.05,2.96)	
ART regimen EFV plus:	ZDV+3TC	105 (53)	20 (19)	1.00	0.37
	TDF+3TC/FTC(±ZDV) ABC+3TC/FTC or ddl+ABC	52 (26) 42 (21)	6 (12) 6 (14)	0.38 (0.07, 1.97) 0.84 (0.16,4.31)	
Duration on ART (years)	1-4	67 (34)	9 (13)	1.00	0.59
	5-8	94 (47)	16 (17)	1.65 (0.36,7.48)	
	9-16	38 (19)	7 (18)	2.08 (0.32,13.39)	

† Other modes of infection include: sexual contact, blood product & unknown; \* Likelihood Ratio Test; ‡ Adjusted for visit week & trial arm

#### Association between adherence measures and confirmed VL $\geq$ 50c/ml adjusted for visit week and trial arm

Figure 3. Association between confirmed VL  $\geq$ 50c/ml & each adherence measure adjusted for visit week & trial arm



- After adjusting for visit week and trial arm, young person report of missed doses in the previous week was most strongly associated with viral rebound (odds ratio (OR) 3.88 [95%CI 1.52,9.93], p=0.006) (Figure 3)
  - Findings were similar in each trial arm (no interaction p=1.0)
- Other adherence measures were also associated with viral rebound, albeit less strongly (Figure 3)

#### Sensitivity and positive predictive value of adherence measures

- At 19/94 (20%) visits where viral rebound occurred and questionnaire data were available, the participant reported missed doses in the previous week; the corresponding sensitivity for caregiver report was 3/41 (7%)
- At 19/168 (11%) and 3/61 (5%) visits where the participant and caregiver, respectively, reported missed doses in the previous week, and VL data were available, viral rebound occurred (positive predictive value)

### Conclusions

- In our study, self-reported missed doses in the previous week helped to identify young people on ART who may require additional adherence support.
- None of the adherence measures used provided a reliable surrogate for viral rebound
- Most participants reporting recent missed doses remained virologically suppressed (independent of trial arm), highlighting a limitation of our work, namely that virological rebound is an imperfect proxy for adherence
- There appeared to be under reporting of poor adherence to treatment as evidenced by viral rebound in the absence of reported missed doses