Substance Use and the Development of Sexual Risk Behaviors in Youth Perinatally Exposed to HIV

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Objective To examine the longitudinal association between sexual behavior and substance use in perinatally HIV-infected (PHIV+) and perinatally HIV-exposed-but-uninfected (PHIV−) youth. **Methods** Growth curve modeling was used with data from $N = 340$ PHIV-exposed youth (60.6% PHIV+; 9–22 years) to estimate the onset of penetrative and unprotected sex across time, adding alcohol and marijuana use trajectories as time-varying covariates and examining HIV-status differences. **Results** The odds of penetrative or unprotected sex more than doubled across time. Alcohol and marijuana use significantly increased the odds of engaging in sex and unprotected sex, with no HIV-status differences. The association between unprotected sex and alcohol use was less salient for PHIV+ than PHIV− youth. **Conclusions** Similar to youth from other populations, PHIV+ and PHIV− youth are increasingly engaging in sex and substance use as they age. Targeted interventions to prevent sexual risk behavior and further HIV transmission should address the influence of substance use.

Key words adolescent HIV; longitudinal; perinatal HIV; sexual risk behavior; substance use.

Introduction

In the United States, nearly 11,000 youth (Centers for Disease Control and Prevention [CDC], 2013) are living with perinatal HIV infection (PHIV+), with 3.3 million youth infected before the age of 15 years globally (UNAIDS, 2012). These youth are at substantial risk for poor health outcomes, including nonadherence to antiretroviral treatment (ART), and thus uncontrolled viremia, as well as transmitting the virus to partners through unprotected sex (Sohn & Hazra, 2013). PHIV+ youth in the United States have now aged into adolescence (CDC, 2013), a developmental period where increases in substance use and sexual risk behaviors are common (Brooks-Gunn & Paikoff, 1997; Kandel, Yamaguchi, & Chen, 1992) and frequently co-occur (Elkington, Bauermeister, & Zimmerman, 2011). Substance use begun in adolescence is associated with poor outcomes, including risky sexual behavior, sexually transmitted infections (STIs), and unintended pregnancy (Cook & Clark, 2005; Elkington, Bauermeister, & Zimmerman, 2010; Guo et al., 2002). These outcomes are particularly salient for PHIV+ youth who are placed at considerable risk for substance use and abuse due to a confluence of risk factors associated with the epidemiology of HIV in women and children earlier in the epidemic when many PHIV+ youth were born. This includes high rates of substance use in HIV+ women, including mothers; residence in impoverished inner-city communities with increased exposure to substance use; and disrupted family attachments due to parental illness and death (Havens & Mellins, 2009; Kang, Mellins, Ng, Robinson, & Abrams, 2008; Mellins & Malee, 2013; Mellins et al., 2007). Despite these risks, no study, to our knowledge, has prospectively examined the association between substance use and sexual risk behavior

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across adolescence in PHIV+ youth. Such data are urgently needed from a public health perspective to inform HIV treatment and prevention interventions.

Sexual Behavior in Perinatally Infected Youth

Studies suggest that PHIV+ youth may experience developmental trajectories of sexual behavior and risk that are different from uninfected peers. Some studies have found that PHIV+ youth delay the onset of sexual behavior (Bauermeister, Elkington, Robbins, Kang, & Mellins, 2012; Brogly et al., 2007) compared with the general population and other groups of vulnerable youth. However, once sexually active, studies indicate that these youth engage in high rates of sexual risk behaviors, including unprotected sex, and report high rates of unintended pregnancy (Elkington, Bauermeister, Brackis-Cott, Dolezal, & Mellins, 2009; Ezeanolue, Wodi, Patel, Dieudonne, & Oleske, 2006; Tassiopoulos et al., 2013). Trajectories of sexual behavior in this population may be influenced by the impact of HIV on development. For example, early and lifelong exposure to HIV infection and treatment may result in the delay of the onset of puberty (Buchacz et al., 2003), significant developmental and neurocognitive problems (Brouwers, Belman, & Epstein, 1991; Nozyce et al., 2006; Smith & Wilkins, 2015), and greater social and emotional immaturity compared with same-aged HIV− peers (Donenberg & Pao, 2005; Havens & Mellins, 2009; Wiener and Mellins, 2012). These challenges to ''normal'' development may influence sexual behavior among PHIV+ youth, resulting in either delayed onset of sexual behavior due to emotional, cognitive, or physical immaturity or, conversely, accelerated onset of risk behavior due to impulsivity or judgment problems. Furthermore, unlike that of their same-aged HIV− peers, the sexual activity of PHIV+ youth carries with it decisions related to partner disclosure and fear of partner infection (Marhefka et al., 2011), all within the context of balancing a desire to attain peer acceptance while managing a stigmatizing illness. As PHIV+ youth age, we must now consider the influence of other developmentally normative behaviors aside from HIV, such as substance use, which may further complicate the sexual development of, and promote sexual risk in, PHIV+ youth, and may be an important focus of HIV prevention and care interventions.

Substance Use, Sexual Risk, and PHIV+

In the United States, 71% of high school students endorsed ever using alcohol, and 40% had used marijuana, with rates increasing across grade levels (CDC, 2012). Substance use has been associated with high rates of sexual risk behavior in adolescents (Graves & Leigh, 1995; Guo et al., 2002; Leigh, 2002; Tapert, Aarons, Sedler, & Brown, 2001). Substance use impairs decision-making ability, reduces risk perception and judgment, and may heighten arousal, reducing the likelihood of using condoms and negotiating safer sex practices (Logan, Cole, & Leukefeld, 2002; McKinnon, 1996). However, the role substance use may play in the development (onset) of sexual behavior and sexual risk as PHIV+ youth age is unknown. As PHIV+ youth age, they must navigate decisions around sexual activity in the context of managing a lifelong stigmatizing and transmittable illness while engaging in developmentally normative behavior, which may include using alcohol and other substances. For some, overprotection by caregivers and withdrawal from social circles to manage a stigmatized identity may result in limited opportunities for engaging in substance use and sexual activity. As such, substance use may be unrelated to sexual risk behavior, as these youth continue to delay sexual onset and risk. However, others may engage in substance use precisely to manage the stress associated with a chronic illness, gain independence, or achieve peer acceptance (King, Delaronde, Dinoi, & Forsberg, 1996). Therefore, substance use may confer increased risk for sexual risk behaviors. To date, few interventions have been developed to prevent risk behaviors, particularly unprotected sexual behavior and substance use in PHIV+ youth. For PHIV+ youth who may already be immune-compromised due to poor adherence, substance use may have particularly negative consequences. These youth may experience CD4 cell decline and increased viral load associated with substance use, and have significant risk for secondary HIV transmission to partners owing to inconsistent condom use related to intoxication (Baum et al., 2010; Rafie et al., 2011; Rudy et al., 2010).

Across the few studies examining the link between substance use and sexual risk in PHIV+ youth, findings have been mixed. Cross-sectional studies suggest that substance use and sexual risk behaviors co-occur (Koenig et al., 2010; Mellins et al., 2012) and that substances such as alcohol and marijuana increase the risk of unprotected sex, even after considering protective effects of family and peer characteristics (Elkington et al., 2009). In contrast, a longitudinal study determined that substance use was not associated with onset of sex (Tassiopoulos et al., 2013). Although informative, these studies examined the influence of substance use during early adolescence and prevalence of both sexual behavior and substance use was low. Examining the prospective association between substance use and sexual behavior across adolescence and into emerging adulthood will increase our understanding of how these two behaviors develop and

co-occur as youth increasingly engage in these developmentally normative behaviors over time.

Study Objectives and Hypotheses

The National Strategy for HIV/AIDS has identified the need for creating HIV prevention programs for HIV+ individuals in areas with high seroprevalence (The White House, 2010). Thus, as a first step to informing needed interventions for PHIV+ youth, the current study, located in New York City (NYC; one of the epicenters of the US epidemic), aims to describe the developmental course of sexual risk behavior in a sample of PHIV+ and perinatally HIV-exposed-but-uninfected (PHIV−) youth and determine the influence of alcohol and marijuana use on sexual risk behavior over time using longitudinal data from Project CASAH (Child and Adolescent Self-Awareness and Health Study), a multisite study of emotional and behavioral outcomes in both PHIV+ and a comparison group of PHIV− youth (Mellins et al., 2009). PHIV− youth were chosen as the comparison group for PHIV+ youth because, with the exception of HIV status, their sociodemographic characteristics are, for the most part, similar. Thus, the current study provides a unique opportunity to explore the contribution of youth's HIV infection to substance use and sexual risk above the influence of environmental factors.

First, we examined the onset of sexual and unprotected sexual behavior over time and whether the onset of behaviors differed by youths' HIV status. Consistent with prior findings, we hypothesized that PHIV+ youth may have a delayed sexual onset compared with PHIV− youth (Bauermeister et al., 2012; Brogly et al., 2007). Second, we examined whether alcohol and marijuana use were associated with the onset of sexual risk and whether this association differed by youth's HIV status. Consistent with prior research in other populations, we hypothesized that alcohol and marijuana would be associated with onset of sexual risk (Graves & Leigh, 1995; Guo et al., 2002; Leigh 2002; Tapert et al., 2001), and that HIV+ youth would demonstrate a stronger association between substance use and sexual risk.

Methods

Participants and Procedures

Data came from Project CASAH (removed for review), a longitudinal study of PHIV+ and PHIV− youth designed to examine differences in mental health and behavioral health outcomes, including sexual and drug use risk behaviors. Participants were initially recruited from four NYC medical centers that provide primary and tertiary care to HIV-affected families throughout NYC to complete two interviews (baseline and follow-up) 18 months apart ($M_{\text{years}} = 1.65$, $SD = 0.45$). Participants included the youth and their primary caregiver with the following inclusion criteria: (1) youth aged 9–16 years with perinatal exposure to HIV (as confirmed by medical providers and charts), (2) cognitive capacity to complete the interviews, (3) English or Spanish speaking, and (4) caregiver with legal ability to sign consent for child participation. To isolate the effect of HIV on mental health and behavioral health outcomes, a comparison group of children from similar environments where the main difference was HIV infection (i.e., all youth were perinatally HIV exposed) was required. In the absence of a large enough pool of PHIV− youth, and similar to other studies of this population (Chernoff et al., 2009), multiple children were recruited from the same family providing they met eligibility criteria. Participants were recruited between 2003 and 2008. Of the 443 eligible participants, 11% refused contact with the research team, and 6% could not be contacted by the site study coordinators. A total of 367 (83%) caregiver–youth dyads were approached, of whom $N = 340$ were enrolled at baseline (77% of eligible families; 206 PHIV+ and 134 PHIV− youth). We were able to retain 82.4% of CASAH participants (166 PHIV+ and 114 PHIV−) between baseline and the follow-up interview.

Although not initially planned, additional funding was secured to continue to follow the CASAH cohort (CASAH-2), which involved re-recruiting families from CASAH for three additional follow-up interviews, each 1 year apart. Families were eligible for CASAH-2 interviews if the youth were at least 13 years old and it had been at least 1 year since they completed their first follow-up (FU1) interview. At the time of these analyses, we were able to re-recruit 79% of the youth (166 PHIV+ and 104 PHIV−) who were initially enrolled in the study; the median time interval between FU1 and the second follow-up (FU2) was 3 years ($M_{\text{years}} = 2.89$, $SD = 1.29$). At FU2, youth's age ranged from 13 to 24 years ($M_{\text{age}} = 16.73$, $SD = 2.74$). We observed minimal but statistically significant differences in follow-up time (in years between assessments) by HIV status between baseline and FU1 ($M_{\text{HIV-negative}} = 1.09$, $SD = 0.42$, $M_{\text{HIV-positive}} = 1.28$, $SD = 0.63$; $t = -3.08$, $p = .005$), and FU1 and FU2 ($M_{\text{HIV-negative}} = 2.46$, $SD = 1.06$, $M_{\text{HIV-positive}} = 3.19$, $SD = 1.35$; $t = -4.48$, $p < .001$). Therefore, in all our statistical models, we accounted for potential differences by including HIV status as a covariate in each of our time-varying predictors (see 'Data Analytic Strategy' section). In this analysis, we include the $N = 324$ youth (195 PHIV+ and 129 PHIV−) with data on all key covariate variables at baseline. There were no differences by youth HIV status,

gender, race/ethnicity, age, sexual behavior, unprotected sexual intercourse, or alcohol or marijuana use between the 324 youth included in these analyses and the 16 youth who were excluded owing to missing data (analyses available from authors).

Data sources for all assessment points included (1) caregiver and youth interviews and (2) medical chart data on viral load and CD4 counts. Caregivers and youth were interviewed separately, but simultaneously when possible, by trained bachelor-level interviewers in English or Spanish. Interviews were conducted at the youth's or caregiver's home, their medical clinic, or our research offices. Institutional review board approval was obtained from all study sites. All caregivers provided written informed consent for themselves and their youth who were <18 years of age; youth provided assent if <18 years and consent if ≥18 years. Monetary reimbursement for time and travel was provided.

Measures

Substance Use

Youth alcohol and marijuana use was assessed by the Diagnostic Interview Schedule for Children (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). This tool, developed for trained lay interviewers, is one of the most well-validated, comprehensive, highly structured diagnostic instruments for psychiatric disorders defined by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994). Youth reported if they had ever used (0 = *No*; 1 = *Yes*) alcohol and/or marijuana at all interviews. Too few youth endorsed use of other drugs (e.g., cocaine, heroin, methamphetamine, prescription drugs) to include in this analysis.

Sexual Behavior

Youth sexual behavior was assessed with the Adolescent Sexual Behavior Assessment (ASBA; Dolezal, Mellins, Brackis-Cott, & Meyer-Bahlburg, 2006). The ASBA contained gateway questions so that participants with no sexual experience were not asked about specific sexual practices. At baseline, the ASBA was administered to approximately half the sample using audio computer-assisted self-interview (ACASI) and to half with face-to-face interview as part of a substudy. No differences were found on rates and types of reported behavior owing to mode of administration (removed for review); at FU1 and FU2, sexual behavior was gathered using ACASI for all youth. Lifetime (yes/no) engagement in penetrative sex (vaginal and/or anal) and unsafe penetrative sex (one or more occasions of penetrative sex without a condom), i.e., behaviors that confer the highest risk of HIV transmission, were examined at each follow-up interview. We aggregated reports of vaginal and anal sex behavior into one variable (''penetrative sex'') given the low frequency of anal sex and high overlap with vaginal sex. Oral sex was not included as a risk behavior, as the overwhelming majority of youth who had engaged in oral sex had also engaged in vaginal sex, rendering the analyses for oral sex and penetrative sex essentially the same (available from authors). Substance use-related risk behaviors (e.g., unprotected sex while drunk or high) were also not included given the significant confound with our independent variable; there were no injection drug use risk behaviors (e.g., needle sharing) in this sample.

Youth Characteristics

Youth HIV status was determined via youth enrollment in HIV primary care clinics, verified by clinicians. Youth demographics included age, gender, and race/ethnicity.

Caregiver Characteristics

Caregiver HIV status was assessed via several self-report questions about personal HIV tests and results (HIV infected vs. uninfected/untested). Self-reported demographics included caregiver age, gender, relationship to the child (birth parent vs. non-birth parent), and household income. Household income was calculated in ranges (1 = ≤$5,000; 5 = $20,000–25,000; 13 = >$150,000).

Data Analytic Strategy

We first examined the baseline sample characteristics as well as prevalence of sex and drug use behaviors across all time points, comparing differences by HIV status using *t* tests and chi-square tests as appropriate (Table I). As PHIV+ youth were approximately 1 year older at FU2, we adjusted for age using logistic regression when examining group differences in prevalence of sex and drug use behaviors at FU2. We used Hierarchical Linear Modeling (HLM; v. 7.0) to design multilevel logistic growth curve models of the cumulative onset of penetrative (vaginal and/or anal) and unprotected penetrative sex across time. While a repeated measures regression performs listwise deletion for cases with missing values in one or more data points, HLM maximizes all available data because its algorithms do not require information across all follow-ups to compute growth estimates for all participants (Raudenbush & Bryk, 2002). Therefore, all $N = 324$ cases were used in this analysis. Given our outcomes are dichotomous, we used the Bernoulli distribution to model our binary logistic regression growth curve models. Similar to survival analysis, this approach allowed

Table I. *Sample Demographics by HIV Status Among a Sample of Perinatally Exposed Youth (n = 324)*

	HIV+ (*n* = 195)		HIV− (*n* = 129)		
Characteristics	*N*	%[a]	*N*	%[a]	*t* test/χ^2
Male	98	50.26	65	50.39	0.001
Age[b]	12.71	2.18	12.40	2.35	−1.42
Race ethnicity					
Black	117	60.00	68	51.94	2.06
Hispanic	69	35.38	57	44.19	2.53
Other[c]	9	4.62	5	3.88	0.10
Caregiver HIV+	61	31.28	88	68.22	42.64***
Caregiver is birth parent	68	34.87	90	69.77	37.84 ***
Household income[d]	5.49	3.26	4.60	2.90	−2.51*
HIV characteristics					
CD4+ cell count[e]	601.36	316.61			
Viral load[f]	17,227.16	47,932.17			
ART	152	79.17			
Sexual behavior					
Penetrative sex at baseline	19	9.84	18	14.17	1.40
Penetrative sex at FU1	34	21.38	26	23.64	0.19
Penetrative sex at FU2[g]	86	56.58	48	48.48	0.63
Unprotected sex at baseline	10	5.18	6	4.72	0.03
Unprotected sex at FU1	15	9.43	13	11.82	0.40
Unprotected sex at FU2[g]	42	27.63	30	30.30	0.50*
Substance use behavior					
Alcohol use at baseline	25	12.82	20	15.50	0.49
Alcohol use at FU1	38	23.46	29	25.66	0.18
Alcohol use at FU2[g]	87	56.86	48	48.98	0.71
Marijuana use at baseline	8	4.10	10	7.75	1.97
Marijuana use at FU1	15	9.26	11	9.73	0.002
Marijuana use at FU2[g]	47	30.72	29	29.59	0.71

Notes. [a]Due to missing data, percents are not generated based on the total for each group.
[b]Mean (*SD*).
[c]''Other'' race/ethnicity category includes: White non-Hispanic, Caribbean English, mixed race, and other non-Hispanic.
[d]Mean (*SD*) of a 12-point scale measuring household income; each point represents a $5,000 increase such that 1 = <$5,000, 2 = $5,001–$10,000, 3 = 10,001–$15,000, etc.
[e]Cells/m^3.
[f]Median (*SD*) copies/ml.
[g]Adjusted odds ratio, after adjusting for youth age at FU2.
FU1 = follow-up 1; FU2 = follow-up 2.
*$p \leq .05$; **$p \leq .01$; ***$p < .001$.

us to estimate the log odds of onset of both penetrative sex and condomless sex over time. In these analyses, once a participant endorses sexual behavior or sexual risk at a given assessment, they are coded as ''1'' in subsequent follow-up assessments. We found three cases had inconsistent responses (two participants noted never having had sex at FU1 even though they had said they had sex at baseline, and one participant noted never having had sex at FU2 when they had said yes at FU1). We cleaned these data prior to running our analyses; our results do not change when we exclude these three cases.

We modeled the onset of youth's sexual behavior (i.e., penetrative and unprotected penetrative sex) over time by including variables at Level 1 (i.e., change over time, e.g., time, alcohol and marijuana use) and Level 2 (i.e., person-centered characteristics, e.g., age, race and ethnicity). Our analysis comprised three analytic steps. First, we examined the log odds of having already had sex at baseline. We adjusted for youth's HIV status, sex, age, and race; Latino ethnicity; and whether they resided with a birth parent. Because 100% of birth mothers were HIV+ by definition and almost all birth parents were the mother, caregiver HIV status and type of caregiver were

highly confounded. Thus, we accounted for the type of caregiver relationship (e.g., birth parent vs. non-birth parent) but did not account for caregiver HIV status in our analytic models given that the two variables were highly confounded. Once baseline differences were accounted for, we modeled the changes in sexual onset over time. Each participant contributed to the growth parameter such that the cumulative odds of sexual onset were modeled across each follow-up. Finally, after modeling the linear change, we added the alcohol and marijuana use trajectories, respectively, as time-varying covariates in our model (Table II). We adjusted for HIV status in each of our time-varying covariates. As an example, we present our Level 1 and Level 2 equations below for onset of penetrative sex:

Level 1 Model

$$\text{Prob}(EVERPENT_{ti}=1|\pi_i)=\phi_{ti}$$
$$\log[\phi_{ti}/(1-\phi_{ti})]=\eta_{ti}$$
$$\eta_{ti}=\pi_{0i}+\pi_{1i}*(Wave_{ti})+\pi_{2i}*(Alcohol_{ti})+\pi_{3i}*(Marijuana_{ti})$$

Level 2 Model

$$\pi_{0i}=\beta_{00}+\beta_{01}*(HIVStatus_i)+\beta_{02}*(Sex_i)+\beta_{03}*(\text{Age}_i)+\beta_{04}*(BioParent_i)+\beta_{05}*(Latino_i)+\beta_{06}*(\text{Race}_i)+r_{0i}$$
$$\pi_{1i}=\beta_{10}+\beta_{11}*(HIV\ Status_i)$$
$$\pi_{2i}=\beta_{20}+\beta_{21}*(HIV\ Status_i)$$
$$\pi_{3i}=\beta_{30}+\beta_{31}*(HIV\ Status_i)$$

We found no support for random effects in our growth term parameters, suggesting that there may be limited variability to model diverse trajectories in our sexual onset growth curves. Consequently, we report our findings as fixed-effect models with robust standard errors. Youth who were not sexually active were included in the analysis of unprotected penetrative sex and substance use to avoid making a Type I error; excluding those not active would increase the likelihood of finding a relationship between substance use and sexual risk.

Table II. *Onset of Sexual Behavior Over Time and Its Association to Alcohol and Marijuana Use Across Adolescence in a Sample of Perinatally Exposed Youth (n = 324)*

	Penetrative sex		Unprotected penetrative sex	
Variables	AOR	95% CI	AOR	95% CI
Baseline				
Intercept	0.16	0.06–0.40***	0.03	0.01–0.08***
Youth HIV+ status	0.76	0.37–1.56	1.50	0.64–3.53
Female	0.63	0.41–0.97*	0.99	0.64–1.54
Age	1.55	1.39–1.74***	1.31	1.16–1.48***
Latino ethnicity	0.80	0.51–1.27	0.81	0.50–1.30
Non-Black	0.10	0.03–0.44**	0.30	0.11–0.83*
Birth parent	1.76	1.08–2.85*	1.40	0.86–2.30
Change over time				
Sex behavior[a]	2.51	1.82–3.47***	2.76	1.89–4.02***
Youth HIV+ status	1.40	0.91–2.14	0.83	0.50–1.35
Alcohol use	7.48	3.68–15.21***	4.32	2.13–8.77***
Youth HIV+ status	0.41	0.17–0.99*	0.38	0.16–0.87*
Marijuana use	2.38	1.10–5.16*	2.17	0.99–4.79*
Youth HIV+ status	2.09	0.72–6.02	1.10	0.38–3.23

Notes. Non-Latinos and Blacks served as referent groups for race/ethnicity comparisons, respectively; Females serve as referent group for sex comparisons.
AOR = adjusted odds ratio; CI = confidence interval.
[a]Sex behavior refers to either penetrative or unprotected penetrative sex, as determined by the dependent variable in each model.
¶$p \leq .10$ *$p \leq .05$ **$p \leq .01$ ***$p \leq .001$.

Results

Sample Characteristics: Differences by HIV Status

Table I presents the baseline sample characteristics, and substance use and sexual risk behavior for both PHIV+ and PHIV− youth. There were no significant differences between PHIV+ and PHIV− youth in age, gender, or race/ethnicity. Families of PHIV+ youth reported a slightly higher average annual income ($25,000–30,000) than families of PHIV− youth ($20,000–25,000); yet, the average across both groups was under the New York State poverty line for a family of four people ($t = -2.51$, $p \leq .05$). As noted, and consistent with other studies of this population, significantly fewer PHIV+ youth were living with a birth parent (34.87% vs. 69.77%; $\chi^2 = 37.84$; $p \leq .001$), and thus, fewer were living with a HIV+ caregiver (31.28% vs. 68.22%; $\chi^2 = 42.64$; $p \leq .001$), as 100% of birth mothers were HIV+ by study definition. This is likely due to the fact that early on in the epidemic, mothers of PHIV+ youth were sicker and thus more likely to pass on the virus to their child (Garcia et al., 1999), and also more likely to pass away with less than optimal treatment.

Among PHIV+ youths, the majority (79.17%) were on ART at baseline. The mean CD4+ cell count was 601.36 (median = 572; $SD = 316.6$) cells/m^3. The median HIV RNA viral load was 17,227.16 copies/ml ($SD =$ 47,932.17); 30% had not been told their HIV diagnosis at baseline, 19% at FU1, and only 4% at FU2.

Prevalence of Substance Use and Sexual Behavior by HIV Status

Penetrative sex (vaginal and anal) increased over time for both groups and was reported by 9.84% PHIV+ and

14.17% PHIV− youth at baseline, 21.38% PHIV+ and 23.64% PHIV− youth at FU1, and 56.58% PHIV+ and 48.48% PHIV− youth at FU2. Similarly, unprotected sex also increased and was reported by 5.18% PHIV+ and 4.72% PHIV− youth at baseline, 9.43% PHIV+ and 11.82% PHIV− youth at FU1, and 27.63% PHIV+ and 30.30% PHIV− youth at FU2. There were no differences in penetrative sex by HIV status at all three time points and no differences in unprotected penetrative sex at baseline and FU1; at FU2, PHIV+ youth were significantly less likely to have reported any unprotected sex, after adjusting for age, compared with PHIV− youth (adjusted odds ratio [AOR] = 0.50; 95% confidence interval [CI] = 0.26–0.95, $p \leq .05$). Among those who were sexually active, unprotected sex was reported by 52.63% PHIV+ and 33.33% PHIV− youth at baseline and 48.84% PHIV+ and 62.50% PHIV− youth at FU2; there were no differences in unprotected penetrative sex by HIV status.

The most prevalent substance used by both groups across all time points was alcohol (12.82%–56.86% PHIV+ youth; 15.50%–48.98% of PHIV− youth). Use of marijuana was less frequent in both groups, but also increased over time (4.10%–30.72% PHIV+ youth; 7.75%–29.59% of PHIV− youth). There were no other differences in substance use or sexual behavior by HIV status at each of the time points.

Onset of Sexual Behavior Over Time and Its Association With Alcohol and Marijuana Use

Table II presents the onset of penetrative sex and onset of unprotected sexual behavior over time and their association with alcohol and marijuana use across adolescence.

Penetrative Sex

Females were less likely than males to report having engaged in penetrative sex at baseline (AOR = 0.63; 95% CI = 0.41–0.97, $p < .05$). Odds of penetrative sex at baseline were more likely among youth who were older (AOR = 1.55; 95% CI = 1.39–1.74, $p < .001$) or lived with a biological parent (AOR = 1.76; 95% CI = 1.08–2.85, $p < .05$). Participants who did not identify as Black were less likely to report penetrative sex at baseline than their Black counterparts (AOR = 0.10; 95% CI = 0.03–0.44, $p < .01$). We noted no baseline differences by Latino ethnicity or HIV status.

The odds of commencing penetrative sex were more than doubled at each additional follow-up for the total sample (AOR = 2.51; 95% CI = 1.82–3.47, $p < .001$); there were no differences in onset of penetrative sex over time by HIV status. The odds of engaging in penetrative sex were substantially more likely if youth reported using alcohol (AOR = 7.48; 95% CI = 3.68–15.21, $p < .001$) and/or marijuana (AOR = 2.38; 95% CI = 1.10–5.16, $p < .05$) over time. PHIV+ youth were less likely to report the onset of sexual behavior across adolescence if they used alcohol than PHIV− youth who used alcohol (AOR = 0.41; 95% CI = 0.17–0.99, $p < .05$). The time-varying association between marijuana use and onset of penetrative sex did not differ by HIV status.

Unprotected Sex

Youth who were older (AOR = 1.31; 95% CI = 1.16–1.48, $p < .001$) were more likely to report engaging in unprotected sex at baseline. Participants who did not identify as Black were less likely to report unprotected sex at baseline than their Black counterparts (AOR = 0.30; 95% CI = 0.11–0.83, $p < .05$). We noted no baseline differences in onset of unprotected sex by gender, HIV status, or living with a biological parent.

The odds of commencing unprotected penetrative sex increased at each follow-up (AOR = 2.76; 95% CI = 1.89–4.02, $p < .001$); we noted no differences in the rate of onset of unprotected sex by HIV status. The odds of engaging in unprotected sex over time were over four times greater if youth reported using alcohol (AOR = 4.32; 95% CI = 2.13–8.77, $p < .001$) and twice as likely if the youth used marijuana (AOR = 2.17; 95% CI = 0.99–4.79, $p = .05$). PHIV+ youth were significantly less likely to engage in unprotected sex across adolescence if they used alcohol compared with PHIV− youth who used alcohol (AOR = 0.38; 95% CI = 0.16–0.87, $p < .05$). The time-varying association between marijuana use and onset of unprotected penetrative sex did not differ by HIV status.

Discussion

In this article, we examined the onset of sexual behavior and unprotected sex across adolescence and the effect of substance use on the timing of these behaviors in a sample of youth perinatally HIV infected or uninfected but perinatally HIV exposed. As expected, the onset of sexual behavior increased over time for both PHIV+ and PHIV− youth, with rates increasing more than fourfold from baseline to FU2, an average of 4.5 years later. The prevalence of sexual activity and sexual risk at each time point was consistent with national trends for both groups (Bruckner & Bearman, 2003; CDC, 2012; Flanigan, 2003) and other studies of PHIV+ youth (Tassiopoulos et al., 2013). Among sexually active youth, a nonsignificant pattern emerged such that PHIV+ youth reported higher

rates of unprotected sex at baseline, a trend which was reversed by FU2. One possible explanation for this finding is that PHIV+ youth are monitored frequently by providers who provide messages and reminders, among other things, about sexual health. In contrast, PHIV− youth are likely not receiving regular medical care and may not be exposed to these messages on a frequent basis.

Although rates of alcohol and marijuana use more than tripled from baseline to FU2, these rates were lower than national rates for both PHIV+ and PHIV− youth (Eaton et al., 2012; Johnston, O'Malley, Bachman, & Schulenberg, 2012), despite both groups residing in high-risk environments for substance use. A large body of literature on resilience in youth suggests that despite exposure to adversity (e.g., residing in impoverished neighborhood with high rates of substance use), some youth still achieve positive outcomes or avoid negative trajectories commonly associated with risk factors (Zolkoski & Bullock, 2012). This process is aided by protective factors that can offset the effect of risk factors (e.g., caregiver monitoring) so that negative outcomes can be avoided or minimized. For youth in the current study, exposure to HIV may serve a protective role with respect to substance use. For example, faced with a life threatening illness youth may choose to avoid behaviors that further threaten their health (e.g., substance use) or HIV+ caregivers may receive education and support from their own medical providers that they communicate to their children. Further research that uses a resilience lens and examines the role of HIV in addition to other factors that offset substance use and other poor outcomes in youth affected by HIV is warranted.

On average, PHIV+ youth were engaging in sex and sexual risk behaviors at a similar pace across adolescence as PHIV− youth. After adjusting for key demographic factors, we found no differences in rate of onset of penetrative sex or unprotected sex across time by youth HIV status. That said, the increase in unprotected sex across adolescence is concerning. Unprotected sex is the most prevalent route of HIV/STI transmission for adolescents in the United States (CDC, 2008), and PHIV+ youth are thus at increased risk for transmitting HIV to others as well as acquiring STIs and possibly other more resistant strains of the virus (Cohen, 2004).

Exacerbating this risk was the finding that alcohol and marijuana were strongly associated with the onset of sexual behaviors in this sample. Youth who used alcohol or marijuana across adolescence were more than twice as likely to engage in sexual debut or unprotected sexual behavior; alcohol was associated with a sevenfold increase in sexual onset at each time point. These findings are consistent with prior studies examining the link between alcohol and marijuana use and sexual risk in youth (Elkington et al., 2010; Guo et al., 2002; Tapert et al., 2001). There are likely different, but potentially related, mechanisms through which substance use increases the risk of engaging in unsafe sexual behavior in these youth. For example, reduced inhibition and impaired judgment due to the effects of intoxication (Logan et al., 2002; McKinnon, 1996), affiliation with high-risk peer groups who use marijuana or alcohol and engage in sexual risk behaviors (Houck et al., 2006), or a confluence of the two (Elkington et al., 2011) may explain the link between sexual risk and substance use. Future studies that use event analysis in addition to social network analytic approaches may shed light on the specific links between sexual risk, alcohol, and marijuana in these youth.

The association between alcohol use, sexual onset, and sexual risk behavior varied by HIV status. Although the association between alcohol use, sexual onset, and unprotected sex was still present for PHIV+ youth, the magnitude of these associations were significantly lower when compared with those observed for PHIV− youth. The current findings characterize the degree to which the onset of sexual activity and sexual risk over time is globally associated with alcohol use in PHIV+ and PHIV− youth. While an important first step, these analyses did not disentangle reasons for the HIV status differences in sexual risk associated with alcohol use, a key step for future intervention development. Qualitative work from this population has revealed that PHIV+ youth liken their HIV status to ''carrying a weapon'' (Marhefka et al., 2011). Therefore, they may be more vigilant about engaging in sexual risk if they are using alcohol. Moreover, given their HIV status, these youth may experience greater monitoring and supervision from caregivers (e.g., have an earlier curfew), which may change the context for alcohol use and sexual risk. Further research that aims to understand potential event level as well as contextual factors related to alcohol use and sexual risk may begin to untangle this relationship in youth infected and affected by HIV and determine how best to approach the role of alcohol use and unprotected sex in interventions for PHIV+ youth.

To our knowledge, this is the first study to identify an association between substance use and sexual risk over time in a sample of PHIV+ and PHIV− youth. However, as with other populations of high-risk youth (Browning, Leventhal & Brooks-Gunn, 2005; Pantin, Schwartz, Sullivan, Prado, & Szapocznik., 2004), future research that uses an ecological approach and examines multilevel risk factors that may mediate or moderate the link between

substance use and sexual risk are necessary. For example, understanding the changing influence over time of family/parent relationships and experiences of childhood sexual abuse or maltreatment, in addition to contextual/structural factors, such as youth's living situation, education/employment, or neighborhood characteristics, will inform age-appropriate prevention interventions that target sexual risk and substance use for youth infected with and exposed to HIV.

Limitations

Several limitations of this study should be noted. Participants were recruited from HIV primary care clinics, and findings may not generalize to youth in other settings. Although we were able to recruit and interview 76% of participants who met criteria for our study in the recruitment sites, this sample of convenience may not reflect the larger population of PHIV+ and PHIV− adolescents, particularly those living outside of NYC or not enrolled in HIV care clinics. We could not determine whether substance use and sexual risk are causally related, correlated traits, or are spuriously associated owing to the effect of other structural variables (e.g., living in high-poverty areas) commonly noted among high-risk youth. Multiple children from the same family were included in this study ($n = 102$ youth). Due to power limitations, we were unable to address this issue by including family as a third level (i.e., family-level clustering) in our analyses. The length of time between FU1 and FU2 was highly variable; in our analyses, we found differences in follow-up length of time between PHIV+ and PHIV− youth. In our multivariate analyses, we adjusted for HIV status in both our baseline and time-varying estimates to reduce potential confounding. The data are self-reported and are subject to issues of social desirability and other biases related to sex and drug use reporting. PHIV+ youth often have delayed puberty due to HIV disease. Given limited data on puberty for this study, we were unable to examine the role of pubertal development in the onset sexual behaviors. We did not capture sexual risk associated with multiple partners or partner HIV status, and as such our estimation of sexual risk may be conservative. Because the majority of youth knew their diagnosis, and disclosure and age were highly confounded in the current sample (youth who were undisclosed to at baseline were all <13, and by FU2 almost all youth knew; Santamaria et al., 2011), we were unable to examine the influence of disclosure on sexual behavior and substance use. Studies that have followed cohorts of PHIV+ youth from early childhood may be better able to tease apart the influence of disclosure on sexual development. We did not capture data on the role of childhood maltreatment or sexual abuse and so could not examine the influence of these variables on the development of sexual behavior and sexual risk over time. Relatedly, we did not ask participants to differentiate between consensual and nonconsensual sex encounters when reporting sexual behavior.

Despite these limitations, findings from the current study have important clinical and policy implications. Twenty-eight percent of PHIV+ youth and 23% of PHIV− youth had engaged in unprotected sex at the FU2 when they were, on average, 17 years old. As PHIV+ and PHIV− youth move into early adulthood, HIV prevention interventions will need to adapt to their changing developmental needs. To date, there are few sexual risk interventions for PHIV+ youth, and those that exist target younger youth (i.e., aged 10–14 years; e.g., McKay et al., 2014). Currently there are no published evidence-based interventions for older PHIV+ youth. Data from the current study show that PHIV+ youth are engaging in risk behaviors as they age and that these patterns of behavioral risk are similar to those of other high-risk youth (e.g., urban minority youth; Romer et al., 1994). Even though PHIV+ youth may not be engaging in more risk behaviors than their PHIV− peers, studies show that PHIV+ youth have greater rates of ART resistance and are more likely to not be virally suppressed than adults with HIV (Tassiopoulos et al., 2013; Van Dyke et al., 2014), suggesting that these youth are at greater risk for transmission to others through unprotected sex. Therefore, interventions for PHIV+ youth are needed and may be adapted from existing interventions developed for other high-risk youth. Sexual risk reduction interventions for older PHIV+ youth that help youth balance their age-normative interests in sexual activity and substance use with health and transmission needs related to their HIV infection, such as partner disclosure, timing of sexual onset, pregnancy intentions, and adherence to treatment and care, may be particularly helpful. We found that PHIV− youth are also engaging in sexual risk behaviors over time, thus increasing their risk for HIV infection, particularly if they are using alcohol. Often, PHIV− youth are not connected to regular health care or other support services as compared with their PHIV+ counterparts and typically reside in high HIV seroprevalence communities (Mellins et al., 2012). The challenge for the field is to find these youth as they age to deliver targeted interventions before they fall out of traditional service systems.

Finally, the data suggest that HIV risk interventions for PHIV+ and PHIV− youth should also address substance use and its link to sexual risk behavior, particularly alcohol

use for PHIV− youth. Given the high risk for transmission in PHIV+ youth, sexual risk reduction interventions that address substance use are critical to reduce their sexual risk behaviors and increased likelihood of spreading the virus (Elkington et al., 2010, 2011). Similarly, substance use treatment and prevention interventions designed for these youth should also address sexual risk. Although rates of substance use are relatively low, our data suggest use is increasing rapidly over time. Clinicians need to be prepared to address this issue as PHIV+ and PHIV− youth age into young adulthood, a highly vulnerable period for substance abuse.

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