Behavioral Health Risks in Perinatally HIV-Exposed Youth: Co-Occurrence of Sexual and Drug Use Behavior, Mental Health Problems, and Nonadherence to Antiretroviral Treatment

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Abstract

In a sample of perinatally HIV-infected (PHIV+) and perinatally HIV-exposed, uninfected (PHEU) adolescents, we examined the co-occurrence of behavioral health risks including mental health problems, onset of sexual and drug use behaviors, and (in PHIV+ youth) nonadherence to antiretroviral therapy (ART). Participants, recruited from 2007 to 2010, included 349 youth, ages 10–16 years, enrolled in a cohort study examining the impact of HIV infection and ART. Measures of the above behavioral health risks were administered to participants and primary caregivers. Nearly half the participants met study criteria for at least one behavioral health risk, most frequently, mental health problems (28%), with the onset of sexual activity and substance use each reported by an average of 16%. Among the sexually active, 65% of PHIV+ and 50% of PHEU youth reported unprotected sex. For PHIV+ youth, 34% reported recent ART nonadherence, of whom 45% had detectable HIV RNA levels. Between 16% (PHIV+) and 11% (PHEU) of youth reported at least two behavioral health risks. Older age, but not HIV status, was associated with having two or more behavioral health risks versus none. Among PHIV+ youth, living with a birth mother (versus other caregivers) and detectable viral load were associated with co-occurrence of behavioral health risks. In conclusion, this study suggests that for both PHIV+ and PHEU youth, there are multiple behavioral health risks, particularly mental health problems, which should be targeted by service systems that can integrate prevention and treatment efforts.

Introduction

WITH THE ADVENT OF highly active antiretroviral treatment (HAART), children with perinatally acquired HIV infection in the United States are reaching adolescence in large numbers.¹ With a longer lifespan comes challenges related to the impact of HIV on health and behavior. Clinical reports reveal substantive mental health problems and risk

behaviors that are barriers to optimal health in perinatally infected (PHIV+) youth,^{2,3} yet there are few studies of behavioral health risks in PHIV+ adolescents and even fewer that include an appropriate comparison groups, such as perinatally HIV-exposed but uninfected (PHEU) adolescents.

The few existing studies with PHIV+ youth indicate high rates of psychiatric problems^{4–6} and the emergence of sexual risk behaviors, including early onset of sexual intercourse and

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sex without condoms, as well as substance use problems during adolescence.⁷⁻¹⁰ Furthermore, studies suggest that a significant percentage of PHIV+ youth fail to adequately adhere to antiretroviral treatment (ART) regimens, resulting in increased viral load and potentially the development of treatment resistant strains of the virus.¹¹⁻¹⁴ Nonadherence, coupled with mental health and substance use problems, as well as sexual risk behavior, place this population at high risk for poor health and quality of life outcomes as well as HIV transmission to sexual partners. In order to inform interventions targeting PHIV+ youth, it is critical to understand the extent to which behavioral health risks, including mental health problems, sexual and drug risk behaviors, and nonadherence occur and coexist. Studies among HIV-infected adults suggest that interventions may be more effective if they integrate prevention and treatment services for populations at high risk for these four co-occurring behavioral health risks.¹⁵

PHIV+ youth may be more vulnerable to the coexistence of behavioral health risks since many are from families living in economically depressed, urban communities affected by racism and discrimination, substance use, loss, violence, and environmental degradation. They typically live with single mothers, many of whom are living with their own HIV infection, often experiencing multiple caretaking transitions due to maternal substance abuse, illness, or death.¹⁶ Studies of other populations have shown that youth with these characteristics are at high risk for mental health problems and for engaging in sexual and drug risk behavior, including early sexual debut at 12-14 years, multiple partners, and sex without condoms.¹⁷⁻¹⁹

Understanding the role of perinatal HIV infection in influencing behavioral health risks and disentangling the effects of HIV from other environmental or psychosocial factors are difficult and few studies have adequate comparison groups. Youth with behaviorally acquired HIV, who share high levels of mental health problems, nonadherence, and sexual risk behaviors, may differ substantially from youth with perinatal HIV exposure in that they are considerably older when first infected and have already engaged in sexual and/or drug risk behavior leading to HIV infection.²⁰⁻²² Perinatally HIV-exposed, but uninfected (PHEU) youth have been considered a more appropriate peer comparison group because, with the exception of HIV infection, they share many sociodemographic characteristics, as well as exposure prenatally and postnatally to maternal HIV infection.⁷ Moreover, given the growing population of perinatally HIV-exposed but uninfected youth in the United States and globally, understanding their psychosocial functioning is an important public health goal in its own right.^{2,3}

In a sample of perinatally HIV-exposed adolescents, including PHIV+ and PHEU youth, participating in one of the largest United States-based studies of this population, this set of analyses examines the prevalence and co-occurrence of four behavioral health risks, mental health problems, onset of sexual activity, substance use, and in PHIV+ adolescents only, ART nonadherence. We hypothesized that both PHIV+ and PHEU youth are at high risk for the co-occurrence of mental health and substance use problems, as well as the onset of sex activity given shared vulnerable environments (both groups recruited from the same clinical settings in similar sociodemographic communities). We hypothesized that PHIV+ youth would present with higher rates of

co-occurring behavioral health risks than PHEU youth given the additional burden of perinatal HIV infection. Finally, we hypothesized that among PHIV+ youth, nonadherence to ART would occur in the context of other behavioral risks, including mental health, substance use, and sex.

Note that although the onset of sex by itself may not be a behavioral problem, a large number of studies have found that early onset of sex is associated with high rates of risky sex in youth, such as having multiple partners and failure to use condoms.^{17,19} For youth living with HIV infection, this is a significant behavioral health risk for themselves and others and thus, onset of sex is considered a behavioral health risk in this study in order to fully understand the secondary HIV prevention and intervention needs of this population.

Methods

Data source and sample

Participants included PHIV+ and PHEU youth enrolled in the Adolescent Master Protocol (AMP) of the Pediatric HIV/AIDS Cohort Study (PHACS). AMP is an ongoing prospective cohort study examining the impact of HIV infection and ART on health, behavioral, and neuropsychological outcomes in older children and adolescents. Participants were recruited from 15 sites, 14 of which are based in academic medical centers and 1 that is a community-based organization with relationships to multiple clinics and agencies. The majority of sites were located in urban settings across the United States and Puerto Rico and provided primary and tertiary care to PHIV+ youth and families. All 15 sites recruited both PHIV+ and PHEU youth. Reflecting the epidemiology of HIV in women and children in the United States, the vast majority of both groups in all settings were from primarily low socioeconomic, ethnic minority communities.

Eligibility criteria for children in AMP included: (a) born to an HIV-infected mother, (b) age 7-15 years, 11 months at study entry, and (c) engaged in medical care and previously enrolled in an approved longitudinal study or having complete HIV medical history available. These analyses focus on youth ages 10 years and older, as 10 is the age at which measures of sexual and drug use behavior are first administered in AMP. Data collected between March 2007 and November 2010 were included.

Procedures

Human subject research review boards at all AMP sites and the Harvard School of Public Health approved the research protocols. Potential participants were identified either through medical chart reviews or case conferences conducted by local site providers. All eligible participants were approached by either their primary care providers or research staff associated with the clinical setting. For all those interested in participating, the AMP protocol was described in more detail, written informed consent for youth and caregiver participation was obtained from parents or legal guardians by the local sites. Written assent was obtained from children in accordance with local Institution Review Board (IRB) guidelines. Given confidentiality and HIPAA regulations, information on patients who refused participation was not available.

Data for this analysis came from the baseline and 6-month interviews with caregivers and youth. The assessments were

administered in English or Spanish by centrally trained psychologists/psychometricians, or via audio-computer assisted self-interview (ACASI). Since the psychosocial assessment was part of a much larger protocol-specified assessment that included cardiac, hearing and language, and neurologic status, the psychosocial assessment could not be completed in one session without undue burden for participants. Therefore, the baseline psychosocial assessment included in these analyses was administered over two sessions. Mental health and demographics were administered at study entry, and the assessment of sexual behavior, substance use, and adherence occurred at the next study visit, on average within 6 months (± 2 months) post-entry visit.

Measures of behavioral health risks

Mental health problems were assessed with the Behavior Assessment System for Children, Second Edition (BASC-2),²³ a well-validated, reliable multidimensional tool used to evaluate children's and adolescents' emotions, self-perceptions, and behavioral functioning. Normative data are based on samples representative of recent US population figures. Since caregivers and youth provide unique perspectives on psychological adjustment,²⁴ we evaluated both, using BASC-2 Self-Report of Personality (SRP) and BASC-2 Parent Rating Scale (PRS).

We defined mental health problems in these analyses as having either a BASC-2 Behavioral Symptoms Index (BSI) or Emotional Symptoms Index (ESI) score in the at-risk (T-score 60–69) or clinically significant (T-score > 70) range.²³ The BSI includes scales measuring hyperactivity, aggression, depression, attention problems, atypicality and withdrawal and reflects overall level of problematic behavior observed by the parent/caregiver. The ESI includes scales measuring social stress, anxiety, depression, sense of inadequacy, self-esteem, and self-reliance and identifies cumulative effects of numerous emotional difficulties reported by the youth.

Sexual behavior was assessed with the Adolescent Sexual Behavior Assessment (ASBA)²⁵ via ACASI. The ASBA is a brief measure of sexual behavior appropriate for the full age range in this study, including younger children via gateway questions. Questions addressed kissing, touching partner's genitals, oral and penetrative (vaginal or anal) sex, and unprotected penetrative sex over their lifetime, with questions addressing both heterosexual sex and same-sex behavior. Sexual activity was defined here as any report of oral, vaginal or anal sex, including heterosexual and same-sex behavior.

Substance use was also assessed with questions via an ACASI developed for the AMP protocol. Questions evaluated current (past 3 months) and ever use of alcohol (more than a few sips at a time) and nonalcoholic substances, including tobacco, marijuana, cocaine, heroin, and other illicit substances. Substance use was defined here as use of any substance in the past 3 months.

Adherence to ART (for PHIV+ youth) was assessed with a questionnaire developed by the AMP team, based on the work of the Adult and Pediatric AIDS Clinical Trials Groups.^{13,26} The questionnaire is administered separately to the caregiver and youth by staff not involved in the clinical medical care of the participant. Participants were asked about their medications, dosing, and the number of missed doses for each medication in the past week, as well as two questions

about the last time medications were missed and a more general categorical estimate of nonadherence over the past 6 months. For these analyses, we defined nonadherence as a report by either the child or caregiver of one or more missed doses to any component of their full ART regimen in the past 7 days. This combined variable was selected based on previous analyses with this sample, as well as other pediatric studies, demonstrating a highly significant association of 7-day recall with concurrent HIV RNA viral load^{12,27} and was equivalent or superior to other adherence variables with longer time frames.²⁷

Covariates

Demographic characteristics included child age (10–12 versus 13–16 years), gender, race (black, white/other/unknown), ethnicity (Hispanic, non-Hispanic), caregiver type (birth mother, other relative, nonrelative), caregiver education (less than high school, yes/no) and family income ($\leq \$20,000$, $> \$20,000$ – $40,000$, $> \$40,000$).

Child health data were obtained from medical charts of PHIV+ participants and included Centers for Disease Control and Prevention (CDC) classification (ever classified as C) and detectable viral load (> 400 copies per milliliter).

Data analysis

For our primary analyses of co-occurring (two or more) behavioral health risks we included sexual activity, substance use, and mental health problems. We grouped individuals into three outcome categories (0, 1, or ≥ 2 behavioral health problems). In a separate set of analyses restricted to PHIV+ youth, we also included a fourth outcome variable, ART nonadherence. We first assessed associations, stratified by infection status, between key demographic and medical characteristics (gender, race, ethnicity, age, income, caregiver type, caregiver education, CDC classification, viral load) and the outcomes using the *t* test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. For modeling, since we were interested in characteristics associated with co-occurrence of two or more behavioral health risks, we used multinomial logistic regression models to identify characteristics independently associated with two or more versus no behavioral health risk outcomes and, separately, one versus no outcomes. We developed separate models for PHIV+ and PHEU youth. We included all variables that were associated in the unadjusted analysis with the outcome ($p \leq 0.10$) in the final models.

Separately, to examine the potential association of HIV-infection status on co-occurrence of behavioral health risks, we included infection status in a model that included both PHIV+ and PHEU youth. We included as potential confounders any characteristics that were associated with the outcome ($p \leq 0.10$) in the unadjusted analysis or that changed the effect estimate for infection status by 15% or more. Analyses were conducted using SAS version 9.1.3 (SAS Institute, Cary, NC); statistical significance was based on $p < 0.05$.

Since a lower proportion of PHIV+ (76%) than PHEU participants (90%) completed the ACASI, we compared participants with and without ACASI data on demographic/caregiver characteristics. Also, as the majority of refusals occurred at one site, we conducted a sensitivity analysis in which we excluded participants from that one site.

Results

Entry and 6-month post-entry AMP visits were completed by 449 participants who were at least 10 years old and eligible to complete the ACASI. Three hundred forty-nine (78%) of these youth (238 PHIV+, 111 PHEU) had complete data on sexual activity, substance use, and mental health problems. Incomplete data were largely due to missing ACASIs. The primary reasons for missing ACASI data were insufficient time and caregiver or participant refusal at the 6-month study visit. In comparisons of youth with and without ACASI data, those younger than 13 years were less likely to have completed ACASIs than were youth 13 years or older (PHIV+: <13 years, 69% completed versus ≥13 years, 81% completed, $p<0.01$; PHEU: 87% versus 98%, $p=0.05$), as were non-Hispanic youth compared to Hispanic youth (PHIV+: 73% versus 85%, $p=0.03$; PHEU: 76% versus 91%, $p<0.001$). There were no other differences on demographic variables, nor were there differences in mental health functioning between youth who did and did not complete the ACASI. When we excluded from the analyses the one site with the majority of ACASI refusals (60%), our results remained qualitatively similar to those of our main analyses.

Sample characteristics

Table 1 summarizes the demographic, caregiver, and health characteristics of the 349 participants. Approximately half of the youth were male and the majority self-identified as black, non-Hispanic. There were several significant differences between PHIV+ and PHEU youth. PHIV+ youth were

slightly older (1 year on average), more likely to be black and non-Hispanic, less likely to be living with their birth mothers, and come from families with higher incomes. These latter two differences concur with a number of previous studies of this population (see Discussion).⁴⁻⁶

Prevalence of behavioral health risks (excluding adherence)

Table 2 summarizes the proportion of PHIV+ and PHEU youth who met each of the study defined criteria for each of the behavioral health risks. For PHIV+ youth and PHEU youth, the most frequently reported behavioral health risk was a mental health problem (26% PHIV+ and 33% PHEU), most frequently with a BSI score in the at-risk or clinically significant range. Eighteen percent of PHIV+ youth and 14% of PHEU youth reported recent substance use. Among those reporting substance use, alcohol was the most prevalent substance reported (58% of PHIV+; 69% PHEU), followed by marijuana (35% PHIV+; 56% PHEU). Sexual behavior was also reported by approximately 16% of youth across both groups; the majority of these, 65% of sexually active PHIV+ youth and 50% of sexually active PHEU youth, reported unprotected vaginal or anal sex, primarily (84%) with opposite gender partners (only 5 PHIV+ and 4 PHEU youth reported same-sex behavior, too small a number to examine differences).

Among the sexually active youth, the mean age of onset was 13 years for PHIV+ (median, 14 years) and 12 years for PHEU youth (median, 13 years) with no significant HIV status group differences ($p=0.22$). There were also no differences

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF 349 PERINATALLY HIV-INFECTED AND HIV-EXPOSED, UNINFECTED CHILDREN AND ADOLESCENTS

Characteristic	Perinatally HIV-infected (PHIV+) n=238	Perinatally HIV-exposed, Uninfected (PHEU) n=111	p Value ^a
Male	119 (50.0%)	54 (48.7%)	0.81
≥13 years	152 (63.9%)	41 (36.9%)	<0.001
Mean age (SD)	13.7 (1.8)	12.7 (1.9)	<0.001 ^b
Race			
Black	162 (68.1%)	68 (61.3%)	0.05
White/other	60 (25.2%)	40 (36.0%)	
Unknown	16 (6.7%)	3 (2.7%)	
Ethnicity			
Hispanic	69 (29.0%)	43 (38.7%)	0.06
Non-Hispanic	169 (71.0%)	67 (60.4%)	
Unknown	0	1 (0.9%)	
Caregiver			
Birth mother	91 (38.2%)	82 (73.9%)	<0.001
Other biological relative	72 (30.3%)	14 (12.6%)	
Non-biological	75 (31.5%)	15 (13.5%)	
Caregiver education (≤high school)	72 (30.3%)	41 (36.9%)	0.21
Annual household income			
≤\$20,000	100 (42.0%)	71 (64.0%)	<0.001
\$20-40,000	70 (29.4%)	16 (14.4%)	
>\$40,000	55 (23.1%)	22 (19.8%)	
Unknown	13 (5.5%)	2 (1.8%)	
Detectable viral load	85 (35.7%)	—	—
Prior CDC class C diagnosis	62 (26.1%)	—	—

^a χ^2 test (unless otherwise specified).

^b t test.

SD, standard deviation; CDC, Centers for Disease Control and Prevention.

TABLE 2. PREVALENCE OF BEHAVIORAL HEALTH OUTCOMES AMONG 349 PERINATALLY HIV-INFECTED AND HIV-EXPOSED, UNINFECTED YOUTH

Behavioral health risk outcome		Perinatally HIV-infected (PHIV+) n=238	Perinatally HIV-exposed, uninfected (PHEU) n=111	p Value ^a
Any current substance use	Yes	43 (18%)	16 (14%)	0.40
	No	195 (82%)	95 (86%)	
Any vaginal, anal, or oral sex	Yes	40 (17%)	17 (15%)	0.73
	No	198 (88%)	94 (85%)	
ESI or BSI risk/clinically significant	Yes	62 (26%)	37 (33%)	0.16
	No	176 (74%)	74 (67%)	
Any missed ART ^b in past 7 days ^c	Yes	74 (34%)	n/a	—
	No	141 (66%)		

^a χ^2 test.^bAntiretroviral treatment.^cTwenty-three missing observations.

ESI, Emotional Symptoms Index; BSI, Behavioral Symptoms Index; ART, antiretroviral therapy.

between PHIV+ and PHEU youth in the prevalence of mental health problems ($p=0.16$), substance use, ($p=0.40$), onset of sexual behavior ($p=0.73$), and unprotected sex ($p=0.50$).

Co-occurrence of behavioral health outcomes (excluding adherence)

Table 3 presents the proportion of PHIV+ and –PHEU youth who reported zero, one, two or all three behavioral health risks. Forty-three percent of PHIV+ and 50% of PHEU youth reported risks in at least one area; 16% of the PHIV+ youth and 11% of PHEU youth met study criteria for two or more behavioral health risks. There were no group differences by HIV status ($p=0.10$). For both PHIV+ and PHEU youth with two or more behavioral health risks, the most frequent co-occurrence was the onset of sex and substance use (42% and 50%, respectively).

Correlates of co-occurrence of behavioral health risks (excluding adherence)

Table 4 summarizes the associations between demographic and caregiver characteristics and two or more (versus no) behavioral health risks. No factors were associated with having one versus no risk outcomes. In the unadjusted analysis, among PHIV+ participants, primary caregiver type was associated with co-occurrence. PHIV+ youth living with their

birth mother had three times the odds of two or more behavioral health risks versus none, as compared to youth who lived with another type of caregiver (e.g., relative or a non-relative). Youth aged 13 years and older had over four times the odds of two or more behavioral health risks as compared to those younger than 13 years. Caregiver type and older age remained significantly associated with co-occurrence of behavioral health risks in the final adjusted model. While not statistically significant ($p=0.09$), detectable viral load was associated with having twice the odds of two or more behavioral health risks.

Among PHEU youth, only older age was significantly associated with co-occurring outcomes. Race, ethnicity, caregiver education, and income were not associated with behavioral health risks among either PHIV+ or PHEU participants, nor was CDC classification for PHIV+ youth.

We also examined co-occurrence of behavioral health risks substituting “unprotected sex” for “any sex.” Although the number of youth reporting unprotected sex is smaller (approximately 55% of the youth who reported sex), the results on predictors of co-occurrence were similar for both groups with one exception; detectable viral load was associated with having two or more behavioral health risks in the PHIV+ participants (data not shown).

PHIV+ behavioral health risks, including adherence

In additional analyses among PHIV+ youth that included ART nonadherence as a fourth behavioral health risk, non-adherence was the most frequently reported risk (34%). The two most frequent combinations of behavioral health risks were (a) mental health problems and nonadherence (23%) and (b) sexual activity, substance use, and nonadherence (20%). In the unadjusted analyses examining correlates of behavioral health risks, detectable viral load and living with a birth mother (versus other caregiver) were significantly associated with having two or more (versus no) behavioral health risks (data not shown). Both remained significantly associated with co-occurring risk outcomes in the adjusted model (detectable viral load: odds ratio [OR]=2.94, 95% confidence interval [CI] 1.30, 6.65, $p=0.01$; birth mother: OR=2.92, 95% CI 1.32, 6.45, $p<0.01$). Older age, while not statistically significant ($p=0.07$), was associated with twice the odds of co-occurring problems.

TABLE 3. NUMBER OF CO-OCCURRING BEHAVIORAL HEALTH RISKS^a AMONG 349 PERINATALLY HIV-INFECTED AND HIV-EXPOSED, UNINFECTED CHILDREN AND ADOLESCENTS

Number of behavioral health risks	Perinatally-infected (PHIV+) n=238	Perinatally-exposed, uninfected (PHEU) n=111
None	137 (57.5)	56 (50.5)
One	63 (26.5)	43 (38.7)
Two	32 (13.5)	9 (8.1)
Three	6 (2.5)	3 (2.7)
		$p=0.10^b$

^aNot including nonadherence to antiretroviral treatment.^b χ^2 test.

TABLE 4. ASSOCIATIONS WITH TWO OR MORE BEHAVIORAL HEALTH RISKS AMONG PERINATALLY HIV-INFECTED AND HIV-EXPOSED, UNINFECTED CHILDREN AND ADOLESCENTS (N=349)

Characteristic	Perinatally infected (PHIV+) n=238		Perinatally exposed, uninfected (PHEU) n=111	
	Unadjusted	Adjusted ^a	Unadjusted	Adjusted ^a
Age ≥13 years	4.43 (1.63, 12.0)	4.66 (1.62, 13.5) ^b	6.88 (1.66, 28.6)	6.90 (1.63, 29.2) ^b
Caregiver is birth mother	3.18 (1.51, 6.71)	3.25 (1.43, 7.39) ^b	0.60 (0.16, 2.33)	
Male	0.82 (0.40, 1.69)		3.09 (0.83, 11.5)	3.10 (0.79, 12.1)
Caregiver <high school education	1.70 (0.80, 3.60)		1.06 (0.28, 3.97)	
Detectable viral load	2.44 (1.18, 5.08)	2.12 (0.95, 4.71)	—	—
Black race	1.68 (0.74, 3.85)		3.00 (0.60, 15.0)	
Hispanic ethnicity	0.75 (0.33, 1.73)		0.50 (0.12, 2.06)	
Annual household income				
≤\$20,000	2.13 (0.78, 5.81)	1.28 (0.43, 3.84)	0.52 (0.11, 2.45)	
\$21,000–40,000	0.62 (0.17, 2.21)	0.52 (0.14, 2.03)	0.53 (0.07, 4.01)	
Unknown	3.81 (0.90, 16.1)	3.82 (0.79, 18.4)	— ^c	
>\$40,000	reference		reference	
Prior CDC class C diagnosis	2.08 (0.96, 4.51)	1.49 (0.63, 3.51)	—	

^aNot including lack of ART adherence.^b*p* < 0.05.^cTwo subjects with unknown income were excluded from model.

Adjusted models include all variables shown. Odds ratios for one vs. no behavioral problems not presented.

CDC, Centers for Disease Control and Prevention; ART, antiretroviral therapy.

HIV infection status and behavioral health risks

PHEU children had almost twice the odds of one versus no behavioral health risks as compared to PHIV+ children (OR = 1.77, 95% CI 1.01, 3.13; *p* = 0.047). However, both groups had similar odds of two versus no outcomes (OR = 0.81, 95% CI 0.36, 1.84, *p* = 0.62).

Discussion

In one of the largest studies of perinatally HIV-infected youth and perinatally HIV-exposed uninfected youth, a high percentage of youth in both groups met study-defined criteria for at least one behavioral health risk, most frequently a mental health problem and, for the PHIV+ youth, ART nonadherence and mental health problems. A number of youth in both groups also reported substance use (most frequently alcohol) and the onset of sex, including a high rate of unprotected sex. Among the youth with two or more behavioral health risks, the most frequent combination was the onset of sex and current substance use. These results suggest that children born to HIV-infected women, regardless of their own HIV status, are at risk for multiple behavioral health risks that require consideration in prevention and health care programs.

Among the behavioral health risks shared by both groups of youth, mental health problems were the most prevalent for both PHIV+ and PHEU youth; roughly one third of youth met criteria for caregiver- or self-reported mental health problems that were in the at-risk or clinically significant category on the BASC-2. It is difficult to compare our data to other studies given differences in measures and criteria. However, the prevalence of mental health problems in our study is greater than expected relative to surveys in the general population,^{28,29} but comparable to the few studies of children living with perinatal HIV infection or uninfected children living with HIV-infected caregivers.^{30–32} Mental health problems during adolescence place youth at heightened risk for chronic mental health disorders in adulthood, as

well as sexual risk behavior, and thus, require early identification and appropriate, evidence-based interventions to promote youth health and mental health, as well as prevent sexual risk behaviors that can lead to HIV transmission. These mental health problems may not be easily detected in a health care provider's office. Our data suggest that incorporating routine mental health assessments into health care systems may be critical to the early diagnosis and treatment of mental health problems as well as prevention among those at risk.

The proportion of youth who had initiated sex or substance use was lower than that reported in many studies of high-risk populations (e.g., runaway youth, youth with psychiatric disorders),^{33,34} and considerably lower than the proportion observed among youth with behaviorally acquired HIV who are typically older and, by definition, have already engaged in sex or substance use.³⁵ Our results correspond with recent investigations of PHIV+ and PHEU youth in whom initiation of sexual behavior and substance use was delayed compared to the general population.^{7,9,36}

These data, in combination with the finding that approximately 70% of participants did not have abnormal BASC-2 composite scores, suggest that despite the likely presence of significant stressors in their lives (e.g., maternal HIV, poverty, family disruption), protective factors that support mental health and prevent early onset of sexual behavior and substance use may be present among many families of PHIV+ or PHEU youth. Further study of resilience is necessary to identify protective factors (e.g., social support, family involvement), with the goal of developing effective prevention programs.

Conversely, among the relatively small percentage of PHIV+ youth who had initiated sex, the rate of unprotected sex was very high (65%) and mean age of onset was young (13 years for PHIV+ and 12 years for PHEU). Furthermore, among PHIV+ youth, ART nonadherence occurred frequently, in the context of detectable viral load, placing these youth at risk for immune suppression and resistance to ART.

Thus, there is a subgroup of PHIV+ youth who are initiating sexual behavior early and engaging in unprotected sex. Coupled with high co-occurrence of ART nonadherence leading to a detectable viral load and mental health problems that may impair judgment, unprotected sex poses a high risk of transmission of HIV to sexual contacts.

These findings underscore the need to focus interventions and services for PHIV+ youth on promotion of positive health outcomes and prevention of secondary HIV transmission to their sexual partners. Also, the clustering of behavioral health risks, especially in the context of inadequately controlled viral load, suggests that models of care that integrate mental health, HIV transmission prevention, and health care services are critical, particularly as the majority of PHIV+ youth in the United States age into adolescence and young adulthood. Pediatric HIV/AIDS programs for perinatally infected youth often integrate these services³⁷; however, adult programs do not necessarily have these resources, which becomes an issue as PHIV+ youth transition to adult care systems.⁴ Moreover, few efficacy-based interventions that integrate services, targeting co-occurring behavioral and health risks have been developed for children or adults living with HIV. One such program, the Healthy Living project for HIV-infected adults, addresses each of these areas in one integrated intervention program that has proven effective in a large multisite clinical trial,³⁸ and one program for children is currently being evaluated.³⁹

Interestingly there were few differences between PHIV+ and PHEU youth. Both groups had similar rates of each of the behavioral health risks, and similar odds of meeting study criteria for two or three behavioral health risks compared to none. Thus, our results highlight the behavioral needs not only of PHIV+ but PHEU youth as well. PHEU youth presented with relatively high rates of mental health problems and, among the sexually active, high rates of unprotected sex. We are close to eradicating perinatal HIV infection in the United States through the widespread use of ART during pregnancy and childbirth.⁴⁰ However, as long as HIV disease continues to affect women, a significant population of youth will continue to be born perinatally HIV-exposed. A number of other studies have also shown that this population of youth is at high risk for mental health problems as well as sexual risk behavior.^{6,41} Unfortunately, HIV-exposed but uninfected youth are often difficult to identify and monitor. They are not followed in comprehensive HIV care clinics, unless they enroll in a limited number of studies such as this one. HIV-infected parents receive medical care in adult HIV clinics that do not typically identify the emotional and behavioral risks of their patients' children. Although PHIV+ youth may have increased access to a range of psychosocial services through their medical clinics, these services may need to be extended to the uninfected children of mothers with HIV-infection, as has now been suggested by the results of several studies.^{41,42}

We identified only two independent demographic predictors of the co-occurrence of risk behaviors. As in studies in other populations, older age was a significant predictor of behavioral health risks for both HIV-infected and HIV-exposed youth.²² Also, among PHIV+ youth, those with biological mother as the primary caregiver were over three times more likely to have two or more comorbidities than those with a relative or nonrelative primary caregiver. The stress of maternal illness, including birth mothers' own comorbid

health, mental health, or substance abuse conditions,^{3,43} may compound the effects of the youth's own HIV infection. Longitudinal studies are needed to disentangle the effects of caregiver and youth HIV infection on PHIV+ youth as well as the myriad other determinants of youth behavior. Moreover, studies are needed to identify potential mediators of this relationship, such as social support or caregiver mental health. That said, there is clearly a need for the development of multilevel family-based interventions to support HIV-infected women and their children, whether infected or not, as there are few efficacy-based interventions available and few service models that have been tested. There is also a need for such interventions for PHIV+ and PHEU youth living with a range of primary caregivers, as behavioral risks were identified among youth living with non-birth parents. Additionally, results indicate that some youth require more intensive services, while others are well-served with consistent monitoring, similar to the pediatric psychology preventative health model as developed by Kazak⁴⁴ for families coping with a recent cancer diagnosis.

There are several limitations to this study. This is a convenience sample. The participants were recruited from HIV primary care clinics and most had participated in previous research studies. Although each study site attempted to recruit all eligible participants and study sites represent a large number of United States-based locations with high HIV seroprevalence, the sample may not fully reflect the larger population of PHIV+ and PHEU adolescents. For example, research studies require regularly scheduled study visits and thus we may have recruited participants more highly compliant with medical care or better supervised by caregivers, and thus underestimated non-adherence or sexual and drug risk behaviors. Although recruited from the same clinics, there were some demographic differences between the PHIV+ and PHEU youth and there may have been other differences unaccounted for in this study. PHIV+ youth were less likely to be living with a birth parent, although this is likely associated with their infection status. As described elsewhere,^{45,46} because the odds of perinatal transmission of HIV increase with maternal illness (i.e., higher viral load), the PHIV+ youths were more likely to have had sicker mothers who were more likely to transmit the virus and may have died earlier with the limited treatment options available when many of these children were born.

An additional limitation is the relatively lower ACASI completion rate among PHIV+ youth. However, when we restricted our analyses to those sites with low refusal rates (resulting in the exclusion of one outlier site which comprised 60% of all refusals), our results remained substantially similar to those from our primary analyses. Additional limitations include the use of cross-sectional data that reduces our ability to assess the temporal relationship between study variables, and issues of social desirability related to self-report instruments, particularly around topics such as mental health, sex, substance use and adherence. However, the use of the ACASI has been demonstrated to reduce social desirability bias.⁴⁷ Also, our caregiver- and self-reported adherence measures were significantly associated with viral load.

It is important to note that our sample was relatively young (mean age of 12 years) which may have resulted in relatively low rates of some behavioral health risks. These young adolescents may not have engaged in many sexual and drug risk

behaviors that typically emerge during middle or late adolescence. Moreover, relatively few of these youth reported same-sex behavior. Psychiatric disorders that more typically emerge in late adolescence or young adulthood might not be present or may be at subthreshold levels for diagnosis. Younger adolescents are likely dependent on their caregivers for medication management and thus adherence may be better than observed in studies of older adolescents.^{48,49} It will be important to follow these youth into older adolescence and young adulthood when more youth begin to report increased sexual behavior, including same-sex behavior, increased alcohol and drug use, and increased responsibility for their own health care, all of which may result in increased behavioral health risk, as has been noted in studies of older adolescents and young adults who acquired HIV through sexual or drug use behavior.^{22,50}

Despite potential differences between youth with perinatally acquired HIV and those who acquired HIV through sexual or drug use behavior, it is possible that as PHIV+ youth age into older adolescence, their needs for intimacy and a healthy sexual life, experience of stigma, need for disclosure of a highly stigmatized and transmittable illness, and difficulties with life-long ART adherence and less family supervision will become similar to young people with behaviorally acquired HIV, warranting similar interventions. Although the perinatal HIV epidemic is diminishing in the United States, this is not true internationally. Future research on intervention and prevention programs for adolescents and young adults in both transmission groups are critically needed to help with transmission prevention, reproductive health, life-long adherence, mental health, and overall quality of life.

In summary, our findings suggest a significant need for targeted service programs for both PHIV+ and PHEU youth, particularly those that address mental health problems, safe sex behavior, and nonadherence. There are now a number of studies that have identified important predictors of the behavioral health risks assessed in this paper, including cognitive function,^{51,52} caregiver supervision and monitoring,⁵³⁻⁵⁵ caregiver mental health,^{11,56} and parent-child relationship factors,^{11,55-57} many of which could be targeted in these services. To date, only a few efficacy-based interventions have been developed that target caregiver-child relationship factors as well as supervision and monitoring to support mental health and reduce risk behavior in PHIV+ youth and youth living with HIV+ caregivers,^{39,58} as well as nonadherence in PHIV+ youth^{39,59} and none of the interventions developed for PHIV+ youth have been tested in large scale randomized control trials. Further study using prospective cohorts may be necessary to identify specific psychosocial mediators among older youth that could be targeted in interventions for multiple behavioral health risks among adolescent children of HIV-infected women, particularly HIV-infected adolescents.

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