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Post-traumatic Stress Disorder and Neurocognitive Impairment in a U.S. Military Cohort of Persons Living with HIV

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Abstract

Objective: Neurocognitive impairment (NCI) is a well-known complication of HIV infection and may be influenced by a number of psychological factors. We examined the relationship between NCI and mental health disorders, including post-traumatic stress disorder (PTSD), in a cohort of 189 active-duty and retired U.S. military men living with HIV.

Methods: Participants completed selected modules of the Composite International Diagnostic Interview (CIDI) to ascertain the presence of PTSD, major depressive disorder and other mental health diagnoses. We also obtained demographic data including history of head trauma via personal interview. NCI was assessed with a comprehensive battery of standardized neuropsychological tests.

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Disclosures: The authors report no conflicts of interest associated with this research study.

Data Availability: All data is stored at the Data Coordination Center of the Infectious Clinical Disease Research Program, 11300 Rockville Pike, Rockville MD, 20852.

Results: The median age of study subjects was 36 years (interquartile range [IQR] 28–43) and median total years of education was 14 (IQR 12–16). NCI was diagnosed in 19% of subjects. Individuals with and without a history of PTSD were similar with respect to most HIV-related characteristics, however, the former were significantly more likely to have a prior AIDS diagnosis. In multivariate analysis, lifetime history of PTSD was independently associated with NCI (OR 6.12; 95% CI 1.85, 20.27), while a history of head of trauma was negatively associated (OR 0.37 95% CI 0.15,0.92).

Conclusions: Our findings demonstrate that PTSD is an important predictor of NCI in this U.S. military cohort. HIV-infected individuals with cognitive difficulties should be screened for mental health disorders including PTSD, and prospective studies of the longitudinal relationship between PTSD and NCI as well as the impact of PTSD treatment on future NCI are warranted.

Keywords

Post-traumatic stress disorder; HIV infection; neurocognitive impairment; military

Introduction

The association between post-traumatic stress disorder (PTSD) and military combat service is well known. While the lifetime prevalence of PTSD in the U.S. is 7–8% (Galea et al., 2012; Gates et al., 2012), estimates in the military of combat-related PTSD are as high as 31% (Richardson, Frueh, & Acierno, 2010). When non-combat trauma, including childhood or adult physical and/or sexual abuse, is considered, prevalence rates of PTSD in servicemembers are even higher (Gierisch et al., 2013). Among persons living with HIV (PLWH), PTSD is one of the more common mental health disorders (prevalence 21–30%), with traumatic events most commonly related to physical or sexual assault or childhood abuse (Fellows et al., 2015; Machtinger, Wilson, Haberer, & Weiss, 2012).

As with clinical depression, the presence of PTSD has been associated with poor cognitive function, including impaired reasoning, memory and concentration (Barrett, Green, Morris, Giles, & Croft, 1996; Leserman et al., 2005; Rock, Roiser, Riedel, & Blackwell, 2014). The effect of PTSD on the development of neurocognitive impairment (NCI) has been described in a number of studies, and the relationship is likely bi-directional (Brewin, Kleiner, Vasterling, & Field, 2007; Vasterling & Verfaellie, 2009). Indeed, deficits in memory and attention are incorporated into the DSM-V criteria for PTSD, (American Psychiatry Association, 2013) while patterns of thought in PTSD may induce further impairment (Vasterling & Verfaellie, 2009). NCI is also common among PLWH, with prevalence estimates ranging from 15–55% (Saylor et al., 2016), particularly in the domains of executive function, learning, and memory (Heaton et al, 2010). Previously, in our cohort of military personnel living with HIV, we reported a 19% prevalence of NCI, which was not associated with HIV-related characteristics (Crum-Cianflone et al., 2013).

Given the observed associations between PTSD and HIV with NCI, individuals living with both HIV and PTSD may be particularly vulnerable to cognitive impairment, as has been demonstrated in two recent studies. Moradi et al. (2013) found that PTSD symptoms were common among PLWH and associated with loss of autobiographical memory. However, this

study lacked standardized diagnostic criteria for PTSD assessment and PTSD symptoms only defined using the experience of receiving an HIV diagnosis as a potentially traumatic event (Moradi, Miraghaei, Parhon, Jabbari, & Jobson, 2013). More recently, Rubin et al. (2016) compared the effects of PTSD on verbal learning, memory and psychomotor speed among women living with and without HIV, finding that PTSD was associated with decreased cognitive scores among both groups. In the same study, HIV infection without PTSD was also associated with lower verbal learning and memory scores; the authors concluded that psychological factors may be as important as HIV status when predicting NCI. Together, these studies provide preliminary evidence of a strong relationship between PTSD and NCI among individuals living with HIV.

Despite this research, the relationship between PTSD and NCI remains relatively understudied, particularly when compared with other mental health disorders (R. Heaton et al., 2010; McClintock, Husain, Greer, & Cullum, 2010), and to our knowledge, the intersection of PTSD, HIV, and NCI has not previously been examined in a military cohort. Given the high prevalence of PTSD among military members, we investigated the relationship between NCI and mental health disorders in a cohort of military personnel living with HIV.

Methods

Between 2009 and 2011, we enrolled 200 military beneficiaries (active duty members, retirees, or dependents, i.e. spouse or domestic partner) living with HIV who were between 18–50 years of age into a cross-sectional study of NCI (Crum-Cianflone et al., 2013). Exclusion criteria included current/recent suicidal ideation, inability or unwillingness to complete study procedures, and presence of a medical condition that could impact the participant's ability to complete the tests (e.g., acute illness). For the present analysis, five military dependents without history of military service were excluded; in addition, owing to small numbers in an otherwise largely uniform sample, six women were also excluded, yielding a total sample of 189 male subjects. All study participants provided written informed consent and the study was approved by a central military institutional review board.

Materials and Procedures

HIV-related characteristics were abstracted from clinical records. These included history of AIDS diagnosis, years living with HIV, current HIV viral load, current CD4 count, CD4 nadir (lowest documented value), and history of antiretroviral therapy (including current ART use). We also obtained data relating to demographics, military rank and duty status, education, substance use, and history of loss of consciousness or serious head injury as obtained by self-report. Illicit drug use was ascertained by a confidential, open-ended series of questions regarding drug use (past and current) and prior failure of military mandatory drug screening. We administered the Composite International Diagnostic Interview (CIDI) to assess DSM-IV diagnoses for current and lifetime history of alcohol use disorder, depression, and PTSD (Kessler and Ustun, 2004). In addition, subjects completed the Beck

Depression Inventory-II (BDI-II) to assess for current depression (Beck, Steer, & Brown, 1996).

All participants underwent a comprehensive battery of standardized neuropsychological tests that included seven cognitive domains verbal fluency, attention/working memory, abstraction/executive functioning, learning, memory (delayed recall), speed of information processing, and complex motor skills (R. K. Heaton et al., 2004; see Figure 1). This standardized battery was designed in accordance with international consensus conference recommendations, is sensitive to HIV-associated neurocognitive disorders, and has published norms that correct for demographic effects [age, education, sex/gender, and (when appropriate) race/ethnicity] (Antinori et al., 2007; R. Heaton et al., 2010). Neuropsychological tests were administered and scored by trained psychometrists, and raw scores were converted to demographically adjusted *t*-scores (M=50, SD=10 in healthy participants). T-scores were then converted to averaged domain-based and global deficit scores (GDS), ranging from 0 (no impairment) to 5 (severe impairment). GDS scores were used to summarize neuropsychological test results. A GDS score ≥0.5 was indicative of neurocognitive impairment, consistent with the literature (R. Heaton et al., 2010).

Statistical Analyses

Descriptive statistics were used to compare individuals with and without a lifetime history of PTSD as defined by the CIDI. Non-parametric tests were used to compare medians; Chi-square and Fisher-exact tests were used to compare percentages between groups. Pearson's correlation test was used to identify relationships between variables. The outcome of interest was NCI, and statistically significant relationships were determined using logistic regression. Odds ratios (OR) for the prevalence of NCI were estimated with 95% confidence intervals (CI). Variables with a *p*-value ≤ 0.10 were entered into a stepwise multivariable model which also adjusted for age, ethnicity and education. Analyses were conducted using SAS software (version 9.0; Cary, NC).

Results

Demographic and clinical characteristics are provided in Table 1. The median age of participants was 36 (interquartile range, 28–44), which included 136 (72%) active-duty, and 53 (28%) retired servicemembers. Twenty-one participants (11.1%) screened positive for a lifetime diagnosis of PTSD, with five of these (2.6% of all participants) meeting diagnostic criteria for current PTSD. An additional 46 participants (23%) screened positive for lifetime history of major depressive disorder using the CIDI; current depression was identified in 4 (2.1%) participants using the CIDI and 14 (7.4%) participants using the BDI (score ≥ 20: moderate depression).

Individuals with lifetime or current PTSD were significantly more likely to screen positive for a depressive disorder on either the CIDI or BDI-II; CIDI-derived variables representing lifetime history of PTSD and depression had a statistically significant correlation (p=0.001, Pearson's coefficient = 0.23). The two groups (PTSD vs. no PTSD) did not differ significantly with respect to history of illicit drug use, alcohol use disorder, history of head trauma or loss of consciousness ≥ 30 minutes, though a trend was observed for the latter

(23.8% vs 10.1%, p=0.065). We also did not observe differences in PTSD prevalence among U.S. military service branches in our cohort (Table 1). With respect to HIV-related characteristics, individuals with PTSD were significantly more likely to have had an AIDS-related diagnosis (23.6% vs 4.2%, $p<0.001$) than individuals without history of PTSD. Current HIV viral loads were also significantly higher among individuals with lifetime history of PTSD compared with those without (median 480 [IQR 48, 3.1×10^4] vs 48 [IQR 48, 2.1×10^3], p=0.025, see Table 2).

Comparing individuals with and without NCI, we did not observe differences with respect to age, ethnicity, prior AIDS diagnosis, years living with HIV or other HIV-related characteristics. Individuals with NCI were significantly less likely to report history of any head injury than individuals without NCI (73% vs 51%, $p=0.01$), and no individuals with NCI reported loss of consciousness ≥ 30 minutes, compared with 13 individuals without NCI. Individuals with NCI were somewhat less likely to have used illicit drugs (3.2% vs 16.9%, $p=0.052$) compared with individuals without impairment; significant differences were not observed with respect to lifetime history of major depressive disorder or alcohol use disorder. Finally, individuals with NCI were more likely to have a lifetime history of PTSD (25.7% vs 7.8%, $p=0.002$).

A multivariate model was constructed and included the following variables: history of head injury; self-reported use of illicit drugs; age; education; ethnicity; and, lifetime history of PTSD. In this final model, lifetime history of head injury (OR 0.37 [0.15, 0.92]) and PTSD (OR 6.12 [1.85, 20.27]) remained independently associated with NCI. These variables remained significant in an exploratory model which included lifetime history of major depressive disorder.

Discussion

We report, for the first time, an association between PTSD and NCI in a U.S. military cohort of MLWH, where individuals with a lifetime history of PTSD were six times more likely to be diagnosed with NCI than individuals without PTSD. Our study's overall prevalence of NCI was low compared with others, but the higher proportion among individuals with a lifetime history of PTSD is noteworthy. While PTSD was highly correlated with current and lifetime history of depression (measured by the BDI-II and CIDI, respectively), current or lifetime depression were unrelated to NCI in our cohort in both univariate and multivariate analyses. We should note, however, that individuals with recent suicidal ideation were excluded from our study.

The relationship between PTSD and NCI among PLWH is understudied, and this study adds to the scant existing literature (Moradi et al., 2013; Rubin et al., 2016). The increased vulnerability of PLWH to PTSD and associated NCI may be explained by several characteristics unique to this population. Compared with the general population, PLWH are more likely to have experienced traumatic events that place them at risk of developing PTSD (Fellows et al., 2015; Machtinger et al., 2012). In one large cohort study, Leserman et al (2005) found that more than half of PLWH reported a history of either sexual or physical abuse, and more than 70% had experienced at least two traumatic events in their lifetime.

Additional studies have found high rates of childhood sexual abuse and sexual victimization or assault among men who have sex with men (MSM) and other groups at risk for HIV infection (Heidt, Marx, & Gold, 2005; Lenderking et al., 1997). Furthermore, the diagnosis of HIV is itself sometimes thought to be a traumatic event, which can result in PTSD-like symptoms, though it is likely prior trauma or history of PTSD may be unmasked or invoked by a new HIV diagnosis (Applebaum et al., 2015; Sherr et al., 2011).

The pro-inflammatory effects of HIV are increasingly understood and may produce synergistic responses with respect to neurocognition and PTSD. While physiological response to acute stress is typically adaptive, chronic exposure to stressful and traumatic experiences and stress hormones can hinder immune mechanisms and increase CNS inflammation, disturbing brain development and function, as well as increasing risk of psychiatric disease and poor cognitive performance (Dinkel, Ogle, & Sapolsky, 2002; Kessler et al., 2010; McEwen, 2000; Radley, Morilak, Viau, & Campeau, 2015). In individuals with HIV or PTSD, these biological processes may partially underlie the elevated rates of NCI observed in these populations, as chronic exposure to stressful and traumatic experiences may partially contribute to disturbances in mood and cognition via amplified inflammation, immune dysregulation, and associated neural alterations (Lupien, McEwen, Gunnar, & Heim, 2009; McEwen, 2000). Though the relation between PTSD and neurocognition among PLWH is increasingly understood, the intersection of immune disorders, mental health, and neurocognitive function requires further study.

The relationship between PTSD and NCI holds particular significance for the clinical care of PLWH with a history of military service. Nonetheless, in current HIV-related clinical research and care provision, PTSD screening is not a standard clinical practice, despite the unique combination of PTSD-related risk factors in this population. As noted above, traumatic events apart from combat, including sexual assault, intimate partner violence and childhood abuse are common among PLWH as well as military service members (Gierisch et al., 2013; Kang, Dalager, Mahan, & Ishii, 2005; Rosen & Martin, 1996; Zaidi & Foy, 1994). Indeed, psychological factors may have greater influence on NCI than physical injury in our military cohort of MLWH, as indicated by the negative association between head injury and NCI in our study.

Here, several factors bear consideration. While TBI has long been associated with NCI (Kinnunen et al., 2010; Langlois, Rutland-Brown, & Wald, 2006), we did not have data to categorize the nature of head injuries in our study, which may have been less severe than typically described in those studies; this would be consistent with the small number of subjects reporting loss of consciousness > 30 minutes. Active-duty MLWH are prohibited from serving in combat, although some individuals may have experienced head trauma before their HIV diagnosis, whether during or prior to military service. Thus, our analysis of the effect of head trauma on NCI is hampered by the lack of standardized classification criteria for the nature of head injury (VA/DoD, 2009) and the reliance on self-report to describe injuries. Still, the negative association remains surprising, and we hypothesize that individuals without significant NCI in our cohort may have been better able to recall their injuries than others.

Last, it is worth characterizing the nature of PTSD in our study. Individuals with PTSD were also more likely to have received a diagnosis of AIDS, suggesting a more advanced state of disease, which may directly or indirectly affect cognitive performance. While age itself was not associated with a diagnosis of PTSD, a trend (p=0.08) was noted where individuals with PTSD had been living approximately seven years longer with HIV. Experiences of stigma following HIV diagnosis, including difficulty obtaining some job promotions or assignments, may have accumulated during this time, and these may have contributed to the development of PTSD in our cohort.

Our study had several limitations. As a cross-sectional study, a causal relationship between PTSD and NCI cannot be inferred. The number of individuals with a lifetime history of PTSD in our survey was somewhat small; studies with larger samples would be useful in further characterizing this relationship. Moreover, our analysis was limited to men with a history of military service; female service members, in turn, have a high prevalence of PTSD, often related to sexual assault, and this group warrants study (Haskell et al., 2010; Kelly, Skelton, Patel, & Bradley, 2011). Data from this study were self-reported and may have underestimated the prevalence of stigmatized behaviors (e.g. substance use). Finally, apart from identifying the diagnosis of PTSD, we did not conduct detailed interviews to understand the underlying trauma (combat or non-combat related). Longitudinal studies are warranted to further elucidate the relationship between PTSD and development of NCI.

Conclusion

Our research demonstrates a strong association between NCI and PTSD among MLWH with a history of military service. Screening for PTSD among PLWH, particularly those with NCI, may be important for clinical management of both HIV and psychological health. In the era of effective antiretroviral therapy and increased virologic suppression limiting the impact of immune suppression on the development of NCI, psychosocial trauma, stressors, or the occurrence of PTSD among individuals living with HIV infection may be of more relevance in the development of NCI than previously recognized. Further research toward understanding the relationship between PTSD and NCI among PLWH should be a research priority, given the high prevalence of both in HIV-infected populations.

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Domain	
Verbal	Wechsler Test of Adult Reading Letter (FAS), category (animals), action fluency (verbs)
Attention/Working Memory	Paced Auditory Serial Addition Task
Visuospatial Functioning	Judgement of Line Orientation Tests (form H) Hooper Visual Organization Test
Information Processing	WAIS-III Symbol Search, WAIS-III Digit Symbol Trail Making Test (TMT) A Stroop Word and Color
Learning/Recall	Hopkins Verbal Learning Test-R Brief Visuospatial Memory Test-R
Abstraction/Executive Functioning	Wisconsin Card Sorting Tests (64-card version) TMT-B Stroop Word and Color Tests
Motor speed and dexterity	Grooved Pegboard Test (both hands)
Effort	Hiscock Digit Memory test

Figure 1.
Neuropsychological Tests/Standard Battery administered to study subjects.

Table 1.

Study participant demographics and characteristics of individuals with and without a lifetime history of post-traumatic stress disorder (PTSD).

	Total (n=189) N(%) or median (IQR[1])	**No lifetime history of PTSD (n=168) N(%) or median (IQR)**	**Lifetime history of PTSD (n=21) N(%) or median (IQR)**	***p*-value**
Age	36 (28,44)	36 (28, 44)	39 (30, 44)	0.490
Active-Duty	136 (72.0)	124 (73.8)	12 (57.1)	0.109
Ethnicity				0.658
White	95 (50.3)	86 (51.2)	9 (42.9)	
African American	52 (27.5)	44 (26.2)	8 (38.1)	
Hispanic	26 (13.8)	23 (13.7)	3 (14.3)	
Asian/Pacific Islander	16 (8.5)	15 (8.9)	1 (4.8)	
Service Branch				0.9846
Army	26 (13.8)	22 (13.1)	4 (19.0)	
Navy	100 (52.9)	90 (53.6)	10 (47.6)	
Air Force	34 (18.0)	31 (18.5)	3 (14.3)	
Marines	24 (12.7)	20 (11.9)	4 (19.0)	
Other	4 (2.1)	4 (2.4)	0 (0.0)	
Education				
Total years	14 (12,16)	14 (12, 16)	14 (12.5, 17)	0.601

[1]Interquartile Range.

Table 2.

Mental health and clinical characteristics of individuals with and without a lifetime history of Post-traumatic stress disorder (PTSD).

	Total (n=189) N(%) or median (IQR[1])	No lifetime history of PTSD (n=168) N(%) or median (IQR)	Lifetime history of PTSD (n=21) N(%) or median (IQR)	*P*-value
Mental health				
Lifetime history of alcohol use disorder	68 (36.0)	57 (33.9)	11 (52.4)	0.097
Current alcohol use disorder	2 (1.1)	2 (1.2)	0 (0.0)	0.789
Lifetime history of illicit drug use[2]	26 (13.8)	22 (13.9)	4 (19.0)	0.515
Current illicit drug abuse	7 (3.7)	7 (4.2)	0 (0.0)	0.432
Lifetime history of Major Depressive Disorder	46 (24.3)	35 (20.8)	11 (52.4)	0.001
Current diagnosis of Major Depressive Disorder	4 (2.1)	1 (0.6)	3 (14.3)	<0.001
BDI Score	3 (1,8)	2 (0, 7)	9 (2, 23.5)	0.000
BDI ≥ 20	14 (7.4)	7 (4.2)	7 (33.3)	0.000
History of Head Injury/Trauma				
Head injury, any severity	131 (69.3)	117 (69.6)	14 (66.7)	0.780
Serious head trauma	22 (11.6)	17 (10.1)	5 (23.8)	0.065
Loss of consciousness (≥ 30 min)	13 (6.9)	11 (6.5)	2 (9.5)	0.611
HIV-related characteristics				
History of AIDS diagnosis	13 (6.9)	7 (4.2)	6 (23.6)	0.000
HIV RNA level (copies/mL)	48 (48,3282)	48 (48, 2.1×10^3)	480 (48, 3.1×10^4)	0.025
Current CD4 count (cells/mm^3)	542 (413,697)	542 (415, 706)	533 (305, 682)	0.282
CD4 nadir (cells/ mm^3)	316 (237,400)	323 (245, 400)	245 (123, 439)	0.106
CD4 nadir < 200 (cells/mm^3)	29 (15.3)	23 (13.7)	6 (28.6)	0.074
On ART	124 (65.6)	113 (67.2)	11 (52.3)	0.176
ART naïve	55 (29.1)	49 (29.2)	6 (28.6)	0.955
Years since HIV diagnosis	5 (2,11)	4.7 (2.1, 10.2)	11.6 (7.4, 16.1)	0.082

[1] Interquartile Range.

[2] N=158 for PTSD- and N=21 for PTSD+.

[3] Antiretroviral therapy.

Table 3.

Factors associated with neurocognitive impairment (GDS[1] ≥ 0.5) in univariate and multivariate analyses.

	Total	NCI – no (n=154) N(%) or median (IQR[1])	NCI – yes (n=35) N(%) or median (IQR[1])	Univariate Odds (95% CI)	Multivariate Odds (95% CI)
Median Age (IQR[2])	36 (28,44)	36 (28, 43)	29 (36, 45)	0.99 (0.95,1.04)	1.00 (0.94,1.07)
Ethnicity					
White	95 (50.3)	77 (50.0)	18 (51.4)	Ref	Ref
African American	52 (27.5)	45 (29.2)	7 (20.0)	1.50 (0.58,3.88)	1.68 (0.55,5.14)
Hispanic	26 (13.8)	18 (11.7)	8 (22.9)	0.53 (0.20,1.40)	0.49 (0.15,1.59)
Asian/Pacific Islander	16 (8.5)	14 (9.1)	2 (5.7)	1.64 (0.34,7.85)	0.91 (0.16,5.1)
Duty Status					
Active-Duty	136 (72.0)	112 (72.7)	24 (68.6)	Ref	
Retired	53 (28.0)	42 (27.3)	11 (31.4)	0.82 (0.37,1.82)	
Education					
Median years of education (IQR)	14 (12,16)	14 (12, 16)	15 (13, 18)	0.84 (0.72,0.99)	0.83 (0.68,1.03)
Mental health					
Lifetime history of alcohol use disorder	68 (36.0)	55 (35.7)	13 (37.1)	0.94 (0.44,2.01)	
Current alcohol use disorder	2 (1.1)	1 (0.7)	1 (2.9)	0.22 (0.01,3.64)	
Lifetime history of illicit drug abuse	26 (13.8)	25 (16.9)	1 (3.2)	0.16 (0.02, 1.26)	0.17 (0.02,1.48)
Current illicit drug abuse	7 (3.7)	6 (3.9)	1 (2.9)	1.38 (0.16,11.82)	
Lifetime history of PTSD	21 (11.1)	12 (7.8)	9 (25.7)	4.10 (1.57, 10.7)	6.03 (1.97,18.43)
Current PTSD					
Lifetime history of Major Depressive Disorder	46 (24.3)	39 (25.3)	7 (20.0)	0.74 (0.3,1.82)	
Current major depressive disorder	4 (2.1)	3 (2.0)	1 (2.9)	0.68 (0.07, 6.69)	
BDI Score (IQR)	3 (1,8)	3 (0, 8.25)	3 (2, 8)	0.99 (0.94,1.03)	
BDI > 20	14 (7.4)	10 (6.5)	4 (11.4)	1.86 (0.55,6.31)	
History of head injury/trauma					
Head injury, any severity	131 (69.3)	113 (73.4)	18 (51.4)	0.38 (0.18,0.82)	0.37 (0.15,0.92)
Loss of consciousness (≥ 30 min)	13 (6.9)	13 (8.4)	0 (0)	N/A	
HIV-related characteristics					
Years living with HIV	5 (2,11)	4.8 (2.3, 10.3)	5.9 (1.6, 14.2)	0.97 (0.92,1.03)	
Viral load (log10 copies/mL)	1.68 (1.68,3.52)	1.69 (1.68, 3.39)	1.68 (1.68, 3.76)	0.88 (0.65,1.19)	
Prior AIDS diagnosis	13 (6.9)	10 (6.5)	3 (8.6)	1.35 (0.35,5.19)	
Current CD4 count (cells/mm^3)	542 (413,697)	526 (413, 682)	606 (377, 737)	1 (1,1)	
CD4 nadir (cells/ mm^3)	316 (237,400)	323 (235, 402)	300 (245, 446)	1 (1,1)	
CD4 nadir < 200 (cells/mm^3)	29 (15.3)	22 (14.3)	7 (20.0)	1.5 (0.58,3.85)	
On ART[4]	124 (65.6)	102 (66.2)	22 (62.9)	0.86 (0.17,4.34)	
ART-naïve	55 (29.1)	44 (28.6)	11 (31.4)	1.34 (0.26,6.88)	

[1] Global Deficit Score.

[2] Interquartile range.

[3] N=148 for NCI- and N=31 for NCI+

[4] Antiretorviral therapy