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Antiretroviral drug use and HIV drug resistance among HIV-infected Black men who have sex with men: HIV Prevention Trials Network 061

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Abstract

BACKGROUND—HPTN 061 enrolled Black men who have sex with men in the United States. Some men with low/undetectable HIV RNA had unusual patterns of antiretroviral (ARV) drug use or had drugs detected in the absence of viral suppression. This report includes a comprehensive analysis of ARV drug use and drug resistance among men in HPTN 061 who were not virally suppressed.

METHODS—The analysis included 169 men who had viral loads >400 copies/mL at enrollment, including three with acute infection and 13 with recent infection. By self-report, 88 were previously diagnosed, including 31 in care; 137 men reported no ARV drug use. Samples from these 169 men and 23 seroconverters were analyzed with HIV genotyping and ARV drug assays.

RESULTS—Forty-eight (28%) of the 169 men had ≥1 drug resistance mutation (DRM); 19 (11%) had multi-class resistance. Sixty men (36%) had ≥1 ARV drug detected, 42 (70%) of whom reported no ARV drug use. Nine (23%) of 39 newly-infected men had ≥1 DRM; 10 had ≥1 ARV drug detected. Unusual patterns of ARV drugs were detected more frequently in newly-diagnosed men than previously-diagnosed men. The rate of transmitted drug resistance (TDR) was 23%

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based on HIV genotyping and self-reported ARV drug use, but was 12% after adjusting for ARV drug detection.

CONCLUSIONS—Many men in HPTN 061 had drug-resistant HIV and many were at risk of acquiring additional DRMs. ARV drug testing revealed unusual patterns of ARV drug use and provided a more accurate estimate of TDR.

Keywords

HIV; drug resistance; antiretroviral drug; Black; men who have sex with men

INTRODUCTION

In the United States (US), men who have sex with men (MSM) account for 66% of new HIV infections and over half of those living with HIV.[1] Black MSM are disproportionately affected by the HIV epidemic.[2] The HIV Prevention Trials Network (HPTN) 061 study evaluated the feasibility of a multi-component intervention to reduce HIV incidence in Black MSM and is the largest longitudinal cohort of Black MSM in the US to date.[3,4] The study enrolled both HIV-uninfected men at a high risk of HIV acquisition and HIV-infected men. HIV incidence in this cohort was 3.0% overall and 5.9% among younger participants (ages 18–30).[3]

HPTN 061 provided important information about the HIV epidemic in Black MSM. By design, most of the HIV-infected men enrolled in HPTN 061 reported that they were unaware of their HIV status (newly diagnosed) or that they were aware of their status (previously diagnosed) but were not in care.[4] However, 54% of the HIV-infected men who reported that they were newly diagnosed had low or undetectable HIV viral loads at enrollment. Although none of these men reported prior or current antiretroviral (ARV) drug use, ARV drug testing revealed that 78% of these men were on ARV treatment (ART), but chose not to disclose this to study staff.[5] Some men had unusual patterns of ARV drugs detected (e.g., two non-nucleoside reverse transcription inhibitors [NNRTIs], a NNRTI with a protease inhibitor [PI], or multiple PIs). A few men had one or two nucleoside/nucleotide reverse transcription inhibitors (NRTIs) detected in the absence of an NNRTI or PI, which suggested that they may have been using ARV drugs for pre- or post-exposure prophylaxis (PrEP or PEP).[5] ARV drugs were also detected in some men with low but detectable HIV viral loads (400–1,000 copies/mL). This was concerning, since exposure to non-suppressive levels of ARV drugs promotes selection of HIV with drug resistance mutations (DRMs),[6] which can be transmitted to others. These findings indicated the need for further evaluation of ARV drug use and HIV drug resistance among Black MSM in the HPTN 061 cohort.

This report presents a comprehensive analysis of ARV drug use and HIV drug resistance among HIV-infected men in the HPTN 061 cohort who were not virally suppressed. By combining ARV drug testing with HIV genotyping, we were able to assess current levels of drug resistance, the risk for increasing drug resistance, and patterns of ARV drug use in this cohort. Inclusion of ARV drug testing in these assessments, rather than relying solely on self-reported ARV drug use, also provided a more accurate estimate of the frequency of transmitted drug resistance (TDR).

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METHODS

Study cohort

HPTN 061 enrolled 1,553 self-identified Black MSM at eight sites in six US cities (Atlanta, Boston, Los Angeles, New York City, San Francisco, and Washington, DC) between July 2009 and October 2010 (NCT 0095129).[3,4] Men were recruited from the community or were referred by their sexual partners; men were eligible for the study if they reported having unprotected anal intercourse with a man in the six months prior to study enrollment. HPTN 061 enrolled HIV-uninfected men, HIV-infected men who reported that they were newly diagnosed, and HIV-infected men who reported that they were previously diagnosed; a maximum of 10 men per study site were enrolled who reported that they were in HIV care.[4] HIV testing was performed at the study sites at enrollment and at the 6- and 12-month follow-up visits.[3] Additional retrospective testing was performed at the HPTN Laboratory Center (Johns Hopkins University, Baltimore, MD).[3,4] Men provided demographic data to an interviewer at the enrollment visit and completed a behavioral assessment and social and sexual network questionnaire using audio computer-assisted self-interview technology at each visit.[3,4] All men were asked about ARV drug use for PrEP or PEP; men were also asked about prior or current ART. Plasma was stored at each visit for laboratory assessments.

Laboratory methods

HIV genotyping was performed retrospectively using plasma samples from men who had viral loads >400 copies/mL, including men who were HIV infected at study enrollment and men who seroconverted during the study. Testing was performed using the ViroSeq HIV-1 Genotyping System (Celera Diagnostics, Alameda, CA). Two samples were analyzed using a modified version of the ViroSeq system that includes a nested PCR step. Plasma samples were also tested for the presence of 15 ARV drugs using a high-throughput, qualitative, high-resolution mass spectrometry assay (four NRTIs: emtricitabine [FTC], lamivudine [3TC], tenofovir [TFV], and zidovudine [ZDV]; two NNRTIs: efavirenz [EFV] and nevirapine [NVP]; and nine PIs: atazanavir [ATV], amprenavir [APV], darunavir [DRV], indinavir [IDV], lopinavir [LPV], nelfinavir [NFV], saquinavir [SQV], tipranavir [TPV], and ritonavir [RTV]).[7] All ARV test results were independently reviewed by two laboratory directors. This assay has a lower limit of identification of 10 ng/mL for all 15 ARV drugs.

Men who had acute HIV infection at enrollment and seroconverters were identified using laboratory methods described previously.[3,4] Men who had recent HIV infection at enrollment were identified using a multi-assay algorithm that includes two serologic assays (the BED capture immunoassay and an avidity assay), CD4 cell count, and HIV viral load; the window period of this multi-assay algorithm for recent infection is 123 days (95% confidence intervals: 99–142 days).[8]

GenBank accession numbers: KM357930-KM358121.

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Statistical methods

Fisher's exact and chi-squared tests were used for univariate analyses. Correlates of HIV drug resistance, multi-class drug resistance (MCR), and ARV drug detection were also compared among men who were included in this sub-study (those with HIV genotyping results) vs. men who were not included in this sub-study (those with viral suppression). Multivariate analyses were attempted via generalized linear mixed models but had inadequate power for modeling the site-to-site variability among covariates. All statistical analyses were performed using SAS, version 9.2 (SAS Institute, Cary, NC).

Ethical considerations

All study participants provided written informed consent for participation in the HPTN 061 study. The study was approved by institutional review boards at each participating institution.

RESULTS

Analysis of HIV-infected men at study enrollment

Study cohort—In HPTN 061, 348 men were HIV infected at enrollment; 163 were virally suppressed (viral load ≤400 copies/mL) and 14 men refused further testing or had no sample available. The remaining 171 men had HIV viral loads >400 copies/mL; genotyping was successful for 169 of those men (men included in this sub-study). Eighty-one (48%) of the 169 men reported that they were newly diagnosed and 88 (52%) reported that they were previously diagnosed; 31 (35%) of the 88 men reported that they were in HIV care. Demographic and behavioral characteristics of the 169 men are shown in Table 1. Compared to the 163 HIV-infected men who were virally suppressed and not included in this sub-study, the 169 men included in this sub-study were more likely to be younger than 30 years old ($P<0.001$) and were less likely to have reported prior or current ART at study enrollment ($P=0.004$ and $P<0.001$, respectively).

HIV drug resistance—At least one DRM was detected in 48 (28%) of the 169 men (Table 1). Nineteen (11%) of the men had MCR, including two (1%) who had HIV that was resistant to all three ARV drug classes (NRTIs, NNRTIs, and PIs). NNRTI-associated DRMs were most common, followed by NRTI- and PI-associated DRMs (Table S1, Supplemental Digital Content); the most prevalent DRMs were K103N/S and M184V/I. In univariate analyses, older age (>30 years), reporting being in HIV care, and reporting prior or current ART use were significantly associated with any HIV drug resistance and with MCR; MCR was also more common among men who reported having no or one sexual partner in the previous six months (Table 1). The frequency of NRTI, NNRTI, and PI resistance in each of the six cities in HPTN 061 is shown in Table S1 (Supplemental Digital Content).

ARV drug detection—None of the men reported ARV drug use for PrEP, and only one reported ARV drug use for PEP. Twenty-one of the 139 men who were asked about ART reported both prior and current ART (30 of the newly-diagnosed men were not asked about ART); 11 men reported prior ART only. At least one ARV drug was detected in samples

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from 60 (36%) of the 169 men (Table 2); 42 (70%) of the 60 men reported no prior or current ARV drug use. ARV drug detection was associated with reporting prior or current ART (P=0.02 and P=0.03, respectively), but was not associated with any of the other demographic or behavioral factors shown in Table 1 (data not shown).

NRTIs and PIs were the most frequently detected ARV drug classes, and FTC was the most frequently detected ARV drug (Figure S1, Supplemental Digital Content). Thirty-one (52%) of the 60 men had ARV drugs detected that were consistent with treatment regimens that are currently recommended or were recommended at the time of study enrollment (2009-2010) by the US Department of Health and Human Services (Table 2).[9–11] Because the half-life of NRTIs is shorter than the half-life of NNRTIs and PIs, detection of a PI or NNRTI alone was considered to be consistent with recommended ART if the PI or NNRTI was included in one of the recommended treatment regimens. Detection of ARV drugs that were consistent with a recommended treatment regimen was more frequent among men who reported that they were previously diagnosed (regardless of whether they reported that they were in care) than among men who reported that they were newly diagnosed (68% vs. 31%, P=0.009).

The remaining 29 men had ARV drugs or combinations of drugs detected that are not consistent with recommended treatment regimens (Table 2). NFV was detected in 13 men (7 had NFV alone) and IDV was detected in 2 men (one had IDV alone); these drugs were no longer recommended for treatment at the time the HPTN 061 study was performed. Thirteen men had a single NRTI detected (nine had ZDV, three had FTC, and one had TFV). Detection of a single NRTI or other ARV drugs and drug combinations that were not consistent with recommended ART was more common among men who reported no prior HIV diagnosis than among men who reported that they were previously diagnosed (69% vs. 32%, P=0.009). The frequency of ARV drug detection in each of the six cities in HPTN 061 is shown in Table S1 (Supplemental Digital Content).

Relationship between HIV drug resistance and ARV drug detection—We next evaluated the relationship between HIV drug resistance and ARV drug use in the 48 men who had drug-resistant HIV at enrollment (Figure S1, Supplemental Digital Content). ARV drugs were more frequently detected in these 48 men than in the 121 men without drug resistance (56% vs. 27%, P<0.001). Men with drug-resistant HIV were more likely to have NRTIs and PIs detected (P=0.001 and P<0.001, respectively), including FTC (P<0.001), TFV (P=0.01), 3TC (P=0.002), RTV (P<0.001), ATV (P=0.01), and LPV (P=0.02). Among the 48 men who had drug-resistant HIV, 18 (38%) had at least one ARV drug detected that was not consistent with the DRMs detected, indicating that they were at risk of acquiring additional DRMs (Table S2, Supplemental Digital Content). We also used the data obtained from ARV drug testing to estimate the rate of TDR. When the rate of TDR was based solely on the frequency of DRMs among the 137 men who reported no prior or current ARV drug use (i.e., based solely on self-report of ARV drug use), the estimated rate of TDR was 23%. When we excluded 14 of the men with DRMs who also had ARV drugs detected (i.e., when ARV drug testing was used in addition to self-report of ARV drug use), the estimated rate of TDR was only 12%. Five (29%) of the 17 men who were classified as having TDR in this assessment had MCR.

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Analysis of newly-infected men

Study cohort—Thirty-nine men in this sub-study were classified as newly infected: three had acute HIV infection at study enrollment, 13 had recent HIV infection at study enrollment (identified using a MAA[8]), and 23 seroconverted during the HPTN 061 study[3]. The 23 seroconverters had a median viral load of 36,078 copies/mL (interquartile range: 5,933 to 85,140 copies/mL) at the first HIV-positive visit. Five additional seroconverters in HPTN 061 were not included in this sub-study (one did not have sufficient sample available from the first HIV-positive visit, and four had viral loads ≤400 copies/mL[7]).

HIV drug resistance—DRMs were detected in nine (23%) of the 39 newly-infected men. No DRMs were detected in any of the acutely-infected men. The NNRTI-associated K103N/S mutation was detected in four (31%) of the 13 recently-infected men and four (17%) of the 23 seroconverters (one of whom also had the NNRTI-associated P225H mutation); one additional seroconverter had the PI-associated L90M mutation.

ARV drug detection—Ten (26%) of the 39 newly-infected men had at least one ARV drug detected. ARV drugs were detected in one (33%) of the three acutely-infected men (NFV and ZDV) and nine (69%) of the 13 recently-infected men (three with NFV, two of whom had the K103N mutation; five with ZDV and one with NVP, none of whom had DRMs). No ARV drugs were detected in samples from the seroconverters at the first HIV-positive visit. None of the 39 newly-infected men reported PrEP or PEP use.

DISCUSSION

In this cohort of Black MSM in the US, 48 (28%) of the HIV-infected men who were not virally suppressed had drug-resistant HIV at study enrollment and 11% had MCR. HIV drug resistance and MCR were associated with older age, reporting being in HIV care, and reporting prior or current ART. We used a novel, high-throughput, multi-drug assay to assess ARV drug use in this cohort. ARV drug testing identified many men who were at risk for acquiring additional DRMs. At least one ARV drug was detected in 27% of the men who did not have drug-resistant HIV, and 38% of the men who had drug-resistant HIV had at least one ARV drug detected that was not associated with their pattern of drug resistance. ARV drug testing also revealed that some men were using ARV drugs that were no longer recommended for HIV treatment (e.g., NFV and IDV) and that some men had unusual patterns of ARV drug use. ARV drug testing also provided a more accurate estimate of the rate of TDR. The estimated rate of TDR in this cohort was 23% when calculated based solely on the rate of drug resistance among men who reported no prior or current ARV drug use. When the results of ARV drug testing were taken into account, the estimated rate of TDR was 12%, which is similar to that reported in other recent, multi-city US studies.[12–15] This should be considered a maximum estimate of TDR, since some men may have taken ARV drugs in the past that were not detected in their samples. It is notable that 29% of the men classified as having TDR had MCR.

ARV drugs were also detected in 10 (26%) of 39 newly-infected men. This group included acutely-infected men, recently-infected men (identified with a multi-assay algorithm), and seroconverters.[3,4,8] Most of these men had NFV or ZDV alone detected. Neither of these

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drugs is currently recommended as part of first-line regimens for PrEP, PEP, or ART.[9,16–18] HIV drug resistance was detected in nine (23%) of the newly-infected men; eight had the K103N/S mutation. The prevalence of drug resistance among these men is higher than the prevalence of drug resistance in other studies of newly-diagnosed or recently-infected MSM in the US.[13,15]

None of the men in this sub-study reported PrEP use, and only one reported PEP use. The first reports of successful use of co-formulated FTC/TFV for PrEP appeared in 2010,[19] after enrollment in HPTN 061 ended. In 2012, Truvada® was approved by the US Food and Drug Administration (FDA) for PrEP in high-risk populations.[16] While this report only included HIV-infected men, some men may have been using PrEP or PEP if they were not aware of their HIV status. In this sub-study, FTC was the most frequent ARV drug detected; TFV was also detected in some men. M184V/I, which confers resistance to FTC and other NRTIs, was the second most common DRM detected in this cohort; this mutation increases susceptibility to TFV.[6] K65R, which is associated with resistance to FTC and TFV,[6] was detected in only one man. These results are relevant to expanded use of Truvada for PrEP among MSM at high risk for HIV acquisition.

Most studies of HIV drug resistance among MSM in the US have focused on men who were failing ART,[20,21] reported they were newly diagnosed,[12–14] or were recently infected.[14,15,22–24] HPTN 061 enrolled both HIV-uninfected and HIV-infected self-identified Black MSM, including men who reported that they were in care.[3,4] This sub-study (which included men with viral loads >400 copies/mL) and our previous report (which included men with low or undetectable HIV viral loads)[5] demonstrate that many men in HPTN 061 chose not to disclose that they were using ARV drugs. Although other studies from both clinical and research settings have also reported undisclosed ARV drug use,[25–27] the frequency of undisclosed ARV drug use was considerably higher in the HPTN 061 cohort than in other studies. Men may have not disclosed past or current ARV drug use because of concerns that it would impact their eligibility for the HPTN 061 study. The study also included monetary incentives and medical services that may have also contributed to nondisclosure due to the high poverty levels in this cohort.[3,4] These findings emphasize the benefit of using objective, biomedical measures to supplement self-reported data on ARV drug use.

We note the following study limitations. First, HIV drug resistance testing was performed using a method based on population sequencing; DRMs present at low levels may not have been detected. Previous studies have shown that minority HIV variants with DRMs can impact ART outcomes[28] and that resistance rates may be underestimated if these minority variants are not taken into account.[29] Second, we also only assessed resistance and ARV drug use for NRTIs, NNRTIs, and PIs. Resistance to and use of other ARV drug classes, such as entry inhibitors and integrase strand-transfer inhibitors (INSTIs), were not assessed. Entry inhibitors and INSTIs are used for ART,[9] and INSTIs are also recommended for PEP.[17] Therefore, the prevalence of HIV drug resistance and ARV drug use in the HPTN 061 cohort may be even higher than what we report here.

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The results in this report should be considered in the context of the evolving landscape of ARV drug use. We detected unusual patterns of ARV drug use in this sub-study and in our previous report.[5] ARV drugs were also detected in 26% of the newly-infected men. In many cases, we were not able to determine the reason for ARV drug use. In addition to ARV drug use for PrEP, PEP, and ART, some men in the HPTN 061 cohort may have been using ARV drugs for other reasons. For example, 3TC and TFV are recommended by the US FDA for treating chronic hepatitis B virus infection,[30] and recent reports suggest that ARV drugs may be useful for treating other conditions.[31] ARV drugs, such as EFV and RTV, are also used for recreational purposes.[32–34] Increasing evidence also suggests that ARV drugs are shared or channeled into illicit markets in some settings, which could compromise ART adherence and expanded use of PrEP.[32,35,36] More research is needed to understand how Black MSM acquire and use ARV drugs. The findings in this report also indicate an urgent need to educate Black MSM about the appropriate use of ARV drugs, to expand the availability of health services for diagnosing and treating HIV in this population, and to ensure that health services are acceptable and effective for Black MSM. The high rate of undisclosed ARV drug use among men in HPTN 061 and other recent reports of undisclosed ARV drug use should raise awareness of the limitations of self-reported ARV drug use in research and clinical settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Author contributions

All authors contributed to manuscript preparation. Additional author roles are listed below.

Iris Chen	Performed drug resistance testing; analyzed laboratory data; contributed to study design; drafted the manuscript
Matthew B. Connor	Data analyst; performed statistical analyses
William Clarke	Developed methods used for antiretroviral drug testing, contributed to study design and data analysis; reviewed results from antiretroviral drug testing
Mark A. Marzinke	Developed methods used for antiretroviral drug testing; contributed to study design and data analysis; coordinated sample and data management for drug testing; reviewed results from antiretroviral drug testing

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Vanessa Cummings	HPTN Network Laboratory Quality Assurance / Quality Control Representative for HPTN 061; assisted with sample and data management
Autumn Breaud	Performed antiretroviral drug testing; reviewed test results
Jessica M. Fogel	Assisted with analysis of laboratory data
Oliver Laeyendecker	Assisted with identification of recently-infected participants
Sheldon D. Fields	Chair of the HPTN 061 Black Caucus; assisted with cultural data interpretations
Deborah Donnell	Statistician; reviewed statistical analyses
Sam Griffith	Project coordinator for HPTN 061
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Carlos del Rio	Principal Investigator for the HPTN 061 site in Atlanta
Manya Magnus	Principal Investigator for the HPTN 061 site in Washington, DC
Sharon Mannheimer	Principal Investigator for one HPTN 061 site in New York City
Darrell P. Wheeler	Protocol Co-chair for HPTN 061; assisted with clinical interpretation of ARV test results and provided general information about the HPTN 061 study
Kenneth H. Mayer	Protocol Co-chair for HPTN 061; assisted with clinical interpretation of ARV test results and provided general information about the HPTN 061 study; Principal Investigator for the HPTN 061 site in Boston
Beryl A. Koblin	Protocol Chair for HPTN 061; assisted with clinical interpretation of ARV test results and provided general information about the HPTN 061 study; Principal Investigator for one HPTN 061 site in New York City
Susan H. Eshleman	Responsible for study design, analyzed data; drafted the manuscript

Conflicts of Interest

None of the authors has a conflict of interest or potential conflict of interest, with the following exceptions: Dr. Eshleman has collaborated on research studies with investigators from Abbott Laboratories (distributor of the ViroSeq HIV-1 Genotyping System). Abbott Laboratories has provided reagents and performed testing for some collaborative studies. Dr. Eshleman received an honorarium in 2009 for a presentation at a symposium sponsored by Abbott Laboratories. Dr. Clarke receives research support from Thermo Fisher Scientific, including monetary support, instrument placement, and reagents. Dr. Clarke also acts as a consultant for Thermo Fisher Scientific.

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Table 1

Association of HIV drug resistance with demographic and behavioral factors.

			Any resistance			Multi-class resistance		
Characteristic		**Total 169**	**Yes 48 (28%)**	**No 121 (72%)**	**P value**	**Yes 19 (11%)**	**No 150 (89%)**	**P value**
Age	≥30 yrs	47 (28%)	7 (15%)	40 (85%)	**0.02**	0 (0%)	47 (100%)	**0.002**
	> 30 yrs	122 (72%)	41 (34%)	81 (66%)		19 (16%)	103 (84%)	
Household income	≥$30,000/yr	131 (78%)	35 (27%)	96 (73%)	0.37	15 (11%)	116 (89%)	1.00
	> $30,000/yr	38 (22%)	13 (34%)	25 (66%)		4 (11%)	34 (89%)	
Employment status	Employed	32 (19%)	9 (28%)	23 (72%)	0.97	4 (13%)	28 (88%)	0.76
	Unemployed	137 (81%)	39 (28%)	98 (72%)		15 (11%)	122 (89%)	
Student	Student	31 (18%)	11 (35%)	20 (65%)	0.33	5 (16%)	26 (84%)	0.35
	Non-student	138 (82%)	37 (27%)	101 (73%)		14 (10%)	124 (90%)	
Health insurance	Yes	105 (62%)	32 (30%)	73 (70%)	0.44	14 (13%)	91 (87%)	0.32
	No	64 (38%)	16 (25%)	48 (75%)		5 (8%)	59 (92%)	
In HIV care[a]	Yes	31 (18%)	15 (48%)	16 (52%)	**0.006**	9 (29%)	22 (71%)	**<0.001**
	No	138 (82%)	33 (24%)	105 (76%)		10 (7%)	128 (93%)	
Education	High school or less	93 (55%)	26 (28%)	67 (72%)	0.89	7 (8%)	86 (92%)	0.09
	At least some college	76 (45%)	22 (29%)	54 (71%)		12 (16%)	64 (84%)	
Substance use[b]	Yes	84 (51%)	25 (30%)	59 (70%)	0.62	8 (10%)	76 (90%)	0.72
	No	80 (49%)	21 (26%)	59 (74%)		9 (11%)	71 (89%)	
	Not available	5	2	3		2	3	
Number of male sexual partners[c]	0–1	33 (20%)	11 (33%)	22 (67%)	0.48	8 (24%)	25 (76%)	**0.008**
	>1	136 (80%)	37 (27%)	99 (73%)		11 (8%)	125 (92%)	
Prior ART[d]	Yes	32 (19%)	17 (53%)	15 (47%)	**0.001**	9 (28%)	23 (72%)	**0.001**
	No	107 (63%)	27 (25%)	80 (75%)		10 (9%)	97 (91%)	
	Reported not being aware of their HIV status	30 (18%)	4 (13%)	26 (87%)		0 (0%)	30 (100%)	
Current ART[d]	Yes	21 (12%)	13 (62%)	8 (38%)	**<0.001**	8 (38%)	13 (62%)	**<0.001**
	No	148 (88%)	35 (24%)	113 (76%)		11 (7%)	137 (93%)	
City	Atlanta	30 (18%)	5 (17%)	25 (83%)	**0.01**	3 (10%)	27 (90%)	0.09
	Boston	14 (8%)	7 (50%)	7 (50%)		1 (7%)	13 (93%)	

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Characteristic		Total 169	Any resistance: Yes 48 (28%)	Any resistance: No 121 (72%)	Any resistance: P value	Multi-class resistance: Yes 19 (11%)	Multi-class resistance: No 150 (89%)	Multi-class resistance: P value
	Los Angeles	41 (24%)	17 (41%)	24 (59%)		8 (20%)	33 (80%)	
	New York City	50 (30%)	10 (20%)	40 (80%)		2 (4%)	48 (96%)	
	San Francisco	10 (6%)	5 (50%)	5 (50%)		3 (30%)	7 (70%)	
	Washington, DC	24 (14%)	4 (17%)	20 (83%)		2 (8%)	22 (92%)	

The table shows demographic and behavioral characteristics of the 169 men who were included in the sub-study and the results from HIV drug resistance testing. Fisher's exact and chi-squared tests were used to compare characteristics of men who did vs. did not have any drug resistance, and men who did vs. did not have multi-class drug resistance. P values <0.05 are bolded. Abbreviations: ART: antiretroviral treatment; yr/yrs: year/years.

[a] Enrollment of men who reported that they were in HIV care was capped at 10 per study site.

[b] Substance use included: inhaled nitrates, smoked and power cocaine, methamphetamine, heroin, non-prescription drug use (Oxycontin, Vicodin, or Xanax), or any other hallucinogens.

[c] Surveys administered at enrollment included questions about activities in the previous six months.

[d] Thirty-two men reported prior and/or current antiretroviral drug use; all of these men reported a prior HIV diagnosis, and 19 reported that they were in HIV care at the time of study enrollment

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Table 2

Antiretroviral drugs detected in men who were HIV infected at enrollment.

	Total	Previously diagnosed[a]	Newly diagnosed[a]
ARV drug(s) detected	60	34	26
Consistent with recommended ART[b]	**31 (52%)**	**23 (68%)**	**8 (31%)**
Consistent with PI-based regimen	24	18	6
PI alone (ATV, LPV, DRV, or RTV)	8	6	2
PI (ATV, LPV, or DRV) ± RTV + NRTI(s)[c]	16	12	4
Consistent with NNRTI-based regimen	7	5	2
NVP alone	3	2	1
EFV alone	1	1	-
EFV + FTC	3	2	1
Not consistent with recommended ART[d]	**29 (48%)**	**11 (32%)**	**18 (69%)**
ZDV alone	9	1	8
NFV alone	7	3	4
FTC alone	3	3	-
TFV alone	1	1	-
IDV alone	1	-	1
FTC/TFV	1	-	1
3TC + NFV	1	1	-
ZDV + NFV	1	-	1
NVP + APV	1	-	1
FTC/TFV + NFV	1	1	-
FTC/TFV + NFV + IDV	1	-	1
FTC/TFV + NFV + LPV + RTV	1	-	1
FTC/TFV + NFV + LPV + RTV + ZDV	1	1	-

The table shows the patterns of antiretroviral (ARV) drugs detected among men who reported that they were previously diagnosed and among men who reported no prior HIV diagnosis (newly diagnosed). Men were tested for the presence of four nucleoside/nucleotide reverse transcription inhibitors (NRTIs), two non-nucleoside reverse transcription inhibitors (NNRTIs), and nine protease inhibitors (PIs, see Methods). Abbreviations: ATV: atazanavir; LPV: lopinavir; DRV: darunavir; RTV: ritonavir; NVP: nevirapine; EFV: efavirenz; FTC: emtricitabine; ZDV: zidovudine; NFV: nelfinavir; TFV: tenofovir; IDV: indinavir; 3TC: lamivudine; APV: amprenavir.

[a] Men were asked whether they were aware of their HIV status at the time of study enrollment.

[b] Criteria used to characterize ARV drugs as consistent with recommended ARV treatment (ART) regimens are described in the text.

[c] The NRTIs detected were either FTC alone or with TFV, or 3TC.

[d] This category includes patterns of ARV drug detection that were not consistent with recommended ART regimens. Drugs that were not recommended as part of pre-exposure prophylaxis, post-exposure prophylaxis, or ART regimens are underlined.