

Original Research

Associations between major depression, health-risk behaviors, and medication adherence among HIV-positive adults receiving medical care in Georgia

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ABSTRACT

Background: There are approximately 1.2 million people in the United States living with HIV, and 25.6% of HIV-positive adults suffer from depression. The purpose of this study is to examine the contribution of depression to substance use and medication adherence among HIV-positive adults receiving medical care for HIV in Georgia.

Methods: Secondary data with a probability sample of 775 HIV-positive adults who took part in the 2009-2013 Georgia Medical Monitoring Project (MMP) were analyzed. Descriptive analyses and multivariate logistic regressions were conducted to assess relationships between depression and current cigarette smoking, injection drug use, other non-injection drug use, and medication adherence, adjusting for sociodemographic covariates (age, gender, race, and education). All analyses accounted for non-response and complex sampling design.

Results: Among HIV-positive adults in Georgia, 8.5% met the criteria for major depression, including 13.7% of women and 6.5% of men. Heterosexual adults had a higher percentage of major depression (10.7%) compared to adults who identified as bisexual (7.4%) or homosexual (5.8%). Major depression was also higher among adults with a high school diploma or GED (12.7%) compared to adults with a higher level of education (5.2%). Major depression was associated with a greater odds of current cigarette smoking (AOR 2.7; 95% CI: 1.5, 5.2) and other non-injection drug use (2.5; 95% CI: 1.4, 4.4), after adjusting for sociodemographic variables. The three measures of medication adherence were not statistically significantly associated with major depression.

Conclusions: As previously observed for the general population, we found, among HIV-positive adults, significant associations between depression and smoking and other non-injection drug use. Because HIV-positive adults have ongoing encounters with healthcare providers, screening and treatment for depression and other co-morbid substance use is needed to reduce an additional health burden in this population.

Key Words: depression; substance use; cigarette smoking; antiretroviral medication adherence; HIV

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INTRODUCTION

Within the United States, approximately 1.2 million people are currently living with human immunodeficiency virus (HIV) infections (CDC - HIV/AIDS). The southern states, including Georgia, have the highest burdens of

HIV (CDC - HIV/AIDS; Southern AIDS Coalition). According to the Georgia Department of Public Health HIV/AIDS Epidemiology Section, 50,436 people were living with HIV in Georgia as of December 31, 2012 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*). In 2011, Georgia

had the sixth highest HIV prevalence among adults and adolescents in the United States and ranked fourth highest for new HIV infections (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*).

Due to the advent of antiretroviral therapy (ART), persons with HIV are living longer. An estimated 36% of HIV-positive persons are prescribed ART medication, and 77% are virally suppressed and adequately adherent to ART medications (CDC - HIV/AIDS). Compared to the general population, persons with HIV still experience mental health disparities, including depression (Do et al., 2014). Depression is a serious mental and emotional disorder in which an individual experiences a loss of interest or pleasure in daily activities, often accompanied by other symptoms, such as changes in sleep patterns, fatigue, and irritability (American Psychiatric Association, 2000). Moreover, in major depressive disorder, individuals experience depressive symptoms for more than 7 days of the previous 2 weeks (American Psychiatric Association, 2000). Compared to the general population, HIV-positive persons are between two to seven times more likely to be diagnosed with major depression (Do et al., 2014; Hinkin, Castellon, Atkinson, & Goodkin, 2001). An estimated 25.6% of HIV-positive adults suffer from depression, and 12.4% suffer from major depression (Do et al., 2014). Depression among HIV-positive persons, and in the general population, has been linked to adverse health outcomes and behaviors, such as cigarette smoking, substance use, and ART medication non-adherence (Arseniou, Arvaniti, & Samakouri, 2014; Mdodo et al., 2015). In more than 95 studies, there was an association of depression with non-adherence to ART medication (Gonzalez, Batchelder, Psaros, & Safren, 2011). However, one investigation found that participants who reported a high number of depressive symptoms were also likely to report a high rate of medication adherence compared to individuals reporting a smaller number of depression symptoms (Berger-Greenstein et al., 2007).

In addition to the association of depression with ART medication non-adherence, depression has been linked to substance use, including cigarette smoking, among both the general population (McClave, McKnight-Eily, Davis, & Dube, 2010; Strine et al., 2012; Trosclair & Dube, 2010) and those with HIV (Burnam et al., 2001; Dausey & Desai, 2003). HIV-positive adults are

twice as likely to smoke compared to the general population, and less likely to quit smoking (quit ratio, 32.4% vs. 51.7%) (Mdodo et al., 2015). It is plausible that nicotine from cigarettes may help mitigate the depressive symptoms (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005). A high prevalence of substance use coupled with mental illnesses is also evident among HIV-positive persons (Burnam et al., 2001; Dausey & Desai, 2003). Between 10% and 28% of persons living with HIV have co-occurring mental illness and substance use disorders (Burnam et al., 2001; Dausey & Desai, 2003). Depression and substance use disorders are also related to low medication adherence, creating a complicated mechanism of disease progression (Magidson et al., 2014).

Currently, little is known about the associations between smoking, medication adherence, and substance use with depression among HIV-positive adults receiving care in Georgia. For persons living with HIV, these adverse health outcomes and behaviors can negatively affect the longevity and quality of life (Helleberg et al., 2015; Gonzalez et al., 2011; Mdodo et al., 2015), and the linkage between depression and these behaviors could inform treatment interventions. The purpose of this study was to examine, by use of data collected for the Georgia Medical Monitoring Project in the years 2009-2013, the association between major depression and current cigarette use, injection drug use, non-injection drug use, and ART medication adherence, among adult Georgians receiving medical care for HIV infections.

METHODS

Institutional Review Board at Georgia State University determined the study to be exempt and approved the research.

Participants/Setting

The Georgia Medical Monitoring Project (MMP) is a surveillance system that collects data on behavioral and clinical aspects of persons living with HIV who are currently receiving medical care ("Georgia Medical Monitoring Project"). For purposes of the present study, a secondary analysis was conducted using aggregate MMP data for 2009, 2010, 2011, 2012, and 2013.

MMP consists of a three-stage, probability sampling method, and Georgia is one of 26 states and cities across the United States to participate ("Georgia Medical Monitoring Project"). MMP

project areas are estimated to include more than 80% of the total HIV/AIDS patients in the United States. To ascertain behavioral information, interviews are conducted either face-to-face or via phone, and medical record abstractions are used to obtain clinical information. To be eligible to participate, individuals were required to be HIV-positive, 18 years of age or older at the time of the interview, and actively receiving medical care for HIV. Data from the Georgia MMP are weighted to produce a representative sample of all adult Georgians receiving medical care for HIV (Blair et al., 2011; Frankel et al., 2012; McNaghten et al., 2007). Once facilities are selected and agree to participate, patient lists are generated, and a sample of 400 Georgia patients are randomly selected.

Independent Variables

In MMP, depression is measured using the Eight-Item Patient Health Questionnaire (PHQ-8) (Kroenke et al., 2009; Kroenke, Spitzer, & Williams, 2001). The PHQ-8 was adopted from the PHQ-9, which assesses the nine criteria associated with depression as defined by the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)* (American Psychiatric Association, 2000). The ninth item, omitted from the PHQ-8, assesses suicidal ideations. Due to the fact that most of the interviewers are not trained mental health providers, this item was removed to create a more widely used tool, the PHQ-8 (Kroenke et al., 2009; Kroenke et al., 2001). The PHQ-8 is closely comparable to the PHQ-9 (Kroenke, Spitzer, Williams, & Löwe, 2010). According to a systematic review of the PHQ-9, the measure has demonstrated internal reliability or 0.86 to 0.89 and external reliability of 0.84 in identifying depression in clinical settings and general population settings (Kroenke et al., 2010).

Methods used to identify individuals with major depression are consistent with the DSM-IV criteria (American Psychiatric Association, 2000) and with methods used in a national MMP study (Do et al., 2014). The PHQ-8 asks if the individuals experienced certain symptoms within the last two weeks. They were considered to have major depression if they had five of the eight symptoms “more than half the days” of the last two weeks, and answered “more than half the days” in response to at least one of the first two questions: 1) “Little pleasure in doing things,” and 2) “Feeling down, depressed, or hopeless” (Do et al., 2014; Kroenke et al., 2009).

Dependent Variables

Injection drug use

Participants who reported that they had used injection drugs in the past 12 months were classified as engaging in injection drug use. The interviewer explained that injection drugs for non-medical purposes include using drugs with a needle, “either by mainlining, skin popping, or muscling” (heroin, cocaine, heroin and cocaine together, crack, methamphetamine, amphetamines, oxycontin, steroids or hormones, or any other drug).

Non-injection drug use

Participants who reported that they had used non-injection drugs in the past 12 months were classified as engaging in non-injection drug use (methamphetamines, amphetamines or stimulants; crack; cocaine; downers such as Valium, Ativan, Xanax; painkillers such as OxyContin, Vicodin, or Percocet; hallucinogens such as LSD or mushrooms; and other drugs such as asecstasy, heroin or opium, marijuana, amyl nitrate, GHB, or ketamine).

Current Cigarette Smoking

Individuals were defined as current smokers if they answered “Yes” to “Have you smoked at least 100 cigarettes in your entire life?” and if they answered “Daily,” “Weekly,” or “Monthly” in response to “How often do you smoke cigarettes now?” (CDC DHDS). Non-smokers included both former smokers (smoked at least 100 cigarettes but does not smoke now) and never smokers (did not smoke at least 100 cigarettes).

ART Medication Adherence

ART medication adherence was assessed using MMP-calculated variables for three measures: dose non-adherence, special instructions non-adherence, and schedule non-adherence. If participants reported less than 100% adherence to doses in the past 3 days, special instructions adherence, or adherence to medication schedule, they were classified as non-adherent in the corresponding category (Beer et al., 2012).

Statistical Analyses

All statistical analyses were conducted in February 2014 using SAS 9.2 (SAS Institute, Inc., Cary, NC). All analyses accounted for the complex survey design and included weights, and cluster and stratum variables. Multivariate logistic regression analyses were conducted to assess associations between major depression

and the four dependent variables while controlling for confounding factors that were identified through bivariate analyses and confounders previously documented in the literature. Chi-Square tests and Fisher Exact tests were performed to assess differences in demographics and outcome categories by depression status.

RESULTS

The overall prevalence of HIV-positive adults with major depression was 8.5% (95% CI: 6.4%,

10.5%) (Table 1). Among females, 13.7% (95% CI: 8.2%, 19.2%) were classified as having major depression, and 6.5% (95% CI: 4.6%, 8.5%) of males met the criteria. Classified as having major depression were 10.7% (95% CI: 7.1%, 14.2%) of heterosexual adults; 7.4% (95% CI: 2.2%, 12.5%) of bisexual adults; and 5.8% (95% CI: 3.2%, 8.3%) of homosexual, gay, or lesbian adults. In this category were 12.7% (95% CI: 8.7%, 16.8%) of persons with a high school education or GED and 5.2% (95% CI: 3.1%, 7.4%) of those with a college education or higher.

Table 1. Demographic characteristics and prevalence of dependent variables among HIV-positive Georgia MMP participants with major depression and without major depression, 2009-2013

	Major Depression		Total MMP Participants		Chi-Square χ^2 (df), p
	N=63*	Percentage (95% CI)	N=775	Percentage (95% CI)	
Gender, n (%)					
Male	37	6.52% (4.59%-8.46%)	548	70.80% (66.12%-75.47%)	10.3 (1), p=0.003*
Female	26	13.71% (8.22%-19.20%)	218	28.08% (23.62%-32.53%)	
Transgender	0	---	9	---	
Race/Ethnicity, n (%)					
Alaskan Native/American Indian	1	---	3	---	7.3 (2), p=0.03*
Asian	0	---	2	---	
Black/African American	35	6.86% (4.29%-9.43%)	543	69.59% (60.65%-68.98%)	
White/Caucasian	20	11.23% (7.22%-15.23%)	187	24.59% (17.98%-25.68%)	
Multi-Racial	7	---	39	4.94% (2.58%-5.62%)	
Sexual Orientation, n (%)					
Homosexual, gay, or lesbian	18	5.77% (3.22%-8.32%)	310	39.84% (33.25%-46.43%)	p= 0.07
Bisexual	7	7.38% (2.24%-12.53%)	86	11.26% (9.20%-13.32%)	
Heterosexual	35	10.69% (7.13%-14.24%)	368	47.63% (42.36%-52.91%)	
Other	2	---	7	---	
Age, n (%)					
18-24	8	---	49	6.60% (4.75%-8.45%)	11.1 (4), p=0.03*
25-34	13	---	108	13.81% (11.35%-16.26%)	
35-44	9	---	208	27.49% (23.95%-31.02%)	
45-54	27	10.95% (7.04%-14.87%)	266	34.57% (31.66%-37.49%)	
≥ 55	6	---	142	17.17% (14.77%-19.57%)	
Education, n (%)					
High School/GED or less	40	12.73%	338	43.11%	11.0 (1),

	Major Depression		Total MMP Participants		Chi-Square
	N=63*	Percentage (95% CI)	N=775	Percentage (95% CI)	χ^2 (df), p
		(8.65%-16.82%)		(37.21%-49.02%)	p=0.01*
Some college or greater	23	5.23% (3.07%-7.39%)	437	56.89% (50.98%-62.79%)	
Current Smoker, n (%)					
Yes	36	61.75% (47.40%, 76.11%)	265	34.51% (30.21%-38.81%)	19.3 (I), p<0.0001*
No	27	38.25% (23.89%, 52.60%)	510	65.49% (61.19%-69.79%)	
Non-Injection Drug Use, n (%)					
Yes	23	37.24% (24.37%, 50.11%)	171	22.34% (18.83%, 25.86%)	8.20 (I), p=0.0042*
No	40	62.76% (49.89%, 75.63%)	604	77.66% (74.14%, 81.17%)	
Injection Drug Use, n (%)					
Yes	2	---	9	---	4.54 (I), p=0.033*
No	61	96.46% (91.83%, 100%)	766	98.84% (97.97%, 99.70%)	
Medication Special Instructions Non-Adherence, n (%)					
Yes	28	66.65% (50.29%, 83.01%)	373	74.04% (69.89%, 78.19%)	1.17 (I), p=0.28
No	14	33.35% (16.99%, 49.71%)	135	25.96% (21.81%, 30.11%)	
Medication Schedule Non-Adherence, n (%)					
Yes	37	66.79% (51.39%, 82.18%)	544	75.81% (72.54%, 79.07%)	2.85 (I), p=0.16
No	18	33.21% (17.82%, 48.61%)	170	24.19% (20.93%, 27.45%)	
Medication Dose Non-Adherence, n (%)					
Yes	45	84.33% (74.23%, 94.43%)	607	85.70% (83.29%, 88.11%)	0.08 (I), p=0.78
No	9	15.67% (5.57%, 25.77%)	99	14.30% (11.89%, 16.71%)	

Note. Weighted percentages were suppressed if estimates had a coefficient of variance >30%. A Gender chi-square test was performed comparing female to male, due to cell size of 0 in transgender depression category. A Race/Ethnicity chi-square test was performed assessing white, black, and other. Other included Asian, American Indian/Alaskan Native, and multiracial due to cell size of 0 in the Asian depression category. A Fisher exact test was performed for sexual orientation instead of Chi-Square test due to cell size <5 in other category.

*Significant p-values <0.05 based on chi-square statistic.

Among adults who met the criteria for major depression, 33.4% (95% CI: 17.0%, 49.7%) reported non-adherence to special instructions for ART medications, compared to 25.2% (95% CI: 21.3%, 29.2%) without major depression (Table 2). Additionally, 33.2%

(95% CI: 17.8%, 33.6%) of adults with major depression reported non-adherence to medication schedule, compared to adults without major depression, 23.4% (95% CI: 20.3%, 26.4%). However, the chi-square statistics for these differences were not

statistically significant. None of the logistic regression results for major depression and ART medication non-adherence were

statistically significant, even after adjusting for age and any drug use.

Table 2. Bivariate and multivariate logistic regression results for the associations between selected health behaviors and major depression among Georgia MMP participants, 2009-2013

	Weighted Prevalence (%)	Unadjusted OR	P-Value	Adjusted OR	P-Value
Current smoking					
Major depression	61.75%	3.43 (1.86, 6.33)	<0.0001	2.73 (1.45, 5.15)	0.002
No major depression	31.99%	1.00 Referent		1.00 Referent	
Non-injection Drug Use					
Major depression	37.24%	2.24 (1.28, 3.90)	0.005	2.48 (1.40, 4.38)	0.002
No major depression	20.97%	1.00 Referent		1.00 Referent	
Injection Drug Use					
Major depression	3.54%	3.87 (1.04, 14.40)	0.04	2.66 (0.73, 9.71)	0.14
No major depression	0.94%	1.00 Referent		1.00 Referent	
Medication Special Instructions Non-Adherence					
Major depression	33.35%	1.48 (0.72, 3.05)	0.28	1.44 (0.67, 3.11)	0.35
No major depression	25.22%	1.00 Referent		1.00 Referent	
Medication Schedule Non-Adherence					
Major depression	33.21%	1.63 (0.82, 3.25)	0.16	1.63 (0.81, 3.30)	0.17
No major depression	23.38%	1.00 Referent		1.00 Referent	
Medication Dose Non-Adherence					
Major depression	15.67%	1.13 (0.50, 2.54)	0.78	1.09 (0.47, 2.53)	0.84
No major depression	14.18%	1.00 Referent		1.00 Referent	

Note. Adjusted based upon bivariate analyses and the presence of confounders in the literature among noted variables. Current cigarette smoking, non-injection drug use, and injection drug use were adjusted for age, gender, race, and education. All of the medication adherence analyses were adjusted for age and any drug use.

*Significant relationships at p<0.05 bolded.

Current cigarette smoking prevalence among adults with major depression was nearly double that of adults without major depression, 61.8% (95% CI: 47.4%, 76.1%) versus 32.0% (95% CI: 27.9%, 36.0%), respectively. After adjusting for age, gender, race, and education, the association between current cigarette smoking and depression was statistically significant (AOR: 2.7, 95% CI: 1.5, 5.2).

Of adults with major depression, 37.2% (95% CI: 24.4%, 50.1%) reported non-injection drug use in the past 12 months, whereas 21.0% (95% CI: 17.5%, 24.5%) of those without major depression reported such use. The non-injection drug most used was marijuana. After adjusting

for age, gender, race, and education, the association between non-injection drug use and major depression was statistically significant (AOR 2.5; 95% CI: 1.4, 4.4).

The prevalence of injection drug use by major depression status was suppressed due to a high coefficient of variation. The Fisher exact test for differences between injection drug use among adults with major depression and adults without major depression was not statistically significant (p=0.16). The unadjusted odds ratio was statistically significant for the association between injection drug use and major depression (AOR 3.9; 95% CI: 1.04, 14.4), however, after adjusting for potential confounders, the

association was no longer significant (AOR 2.7; 95% CI: 0.7, 9.7).

DISCUSSION

To our knowledge, the present study is one of the first to examine the relationship between major depression and selected health behaviors among adults living with HIV in Georgia who are currently receiving medical care. Major depression was more prevalent among persons with HIV compared to the prevalence among the general population of U.S. adults (4.1%) (Do et al., 2014). This finding is not unexpected, since HIV-positive adults face adversities that may increase the risk of developing depression and depressive symptoms (Arseniou et al., 2014; Valente, 2003). HIV-positive individuals tend to have feelings of helplessness, a loss of hope, and despair associated with their HIV diagnosis, which can lead to the onset of depressive disorders (Leserman, 2008; Valente, 2003). A loss of social support, medication side effects, and distress associated with HIV status have also been linked to depression (Valente, 2003). In addition to psychosocial factors, biological processes may be involved in the relationship between depression onset and HIV infection (Leserman, 2008). Although the biological mechanisms are not known, a theory is that HIV infection of the central nervous system may lead to depression through damaged neurons and impaired synapse function (Valente, 2003).

An aspect of the association between depression and HIV infection is that the chronicity of depression may affect the progression of HIV disease (Leserman et al., 2002; Leserman, 2003; Leserman, 2008). For example, one study found that, after controlling for ART medication adherence, HIV-positive women with clinical depression were twice as likely to die from AIDS compared to HIV-positive women without clinical depression; clinically depressed women also had significantly lower CD4+ cell counts compared to women without depression (Ickovics et al., 2001). These results indicate that, regardless of ART treatment, the effect of depression on HIV disease progression warrants attention by care providers who screen, diagnose, and treat depression in their HIV-positive patients.

As found in the general population (Davis, Uezato, Newell, & Frazier, 2008), our findings indicate that HIV-positive adults with major depression engaged in non-injection drug use

more frequently than HIV-positive adults without major depression. The use of such substances may exacerbate depressive disorders and increase engagement in other health risk behaviors, such as unprotected sex, which may lead to HIV transmission (Molitor, Truax, Ruiz, & Sun, 1998). Thus, the treatment of depression and co-morbid substance use disorders for HIV-positive persons has implications for the prevention of HIV transmission.

In our sample, the association between cigarette smoking and depression among HIV-positive adults is consistent with findings for the general population, in which 36.1% of adults with mental illness smoke cigarettes (McClave, McKnight-Eily, Davis, & Dube, 2010; Strine et al., 2012; Trosclair & Dube, 2010). Nicotine has psychoactive properties and may be used as self-medication to ease symptoms of depression (McClave et al., 2010; Strine et al., 2012; Trosclair & Dube, 2010). Compared to the general population, HIV-positive persons who smoke are at an increased risk for cardiovascular disease, pneumonia, lung cancer, and liver cancer (Helleberg et al., 2013). There is also a substantial increase in mortality among smokers living with HIV (2013). These findings warrant interventions targeted at mitigating cigarette smoking among HIV-positive persons.

Although, in more than 95 studies, the association between depression and medication non-adherence has been demonstrated (Gonzalez et al., 2011), in our study, the three measures of medication non-adherence were not associated with major depression. One possible reason for the lack of relationship found between depression and medication non-adherence is that persons who are regularly retained in medical care may receive close monitoring, such that their medication adherence does not lapse. Future studies should include longitudinal designs that monitor and collect relevant information about patterns of medication adherence among persons with and without depression.

Several limitations in our study should be noted. All measures examined were self-reported, which introduces the possibility of recall bias and/or report bias (social desirability). In particular, reported injection drug use was low, which could be due to underreporting because of social desirability or recall bias. Due to the small sample of transgender persons, we were unable to conduct analyses for this group. Future studies

should include larger sample sizes of transgender persons in examining the relationship between depression and behaviors. In our study, injection drug users composed a small sample size, and it is possible that we had insufficient power to detect associations between depression and injection drug use. Future studies will benefit from larger sample sizes. The MMP questionnaire does not assess whether or not the individual is taking antidepressant medication. By knowing whether or not an individual is taking antidepressants, analyses could be conducted to assess whether persons with untreated depression experience more adverse health outcomes than those with treated depression. Lastly, the burden of depression among HIV-positive adults currently receiving care may underestimate the overall burden of depression among HIV-positive adults. Those seeking medical care may be more health-conscious and may have fewer adverse health behaviors than the general HIV-positive population.

The prevalence of major depression among HIV-positive adults receiving medical care has implications for treatment of depression and for screening for HIV-positive persons. HIV-specific care providers have guidelines for screening and treatment of depression (Aberg et al., 2009). Although recommended as part of HIV medical care guidelines, screening for depression has not been consistently implemented in HIV care provider settings. For HIV care providers, the PHQ-9 is a feasible screening tool (Shacham et al., 2009).

CONCLUSIONS

Future studies should investigate the associations between major depression, health behaviors, and medication adherence in alternative populations, such as urban adults compared to rural adults. Moreover, to inform clinical interventions, studies are needed to determine the biological association between major depression and HIV. Future research should also evaluate the effectiveness of behavioral interventions aimed at mitigating drug use and cigarette use among persons living with HIV who are also experiencing depression.

Depression and the potential co-occurrence of cigarette smoking and non-injection drug use negatively affect the overall treatment for HIV-positive persons by reducing the quality and longevity of life. The use of non-injection drugs

among HIV-positive persons may also increase the risk of HIV risk behaviors (Molitor, Truax, Ruiz, & Sun, 1998), thus increasing the risk for HIV transmission. Treating depression and these potentially co-occurring adverse health behaviors among HIV-positive adults may increase the overall well-being of persons living with HIV.

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