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Recently formed age-disparate partnerships are associated with elevated HIV-incidence among young women in South Africa

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Abstract

Objective: Cross-sectional and cohort studies draw different conclusions on whether age-disparate partnerships increase HIV-acquisition risk for young women. We investigated whether age-disparities were associated with HIV-infection risk early in relationships. This could result in the exclusion of women who seroconverted during high-risk age-disparate partnerships from cohort studies of HIV-incidence – which exclude HIV-positive women – and explain null findings in these studies.

Design: Prospective cohort study

Methods: We used data on 15–24 year-old, HIV-negative women in heterosexual partnerships (N=830) in KwaZulu-Natal, South Africa. The association between age-disparate partnering (i.e.,

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Authors' contributions

ABMK is the principal investigator of the HIV Incidence Provincial Surveillance System (HIPSS). ABMK, CC, and DK, were responsible for HIPSS study operations and quality assurance. BMB, AV, ABMK and GG were responsible for the concept of the analysis for this paper. All authors contributed to the interpretation of the data, and manuscript preparation; all authors approved the final version of the report.

Conflicts of Interest and Source of Funding

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male partner ≥5 years older) and subsequent HIV-seroconversion was assessed using Cox hazard models. We examined heterogeneity in HIV-acquisition risk by duration of partnership (defined by quartiles) at cohort enrolment.

Results: During 1139 person-years (mean: 1.4 years) of follow-up, 54 (6.5%) women seroconverted, a weighted HIV-incidence estimate of 4.41/100 person-years (95% CI 3.30–6.06). HIV-acquisition risk did not differ significantly between women in age-disparate vs. age-similar partnerships (aHR 1.10, 95% CI 0.55–2.21). However, for women in the shortest partnership quartile (<1.09 years) at baseline, risk of HIV-seroconversion was higher for women in age-disparate partnerships (aHR 3.13, 95% CI 1.02–9.65, p=0.047). HIV-acquisition was not statistically different by partnership type among women in longer partnerships.

Conclusions: The association between age-disparate partnerships and HIV-acquisition risk is evident early in young women's relationships. Results provide a potential explanation for null findings in cohort studies, whose research designs may exclude women in such partnerships, and affirms the elevated risk of HIV acquisition for young women in age-disparate relationships.

Keywords

HIV acquisition; HIV incidence; HIV infection risk; age-disparate sexual relationships; partner age difference; intergenerational partners; South Africa

Introduction

HIV-infection risk remains high among young women in sub-Saharan Africa. In 2016, 26% of new HIV infections in eastern and southern Africa occurred among 15-to-24 year-old women, who make up only 10% of the population [1]. In South Africa alone, approximately 2000 young women were infected with HIV every week in 2016 [2].

Evidence is currently mixed on age-disparate partnerships – those in which the male partner is five or more years older – as an HIV-infection risk factor for young women. Evidence from several sources indicates that partnering with older men increases risk of HIV-infection for young women [3–9]. This evidence aligns with epidemiological data: older male partners are more likely to be HIV-infected with an unsuppressed viral load than younger partners [6]; and behavioural data: condomless sex [10–13], transactional sex [13], higher frequency of sex [14–16], and concurrent sexual partnering [17], are more prevalent in age-disparate partnerships.

In contrast, three longitudinal studies in South Africa have shown no association between age-disparate partnerships and HIV-acquisition among young women [18–20]. These cohort studies have brought into question the efficacy of HIV-prevention interventions targeting age-disparate partnerships [21]. However, a potential source of bias in longitudinal studies is selection into prospective cohorts. Cohort studies of HIV incidence exclude HIV-positive individuals at baseline. As age-disparate partnerships are characterised by significantly greater sexual risk behaviour, one would expect HIV-transmission to occur more rapidly within sero-discordant age-disparate partnerships than in age-similar partnerships. Eligibility criteria for cohort studies would consequently result in the exclusion of a greater proportion of women already infected within age-disparate partnerships, and thus in relatively fewer

HIV-negative women remaining at risk of HIV-infection within these partnerships. That is, the effect of age-disparities in increasing HIV-acquisition for young women may have occurred prior to cohort selection in many cases, as might seem to be indicated by positive associations in cross-sectional studies.

The potential bias from selection effects of this nature in cohort studies would vary based on the length of women's relationships at study eligibility assessment, with the smallest effects among women in newly formed relationships. We used prospective cohort data on 15-to-24 year-old HIV-negative women to assess heterogeneity in the relationship between age-disparate partnering and HIV seroconversion by partnership duration at cohort enrolment. The hypothesis was that age-disparate partnerships would be associated with an increased risk of HIV-acquisition within more recent partnerships, with weaker associations for partnerships of longer duration.

Methods

We used longitudinal data on participants testing HIV-negative during the 2015/16 survey of the HIV Incidence Provincial Surveillance System (HIPSS), conducted from July 2015 to June 2016 in two sub-districts (Vulindlela [rural] and Greater Edendale [peri-urban]) in KwaZulu-Natal, South Africa [22]. This province has the highest HIV prevalence in South Africa [23], with HIV prevalence of ~44% among 15-to-49 year-old women in the study region [24]. Baseline survey participants (N=10,236; 15–49 years old) were selected by 1) selecting households using a two-stage random sampling of enumeration areas and then households; 2) randomly selecting one individual per household. Cohort follow-up was conducted from November 2016 to August 2017. At baseline and follow-up, venous blood samples were collected from all participants for HIV-antibody testing, and face-to-face questionnaires were administered.

Laboratory HIV testing was done using fourth generation HIV enzyme immunoassays to test for HIV antibodies and antigens using enzyme Biomerieux Vironostika Uniform II Antigen/Antibody Microelisa system (BioMérieux, Marcy I'Etoile, France) and HIV 1/2 Combi Roche Elecys (Roche Diagnostics, Penzberg, Germany). Positive tests were confirmed with a Western-Blot (Biorad assay, Bio-Rad Laboratories, Redmond, WA 98052, USA).

The primary outcome was HIV seroconversion. The date of seroconversion was assumed to be the mid-point between the baseline and follow-up survey dates. The exposure of interest was the difference in age between the participant and her male partner at enrolment. Data were collected on participants' three most recent sexual partners (within the previous five years). Two measures of partner age differences were created using data on current (i.e., had not ended) heterosexual partnerships at baseline. (1) A binary variable to identify age-disparate partnerships. (2) A continuous variable of the difference in age between partners (number of years the male partner was older), left censored at zero. For women in multiple, heterosexual partnerships at baseline (n=32, 4%), data on the most recent sexual partner were used.

Cox proportional hazard models, as in previous cohort studies [18,19], were used to assess the relationship between HIV-acquisition and each measure of partner age difference. Multivariable models included potential sociodemographic and behavioural confounders: participant age; education (secondary school completion); area of residence (urban vs rural); concurrent sexual partnerships (i.e., multiple, heterosexual partnerships at baseline); relationship duration (quartiles); alcohol consumption; and household income. Relationship duration was categorised into quartiles to allow for non-linear associations with HIV risk, which may arise as a result of reproduction decision-making changes during relationships.

To assess heterogenous effects of age-disparity on HIV-acquisition by partnership duration, we included an interaction term: age-disparate partnerships (0/1) multiplied by partnership duration quartiles. Quartiles were used to create a category (quartile 1) of individuals in partnerships of less than one year, our *a priori* definition of a recently established relationship. As this choice was arbitrary, we tested the robustness of results using partnership duration tertiles, and using quintiles of partnership duration. All models were estimated in Stata (15.1) with cluster-robust standard error estimation, using enumeration areas as the clustering unit, and applied survey weights.

Results

1,861 women aged 15-to-24 years were eligible for this cohort study, and 1,411 (76%) enrolled (see Figure S1, supplemental digital content (SDC) 1). The analytical sample (N=830) excluded 567 women not in a sexual partnership at baseline and 14 women in same sex partnerships. Participants were followed for a total of 1,139 person-years of follow-up (mean:1.4 years). Days to follow-up ranged from 314 to 777, with a mean of 518 (standard deviation 87), and median of 501.

Our sample (see Table S1, SDC 1) comprised Black African participants, predominately 20-to-24 years old (65%), with a mean age of 20.5 years. 27.3% of women (95% CI:23.5–31.0) were in an age-disparate partnership at baseline. The mean partnership duration was 2.95 years (standard error: 0.097; range: 0–15.59 years (outlier of 23.43 years excluded)), with 23% of partnerships starting in the year preceding the baseline.

Fifty-four (6.5%) women seroconverted between baseline and endline (4.41 per 100 person-years, 95% CI:3.30–6.06, see Table 1). The difference in crude HIV-incidence between women in age-disparate and age-similar partnerships was small and not statistically significant (4.85 vs 4.25, p=0.708). The adjusted hazard ratios (aHR) for the association between HIV-acquisition and a) age-disparate partnering (aHR:1.10; 95% CI:0.55–2.21), and b) partnership age differences in years (aHR:1.04, 95% CI:0.94–1.14) were small and not statistically significant.

Substantial differences in crude HIV-incidence were evident between women in age-similar and age-disparate partnerships by partnership duration (see Table S3, SDC1). Among partnerships of less than 1.09 years duration (quartile 1), HIV-incidence was approximately three times higher for women in age-disparate partnerships compared to women with similar-aged partners (11.83 vs 3.59 per 100 person-years). In contrast, HIV-incidence was

lower among women in age-disparate partnerships for each of the other partnership duration quartiles. Among age-disparate partnerships, 44% (8/18) of HIV infections occurred in those that began the relationship 1.08 years, or fewer, prior to the baseline survey.

Figure 1 presents hazard ratios for each of the partnership duration quartiles, calculated using Cox proportional hazard models with interaction terms for age-disparity and each partnership duration quartile (for model coefficients, see Table S4, SDC1). Among women reporting the shortest 25% of partnerships at baseline, those in age-disparate partnerships were significantly more likely to seroconvert (aHR 3.13, 95% CI: 1.02–9.65, p=0.047). Note, the mean duration of partnerships in quartile 1 was similar across partnership type (age-disparate: 0.55 years, age-similar: 0.61 years; p=0.197). HIV-acquisition was not statistically different by partnership type among women in longer-length partnerships.

Sensitivity analyses showed that heterogenous age-disparate effects by partnership duration were not sensitive to adjustment of the partnership duration measure to tertiles, or to quintiles (see Figures S2 and S3, SDC1). Additional analysis was conducted among a different sample in newly established relationships: 15-to-24 year-old women (N=209) who were not in a sexual partnership at baseline but reported a sexual partner in the 12 months prior to the follow-up survey. This analysis (see Table S5, SDC1) also found a positive association between HIV acquisition and a) age-disparate partnerships (aHR: 2.71, 95% CI:0.69–10.61, p=0.150) and b) years age-difference between partners (aHR:1.22, 95% CI:1.02–1.46, p=0.031).

Discussion

Recent cohort studies have found no association between age-disparate partnering and HIV-acquisition among women in South Africa [18–20]. These findings have led policymakers to question whether programs to mitigate risks from age-disparate partnerships are an effective HIV-prevention strategy for young women. Our results challenge this interpretation. Specifically, we found that a null relationship between age-disparate partnering and HIV incidence masked substantial heterogeneity in HIV-infection rates by length of partnership. Within recently formed partnerships at cohort enrolment, HIV-seroconversion was significantly more likely for women with age-disparate partners.

Study results suggest that the null findings in previous cohort studies of HIV incidence [18–20] may have resulted from analytical designs that excluded HIV-positive women. A large effect of age-disparity on HIV-acquisition early in partnerships would result in a high proportion of *high-risk* age-disparate partnerships being excluded from cohort studies. This would lead to the selection of a sample comprised predominantly of individuals in lower-risk partnerships, which would bias estimates of the impact of age-disparate partnerships on HIV incidence towards the null, and/or make it difficult to detect meaningful associations due to loss of statistical power. Selection effects in particular may provide a potential explanation for why, unlike cohort studies, cross-sectional studies typically do find a positive association between age-disparities and HIV-positivity. Cross-sectional studies, by design, do not exclude HIV positive women.

We acknowledge several study limitations. Both incomplete reporting of sexual partners, which is likely in surveys [25], and misclassification of whether a partnership had ended might have led to selection bias. Self-reported partner age [26], and partnership duration might also be measured imperfectly. Social desirability bias might have increased the likelihood of underreporting male partners' age in the region, given a recent campaign discouraging partnerships with older men. In addition, our study was conducted in a relatively small geographic region, which creates uncertainty about the external validity of the results. Finally, small sample bias might have influenced our results.

In conclusion, our study provides evidence of a significantly elevated HIV-acquisition risk among young women in more recently established age-disparate partnerships. This finding provides a plausible explanation for the lack of association between age-disparities and HIV-incidence found in previous cohort studies in South Africa. Our results provide further evidence that targeting risks associated with age-disparate partnerships may be effective in reducing HIV-incidence rates among young women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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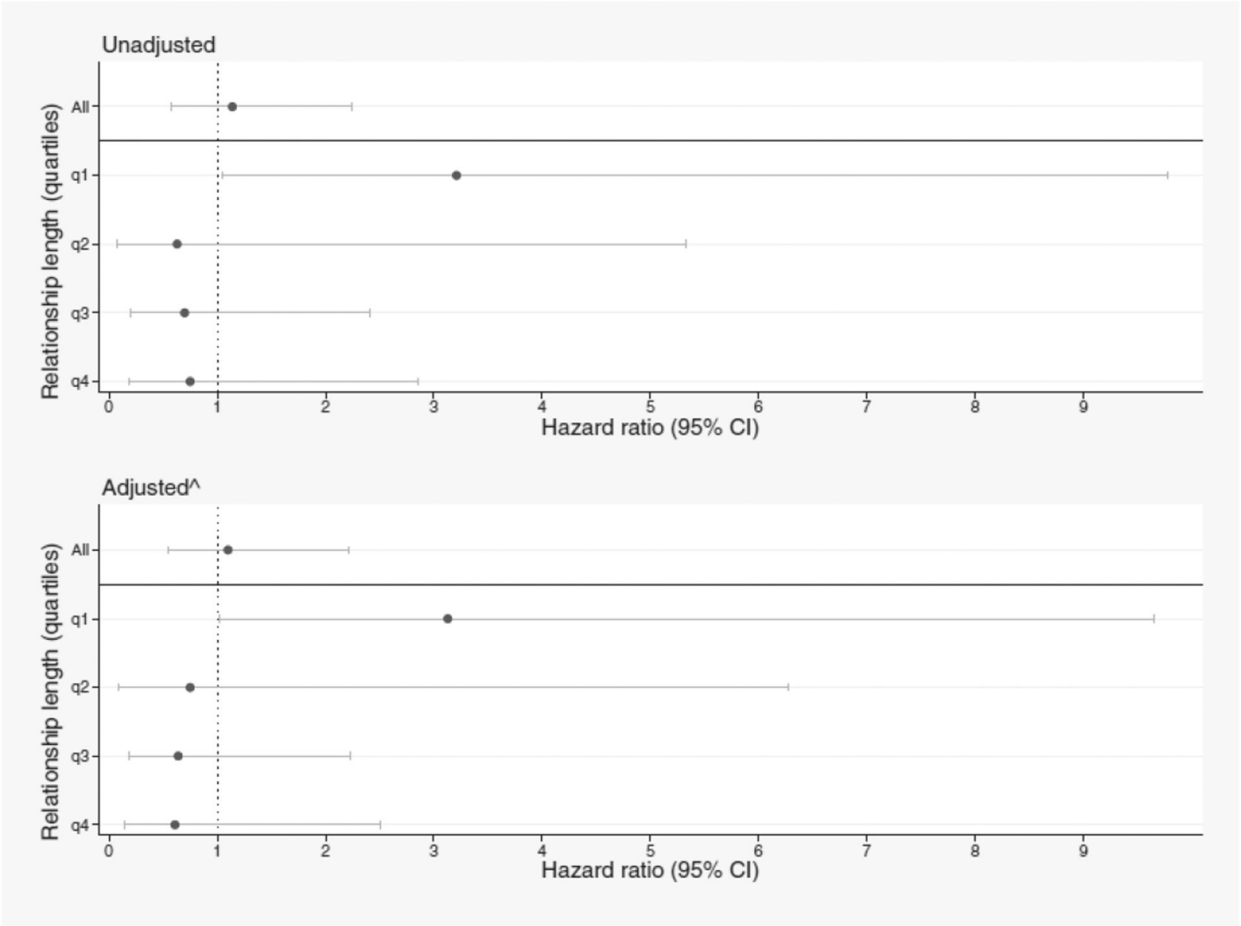

Figure 1.

Hazard ratios for the association between HIV acquisition and age-disparate partnerships (reported at baseline) among 15-to-24 year-old women (N=830), by partnership duration (quartiles). Hazard ratios estimated using Cox proportional hazard models with interactions between age-disparate partnerships (0/1) and relationship duration quartiles. Âdjusted models included the following control variables: participant age (years); education (completion of secondary schooling (grade 12) or not); area of residence (urban vs rural); concurrent sexual partner at baseline (no/yes); household income (≤R2500, R2501–6000, >R6000) and alcohol use (whether the respondent drinks alcohol/not).

Table 1:

Association between HIV acquisition and age differences within partnerships at baseline among 15-to-24 year-old women in KwaZulu-Natal, South Africa (2015–2017)

	unweighted data		weighted data		
	HIV infections/ person-years	**HIV Incidence (per 100 person-years)**	**HIV Incidence (per 100 person-years)**	**Unadjusted Cox proportional hazard model**	**Adjusted Cox proportional hazard model[a]**
		(95% CI)	**(95% CI)**	**HR (95% CI)**	**aHR (95% CI)**
All women (15–24 yrs old)	54/1138.69	4.74 (3.63–6.19)	4.41 (3.29–6.06)		
Independent variable 1					
Age-disparate partnership					
No	36/830.83	4.33 (3.13–6.01)	4.25 (2.97–6.29)	ref	ref
Yes	18/307.87	5.85 (3.69–9.28)	4.85 (2.91–8.67)	1.14 (0.58–2.25)	1.10 (0.55–2.21)
Independent variable 2					
Partnership age-difference (in years, 0–27)				1.04 (0.95–1.14)	1.04 (0.94–1.14)

Notes: 95% CI: 95% confidence interval; HR: hazard ratio; aHR: adjusted hazard ratio

[a]Multivariable Cox proportional hazard model controlling for participant age (years); education (completion of secondary schooling (grade 12) or not); area of residence (urban vs rural); relationship duration (quartiles); concurrent sexual partner at baseline (no/yes); household income (≤R2500, R2501–6000, >R6000) and alcohol use (whether the respondent drinks alcohol or not).

See Table S2, Supplemental Digital Content 1, for the full multivariable Cox proportional hazard models of HIV acquisition.