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# Psychological Symptoms Among 2032 Youth Living with HIV: A Multisite Study

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#### **Abstract**

This study determined the prevalence and patterns of psychological symptoms in adolescents and young adults living with HIV (YLWH) in medical care and relationships between psychological symptoms, route and duration of infection, and antiretroviral treatment (ART). A clinic-based sample of 2032 YLWH (mean age 20.3 years), recruited from 20 adolescent medicine HIV clinics, completed a cross-sectional survey of health behaviors and psychological symptoms using the Brief Symptom Inventory (BSI). Overall, 17.5% of youth reported psychological symptoms greater than the normative threshold on the Global Severity Index. A wide variety of symptoms were reported. The prevalence of clinical symptoms was significantly greater in youth with behaviorally acquired HIV compared to those with perinatally acquired infection (20.6% vs. 10.8%, OR = 2.06 in Multiple Logistic Regression (MLR)), and in those not taking ART that had been prescribed (29. 2% vs. 18.8%, OR = 1.68 in MLR). Knowing one's HIV status for more than one year and disclosure of HIV status were not associated with fewer symptoms. A large proportion of YLWH have psychological symptoms and the prevalence is greatest among those with behaviorally acquired infection. The high rate of psychological symptoms for youth not taking ART that is prescribed is a cause for concern. Symptoms do not appear to be a transient reaction to diagnosis of HIV.

# Introduction

IV INFECTION IS DISPROPORTIONATELY a disease of adolescence, with individuals aged 16–24 years showing the highest rate of new infections compared to other age groups. <sup>1–3</sup> Although there are a number of studies that document the prevalence of psychological symptoms among children living with HIV, <sup>4–7</sup> there are fewer that address this issue among adolescents, and none with a large cohort of behaviorally infected youth in this era of simplified treatment regimens. Examination of psychological symptoms and emotional distress among adolescents living with HIV is critical because they are associated with worse quality of life, <sup>8,9</sup> poorer health, <sup>8,10</sup> less adherence to antiretroviral medication (increasing the likelihood for secondary transmission of HIV), <sup>11–14</sup> greater substance use, <sup>6,15–17</sup> and more sexual risk behavior. <sup>6,16,18,19</sup> For example, a study, using a

portion of the same data set used for this report, examined 1712 youth in care for HIV at fifteen adolescent medicine HIV clinics and found one subgroup that was identified through latent class analysis based on higher levels of sexual risk and substance use. The group was also more likely to report mental health concerns, less likely to be taking anti-retroviral treatment (ART), and had higher viral loads compared to those in the other groups.<sup>20</sup>

Despite indications that mental health disorders occur frequently among adolescents and young adults living with HIV (YLWH) and evidence of a contribution of emotional distress to risk behaviors and health, to date little research has been conducted on the prevalence and patterns of psychological symptoms among these youth. Six studies provide quantitative data on the prevalence of significant, current mental symptoms among YLWH. The studies used different measures of psychological symptoms, and sample sizes were

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small, limiting the generalizability of the findings. Three studies reported clinical diagnoses. Pao et al.<sup>21</sup> conducted structured clinical interviews with 34 YLWH (mean age 18.5 years) in an adolescent clinic and found that most had an Axis 1 diagnosis, commonly major depression (44%). Another study examined 174 youth (mean age 21) in a HIV clinic and found that 17% had an anxiety disorder and 15% a major depressive disorder based on a clinical interview. <sup>22</sup> In another study, a computerized interview was used to screen specifically for depression in 147 young women living with HIV (mean age 20.6 years) and found a rate of 10%. 23 Two studies report the prevalence of significant psychological symptoms based on exceeding the threshold on standardized scales. In a sample of 230 YLWH (mean age 16.1 years), 18% reported elevated anxiety on the Children's Manifest Anxiety Scale and 17% elevated depression on the Child Depression Inventory.<sup>24</sup> Among 166 YLWH (mean age 16.8 years), 21% scored above the threshold for internalizing symptoms (e.g., depression, anxiety) and 30% for externalizing (e.g., conduct problems) as measured by the Achenbach Youth Self Report.<sup>25</sup> A study with 66 YLWH found that 50% "scored above the cutoff for significant mental health symptoms on the Brief Symptom Inventory (BSI)."<sup>26</sup> Other studies have administered the BSI to YLWH but have used the scale as part of a correlation matrix or variable model.<sup>27-29</sup> Mean scores for the samples were not reported, so the prevalence of clinically significant psychological symptoms cannot be determined. In total, these studies suggest a substantial prevalence of psychological symptoms for youth living with HIV, especially for symptoms of depression and anxiety. However, these studies are limited by their small sample sizes and their focus on only selected diagnoses or broad measures of symptoms, such as internalizing or externalizing.

It is important to examine patterns of significant symptoms reported by youth living with HIV in order to plan for available treatments and to enhance screening efforts. In addition, studies have not examined differences in symptoms based on route of HIV acquisition. Several studies report on psychological profiles of children or younger adolescents with perinatally acquired HIV, but the patterns may change as youth age and have access to medical and psychological treatment. In addition, the extent and patterns of symptoms may be different for those with behaviorally acquired HIV, as some studies have demonstrated high rates of risk behaviors, substance use, and psychological symptoms. <sup>15,18,19,30–32</sup>

It has been suggested that youth with behaviorally acquired HIV progress through stages in their acceptance and adaptation to the disease. An intense, emotional reaction is a common initial response to learning of one's infection,<sup>33</sup> followed by a transition to acceptance of treatment,34 more active coping with the disease, 35 greater medical adherence, 11 and disclosure of infection to others. 36 Hosek et al. 37 have proposed an empirically-based ecological model of stressors faced by youth during the first year of their HIV diagnosis. The model describes a range of stressors that may be confounded by the typical challenges of normal adolescent development, and further exacerbated by living with a highly stigmatized illness and, for some, the stigma of a nonmajority sexual orientation.<sup>38–41</sup> Qualitative data demonstrate that the initial period of acceptance after learning of one's infection is extremely challenging for youth as they reported intense feelings of depression, isolation, and at times, suicidal

ideation.<sup>37</sup> Acceptance of treatment, including ART, coincides with fewer psychological symptoms. Youth with perinatal infection have known of their infection and have been engaged with healthcare longer, on average, than those with behaviorally acquired HIV. The greater length of time to adjust to the diagnosis and to receive health services should be associated with fewer psychological symptoms. Although there is some evidence for these associations, <sup>4,9,16,17,30</sup> they have not been verified in a large and diverse sample.

A greater understanding of the psychological symptoms among youth served by the clinics would enable the development of more targeted programs for YLWH. This article examines cross-sectional survey data from a large scale, multi-site study in a population of YLWH who were receiving clinic-based medical care in order to describe and compare the extent and patterns of psychological symptoms reported by youth based on method of acquisition of HIV (behavioral vs. perinatal).

It was hypothesized that significant psychological symptoms would be more prevalent among those with behaviorally acquired HIV than in those with perinatally acquired HIV because of factors described above and that symptoms would be more prevalent among males with a non-majority sexual orientation. Because of the stress associated with receiving a HIV diagnosis, it was hypothesized that more psychological symptoms would be found in the first year after learning of one's diagnosis.

Psychological symptoms were hypothesized to be a barrier to disclosure of HIV by the youth to others and be greater among those who had been prescribed ART but were not taking it. Data on the complex multifactorial relationships between mental health symptoms, risk behaviors (sexual and substance use), medication adherence, and health indices will be reported in subsequent publications.

#### Methods

## **Participants**

Location of recruitment. From December 2009 through January 2012, youth living with HIV or AIDS were recruited from 20 adolescent medicine clinics that provide a range of services to YLWH and are part of the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) to participate in a cross sectional survey. Sites are listed in the acknowledgements.

Eligibility criteria. To be eligible, youth had to be: (1) 12 through 24 years of age; (2) living with HIV/AIDS; (3) aware of their HIV positive status; (4) engaged in care in one of the ATN's adolescent medicine treatment units or affiliates; and (5) able to understand English or Spanish.

Consenting procedures. Youth were recruited at 20 adolescent medicine treatment units (ATMUs) that were a part of the ATN between 2009 and 2012. Research staff approached all youth meeting eligibility criteria during one of their regularly scheduled clinic visits to describe the study. After a thorough explanation of the study and its procedures, staff obtained signed informed consent from all youth who agreed to participate. In cases where parental consent was needed, youth assent was obtained after parental consent was given.

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Study procedures and final sample size. The 20 sites obtained informed consent from 2216 participants. Screening data was available from 18 of the sites, which enrolled 91% of the participants. Those 18 sites screened 2325 patients and 95% were eligible. 91% of the eligible subjects were enrolled. 2032 of the available 2216 surveys from all 20 sites had data on the Brief Symptom Inventory (the key outcome variable for this study), and data for gender and route of transmission (primary predictor variables). These 2032 surveys comprised the sample used for analysis. A 45-min audio-computer assisted self-interview (A-CASI) was followed by a 5-min debriefing interview. The encrypted A-CASI data was transferred to the ATN Data Coordination Center secure website without any personally identifiable participant information. The procedures were approved by the Institutional Review Boards at each participating site as well as those from the members of the protocol team. Participants were given a small compensation determined by each site's IRB for their time and effort. Sites did not have access to any of the participants' responses to the A-CASI.

## Psychosocial assessment

The psychosocial assessment was designed to assess several domains. The following measures, which took a total of 10–15 min to complete, were used in this analysis. Other domains (medical adherence, sexual and substance risk, health indices) will be reported in other publications.

Demographic and HIV-related variables. Age, birth gender, race and ethnicity, self-identified route of infection with HIV (How do you think you got HIV? Perinatal = "I was born with it"; Behavioral = "sex with a man, sex with a woman, injection drug use"), time since knowledge of HIV status (>1 year, ≤1 year), sexual orientation ("straight, gay, lesbian, queer, bisexual, questioning"), refusal of ART ("Has your doctor offered or prescribed pills or other medicines for your HIV infection but you never took them?" Yes/No), and disclosure of HIV infection to others ("disclosed HIV to anyone?" Yes/No) were collected.

Mental health. The Brief Symptom Inventory (BSI) was used to assess mental health issues. 42 The BSI is a 53 item measure that yields nine primary symptom subscales (see Table 2) and a Global Severity Index (GSI). Symptom subscales include: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism. Items have the following response options: not at all (0), a little bit (1), moderately (2), quite a bit (3), extremely (4). Internal consistency for the subscales (dimensions) ranged from 0.71 to 0.85. The Global Severity Index combines information about number of symptoms and intensity of distress and has often been used as a measure of general psychological distress and symptomatology. 26,42 The internal consistency of the GSI has been reported as 0.98. 43

#### Data analysis

Because the BSI has separate norms for males and females, separate analyses were run for each gender. Differences between groups were examined using t-tests for BSI subscale scores and chi-square tests for the proportion of youth above the threshold of the BSI norms (T score >63) for being "considered a positive case." Symptoms greater than the threshold will be termed "clinically significant" for this report, although establishing a diagnosis is beyond the scope of any screening instrument. Because the mean age of the sample was 20.3 years, adolescent norms were used since the adult norms are based on a sample with a mean age of 46 years. When age was significantly different between groups to be compared, an ANCOVA was used, rather than a t-test, to control for age. Finally, the association of the GSI of the BSI with variables found to be significant in univariate comparisons was examined using logistic regression. SPSS version 15.0 was used to analyze the data.

#### **Results**

## Description of sample

Of the 2032 YLWH whose data was analyzed for this report, 1370 were males (67% of total) and 662 were females

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

	Sa	ımple	Perinatal		Behavioral			
	% or M	N or SD	% or M	N or SD	% or M	N or SD	$X^2$ or $t$	p
Gender							209.80	< 0.001
Male	67.4%	1370/2032	44.9%	282/628	77.5%	1088/1404		
Female	32.6%	662/2032	55.1%	346/628	22.5%	316/1404		
Ethnicity							0.002	0.952
Hispanic	19.4%	392/2025	19.4%	121/623	19.3%	271/1402		
None Hispanic	80.6%	1633/2025	80.6%	502/623	80.7%	1131/1402		
Race							0.795	0.977
Asian/Pacific Islander	1.0%	21/2014	0.8%	5/615	1.1%	16/1399		
Black/African American	68.2%	1374/2014	68.0%	418/615	68.3%	956/1399		
Native American	0.9%	19/2014	0.8%	5/615	1.0%	14/1399		
White	12.8%	258/2014	12.8%	79/615	12.8%	179/1399		
Mixed	10.7%	216/2014	11.1%	68/615	10.6%	148/1399		
Other	6.3%	126/2014	6.5%	40/615	6.1%	86/1399		
Age	20.25	2.14	18.10	2.93	21.22	2.04	27.66	< 0.001

Table 2. Proportion of Youth Living with HIV Above Thresholds on Subscales the Brief Symptom Inventory

	M			
	Perinatal transmission (% above threshold) N=282	Behavioral transmission (% above threshold) N=1088	$\chi^2$	p
Global Severity Index	6.6	19.8	25.39	< 0.001
Anxiety	4.0	17.6	32.32	< 0.001
Somatization	4.7	15.8	23.26	< 0.001
Obsessive compulsive	11.5	22.6	16.90	< 0.001
Depression	7.9	23.8	34.17	< 0.001
Hostility	6.4	14.5	13.20	< 0.001
Phobic anxiety	4.3	15.7	24.93	< 0.001
Paranoid	8.2	19.4	19.66	< 0.001
Psychoticism	11.3	21.6	14.70	< 0.001
Interpersonal sensitivity	5.1	18.1	28.90	< 0.001

	Fer			
	Perinatal transmission (% above threshold) N=346	Behavioral transmission (% above threshold) N=316	$X^2$	p
Global Severity Index	14.2	23.2	8.49	0.004
Anxiety	6.1	16.0	16.35	< 0.001
Somatization	16.8	25.8	8.0	0.005
Obsessive compulsive	16.4	25.8	8.68	0.003
Depression	17.8	24	3.81	0.051
Hostility	15.0	21.2	4.26	0.039
Phobic anxiety	12.6	18.8	4.75	0.029
Paranoid	21.2	24.5	1.02	0.313
Psychoticism	12.4	26.3	20.34	< 0.001
Interpersonal sensitivity	14.7	20.2	3.36	0.067

(33%) with a mean age of 20.3 years. The sample was predominantly racial/ethnic minority, with 68.2% identifying racially as black/African American, 12.8% white, and 10.7% Mixed (Table 1). Ethnically, 19.4% identified as Hispanic/Latino. The most frequently reported route of HIV infection for males was from "sex with a man" (74.1%), followed by perinatal infection (20.1%). Women most frequently reported their route of HIV infection as perinatal infection (50.6%), followed by "sex with a man" (47.0%). Of those with behaviorally acquired infection, 45.1% had been diagnosed with HIV infection within the last 12 months.

Of the 2032 participants, 17.5% reported symptoms greater than the threshold to be considered significant on the GSI, with 20.6% of youth with behavioral infection and 10.8% of those with perinatal infection reporting clinically significant symptoms (>T score of 63). Table 2 reports the proportion of youth above the BSI thresholds for each subscale by route of infection for males and females. A greater proportion of youth with above threshold symptoms was found among those with behavioral infection on most subscales. There were no differences among the males with behavioral infection based on sexual orientation (heterosexual vs. nonheterosexual) [data not shown].

Those who were behaviorally infected were significantly older [21.2 (SD=2.04)] for behaviorally infected vs. 18.1 (SD=2.92) for perinatally infected, t=27.66, p<0.001, so age was controlled in the subsequent analyses. Table 3 shows

the mean BSI subscales scores for the four groups. For males, those with behavioral HIV infection were significantly more likely to report symptoms on each of the ten scales. Among males with behavioral infection, the only difference based on sexual orientation was that those with a heterosexual orientation reported more paranoid symptoms [7.45 (5.33) vs. 6.43 (5.06) F=4.50, p=0.034; other data not shown]. For females, the behavioral group, compared to the perinatal, reported more symptoms for eight of the ten scales (except depression and phobic anxiety, p>0.05).

Chi-square analyses (Table 4) found that in the behaviorally infected group there was a greater proportion of youth with significant mental symptoms among those not taking ART that had been prescribed (29.2% vs. 18.8%) but this difference was not found in the perinatal group. Also, length of time knowing one's HIV status and disclosureof HIV status were not associated with psychological symptoms.

A multiple logistic regression (MLR) examined the association of clinically significant GSI scores with age, route of transmission, and not taking ART that was prescribed (Table 5). Because most males with behavioral transmission were nonheterosexual, only the transmission category was entered into the regression to avoid multicolinearity. Gender was not entered because it was not associated with GSI scores. The odds of having a clinically significant GSI score were significantly greater for those with behavioral transmission

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TABLE 3. MEAN SUBSCALE SCORES ON THE BRIEF SYMPTOM INVENTORY AMONG YOUTH LIVING WITH HIV

	M			
	Perinatal transmission N = 282	Behavioral transmission N=1088	$F^{\mathrm{a}}$	p
Global Severity Index	0.65	1.04	36.13	< 0.001
Anxiety	0.45	0.88	32.08	< 0.001
Somatization	0.47	0.81	26.70	< 0.001
Obsessive compulsive	0.93	1.17	8.57	0.003
Depression	0.64	1.17	33.25	< 0.001
Hostility	0.85	1.13	20.03	< 0.001
Phobic anxiety	0.34	0.66	22.53	< 0.001
Paranoid	0.95	1.31	23.50	< 0.001
Psychoticism	0.63	1.03	22	< 0.001
Interpersonal sensitivity	0.59	1.12	41.26	< 0.001

	Fer			
	Perinatal transmission N = 346	Behavioral transmission N=316	$F^{a}$	p
Global Severity Index	0.86	1.05	11.01	0.001
Anxiety	0.61	0.77	6.44	0.011
Somatization	0.63	0.84	11.5	0.001
Obsessive compulsive	1.05	1.16	4.34	0.038
Depression	0.96	1.16	3.34	0.068
Hostility	1.01	1.18	10.69	0.001
Phobic anxiety	0.53	0.62	3.08	0.080
Paranoid	1.21	1.39	8.97	0.003
Psychoticism	0.77	1.06	16.53	< .001
Interpersonal sensitivity	0.99	1.14	5.76	0.017

<sup>&</sup>lt;sup>a</sup>ANCOVA controlling for Age

(OR = 2.06) and those not taking ART that was prescribed (OR = 1.68), while controlling for age in the MLR.

# **Discussion**

This study is the largest report to date of the psychological symptoms of YLWH who are in care. Overall, 18% of youth reported symptoms beyond the threshold considered clinically significant for the BSI, compared to 10–50% reported in previous studies. The rate of 18% may be a more accurate estimate of clinically significant symptomatology because prior studies have been limited by smaller and less diverse samples. In addition, there was no distinct pattern to

the symptoms reported. For example, youth were as likely to experience hostility as they were anxiety or depression. This wide range of symptomatology suggests that health care providers need to be alert to the full spectrum of emotional and behavioral problems with which youth may present and have appropriate interventions available. It also suggests that even though behavioral acquisition of HIV may be associated with impulsive, risky behaviors, such as unsafe sex and substance use, many youth may be withdrawn and distressed.

YLWH with behaviorally acquired infection, compared to those with perinatal infection, had twice the odds (21% vs. 11%, OR = 2.06 in MLR) of reporting clinically significant psychological symptoms. It is possible that greater access

Table 4. Association of Global Severity Index Scores with ART Refusal, Having Disclosed HIV Status, and Time Knowing HIV Status

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Transmission group	Variable	GSI elevated (%)	$X^2$	p
Perinatal	ART refusal—Yes -No	10/76 (13.2%) 53/503 (10.5%)	0.468	0.494
Behavioral	ART refusal—Yes -No	209/1109 (18.8%) 66/226 (29.2%)	12.31	< 0.001
Perinatal	Have disclosed—Yes -No	45/379 (11.9%) 16/183 (8.7%)	1.25	0.264
Behavioral	Have disclosed—Yes -No	245/1175 (20.9%) 31/165 (18.8%)	0.377	0.539
Behavioral	Time knowing HIV status ≤1 year >1 year	130/602 (21.6%) 145/733 (19.8%)	0.664	0.415

Table 5. Logistic Regression of Factors Associated with Elevated Global Severity Index Scores

	В	SEB	Wald	OR	95% CI
Age (>18) Behavioral	0.03 0.72	0.17 0.17	0.03 18.90	1.03 2.06 <sup>b</sup>	0.74–1.44 1.49–2.86
transmission ART refusal	0.52	0.16	11.86	1.68 <sup>a</sup>	1.25-2.25

Final Model: n=1, 924.  $X^2$  (3)=39.56, p<0.001. Nagelkerke  $R^2=0.034$ .

over time to medical and psychological treatment by those with perinatal infection accounts for their reduced risk. In fact, the prevalence of 10.8% among youth with perinatally acquired HIV is very close to rates found in community samples without specific health conditions and suggests a generally successful adaptation to illness for this group. 42 In the group with behaviorally acquired infection, HIV is contracted by risk behaviors that may be associated with psychological symptoms, which could account for that group's greater report of symptoms. Further, symptoms in this group were no less prevalent in those who had known of their infection for more than one year as compared to newly diagnosed youth. Thus, the passage of time and the initial access to care and psychological treatment in clinics does not diminish the prevalence of psychological concerns among youth.

In HIV treatment clinics, ART has become widely used, and is used earlier in the course of infection. Indeed, 83% of the participants with behaviorally acquired HIV were taking ART. Unfortunately, the odds was two-thirds greater of reporting clinically significant psychological symptoms (29% vs. 19%, OR = 1.68 in MLR) among those not taking ART that was prescribed compared to those taking medication, even when accounting for the impact of age and route of transmission. Several factors could account for this finding, either independently or in concert. It is possible that mental health issues preclude some youth from considering taking medications or providers are more reluctant to prescribe them. It is also possible that some youth begin on ART treatment and their mental health improves in parallel to their physical health. No matter the cause, health care providers should be particularly alert to mental health concerns of those not on ART because of the increased risk of transmission and the potential for psychological symptoms to reduce their quality of life.

Those who had disclosed their HIV infection to others were just as likely to report psychological symptoms as those who had not. Several factors related to disclosure were not examined in this study, such as the number of people told, the quality of the relationships, and the perceived outcome of disclosure. These important factors could interact with mental health issues. <sup>45</sup> In any case, the act of disclosure is not a guarantee of fewer mental health concerns.

This study has several limitations. The study examined cross-sectional data that were collected at one point in time and thus causal relationships cannot be identified. These data cannot determine changes that may occur in mental health as individuals live with and manage their HIV infection. The

measure of psychological symptoms was a self-report screening tool, rather than structured psychiatric diagnosis derived from a clinical interview. However, the BSI has been widely used and assesses a wide range of emotional and behavioral symptoms. Most information was obtained via self-report and thus can be inaccurate. Efforts were made, however, to increase accurate reporting by means such as the use of confidential computer assisted administration. One recent study in the ATN found that the use of computer assisted self-reporting of drug use had high rates of concordance with toxicology results in youth with HIV infection.<sup>46</sup> Finally, all participants are currently receiving some type of medical or psychosocial care through adolescent medical care clinics. Thus, youth with HIV infection who are not engaged in the medical system are not represented in this sample. It is possible that these youth may have different patterns of psychological symptoms from those identified in

In summary, this study presents data on the prevalence and correlates of psychological symptoms among one of the largest samples of adolescents and young adults with HIV infection who are receiving medical care drawn nationally from 20 different sites across the country. The results of this study suggest that a significant number of youth are troubled by mental health issues and the prevalence is greatest among those with behaviorally acquired infection. Psychological symptoms of all types are reported ranging from depression and anxiety to hostility and paranoia. Symptoms are not fewer if individuals have known of their infection longer or have disclosed their infection to others. Adjustment to living with HIV is a complex process and each new event, such as disclosure, may relieve some issues and bring others into focus. The small proportion of youth not taking ART that had been prescribed had very high rates of psychological symptoms and is a cause for concern, given the increased chance of HIV transmission with greater viral loads and the decreased quality of life with more mental health issues. Engaging these youth in psychiatric treatment is critical and may require multiple, innovative approaches that are tailored for each person. It is left to future research to examine these patterns of psychological symptoms over time in adolescents and young adults living with HIV. Symptoms need to be examined in relation to the many important, changing, factors in the lives of youth such as their engagement in care, health status, substance use, employment, housing status, and available social supports. 45,47 It is likely that programs will need to acknowledge the relevance of all of these factors in order to adequately address the mental health concerns of the youth whom they serve.

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 $<sup>^{</sup>a}p = 0.001; ^{b}p < 0.001.$ 

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# **Author Disclosure Statement**

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