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Predictors of over-reporting HIV pre-exposure prophylaxis (PrEP) adherence among young men who have sex with men (YMSM) in self-reported vs. biomarker data

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Abstract

Young men who have sex with men (YMSM) face a disproportionately high burden of HIV. Oral pre-exposure prophylaxis (PrEP) is effective in preventing HIV acquisition, but adherence to PrEP among YMSM may be inadequate. Medication adherence may be assessed via biomarkers, which are expensive and invasive, or via self-report through Audio Computer Assisted Self-Interview (ACASI), which may result in over-reporting of adherence. In this paper we assess the potential of a new method of self-report, the Interactive Questionnaire System (iQS), in validly estimating true adherence rates. PrEP adherence among 167 YMSM aged 15 to 23 was measured via dried blood spot (DBS), ACASI, and iQS twice over a 24-week study period. Both ACASI- and iQS-reported data revealed that over 40% of individuals self-reporting adequate PrEP adherence had DBS-estimated drug levels indicating inadequate adherence. Adjusted logistic repeated measures random intercept regression analyses indicated that younger YMSM had higher odds of over-reporting adherence than older YMSM – each one year increase in age was associated with 0.79 times the odds of over-reporting adherence (95% CI:0.63, 0.98; p-value=0.031), and being African American was associated with 3.22 times greater odds of over-reporting than non-African Americans (95% CI:1.51, 6.90; p-value=0.0003). These results suggest that ACASI and iQS methods of self-report significantly overestimate true PrEP adherence rates among YMSM, and that the odds of over-reporting adherence may be affected by both age and race.

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COMPLIANCE WITH ETHICAL STANDARDS:

ETHICAL APPROVAL: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT: Informed consent was obtained from all individual participants included in the study.

Keywords

HIV; pre-exposure prophylaxis; adherence; adolescents; men who have sex with men

INTRODUCTION

Better Human Immunodeficiency Virus (HIV) prevention strategies are urgently needed for key populations. While HIV incidence in the United States (U.S.) has remained stable over recent years, HIV incidence is increasing among men who have sex with men (MSM), and especially among young MSM (YMSM) aged 13 to 24 years (1). Male-to-male sexual contact is the primary route for HIV transmission in the U.S., and was responsible for 29,771 new HIV cases in the U.S. in 2014 (2). Considering that there were 44,073 incident cases of HIV in the U.S. overall in 2014, MSM represent over 67% of new HIV infections, despite the fact that MSM make up less than 5% of the U.S. population (1–3). YMSM also face a disproportionate burden of HIV, with approximately 7,100 infections in this population in 2014, and an increasing HIV incidence (2). Black and Latino YMSM faced an 87% increase in HIV incidence from 2005 to 2014, while white YMSM faced a 56% increase in HIV incidence during this period – such drastic increases in HIV incidence have seldom been seen in any other population groups in the U.S. (4,5).

Numerous studies have shown pre-exposure prophylaxis (PrEP) to be efficacious in the prevention of HIV among MSM in clinical trials (6–9). However, PrEP efficacy is highly dependent on medication adherence (10). Although it is prescribed as a once daily oral medication, PrEP's emtricitabine and tenofovir disoproxil fumarate (FTC/TDF) drug concentrations may reach adequate levels to confer protection against HIV when taken at least four times a week (9). However, previous PrEP trials have shown that adherence rates are often low, and thus drug concentrations often fail to reach protective levels in study populations (9,11,12). Poor PrEP adherence has been documented in both women and MSM (12–14). Recently, two PrEP trials conducted among HIV negative women in sub-Saharan Africa were halted due to futility as a result of extremely low adherence levels (12,14). In both trials, the adherence rates self-reported via Audio Computer Assisted Self-Interview (ACASI) were relatively high, although only about one quarter to one third of plasma samples had any FTC/TDF detectable (12). MSM in the placebo-controlled iPrEx trial self-reported PrEP adherence of over 90% in computer-assisted self-interview (CASI), but peripheral blood mononuclear cells (PBMC) indicated that of those in the PrEP treatment arm, only 53% of subjects had any FTC/TDF detectable (15). In the iPrEx open-label extension (OLE), overall adherence was higher, at 71% (9). Among those who had drug measurements during both the iPrEx placebo-controlled trial, and iPrEx-OLE, the proportion of those with FTC/TDF detected was higher in iPrEx-OLE (9). It is possible that our study may reveal similar PrEP adherence rates as was found in iPrEx-OLE, and greater adherence rates than was found in iPrEx, due to the generally higher adherence levels found in open-label vs. placebo-controlled PrEP studies (16). However, it is probable that participants in our study may have lower adherence rates than those enrolled in iPrEx-OLE, given that our study population consists of YMSM, a population that may face greater barriers to PrEP adherence (13,17). The first study to pilot PrEP among YMSM found large discrepancies

between self-reported adherence and detected drug levels in blood, adding to the evidence that adherence to PrEP is lower than reported across populations, and adherence self-reported via ACASI may be invalid (13,18).

Although biomarker data may be considered the “gold-standard” for adherence measurement, obtaining biological samples is expensive, invasive, and associated with high burdens for patients, researchers, and healthcare workers. ACASI, though potentially less biased than face-to-face interviews, may result in over-reporting of behaviors that are perceived as positive, and under-reporting of behaviors deemed more negative (19). Medication adherence, considered a socially desirable behavior, is thus often over-reported when assessed via ACASI self-report in HIV PrEP trials, as reported above (19). To address this issue, a new method to report adherence, the Interactive Questionnaire System (iQS), was developed to assess the potential of an alternative self-reporting system for adherence measurement. The iQS required higher participant interaction with the survey system, as compared with ACASI, and involved the use, customization, and interaction with a user-designed avatar. This analysis compares differences in adherence reporting between iQS or ACASI as compared to the levels of drug detected in blood, and examines the predictors of discrepancies between self-report (iQS and ACASI) and biomarker methods of adherence reporting. This study was nested within ATN-110/ATN-113, in order to examine discrepancy in adherence reporting in greater detail. This research is crucial to examine the validity and explore potential correlates of discrepancies between self-reported and biomarker-reported PrEP adherence among YMSM at high risk for HIV acquisition.

METHODS

The NICHD-funded Adolescent Medicine Trials Network (ATN) conducted clinical trials of daily oral PrEP safety and efficacy among YMSM in 16 urban sites in the U.S. (ATN-110 and ATN-113). Participants at 12 of the 16 sites were offered enrollment in a sub-study evaluating iQS, entitled “Structural and Partnership Factors Affecting Adherence to Pre-Exposure Prophylaxis (PrEP) among Young Men who have Sex with Men” (ATN-123). The 12 participating sites were located in Baltimore, Boston, Chicago, Denver, Detroit, Houston, Los Angeles, Memphis, Miami, New Orleans, Philadelphia, and Tampa. On or prior to their ATN-110/ATN-113 week 24 visit, participants were offered participation in ATN-123. ATN-123 began recruiting participants in July 2013, and completed enrollment in July 2015 with 167 participants. All enrollees in ATN-123 were given the option of taking the iQS at the study site, on a personal mobile device, or on a personal computer. This was operationalized slightly differently across sites, as there were some barriers to confirming study activity enrollment for those who selected out of study site options. All participants were compensated $10–$45 for completing each iQS – compensation amount was determined by each site according to its research standards. Signed informed consent was obtained from all ATN-123 participants prior to any study activities. Participants consented to completing iQS questionnaires upon enrollment in ATN-123. Individuals enrolled in ATN-123 had previously consented to providing dried blood spot (DBS) samples and completing ACASI questionnaires through their participation in ATN-110/ATN-113. The study protocol was reviewed and approved by the IRBs at each study site and the UCLA IRB.

The iQS was completed at two timepoints – timepoint one corresponded to ATN-123 baseline, when iQS was first introduced to participants; timepoint two occurred 24 weeks after timepoint one, and marked the conclusion of ATN-123. The baseline of iQS corresponds to ACASI week 24, while the second timepoint of iQS corresponds to ACASI week 48; participants who enrolled in ATN-123 were first introduced to PrEP 24 weeks prior to ATN-123's baseline. Questions regarding PrEP adherence asked in iQS were identical to those asked in ACASI. For both self-report methods, individuals were presented with a calendar representing the previous month, and were prompted: "This calendar represents the past month. Now please fill in the days you took your study pill…"

Those subjects with missing DBS data at timepoints one or two had DBS data imputed from a previous clinic visit no more than 12 weeks prior to the corresponding ATN-123 site visit, as not all participants gave DBS samples on the same dates that iQS self-interviews were administered (Table I). Subjects with no DBS data available for up to the 12 weeks prior to ATN-123 baseline or ATN-123's conclusion at week 24 were excluded from analyses. Those participants missing adherence data on self-report and/or DBS were determined via regression analyses to not be significantly different from participants included in full analyses with regards to age, race, study site, heavy alcohol use in the past month, any non-marijuana drug use in the past month, socioeconomic status, or any other relevant covariate. We thus expect that excluding subjects with missing adherence data from analyses will not induce bias.

Proportions of participants with adequate PrEP adherence were reported for all three adherence measurement methods – DBS, ACASI, and iQS – by timepoint. Participants were considered "adequately adherent" if they took PrEP at least four times a week – reflected in ACASI/iQS as self-reported drug-taking at least four times a week for the previous 30 days, and by DBS drug levels of 700fmol/punch or greater (20). In order to determine whether differences in proportions of subjects with adequate adherence exist between iQS, ACASI, and DBS, and across timepoints, McNemar's Test, a test of marginal homogeneity, was utilized. McNemar's Test was performed to compare iQS vs. ACASI, iQS vs. DBS, and ACASI vs. DBS at timepoints one and two. This test was selected to determine whether there existed discrepancies between reported adequate adherence between the three measurement methods, by timepoint. Frequencies and percentages of participants reporting preference of adherence measurement method were also tallied at each timepoint.

Crude and adjusted mixed logistic regression models with random intercept were utilized to determine which covariates were associated with over-reporting of medication adherence in self-report, while adjusting for clustering induced by having repeated measures on subjects across the two time points. For these regression analyses, ACASI was utilized as the self-report measure in logistic regression analyses, as adherence measures between ACASI and iQS were not significantly different – as confirmed by McNemar's Test (Table III) – and ACASI adherence data was more complete than was iQS data (Table I). Study participants were classified as over-reporting adherence if they self-reported taking PrEP at least four days a week, but their DBS data revealed TFV levels of less than 700 fmol/punch, the minimum drug level expected among individuals taking PrEP four days a week (20). Variables included in bivariate crude regression models included: age; race; been drunk in

the past month; taken any non-marijuana recreational drugs in the past month; number of sex partners in the past three months; currently in school; currently living with parents; ever received public assistance; and sexual identity. Variables included in adjusted regression model included: age; race; currently living with parents; been drunk in the past month; and ever received public assistance. Variables for inclusion in the adjusted model were selected based on the 10% change in effect estimate criterion. This method of variable selection has been shown to produce more reliable models than variable selection that is based solely on statistical significance of covariates (21). All analyses were performed using SAS 9.4.

RESULTS

All 167 participants enrolled in ATN-123 with non-missing self-reported and DBS-determined data at timepoint one were YMSM, per enrollment criteria for ATN-110 or ATN-113, with a median age of 20 years (range of 15 to 23 years). Table II describes characteristics of participants overall and by over-reporting of adherence status, comparing adherence measured by ACASI to adherence confirmed by DBS, at timepoints one and two. While close to half of the participants were older YMSM, aged 21–23, about 40% were ages 18–20, and 12% were ages 15–17. It is apparent that younger participants tended to over-report more frequently than the older YMSM in this sample. The majority of study participants self-identified as gay, while about 18% were bisexual, and the remainder had some other sexual identity. Most study participants were African-American (55.8%), followed by non-Hispanic White (17.6%), Hispanic (15.2%), and other (11.5%). Participants had a range of education levels, although the majority had a high school diploma or less, which is unsurprising considering the young age of the study population. Just over half of ATN-123 participants had received some type of public assistance in the past, whether it be food stamps, social security, medical benefits, free school lunches, or other public aid. A fairly high proportion (75.8%) reported being drunk in the past month, and 21.8% reported any non-marijuana drug use in the past month. Participants most commonly had 1 or 2 sex partners in the past 3 months, while 13.9% did not report any sex partners in the past 3 months, and 36.7% reported 3 or more partners.

The proportion of participants achieving adequate adherence varied by adherence measurement method, with DBS data recording a lower percentage of adherent participants than either self-report method (Table III; Figure 1). This discrepancy in proportion of adequately adherent individuals between self-report and biomarker data was apparent at both timepoints. A relatively large proportion of participants reported adequate adherence via iQS and ACASI at both timepoints (Figure 1; 86.6% adherent at iQS timepoint one; 82.6 % adherent at ACASI timepoint one; declining to 69.3 % adherent at iQS timepoint two and 74.1% adherent at ACASI timepoint two), but DBS-estimated adherence was considerably lower than self-reported data. According to DBS, only 45.9% of participants were adequately adherent at timepoint one, decreasing to 38.8% at timepoint two. While iQS, ACASI, and DBS all revealed declining adherence over time, the extent of mismatch in adequate adherence between self-report and biomarker remained relatively large.

The results of McNemar’s test revealed that at timepoints one and two, for comparisons both between iQS and DBS, and between ACASI and DBS, adherence levels were not

homogenous (p-values <0.001; Table III). Such results provide evidence that adequate adherence levels are significantly different when measured by self-report vs. by biomarker. However, homogeneity between measures could not be rejected when comparing the two self-report measures (iQS vs. ACASI) at both timepoints one and two. iQS and ACASI may thus be expected to provide similar data on adherence.

When comparing similarity between measurement methods between timepoints, adherence measurements revealed that for all three methods, adherence appeared to decline over time (Figure 1). As determined by DBS data, 43 participants maintained adequate adherence across timepoints, 50 maintained inadequate adherence across timepoints, 20 participants had adequate adherence at timepoint one but dropped to inadequate adherence at timepoint 2, while 8 participants had inadequate adherence at timepoint one but improved to adequate adherence at timepoint 2.

Over-reporting of adherence via ACASI self-report, as compared with DBS, was fairly common, occurring in 37.1% (59 out of 159) and 40.2% (45 out of 112) participants at timepoints one and two respectively. The discrepancies reported between self-reported and biomarker-determined data were almost entirely due to participants over-reporting their adherence in self-report, as compared to their DBS-determined drug levels. There was only one instance of an individual with adequate adherence as confirmed by DBS underreporting his adherence status in ACASI, and only three instances of individuals with adequate adherence by DBS underreporting their adherence statuses in iQS.

When asked about their preferred method of self-report for measuring their adherence to PrEP, at iQS baseline the majority of participants reported preference of ACASI over iQS. While preference of ACASI over iQS persisted at iQS week 24/ACASI week 48, the difference in percentage of participants preferring ACASI over iQS declined. At timepoint one, 68.5% (74 out of 108) participants preferred ACASI over iQS. This dropped to 58.9% (43 out of 73) preferring ACASI over iQS at timepoint two.

Crude mixed logistic regression random intercept models estimating the odds of over-reporting adherence via self-report indicated that, without controlling for any other variables, age, race, and living with parents were significant predictors of over-reporting adherence in ACASI (Table IV). For each one year increase in age, without controlling for any other variables, participants had 0.76 times the odds of over-reporting, as compared to those participants one year younger, indicating that as age increases, the odds of over-reporting decreases (95% CI: 0.65, 0.90; p-value=0.001). In the crude model, African American participants had 3.21 times greater odds of over-reporting, as compared to non-African American participants (95% CI: 1.69, 6.08; p-value=0.0004). Living with parents was also associated with over-reporting adherence in the crude mixed model; those YMSM who lived with their parents had 2.72 times greater odds of over-reporting adherence, as compared with YMSM who did not live with their parents (95% CI: 1.47, 5.01; p-value=0.002). No other covariates revealed significant associations with over-reporting status in the crude models.

The adjusted mixed logistic regression random intercept model indicated that, after controlling for all other variables in the model (age; race; living with parents vs. not living with parents; any binge alcohol drinking in the past month; and ever received public assistance), both age and race remained significantly associated with over-reporting, while living with parents was trending towards significance (Table IV). All else equal, each one year increase in age was associated with 0.79 times the odds of over-reporting PrEP adherence, indicating that as age increases, odds of over-reporting decreases (95% CI: 0.63, 0.98; p-value=0.031). All else equal, African-Americans had 3.22 times higher odds of over-reporting adherence status than non-African Americans (95% CI: 1.51, 6.90; p-value=0.003). While living with parents had a p-value marginally greater than 0.05 (p-value=0.058), it appears that living with parents may also be positively associated with over-reporting adherence, after adjusting for other covariates (OR = 2.13; 95% CI: 0.97, 4.66).

DISCUSSION

These findings confirm large discrepancies in adherence reporting between self-reported (both ACASI and iQS) and biomarker-identified levels of use of pre-exposure prophylaxis among young men who have sex with men across multiple cities in the U.S. In the setting of a clinical trial, a different approach to collecting self-reported data (i.e. iQS) did not improve the accuracy of such reports, and collection of adherence data revealed a higher proportion of incomplete data for adherence measured when collected via iQS vs. ACASI. Adherence reports were similar between the two methods of self-report at both timepoints; discrepancies between PrEP adherence measured in ACASI and iQS compared to blood drug levels suggest substantial over-reporting of adherence through these subjective methods. DBS, ACASI, and iQS-reported adherence levels all decreased over time, but self-reported data revealed large over-estimations of DBS-estimated adherence levels; approximately 40% of individuals self-reporting adequate adherence at both timepoints over-reported their adherence, as estimated by DBS (Figure 1), emphasizing the need for biomarkers to accurately assess adherence.

Of note, the YMSM in this study generally tended to prefer ACASI over iQS, which may be because all participants in ATN-123 had previous experience with ACASI in the parent study (ATN-110/113) prior to their enrollment in ATN-123. Participants may have preferred ACASI over iQS simply due to their familiarity with ACASI. Supporting this possibility is that the percentage of participants preferring iQS increased by timepoint two. Thus, participants may have preferred iQS after they gained more familiarity in this method of self-report. In future studies, participants should have equal experience with each method in order to get a more accurate measurement of self-report measure preference.

Our finding that younger age was associated with discrepancies in adherence reporting may be due to a variety of factors. Firstly, adolescent boys may be more concerned about getting in “trouble” with researchers if they report poor adherence to PrEP, while young men in the study may be more aware that they will not get in trouble if they report low adherence levels. Age may also be associated with tendency to over-report, and adolescence may be a period associated with a time of particular vulnerability to adhere to social norms, such as medication adherence (22). Furthermore, adolescents may face heightened susceptibility to

social desirability bias, and younger individuals may thus provide answers that conform with what they expect would be deemed acceptable by the researchers (23). These findings suggest that younger study participants should be encouraged that their answers to any questions on self-interview will be confidential, that truthful answers are most helpful to researchers, and that they will not face negative consequences from the research team for their answers.

Despite the fact that living with parents failed to reach statistical significance in the adjusted model, it is possible that living with parents is a relevant factor that acts as a barrier for YMSM to properly report their PrEP use. YMSM living with parents may not wish to disclose their sexual orientation, sexual activity, and/or their PrEP use to their parents, and may be similarly uncomfortable disclosing PrEP use concerns to researchers. Additionally, if YMSM are with their parents at the time they are scheduled to take their daily PrEP dose, their ability to adhere may be hindered, and PrEP use associated with a need to act covertly. It was noted in iPrEx's qualitative study that as PrEP has a distinctive appearance, some MSM in the study said that carrying PrEP attracted unwanted attention from others (24). Researchers should be aware that being able to discreetly take and discuss PrEP may be important for MSM in general, and may be particularly crucial for YMSM who live in households with their parents.

The fact that race, and particular that being African American, was significantly associated with over-reporting is particularly concerning, as this population group is the most vulnerable to HIV acquisition in the U.S. (4,5). The need to understand barriers that prevent African American YMSM from being able to adhere to PrEP is thus crucial. Findings from this study indicate that barriers currently exist that prevent African American YMSM from being able to disclose personal and sensitive information to researchers. It is possible that health researchers are currently insufficiently able establish rapport with young African American males, which leads to a lack of trust between the researcher and participant. Previous studies have found that African American boys and young men, and particularly African American YMSM, may be more likely than their non-African American counterparts to distrust or be wary of medical professionals (25–27). This distrust is rooted in historical fact, as 400 African American men in the Tuskegee Syphilis study were unethically and inhumanely denied treatment from 1932 to 1972 (25). Although eliminating such distrust will be difficult, there are ways in which African American YMSM can be encouraged to trust health research, like PrEP studies, from which they may benefit. For example, having a greater number of young African American males on research teams, and as physicians, nurses, and other clinicians at clinic sites, may allow young African American men to feel greater comfort, trust, and encouragement to participate in health research. Current health professionals should also receive further training in cultural competence in order to improve researcher-participant and provider-patient interactions, communications, trust, and understanding (25).

Age, race, and, potentially, living with parents are associated not only with over-reporting of PrEP adherence, but also with poor DBS-estimated PrEP adherence. Young, African American MSM who live with their parents are less likely to accurately self-report their PrEP adherence, and less likely to properly adhere to PrEP, as compared to older, non-

African American YMSM who do not live with their parents. This suggests that these individuals would benefit from support to encourage both daily PrEP-taking and accurate self-reporting even when adherence is low.

This study relies on the assumption that DBS is a valid method of measuring PrEP for individuals enrolled in ATN-123. While DBS is generally considered to be an accurate, valid, and accepted method of determining PrEP adherence (28,29), the performance of DBS as a measure of PrEP adherence across different age and racial groups continues to be assessed.

LIMITATIONS

ATN-123 faced some notable limitations. Firstly, although compensation amounts were determined prior to study initiation, in practice there were variations in compensation amounts given to participants across study sites. Although lower compensation for certain participants did not negatively impacted study retention rates for iQS, it may have reduced enthusiasm for the method. It may have been perceived as more burdensome because the compensation for participating in the sub-study was as low as $10 in some sites, which may have been inadequate for the participants' time, but up to $45 in others, though participants were not aware of the compensation discrepancies. Additionally, a 30-day recall of medication adherence was utilized, which may pose difficulty for accurate reporting of medication-taking . Future studies could utilize less burdensome recall periods to asses if that improves reporting. Thirty day recall, however, has previously been demonstrated as having lower rates of over-reporting of HIV medication adherence, as compared with three day or seven day recall (30). An additional limitation was the operationalization of the iQS. The prototype avatar was conceptualized as realistic, customizable, interactive, and visually appealing. In practice, however, due to technological limitations, the avatar was a simplified, juvenile cartoon figure with minimal customization options and only minimally interactive. To assess the potential for an interactive mode to improve adherence, future studies will need avatars that are more like virtual humans and more appealing. This study also experienced loss to follow up, which resulted in a loss of sample size and the potential that those participants who were lost may have faced different barriers to PrEP adherence than participants who were retained in the study. Although loss to follow up was not found to be associated with PrEP adherence or other measured covariates, losing participants affected sample size, which may have impacted statistical efficiency. The reasons for loss to follow up, especially for iQS, must be explored in more depth.

CONCLUSION

The results of ATN-123 provide further evidence that self-report methods of adherence to PrEP in clinical trials suffer from considerable over-reporting and likely do not accurately capture true levels of medication adherence. Discrepancies between self-reported and biomarker-determined PrEP adherence are not uniform across participants, however, and individuals who are younger, African American, and possibly those who live with their parents may be more likely to over-report medication adherence, as compared to older, non-African American individuals who do not live with their partners. These findings indicate

that young, African American YMSM individuals may feel uncomfortable disclosing concerns regarding PrEP use, and that mistrust of health professionals and social desirability bias may impact PrEP use reporting among this population.

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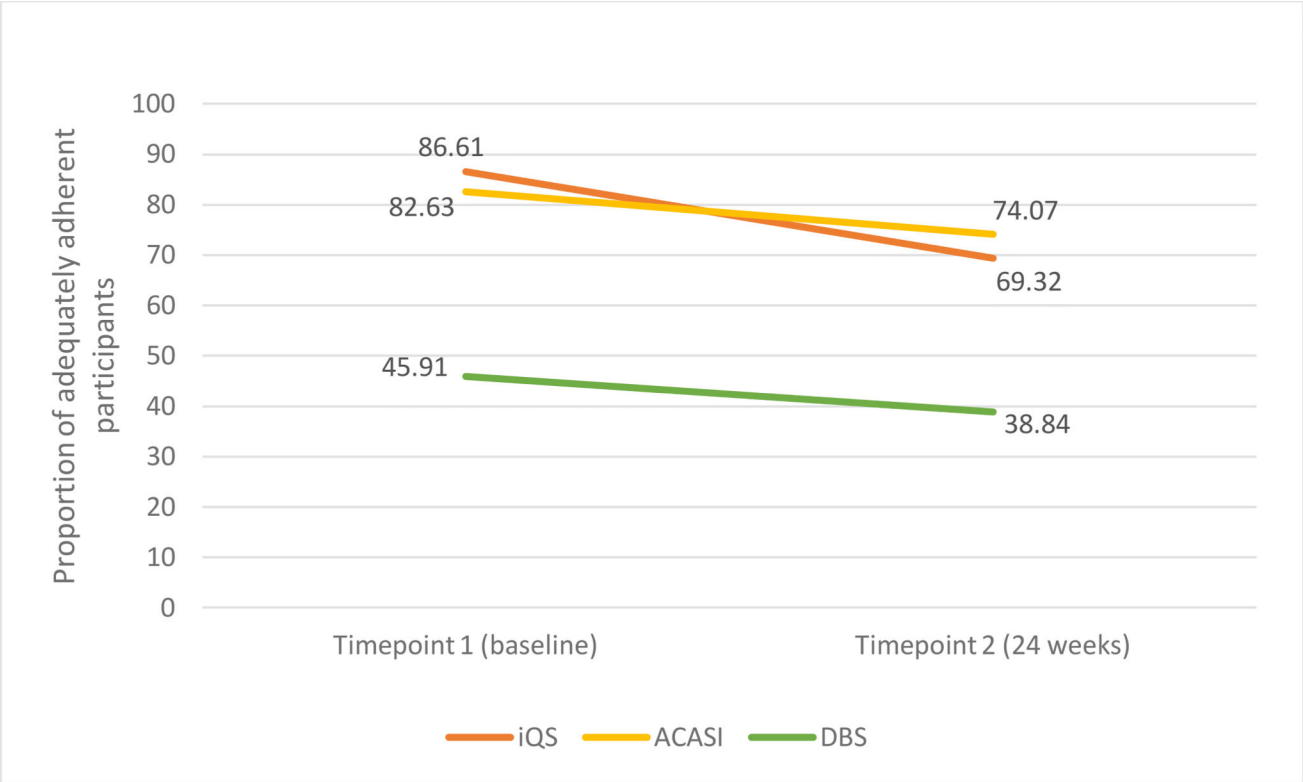

Figure 1.
Changes in percentage of participants with adequate PrEP adherence from timepoint 1 to timepoint 2, by adherence measurement method

Table I

Number of participants with non-missing vs. fully-missing adherence data by data collection method and timepoint.

	Timepoint 1		Timepoint 2	
Data collection method	**Number non-missing**	**Number missing adherence data**	**Number non-missing**	**Number missing adherence data**
ACASI	167	0	135	32
iQS (n=137)	123	14	86	51
DBS (n=167)	159*	8	121*	38

*Since participants didn't always give DBS samples at timepoints that exactly corresponded with ACASI and iQS administration dates, DBS data from up to the previous 12 weeks were imputed for timepoints 1 and 2. For timepoint 1, 20 participants had DBS imputed from up to 12 weeks prior to ACASI/iQS timepoint 1; for timepoint 2, 24 participants had DBS imputed from up to 12 weeks prior to ACASI/iQS timepoint 2.

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Table II

Sociodemographic information about ATN-123 study population, by over-reporting of adherence status at both timepoints

	ATN-123 (N=167)									
	Overall (N=167)		Over-reported at timepoint 1 (N=59)		Did not over-report at timepoint 1 (N=100)		Over-reported at timepoint 2 (N=67)		Did not over-report at timepoint 2 (N=45)	
Demographics	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Age (N=167)										
15–17 years	20	12.0	13	22.0	7	7.0	9	20.0	7	10.4
18–20 years	67	40.1	27	45.8	38	38.0	21	46.7	22	32.8
21–23 years	80	47.9	19	32.2	55	55.0	15	33.3	38	56.7
Race/Ethnicity (N=165)										
Black	92	55.8	42	72.4	43	43.4	30	68.2	30	45.5
White	29	17.6	4	6.9	25	25.3	6	13.6	13	19.7
Hispanic	25	15.2	8	13.8	16	16.2	6	13.6	12	18.2
Other	19	11.5	4	6.9	15	15.6	2	4.5	11	16.7
Sexual identity (N=166)										
Gay	124	74.7	43	72.9	74	74.7	32	72.7	55	82.1
Straight	3	1.8	1	1.7	2	2.0	1	2.3	1	1.5
Bisexual	29	17.5	11	18.6	17	17.2	9	20.5	6	9.0
Other	10	6.0	4	6.8	6	6.1	2	4.5	5	4.5
School status (N=167)										

	ATN-123 (N=167)									
	Overall (N=167)		Over-reported at timepoint 1 (N=59)		Did not over-report at timepoint 1 (N=100)		Over-reported at timepoint 2 (N=67)		Did not over-report at timepoint 2 (N=45)	
Demographics	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
In school	93	55.7	34	57.6	57	57.0	23	51.1	42	62.7
Not in school	74	44.3	25	42.4	43	43.0	22	48.9	25	37.3
Ever received any public assistance (N=167)										
Yes	88	52.7	36	61.0	49	49.0	28	62.2	34	50.7
No	79	47.3	23	39.0	51	51.0	17	37.8	33	49.3
Currently live with parents (N=167)										
Yes	78	46.7	34	57.6	37	37.0	30	66.7	25	37.3
No	89	53.3	25	42.4	63	63.0	15	33.3	42	62.7
Been drunk in the past month (N=124) *										
Yes	94	75.8	34	79.1	56	72.7	21	61.8	38	70.4
No	30	24.2	9	20.9	21	27.3	13	38.2	16	29.6
Taken any non-marijuana drugs in the past month (N=165)										
Yes	36	21.8	11	18.6	23	23.2	9	20.0	11	16.4
No	129	78.2	48	81.4	76	79.2	36	80.0	56	83.6
Number of sex partners in the past three months (N=166)										
0	23	13.9	11	19.0	7	7.0	6	13.3	3	4.5
1 or 2	82	49.4	25	43.1	54	54.0	33	73.3	38	56.7

	ATN-123 (N=167)									
	Overall (N=167)		Over-reported at timepoint 1 (N=59)		Did not over-report at timepoint 1 (N=100)		Over-reported at timepoint 2 (N=67)		Did not over-report at timepoint 2 (N=45)	
Demographics	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
3 or more	61	36.7	22	37.9	39	39.0	6	13.3	26	38.8
In a serious relationship (N=138)										
Yes	47	34.1	17	37.0	28	32.2	14	40.0	15	37.5
No	91	65.9	29	63.0	59	67.8	21	60.0	30	66.7
Age (Years)										
Median					20					
Interquartile					3					
Range					15–23					

*The lower sample size for this variable is indicative of participants choosing not to answer alcohol-related questions in ACASI/iQS self-interviews

Table III

Proportion of adequate adherence (at least 4 pills reported taken per week via iQS or ACASI, or DBS drug levels of 700 fmol/punch TFV or greater), by adherence method and timepoint; and discordance of adequate adherence between adherence measurement method by timepoint

		Adequate adherence N (%)	iQS Kappa (CI; p-value)	ACASI Kappa (CI; p-value)	DBS Kappa (CI; p-value)
iQS	**Timepoint 1**	110 (86.6)	---	0.73 (0.56–0.90; 0.10)	0.27 (0.14–0.39; <0.001*)
	Timepoint 2	61 (69.3)	---	0.71 (0.53–0.89; 0.32)	0.19 (0.04–0.34; <0.001*)
ACASI	**Timepoint 1**	138 (82.6)	0.73 (0.56–0.90; 0.10)	---	0.30 (0.19–0.40; <0001*)
	Timepoint 2	100 (74.1)	0.71 (0.53–0.89; 0.32)	---	0.27 (0.16–0.39; <0.0001*)
DBS	**Timepoint 1**	73 (45.9)	0.27 (0.14–0.39; <0.001*)	0.30 (0.19–0.40; <0001*)	---
	Timepoint 2	47 (38.8)	0.19 (0.04–0.34; <0.001*)	0.27 (0.16–0.39; <0.0001*)	---

*p-value<0.001

Table IV

Crude and adjusted logistic repeated measures random intercept regression models for each covariate, modeling over-reporting of self-reported (via ACASI) vs. DBS-confirmed medication adherence on covariates.

	Crude			Adjusted		
	Odds Ratio	**95% CI**	**p-value**	**Odds Ratio**	**95% CI**	**p-value**
Age (per 1 year increase)	0.76	0.65 – 0.90	0.001 *	0.79	0.63 – 0.98	0.031 *
Race						
Non-African American	Ref.	-	-	Ref.	-	-
African American	3.21	1.69 – 6.08	0.0004 *	3.22	1.51 – 6.90	0.003 *
Living with parents	2.72	1.47 – 5.01	0.002 *	2.13	0.97 – 4.66	0.058
Been drunk in the past month	0.88	0.43 – 1.81	0.73	1.35	0.61 – 2.98	0.45
Ever received public assistance	1.65	0.89 – 3.07	0.11	1.05	0.50 – 2.21	0.89
In a serious relationship	1.26	0.65 – 2.43	0.49	--	--	--
Taken any drugs other than marijuana in the past month	0.94	0.45 – 1.97	0.86	--	--	--
Number of sex partners in the past 3 months (per 1 partner increase)	0.99	0.93 – 1.05	0.75	--	--	--
In school	0.85	0.46 – 1.59	0.61	--	--	--
Sexual identity						
Gay	Ref.	--	--	--	--	--
Straight	1.24	0.15 – 9.98	0.84	--	--	--
Bisexual	1.40	0.63 – 3.12	0.40	--	--	--
Other	1.00	0.31 – 3.26	1.00	--	--	--

* p-value <0.05