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Factors associated with incident HIV infection versus prevalent infection among youth in Rakai, Uganda

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Abstract Factors associated with prevalent and incident HIV infection were compared among sexually experienced Ugandans aged 15–24. Most factors were similar. However, in women, older age and current marriage were associated with prevalent, but not incident, infection. It is important to recognize the limitations of prevalence analyses for identifying at-risk youth.

1. Introduction

Youth (15–24 years) represent 39% of all new HIV infections [1], and nearly 80% of the 5 million youth living with HIV reside in Sub-Saharan Africa (SSA) [2].

Most studies examining the factors associated with HIV infection in SSA youth have been cross-sectional with prevalent, not incident, infection as an outcome [3]. Prevalent infections in youth are likely to be relatively recent because of the recent initiation of sex, and therefore, factors associated with prevalent infection may approximate those of incident HIV. However, without a formal comparison, this remains an untested hypothesis. Epidemiologic principles [4] and available comparisons [5] suggest they might differ.

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This study investigated whether similar factors were associated with incident [6] and prevalent HIV infection among youth in the Rakai District of Uganda.

2. Materials and methods

This study used a prospective longitudinal study design. The study population was sexually experienced youth participating in the on-going Rakai Community Cohort Study (RCCS) between March 1999 and April 2008. The RCCS is an open cohort of residents aged 15—49 years from 50 communities in the Rakai district of southwestern Uganda. Communities are surveyed approximately annually [7].

Between March 1999 and April 2008 there were 7 RCCS survey rounds and 15,173 participants 15—24 years of age who ever had sex and were tested for HIV. These participants are eligible for the analysis of prevalent infection. Incident analyses were restricted to initially HIV-negative youth who were followed up at one or more study visits with no more than 1 survey round missing (n = 6741). HIV status was determined by two separate ELISA tests and confirmed by HIV-1 western blot [7].

Institutional review board (IRB) approvals were obtained from the Uganda Virus Research Institute's Science and Ethics Committee, Uganda National Council for Science and Technology, and IRBs at Columbia and Johns Hopkins universities and Western IRB in the United States.

2.1. Analyses

A recently published incident analysis which estimated incident rate ratios (IRR) [6] was compared with analyses in which the outcome was prevalent HIV. Prevalence rate ratios (PRR) were estimated using modified Poisson regression [8] with generalized estimating equations (GEE) and robust standard errors to account for repeated observations per person. To address concerns that results could be biased toward participants with multiple observations, additional analyses were performed in a subsample wherein one observation was chosen at random per individual. The results (not shown) were similar to those presented in this paper.

This study presents unadjusted and multivariate analyses. For multivariate models, variable selection was conducted by first performing backward selection in domain-specific models (domains: demographic, sexual behaviors, alcohol use and sexually transmitted infection [STI] symptoms) and then backward selection in models containing statistically significant factors from the domain-specific models [6].

For all factors, incident HIV and prevalence analyses were qualitatively compared by measures of association, magnitude, statistical significance and inclusion in the multivariate model. Additional analyses were conducted to explore differences observed between the prevalent and incident analyses with respect to age and marital status.

3. Results

Among the 15,173 sexually experienced youth, there were 27,228 observations eligible for the analysis of prevalent HIV infection and 12,111 for the incidence analysis. Most observations eligible for the prevalence, but not the incidence, analysis were baseline observations (87.0%). HIV prevalence at baseline was 2.5% in young men and 9.9% in young women.

In the unadjusted analyses, most factors associated with incident infection were similar to prevalent infection (Table 1). Among young men, incident and prevalent HIV were positively associated with older age, marital status, not being enrolled in school, alcohol consumption, number of sexual partners, sexual concurrency and STI symptoms. Never having attended school was associated with prevalent (PRR: 2.46; confidence interval (CI): 1.40—4.32), but not incident, infection (IRR: 0.63; CI: 0.09—4.45).

Among young women, both incident and prevalent HIV infection were positively associated with residence in a trading village, former marriage, not being enrolled in school, number of partners, concurrency and STI symptoms (Table 1). Older age was positively associated with prevalent (PRR: 1.79; CI: 1.62—1.98), but not incident, infection (IRR: 0.92; CI: 0.64—1.33). Current marriage was negatively associated with incident (IRR: 0.55; CI: 0.37—0.81), but not prevalent, infection (PRR: 1.12; CI: 0.96—1.29).

The strength of association was generally greater in the incident analyses for sexual behaviors and STI symptoms (Table 1). For some factors, including condom use and alcohol consumption in young women, the measures of association were similar between the unadjusted incident and prevalent analyses, but statistical significance was constrained by sample size. More factors were selected for the multivariate model in the prevalence than incidence analyses, including older age, condom use and additional STI symptoms

Table 1 Associations with incidence and prevalent HIV infection among sexually experienced young men and women (15–24 years-old), Rakai District, Uganda, 1999–2008.

	# Incident HIV+/ py	Unadjusted IRR(95% CI)	Adjusted IRR (95% CI)	# Prevalent HIV + obs/ total obs	Unadjusted PRR(95% CI)	Adjusted PRR (95% CI)
MEN						
Total	56/6772			9809/11,680		
Age (years)						
15–19	7/1969	1		23/4194	1	1
20–24	49/4803	2.87 (1.30–6.32)		264/7486	5.57 (3.91–7.94)	3.06 (2.11–4.45)
Community type						
Rural	43/5554	1		222/9426	1	
Trading village	13/1217	1.38 (0.75–2.55)		65/2212	1.10 (0.79–1.54)	
Marital Status						
Never married	22/4480	1	1	97/7849	1	1
Currently married	24/2100	2.33 (1.31–4.14)	1.64 (0.90–2.99)	151/3522	3.53 (2.71–4.59)	1.98 (1.45–2.71)
Formerly married	10/191	10.65 (5.14–22.07)	5.57 (2.51–12.36)	39/309	6.23 (3.89–10.00)	3.37 (2.09–5.44)
Highest Level of Schooling Attended						
No schooling	1/155	0.63 (0.09–4.45)		19/336	2.46 (1.40–4.32)	
Primary schooling	46/4483	1		203/7517	1	
Secondary schooling	9/2084	0.42 (0.21–0.86)		64/3644	0.68 (0.49–0.95)	
Tertiary schooling	0/50			0/141		
Current Student						
No	55/5519	1		279/9459	1	1
Yes	1/1253	0.08 (0.01–0.58)		8/2221	0.20 (0.13–0.32)	0.57 (0.33–0.99)
Drank alcohol in last 30 days						
No	19/4250	1	1	96/7115	1	1
Yes	37/2522	3.28 (1.89–5.69)	2.08 (1.15–3.77)	191/4563	2.32 (1.85–2.92)	1.68 (1.33–2.11)
Number of sexual partners in the past 12 months						
0	2/752	0.53 (0.12–2.29)	0.64 (0.15–2.75)	6/1481	0.42 (0.27–0.64)	0.65 (0.38–1.14)
1	16/3172	1	1	96/5317	1	1
2	19/1766	2.13 (1.10–4.13)	1.56 (0.78–3.14)	97/2853	1.56 (1.24–1.98)	1.32 (1.05–1.67)
3+	19/1082	3.48 (1.80–6.73)	1.85 (0.87–3.93)	88/2028	1.83 (1.35–2.46)	1.30 (0.96–1.76)
Number of sexual partners from outside the community in the past 12 months						
0	27/4105	1		138/7024	1	
1	12/1768	1.03 (0.52–2.03)		78/2960	1.07 (0.86–1.34)	
2+	17/898	2.88 (1.58–5.24)		71/1694	1.55 (1.16–2.08)	

(*continued on next page*)

Table 1 (*continued*).

	# Incident HIV+/ py	Unadjusted IRR(95% CI)	Adjusted IRR (95% CI)	# Prevalent HIV + obs/ total obs	Unadjusted PRR(95% CI)	Adjusted PRR (95% CI)
Concurrent partner at time of interview						
No	36/5492	1		204/9689	1	
Yes	20/1279	2.38 (1.39—4.10)		83/1991	1.70 (1.33—2.17)	
Condom use in past 12 months						
Never/Inconsistently	44/4658	1		84/4125	1	1
Always	12/2113	0.60 (0.32—1.13)		203/7554	0.55 (0.41—0.74)	1.05 (0.72—1.54)
STI symptoms in past 12 months						
Genital ulcer	21/646	5.69 (3.34—9.69)	3.56 (1.97—6.41)	85/1031	2.63 (1.95—3.54)	1.70 (1.26—2.28)
Genital discharge	10/331	4.23 (2.17—8.28)		34/551	1.81 (1.18—2.76)	
Frequent urination	5/123	5.31 (2.19—12.90)		18/239	1.79 (0.98—3.27)	
Painful urination	14/636	3.10 (1.70—5.64)		58/1142	1.80 (1.35—2.40)	1.40 (1.08—1.81)
Pain during intercourse	4/164	3.09 (1.13—8.45)		11/308	1.13 (0.60—2.10)	
Bleeding during intercourse	0/35			3/76	1.06 (0.42—2.66)	
Lower abdominal pain	7/378	2.41 (1.10—5.27)		22/601	1.40 (0.99—1.99)	
Genital warts	2/64	3.88 (0.97—15.41)		7/101	1.99 (0.96—4.14)	
WOMEN						
Total	148/10,520			15,631/17,132		
Age (years)						
15—19	39/2614	1		290/6748	1	1
20—24	109/7907	0.92 (0.64—1.33)		1211/12,754	2.08 (1.89—2.28)	1.79 (1.62—1.98)
Community type						
Rural	107/8489	1	1	1109/15,389	1	1
Trading village	41/2031	1.60 (1.12—2.28)	1.48 (1.04—2.11)	388/4042	1.22 (1.07—1.39)	1.17 (1.03—1.33)
Marital Status						
Never married	43/2681	1	1	287/5374	1	1
Currently married	86/7434	0.72 (0.50—1.04)	0.55 (0.37—0.81)	941/13,009	1.57 (1.38—1.79)	1.12 (0.96—1.29)
Formerly married	19/405	2.93 (1.73—4.94)	1.73 (1.01—2.96)	273/1119	3.67 (3.11—4.32)	2.14 (1.80—2.55)
Highest Level of Schooling Attended						
No schooling	8/433	1.24 (0.61—2.53)		96/891	1.37 (1.09—1.73)	0.85 (0.68—1.06)
Primary schooling	97/6532	1		1012/11,979	1	1
Secondary schooling	43/3505	0.83 (0.58—1.18)		382/6449	0.64 (0.56—0.74)	0.66 (0.51—0.84)
Tertiary schooling	0/26			10/120	0.93 (0.50—1.74)	0.82 (0.42—1.56)
Current Student						
No	145/9676	1	1	1468/17,839	1	1
Yes	3/844	0.24 (0.08—0.74)	0.22 (0.07—0.72)	33/1663	0.29 (0.22—0.37)	0.52 (0.39—0.70)

Table 1 (*continued*).

	# Incident HIV+/ py	Unadjusted IRR(95% CI)	Adjusted IRR (95% CI)	# Prevalent HIV + obs/ total obs	Unadjusted PRR(95% CI)	Adjusted PRR (95% CI)
Drank alcohol in last 30 days						
No	108/8112	1		972/14,568	1	1
Yes	40/2407	1.25 (0.87—1.79)		529/4930	1.29 (1.20—1.39)	1.13 (1.05—1.22)
Number of sexual partners in the past 12 months						
0	5/480	0.82 (0.34—1.98)	0.59 (0.21—1.60)	68/1022	0.88 (0.74—1.05)	1.01 (0.84—1.20)
1	122/9545	1	1	1175/16,967	1	1
2	18/444	3.17 (1.96—5.12)	2.27 (1.36—3.81)	196/1253	1.58 (1.41—1.78)	1.46 (1.29—1.65)
3+	3/52	4.54 (1.49—13.81)	2.16 (0.82—5.70)	62/257	2.25 (1.80—2.82)	1.70 (1.34—2.13)
Number of sexual partners from outside the community in the past 12 months						
0	107/8656	1		1066/15,352	1	
1	38/1736	1.77 (1.23—2.55)		340/3711	1.15 (1.04—1.27)	
2+	3/129	1.88 (0.61—5.84)		94/437	2.02 (1.68—2.44)	
Concurrent partner at time of interview						
No	141/10,318	1		1425/19,085	1	
Yes	7/202	2.54 (1.21—5.31)		76/417	1.86 (1.55—2.22)	
Condom use in past 12 months						
Never/Inconsistently	137/9431	1		899/12,935	1	1
Always	11/1086	0.70 (0.38—1.28)		601/6559	0.77 (0.68—0.88)	1.07 (0.92—1.25)
STI symptoms in past 12 months						
Genital ulcer	31/1179	2.10 (1.42—3.09)		351/2232	1.68 (1.53—1.85)	1.38 (1.25—1.52)
Genital discharge	63/2991	1.87 (1.35—2.57)		637/5610	1.43 (1.33—1.54)	
Vaginal discharge	58/2489	2.08 (1.50—2.88)		537/4575	1.44 (1.34—1.55)	
Vaginal itching symptoms	95/4081	2.83 (2.03—3.94)	2.32 (1.63—3.29)	838/7405	1.59 (1.48—1.70)	1.31 (1.21—1.41)
Unpleasant vaginal odor	24/1018	1.81 (1.18—2.78)		208/1747	1.37 (1.23—1.52)	
Frequent urination	25/1031	1.87 (1.22—2.86)		212/1944	1.23 (1.12—1.36)	
Painful urination	33/1174	2.22 (1.52—3.26)	1.59 (1.07—2.36)	300/2449	1.38 (1.26—1.51)	1.14 (1.04—1.25)
Pain during intercourse	19/1070	1.30 (0.81—2.09)		196/2123	1.11 (1.00—1.23)	0.94 (0.85—1.04)
Bleeding during intercourse	3/117	1.85 (0.61—5.55)		36/294	1.35 (1.08—1.70)	
Lower abdominal pain	53/3291	1.23 (0.88—1.71)		590/6199	1.17 (1.10—1.25)	
Genital warts	12/250	3.62 (2.05—6.39)	2.57 (1.43—4.61)	105/539	1.70 (1.42—2.04)	1.41 (1.18—1.67)

py = person-years; IRR = incidence rate ratio; CI = confidence intervals; obs = observations; PRR = prevalence rate ratio.

in young men and women; current school enrollment in men; and alcohol consumption and the highest level of school in women.

Exploratory analyses were conducted for factors that had a different relationship between prevalent and incident analyses. With respect to age, a similar pattern was seen by single year of age as was seen by age group. In young men, prevalence and incidence increased with age (PRR: 1.41; CI: 1.34—1.49; IRR: 1.22 CI: 1.06—1.40). In young women, prevalent HIV infection increased with age (PRR: 1.17; CI: 1.15—1.19), but not incident infection (IRR: 0.98 CI: 0.91—1.05). Associations between current marriage and HIV in young women differed by age group. Current marriage was associated with prevalent HIV among 15—19 year-olds (PRR: 1.60 CI: 1.24—2.06), but not 20—24 year-olds (PRR: 1.11 CI: 0.96—1.28) (interaction p-value < 0.001). In the incidence analysis, the reduced risk of HIV among currently married women was only seen in 20—24 year-olds (IRR: 0.55 CI: 0.35—0.86) and not 15—19 year-olds (IRR: 1.22 CI: 0.64—2.36) (interaction p-value = 0.047).

4. Discussion

Factors associated with prevalent HIV infection were mostly similar to those associated with incident infection among sexually experienced Ugandan youth. Given that most studies of HIV infection in youth are prevalence analyses [3], this is reassuring. However, key risk factors differed. Age and marriage among young women were associated with prevalent HIV infection, but neither was associated with increased risk for incident infection.

The differences seen in effect of age and marriage likely stem from the limited ability of prevalence analyses to account for duration of disease and exposure. A key epidemiologic principle is prevalence which is roughly equal to incidence multiplied by duration of disease [4]. Thus, age or other covariates that are correlated with duration of infection may affect prevalence but not incidence. Also, as a cumulative measure, prevalence does not account for duration of exposure to risk. This period is relatively short in Rakai for never married, sexually experienced women (~2.1 years) and thus, compared with the longer married state, cumulative prevalence will likely be lower [9]. This helps explain the discrepancy seen wherein current marriage is associated with a reduced risk of incident HIV, but increased likelihood of prevalent HIV shown here and elsewhere [3,9—11].

In general, the magnitude of associations was greater for the incidence analyses. Recent reports may not reflect risk at the time of infection for prevalent cases, even among youth. Moreover, risk behaviors may decline following HIV diagnosis [10]. Thus, a smaller effect size might be expected in the prevalence analysis for sexual behaviors and STI symptoms in the prior year.

There was greater power in the prevalence analyses, which had a larger sample size compared with incidence analyses. This would also affect statistical significance and, in turn, inclusion into the multivariate model.

Comparisons between prevalent and incident HIV infection risk factors are rare in SSA. Braunstein et al. [5] compared incidence analyses from longitudinal studies in Zimbabwe and Uganda to prevalence analyses using the Demographic and Health Surveys (DHS) and found older age was associated with prevalent and not incident infection. The benefit of this internal comparison is that there is less concern that differences seen between analyses were driven by underlying differences between the observed populations.

One reason why there are few comparisons of incident and prevalent risk factors is studies of incidence in SSA are rare. While longitudinal cohort studies are valuable for assessing causality, these studies are complex, lengthy and costly. Laboratory methods have been developed to identify recent HIV infection in cross-sectional studies, but have limited specificity particularly in populations where non-B subtypes predominate, such as Uganda [11,12].

This study has limitations. Our prevalence analysis was performed within an ongoing cohort study. To address the potential effect of multiple observations, robust variance estimates were used and an additional sensitivity analysis on randomly selected individuals was performed. When comparing incident and prevalent analyses, differences in eligibility criteria (i.e., observation time) meant that samples may have differed in terms of survey availability, mobility and information on timing of infection. Any comparison of prevalence and incidence will be influenced by factors that already influence cross-sectional and longitudinal studies, including refusal to consent or to be tested and loss to follow-up. Social desirability bias and recall error were possible in both the incidence and prevalence analyses.

In the recently disseminated U.S. PEPFAR Blueprint, evidence-based approaches were emphasized, including the goal to ''target and tailor programing for sexually active and most-at-risk

youth based on patterns of behavior and their needs [13]''. Research, surveillance, treatment, and prevention programs should be based on best practices in epidemiology. This study and others suggest that HIV prevalence studies have their limitations in identifying youth at risk for HIV infection. In this study, prevalence analyses did not accurately predict the lack of risk observed for age and marital status in incident analyses.

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Conflict of interest

The authors have no conflicts of interest to disclose.

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