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HIV and HSV-2 incidence among Adolescent Mothers in South Africa: A Longitudinal Analysis of HIV Prevention Trials Network 068 Data

Allison K. Groves, PhD[1], **Nivedita L. Bhushan, PhD**[2], **Marie C.D. Stoner, PhD**[3], **F Xavier Gómez-Olivé, PhD PhD**[4,5], **Kathleen Kahn, PHD**[4,5], **Audrey E. Pettifor, PhD**[2,4]

[1]Department of Community Health and Prevention, Drexel University, Philadelphia, PA, USA

[2]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[3]Women's Global Health Imperative, RTI International, Berkeley, California, USA

[4]MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, Gauteng, South Africa

[5]INDEPTH Network, Accra, Ghana

Abstract

Background: Adolescent motherhood is common in South Africa and occurs against a backdrop of high HIV risk. While childbearing during adolescence may result in social and economic strain that may negatively impact health, there has been limited study of whether adolescent motherhood increases risk of HIV or HSV-2 acquisition or engagement in high-risk sexual partnerships.

Setting: Data are from HIV Prevention Trials Network (HPTN) 068, a longitudinal conditional cash transfer study of adolescent girls and young women (age 13–23) in rural South Africa.

Methods: We used survival analysis to estimate hazard ratios to determine if adolescent motherhood (live birth before 20 years) predicted incident HIV and incident HSV-2 and GEE for behavioral risk ratios to determine if adolescent motherhood was associated with transactional sex and age-disparate partnerships.

Results: Of 2,452 adolescent girls and young women who were HIV-negative at baseline, 5% were adolescent mothers; 16% were adolescent mothers by the end of the study period. After controlling for covariates, adolescent motherhood predicted incident HSV-2 acquisition (AHR: 1.30, 95% CI: 1.01–1.95), but not HIV acquisition (AHR: 1.19, 95% CI: 0.76–1.86). Adolescent motherhood was also associated with being in an age-disparate partnership (ARR: 1.30, 95% CI: 1.07–1.58), but not transactional sex.

Conclusion: Adolescent motherhood increased risk of HSV-2 and engagement in age-disparate partnerships, both known risk factors for HIV infection. STI screening and/or tailored combination

CORRESPONDING AUTHOR: Ali Groves, 3215 Market Street 416, Philadelphia, PA 19140 USA, aligroves@drexel.edu, Fax: 267.359.6109, Phone: 267.359.6274.

HIV prevention interventions that account for the context of adolescent motherhood are critical to maximize adolescent mothers' long-term health and to meet UNAIDS 95–95-95 targets by 2030.

Keywords

adolescent mother; teen pregnancy; HIV; HSV-2; age-disparity; transactional sex

Introduction

Adolescent motherhood is common in South Africa and occurs against a backdrop of high HIV and Herpes Simplex Virus type 2 (HSV-2) risk. Nearly one third of South African women have given birth before the age of 20.[1] Adolescent pregnancy is associated with increased risk of mortality for mothers and infants.[2] Specifically, in lower and middle income countries, the leading cause of death for adolescent girls between ages 15–19 is due to complications of pregnancy and childbirth,[3] and infants of mothers under 20 are significantly more likely to be stillborn or to die in the first week of life than infants of mothers 20–29.[4]

At the same time, adolescent girls and young women (AGYW) bear a disproportionate burden of HIV and HSV-2 in the region. In South African studies with general populations, the estimated HIV prevalence among adolescent girls between 15–19 is 5.8%[5]. Moreover, HIV incidence among adolescent girls between 15–19 years is four-to-five times higher than among adolescent boys of the same age.[6] The estimated prevalence of HSV-2 among adolescent girls between 15–19 in the African region is 21.7%[7]. Furthermore, adolescent girls in South Africa are more than three times more likely to be HSV-2 infected than adolescent boys.[8] HSV-2 is a sexually transmitted infection that can lead to ulcerative infection of the genitals[9], in rare cases is associated with negative pregnancy outcomes[10], and finally, is associated with increased risk of HIV acquisition.[11,12]

Despite extraordinarily high levels of pregnancy, HIV and HSV-2 among adolescent girls, there has been limited study of whether HIV and HSV-2 acquisition are negative consequences of adolescent motherhood. In a longitudinal study in the Eastern Cape with adolescents between the ages of 15–26, early adolescent motherhood (pregnant before 16 years) was associated with a three-fold increase in HIV acquisition, but later adolescent motherhood (pregnant between 16–19 years) was not associated with increased risk of HIV acquisition.[13] However, the participants in the cohort study were high risk (i.e., they had an earlier average age of sexual initiation than the national average and almost 9 out of 10 had a history of being sexually active at baseline), potentially limiting the generalizability of the findings. In another prospective study in Uganda, the unadjusted rate ratio of incident HIV among pregnant adolescents aged 15–19 was 2.82 (95% CI: 1.25–6.24) compared to non-pregnant and non-lactating adolescents;[14] however, the authors did not examine whether the incident rate ratio (IRR) of HIV was higher among pregnant adolescents after adjusting for confounders.[14] Interestingly, the authors did find that pregnant adolescents between ages 15–29 (broader age categorization) had a higher adjusted IRR of HIV acquisition (IRR: 2.15, 95% CI: 1.33–3.47) than non-pregnant and non-lactating women in the same age group. Of note, neither study examined adolescent motherhood continuously in alignment

with the World Health Organization (WHO) definition of adolescence (10–19 years).[15] As far as we know, no other studies in sub Saharan Africa have examined the relationship between adolescent motherhood and incident HIV infection and/or incident HSV-2.

Contributing to the knowledge deficit is a gap in understanding of whether there are differences between adolescent mothers and adolescent non-mothers in sexual risk behaviors or sexual partnership types, especially those which might be motivated, at least in part, by a need to fulfill basic needs.[16,17] Such behaviors include transactional sex, or "non-commercial, non-marital sexual relationships motivated by an implicit assumption that sex will be exchanged for material support or other benefits (pg. 187)"[16] as well as engagement in age-disparate partnerships, or a relationship in which the age difference of one's sexual partner is 5 years or more.[18] In both cases, male provision, or young women's dependence on male partners for financial and/or material support, may result in young women's weakened relationship power, affecting their ability to negotiate safe sex and subsequently increasing their susceptibility to HIV and/or HSV-2.[18,19]

Becoming an adolescent mother can contribute to economic strain in households, and as such, may increase their engagement in transactional sex and/or age-disparate partnerships. Most pregnancies among South African adolescents are unplanned and occur among unmarried adolescents.[20–22] For many families, adolescent pregnancy is the first acknowledgement of the fact that the adolescent is sexually active.[23] Per qualitative research in rural South Africa, adolescent mothers most commonly live with their natal families during pregnancy and after childbirth. Young mothers' natal families tend to prioritize the solicitation of financial and social support from the father's family over cementing the union, with varying degrees of success.[24,25] Thus, it is not uncommon for the adolescent pregnancy (and subsequent motherhood) to result in economic strain within the household. In accordance with existing literature in which household-level poverty is associated with increased transactional sex,[16,26–29] we posit that adolescent mothers will be more likely than non-adolescent mothers to engage in transactional sex and/or seek older partners to offset the costs of having a child in adolescence.

Therefore, the purpose of this longitudinal analysis is twofold: (1) to determine whether adolescent motherhood is associated with an increased risk of incident HIV and HSV-2 infection among South African girls; and (2) to examine whether adolescent mothers are more likely than non-adolescent mothers to engage in transactional sex and age-disparate relationships.

Methods

Study setting

The data for the current study come from HPTN 068, a phase III randomized controlled intervention trial which assessed whether a conditional cash transfer intervention (CCT) reduced young women's risk of HIV acquisition (for more details on study design, questionnaires, and laboratory procedures see the baseline and main trial publications).[30,31] The study took place in Mpumulanga province, South Africa. Participants resided in the Agincourt health and socio-demographic surveillance system (HDSS) site, which includes

28 villages in a deprived and densely populated, but rural area in Mpumalanga province in north-east South Africa, and has an HIV prevalence of 45% among individuals between the ages 15–84.[32]

Recruitment and retention of original sample

Starting in 2011, HPTN 068 enrolled 2,533 young women, aged 13 to 20, who were attending high school grades 8 to 11, not currently pregnant, and had at least one parent/guardian in their household. Young women were then randomized to receive a monthly cash transfer conditional (CCT) on 80% school attendance each month. Young women were eligible to receive this transfer until the completion of grade 12.

The intervention trial visits occurred approximately annually and include baseline (T_1), year 1 (T_2), year 2 (T_3), and year 3 (T_4) assessments. Girls exited the intervention trial when they completed high school or when the study ended. The last intervention study visit (or "main study" visit) to assess the impact of the CCT occurred in March of 2015. Girls exited the intervention study when they completed grade 12 or when the intervention ended, and as such, there is variability across participants in the number of follow up visits completed during the cash transfer trial. Nearly all participants (i.e., 91%) completed at least one follow up assessment during the CCT prior to completing grade 12 or exiting the study. Following the main study (2011–2015), one additional assessment (T_5) with all available participants was conducted approximately one year after the conclusion of the intervention trial. All 2,533 participants were eligible to complete the post-intervention assessment, and more than 80% of participants completed the post-intervention visit. In total, young women who enrolled in HPTN 068 could participate for a period of 6 years, ranging from 2011–2017.

Each study visit included an Audio Computer-Assisted Self-Interview (ACASI). The ACASI contained self-reported information on pregnancy, sexual behaviors, and other characteristics of the AGYW and her sexual partners. HIV and HSV-2 testing were also conducted at all study visits. The research was approved by the IRB at the Division of AIDS, the University of North Carolina (UNC), the University of Witwatersrand, and the Mpumalanga Department of Health.

Measures

HIV and HSV-2 were assessed from biological specimens collected at follow up assessments. Adolescent motherhood, sexual relationship, and all other covariates were taken from the ACASI interviews.

Adolescent motherhood was based on an adolescent's current age and an adolescent's response to the following item: "How many living children do you have, that you have given birth to?" Those who were aged 19 and younger and reported a living child were coded as 1 for adolescent motherhood, all others were coded as 0. Once an adolescent mother reported a living child, she was considered exposed to adolescent motherhood for all follow-ups.

HIV incidence was determined using two HIV rapid tests performed in parallel followed by a confirmatory test, if one or both rapid results were HIV reactive. Detailed procedures for HIV testing and laboratory procedures are described in the trial paper.[31]

Herpes Simplex Virus Type 2 (HSV-2) incidence was determined using the Herpes Simplex Virus Type 2 IgG ELISA assay (Kalon Biological, LTD Guildford, UK) using an index cutoff of 1.5),[33] followed by a confirmatory test at the HPTN laboratory center. Detailed procedures for HSV-2 testing and laboratory procedures are also described in the trial paper.[31]

Transactional sex and frequent transactional sex were measured drawing on questions from the sexual partner grid, in which women were asked about sexual behavior in the past three months with up to three partners at each follow up visit. First, we constructed a binary measure based on women's response to the following two questions: "did you feel like you had to have sex with [initials] because they gave you money?" or to "did you feel like you had to have sex with [initials] because he gave you things [airtimes, cellphone, groceries, etc]?" Women who responded yes to either were coded as 1 for transactional sex; those who respond no to both questions were coded as '0'. We also created an additional binary measure, frequent transactional sex, where women received a '1' for transactional sex with a partner that gave money or gifts frequently (*frequent transactional sex*) and 0 if either 1) no transactional sex; or 2) transactional sex with infrequent exchange (*infrequent transactional sex*). Frequent exchanges were defined as receiving money weekly or gifts 'often' or 'always', in contrast to infrequent exchanges (having received money once or monthly and gifts 'a few times' or 'once' or 'none').[19]

Age-disparate partnership was measured as having had at least one sexual partner >5 years older at each follow-up visit. Girls who did not report a partner at a given visit were coded as not being in an age-disparate partnership. If all partner ages were missing, then it was coded as missing.

Covariates include the following baseline measures: age of young woman at baseline and HPTN 068 study intervention arm assignment. Time-varying lagged controls include schooling (current grade in school), physical intimate partner violence, orphan status, ever had sex, socioeconomic status (measured as quartiles of per-capita household consumption), and depression. These variables were selected a priori and have been shown to be associated with incident HIV infection, HSV-2 infection, and HIV-related sexual behaviors among AGYW in Southern Africa[34–38]. The construction of various covariates has been described in prior publications[26,29,31,33].

Analysis

First, we described participant characteristics and outcomes at baseline. Second, we used separate Cox proportional hazard regression models to estimate unadjusted and adjusted hazard ratios (AHR) for the relationship between adolescent motherhood, incident HIV infection, and incident HSV-2 infection. Adolescent motherhood was treated as a time-varying covariate in the models. The origin for each AGYW for the survival analysis was the date where they became sexually active (i.e., reported ever having had sex). Note that if an AGYW reported being sexually inactive (i.e., never having had sex) but had a child (n=13), we recoded them as sexually active. As sexual initiation would have occurred sometime between surveys, the time they entered the risk set was the time of the last survey. If they were sexually active at baseline, this date was the date of enrolment in the study. Time

was modelled in continuous months from this date of origin until date of detection of HIV or HSV-2 infection, date of visit before loss to follow up, outmigration or administrative censoring at the last visit. Finally, we used separate log-binomial regression models to estimate unadjusted and adjusted risk ratios (ARR) for the association between adolescent motherhood and sexual behaviors (transactional sex and age-disparate partnerships). The adolescent motherhood exposure was lagged by one time point; the exposure was from the previous time point and the outcomes were sexual behaviors in the past three months measured at the current time point. We fit GEE models to account for the non-independent repeated measures from the same participant using an exchangeable correlation structure for the working correlation matrix. All models were adjusted for covariates described previously. All analyses were conducted using StataSE, version 14.2 (College Station, TX).[39]

To examine the robustness of our findings we undertook the following sensitivity analysis: we examined the exposure of motherhood on outcomes for all women in the sample (i.e., inclusive of young adult women between 20–23 who were mothers), and the pattern of results were similar. We did not have statistical power to examine whether there were differences in outcomes for subsets of adolescent mothers (i.e., very young (14–17) and older adolescents (18–19)).

Results

As seen in Table 1, of 2,452 AGYW whom were HIV-negative at baseline, 6% were adolescent mothers at baseline (n=149). By the end of the study period, just over one in six (16%) were adolescent mothers (n=318).

At baseline, adolescent mothers were less likely to report both parents living (60% vs 67%, p=.001) and were more likely to be in the poorest SES quintile (40% vs 31%, p=.019) (Table 1). Furthermore, adolescent mothers at baseline had higher sexual risk than non-mothers; they were significantly more likely to have ever had sex (93% vs 21%, p<.001), were more likely to report unprotected sex in the past 3 months (38% vs 6%, p<.001), were more likely to report ever having an older partner (19% vs 4%, p<.001), and more likely to report ever having had transactional sex (17% vs 2%, p<.001).

Table 2 reports the hazard ratios for the association between adolescent motherhood on HIV incidence and HSV-2 incidence in the entire sample. In unadjusted analyses, adolescent motherhood was not associated with increased risk of HIV acquisition for adolescent motherhood (hazard ratio (HR): 1.28, 95% CI: 0.87, 1.88)), though the observed trend was in the hypothesized direction. After adjusting for covariates, the association between adolescent motherhood and HIV incidence was further attenuated (adjusted hazard ratio (AHR): 1.19, 95% CI: 0.76, 1.86)). Adolescent motherhood was associated with HSV-2 incidence in both unadjusted (HR: 1.44, 95% CI: 1.01, 2.06) and adjusted analysis (AHR: 1.30, 95% CI: 1.01, 1.95).

Finally, Table 3 reports the associations between adolescent motherhood and the following outcomes: involvement in an age-disparate relationship, transactional sex, and frequent

transactional sex. Adolescent motherhood was associated with a higher likelihood of having an older partner in the past three months in unadjusted (RR: 3.32, 95% CI: 2.91, 3.80) and adjusted analysis (ARR 1.30, 95% 1.07–1.58). Adolescent motherhood in the past year was positively associated with transactional sex and frequent transactional sex in the past three months (risk ratio (RR): 3.72, 95% CI 3.26–4.25; RR: 3.49, 95% CI 2.86–4.25, respectively)); however, the results for both estimates were attenuated after adjusting for covariates (adjusted risk ratio (ARR): 1.10, 95% CI: 0.92–1.31; ARR: 0.78, 95% CI 0.54–1.13, respectively)).

Discussion

Adolescent motherhood was associated with increased incident HSV-2 and with having engaged in an age-disparate relationship in the past three months. While we did not see a significant effect of adolescent motherhood on HIV, our results suggest that having a child as an adolescent increases young women's HIV-related risk.

As far as we know, this is the first study to demonstrate an association between adolescent motherhood and HSV-2 incidence. HSV-2 on its own can lead to significant morbidity (ulcerative infections of the genitals)[9] and in rare cases, neonatal morbidity and mortality.[10] HSV-2 infection increases one's risk of HIV acquisition by nearly threefold,[11] and the risk may be even greater among those newly infected.[12]

In addition, we found that adolescent motherhood may similarly affect risk of incident HIV. First, there were similar point estimates between HIV and HSV-2. Second, HIV and HSV-2 are associated,[40] and HSV-2 is often used as a proxy for HIV.[41] Finally, the point estimate is above 1, which is indicative of an effect, however, we did not have a large number of HIV infections among all adolescents or among adolescent mothers, which limited power to see a significant association. These findings are somewhat aligned with the only other study to examine the longitudinal relationship between adolescent motherhood and HIV.[13] In that study, while very young adolescent mothers (<16 years) had increased risk of HIV acquisition, older adolescent mothers (16–18) did not. Though we were underpowered to examine whether the association varied by age, a strength of our analysis is the continuous examination of motherhood across a broader age range of adolescents.

Given the link between adolescent motherhood and incident HSV-2 (and to a lesser extent, HIV), we also explored whether adolescent mothers were more likely to engage in sexual partnerships that might be motivated at least in part by a need to fulfill basic needs related to the economic costs of childbirth. Consistent with our hypothesis, adolescent mothers were significantly more likely than non-adolescent mothers to be in age-disparate partnerships. Our longitudinal results build on the cross-sectional findings previously reported by Christofides et al., in which mothers were more likely to report being in age-disparate relationships at baseline than non-adolescent mothers.[13] On the other hand, the differences in transactional sex between adolescent mothers and non-adolescent mothers were attenuated after adjusting for confounders. Findings suggest there may be meaningful differences in adolescent mothers' engagement in age-disparate relationships and in transactional sex. That is, adolescent mothers may be more likely than non-adolescent

mothers to seek partnership with an older man because they perceived older men will be able to provide needed economic stability. On the other hand, there may be no difference between adolescent mothers and non-adolescent mothers in engagement in transactional sex because transactional sex in this context may not be driven by basic needs, but rather by desires to improve social status and/or to receive material expressions of love.[42] Qualitative research with adolescent mothers is needed to shed additional light on how economic needs following childbirth shape sexual partnership formation and sexual behavior. Further, given that economic need may increase engagement in concurrent, or overlapping sexual relationships[43,44], future research might also examine whether adolescent mothers are more likely than non-adolescent mothers to engage in concurrent sexual partnerships.

Our study has several limitations. First, adolescents who were not enrolled in school or were pregnant at baseline were not eligible to participate in the original trial. Relatedly, adolescents had to be aged >13 years or older to participate in the original trial. As such, our sample likely excludes adolescents highly vulnerable to future HIV infection, including very young adolescent mothers (i.e., those between 10–12 years), which may underestimate effect estimates. Second, we are not able to determine from our survey items whether the sexual partners that adolescent mothers identified at the follow up surveys were the fathers of their children. Quantitative research to describe trajectories and outcomes of adolescents' relationships with the father of their children both during and after pregnancy are needed. Relatedly, measurement of the onset of adolescent motherhood and of sexual risk behaviors is imperfect: young women could have become an adolescent mother at any time in the past year and young women report their engagement in transactional sex and/or having an older partner in the past three months. Given such, there may be some young women who were pregnant or had just given birth at the time of engaging in sexual risk. Finally, it is possible that it is the pregnancy itself – and not motherhood – that contributes to vulnerability to HIV. We lack the data to assess if findings change when we include all teenagers who report pregnancy (which includes those who miscarried or terminated their pregnancy) as compared to those who report a live birth.

Despite these limitations, our study provides novel evidence that adolescent mothers comprise a subset of AGYW at increased risk of incident HSV-2 infection and age-disparate sex, both known risk factors for HIV infection. While existing prevention and treatment options for HSV-2 are somewhat limited,[45] an effective vaccine against HSV-2 could yield substantial health gains for adolescent girls broadly, and adolescent mothers, specifically.[40,46] In addition, interventions that reduce teen pregnancy by increasing adolescent access to sexual health education and contraception,[47] are likely to reduce HIV risk long-term. Moreover, given the high prevalence of adolescent motherhood in South Africa, HIV prevention interventions tailored for adolescent mothers are also critical. While evidence of effective programs for adolescent mothers is nascent,[48,49] combination prevention interventions which increase pregnant and parenting adolescents' access to female-controlled prevention methods like pre-exposure prophylaxis (PrEP), offered alongside other social and structural interventions, may be particularly promising avenues for future evaluation. It is equally pressing to identify and scale up interventions which increase adolescent mothers' access to contraception postpartum to reduce repeat pregnancy during adolescence.

Given that adolescents in Africa are the fastest growing population in the world,[50] prevention of HIV among adolescent mothers is necessary to ending the AIDS epidemic by 2030,[51] and to ensuring the health and well-being of the continent.

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Table 1.

Participant Characteristics by Adolescent Motherhood at Baseline (N = 2542)

	All Participants* (N = 2452)		Adolescent mothers (N = 149)		Not Adolescent mothers (N = 2303)		Difference Between Groups
	N	%	N	%	N	%	P-Value
Demographics							
Age							
13–14	739	29%	2	1%	737	32%	
15–16	1009	40%	30	20%	979	43%	
17–18	505	20%	91	61%	414	18%	
19–21+	109	4%	26	17%	83	4%	p < 0.001
Orphanhood							
Both Parents Living	1,625	64%	89	60%	1,536	67%	
One Parent Living	519	20%	49	33%	470	20%	
No Parents Living	102	4%	6	4%	96	4%	
Unknown	206	8%	5	3%	201	9%	0.001
Socio-Economic Position							
1st Quintile (Poorest)	766	30%	60	40%	706	31%	
2nd Quintile	460	18%	30	20%	430	19%	
3rd Quintile	388	15%	24	16%	364	16%	
4th Quintile	432	17%	23	15%	409	18%	
5th Quintile (Richest)	312	12%	12	8%	300	13%	0.019
Sexual Behaviors							
Ever Had Sex							
Yes	620	24%	139	93%	481	21%	
No	1,742	69%	10	7%	1,732	75%	p < 0.001
Any Unprotected Sex in Past 3 Months							
Yes	184	7%	56	38%	128	6%	
No	2,160	85%	89	60%	2,071	90%	p < 0.001
Any Older Partner (> 5 Years)							
Yes	129	5%	29	19%	100	4%	

	All Participants* (N = 2452)		Adolescent mothers (N = 149)		Not Adolescent mothers (N = 2303)		Difference Between Groups
	N	%	N	%	N	%	P-Value
No	2,195	86%	118	79%	2,077	90%	p < 0.001
Any Transactional Sex							
Yes	82	3%	25	17%	57	2%	
No	2,128	84%	104	70%	2,024	88%	p < 0.001
Frequency of Transactional Sex							
Frequent	39	2%	9	6%	30	1%	
Infrequent or None	2,413	95%	140	94%	2,273	99%	p < 0.001

*Totals do not sum to 100% due to missing data

Table 2.

HIV and HSV-2 Incidence by Adolescent Motherhood

	Unadjusted		Adjusted^		Unadjusted		Adjusted^	
	HIV		HIV		HSV-2		HSV-2	
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI
Adolescent Motherhood	1.28	(0.87, 1.88)	1.19	(0.76, 1.86)	1.44*	(1.01, 2.06)	1.30*	(1.01, 1.95)

*p < 0.05

^Estimates adjusted for age, 068 intervention arm, in school, assets, orphanhood, ever having sex, intimate partner violence, and depression

Table 3.

Sexual Behaviors by Adolescent Motherhood

	Unadjusted		Adjusted^	
	RR	**95 % CI**	**RR**	**95 % CI**
Transactional Sex (Binary: Any vs No)				
Adolescent motherhood	3.72*	(3.26, 4.25)	1.10	(0.92, 1.31)
Transactional Sex (Binary: Frequent vs Infrequent)				
Adolescent motherhood	3.49*	(2.86, 4.25)	0.78	(0.54, 1.13)
Any Older Partner (> 5 Years)				
Adolescent motherhood	3.32*	(2.91, 3.80)	1.30*	(1.07, 1.58)

*p < 0.05

^Estimates adjusted for age, 068 intervention arm, in school, SES, orphanhood, ever having sex, intimate partner violence, and depression

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