

A Protective Effect of Circumcision Among Receptive Male Sex Partners of Indian Men Who Have Sex with Men

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Abstract The role of circumcision in the transmission of human immunodeficiency virus (HIV) among men who have sex with men (MSM) in resource restricted regions is poorly understood. This study explored the association of circumcision with HIV seroprevalence, in conjunction with other risk factors such as marriage and sex position, for a population of MSM in India. Participants ($n = 387$) were recruited from six drop-in centers in a large city in southern India. The overall HIV prevalence in this sample was high, at 18.6%. Bivariate and multivariable analyses revealed a concentration of risk among receptive only, married, and uncircumcised MSM, with HIV prevalence in this group reaching nearly 50%. The adjusted odds of HIV infection amongst circumcised men was less than one fifth that of uncircumcised men [adjusted odds ratio (AOR) 0.17; 95% CI 0.07–0.46; $P < 0.001$]. Within the group of receptive only MSM, infection was found to be lower among circumcised individuals (AOR, 0.30, 95% CI 0.12–0.76; $P < 0.05$) in the context of circumcised MSM engaging in more UAI, having a more recent same sex encounter and less lubricant use when compared to uncircumcised receptive men. To further explain these results, future studies

should focus on epidemiologic analyses of risk, augmented by social and sexual network analyses of MSM mixing.

Keywords Circumcision · Men who have sex with men · India · HIV prevention · Sexual behavior

Introduction

A number of studies have examined the association of circumcision and HIV among men who have sex with men (MSM) and have been reviewed in detail elsewhere [1, 2]. The main conclusion from these studies in aggregate suggests that there is little evidence of circumcision reducing the risk of HIV acquisition among MSM, although one study in Australia did find lower rates of HIV infection among circumcised insertive only MSM [3]. In resource limited settings, however, studies of circumcision and MSM are less conclusive, with one study in Peru demonstrating a marginally lower likelihood of HIV seroconversion among circumcised men [4], and another demonstrating decreased likelihood of HIV infection among insertive MSM in South Africa [5].

It is plausible that sex position in conjunction with circumcision plays a role in HIV acquisition among MSM, with circumcised insertive only individuals having less risk of acquisition [3, 5]. However, there is little evidence for the benefits of circumcision in most western settings [6], even with stratification for sex position and a particular focus on insertive only sex participants [7–10]. Studies suggest that the sexual behaviors and practices of MSM vary considerably across and even within cultures, resulting in diverse risk patterns [11]. In several Western settings it has been shown that only a minority of MSM predominantly or exclusively practice a given sex position; rather the majority shift

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modality depending upon setting and partner contexts [12] and can be characterized as dual or versatile [3, 10]. In other settings, MSM are differentiated and identified based on their role in sexual relations with other men, e.g., distinctions such as *activo* versus *passivo* in Latin America [13] or *kothi* versus *panthi* in India [14]. These distinctions generally follow normative sex positioning roles and insertive partners are less stigmatized or viewed as normal. While there is some flexibility in this structure in that some MSM are both insertive and receptive, e.g., Double-Deckers in India, the majority of indigenous MSM identify themselves and others according to this schema as there is more widespread adherence to exclusively one sex position. Greater attention is required to understand the patterns of social and behavioral conduct in these settings and their role in HIV transmission, especially given forthcoming novel biologic HIV prevention interventions [15] which are likely to be promoted within MSM populations broadly.

In India, MSM represent a heterogeneous group at high-risk for HIV infection [16]. In addition to a distinct gay identity, other identities based upon sex position preference exist [11]. These identities include considerable segments of the MSM community, and could help further understandings of the role of circumcision in HIV acquisition. The possible protective effect of circumcision could be of additional interest given high rates of marriage (to women) and bisexuality in this setting [16, 17], thus the potential for bisexual MSM to be a bridge population for transmission of HIV outside of MSM networks. In one study in India, the role of circumcision as protective against HIV has been determined for men attending a sexually transmitted disease clinic [18], however, the majority of this group was exclusively heterosexual. Recent reports [17] of subgroups of MSM such as married MSM being at increased risk for HIV infection have not accounted for important behavioral characteristics (e.g., sex position preference) or biologic characteristics (e.g., circumcision status) of these MSM. The present study was conducted to determine the relationship between circumcision, HIV status and other social and behavioral modifiers of this potential relationship among MSM. Participants were recruited within the state of Andhra Pradesh, which has the highest HIV prevalence in India (0.75 for women and 1.22 for men) [19], in the city of Hyderabad, which is 41% Muslim and holds one of the most concentrated Muslim populations in the country [20].

Methods

Participants and Setting

The study was conducted at six MSM drop-in centers managed by a local community based organization (CBO),

Mithrudu (“Friend”), between August 2008 and June of 2009. Drop-in centers are small private apartments/office spaces where MSM CBOs gather and provide social and clinical services to the community. MSM between the ages of 18–49, who were fluent Hindi or Telugu speakers, identified as men, and reported having anal intercourse with another man in the past 12 months were eligible for participation. A convenience sample of clients presenting at the drop-in centers was generated from all individuals entering the drop-in centers which were approached by an outreach worker and assessed for eligibility as candidate participants. One trained research assistant subsequently collected written informed consent, performed the interview, and conducted the HIV VCT procedures on all eligible and consenting study participants. The protocol and procedures were approved by the appropriate ethics committees in India and the United States. Study participants were provided HIV test results as well as referral for additional services when appropriate.

Data Collection

Confidential interviews were administered in person by one trained research assistant with 5 years experience working with this population. Interviews were conducted to obtain social, behavioral and biologic information and other risk factors that may be associated with the occurrence of HIV in this population. Social strata information included age, education, marital status, occupation, income, religion and caste. The caste system is a social class hierarchy upheld in India, and categories used for caste were those defined by the Government of India (from highest to lowest) as forward caste, backwards caste, scheduled caste, and scheduled tribe. All references to marriage in our questionnaire and in our data referred to marriage between a man and a woman. Information relevant to this paper included recency of last intercourse with a male sex partner, sex position preference with male partners (e.g., insertive, receptive, dual), HIV testing history (e.g., date of last test, location and results), self-reported circumcision status, and unprotected anal intercourse (UAI) with last sex partner. HIV testing was conducted using standard methods and kits for detecting HIV-1/2 utilizing minimally invasive sampling strategies, and included three sequential antibody tests in accordance with National AIDS Control Organization guidelines [21] (First Response HIV 1–2.0, PMC Medical, India; Determine HIV 1/2, Inverness Medical, USA; Capillus HIV-1/HIV-2, Trinity, Ireland). HIV test results were provided to all study participants following the study survey during the post-test counseling phase of the visit. Study participants who were found to be infected were referred to local centers with capacity for government approved CD-4 testing and/or HIV therapy.

Analysis

The primary goal of this study was to determine the association between HIV seroprevalence, circumcision, and other potential socio-behavioral risk factors in MSM. Chi-square or Fisher's exact statistics were used for bivariate analyses. For all estimates of the odds ratio, 95% confidence intervals were calculated to assess precision and statistical significance. Multiple logistic regression was conducted on HIV status using predictor variables statistically significant from bivariate analyses: participants' age, education, circumcision, marriage status, sex position preference, UAI, recency of last sex with a man, lubricant use, alcohol use, and any STI symptoms. Adjusted odds ratios (AORs) with 95% confidence intervals (95% CI) were reported with p values less than 0.05 considered statistically significant. A backwards selection process was used to identify those variables that were the strongest independent predictors of HIV seroprevalence in the final model. STATA (version 11.0) was used for statistical analyses.

Results

Socio-Demographic Description of Sample

A total of 387 MSM were enrolled for participation. Socio-demographic characteristics of the MSM in this sample are presented in Table 1. Overall the sample was relatively young, with a median age of 26 (IQR 24–30 years); 94.8% of the sample was 40 or younger. Less than one third (30.6%) of the MSM were married, which in large part may be due to the overall youth of the sample. Among men in their thirties 59.3% were married, while 77.8% of men in their forties were married. Only 1.8% of the unmarried sample reported being separated or divorced. The majority of men were Hindu (62.5%), almost one third were Muslim (31.8%), and the remaining MSM were Christian (5.7%).

The MSM in this sample were relatively broadly distributed across our indicators of socio-economic status, though compared to studies of MSM in wealthier countries these levels may seem low [22]. Over two thirds of the sample (68.4%) completed 10 or less years of schooling. In regard to occupation, the rate of unemployment was low (6.5%), however, one fifth of participants reported begging or sex work as their primary occupation (19.0%), while another 15.9% worked as laborers. Just over one quarter (27.3%), the largest portion of the sample, reported work in the service industry. An additional 7.7% reported transport related work, 12.5% were professionals, and just over 10% of the participants were students. About three quarters (73.1%) of the sample reported a monthly income with a

Table 1 Socio-demographic characteristics of men who have sex with men in Hyderabad India ($n = 387$)

Characteristic (N) ^a	%
Age (386)	
Less than 20 years	6.2
20–24 years	27.2
25–29 years	36.8
More than 29 years	29.8
Education (361)	
Primary (<6)	11.6
Secondary (6–10)	56.8
Higher (11–12)	20.5
College (>12)	11.1
Marital Status (386)	
Unmarried/divorced	69.4
Married	30.6
Occupation (352)	
Begging and sex work	19.0
Labor	15.9
Professional	12.5
Service	27.3
Student	11.1
Transport related	7.7
Unemployed	6.5
Monthly income in Indian rupees (\$US) (283)	
<3500 (\$90)	18.7
3500–4999 (\$90–125)	31.4
5000–6499 (\$125–165)	32.5
≥6500 (\$165)	17.3
Religion (387)	
Christian	5.7
Hindu	62.5
Muslim	31.8
Caste (387)	
Forward caste	8.8
Backwards caste	22.2
Scheduled caste	26.4
Scheduled tribe	8.3
Not applicable	34.4
Circumcision (382)	
Uncircumcised	63.1
Circumcised	36.9

^a Number non-missing. Variable totals may not equal sample total due to missing data

mean of about 5000 INR (~\$110). Close to two thirds of the MSM associated with a specific caste (65.6%), with less than a tenth of the sample belonging to the highest status caste (8.8% forward caste).

Circumcision is highly correlated with religion in India, and in our sample 99.2% of the 123 Muslim men self-

reported circumcised status. This is compared to just over a quarter (27.3%) of the 22 Christians and only 5.5% of the 237 Hindu men. Five of the Hindu men did not answer the question about circumcision, and these five cases were excluded from the multivariate analyses.

Distribution of Behavior and Risk Practices

Table 2 presents the distribution of sexual behaviors and risk associated with HIV transmission, as well as HIV status and CD4⁺ lymphocyte counts for our sample of MSM. In India, socially recognized distinctions between MSM are made based on their role in sex with other men, which we refer to as sex position. Almost two thirds (64.5%) of our sample assumed the exclusively receptive role in sex with other men; 20.5% reported being insertive only in sex with men. An additional 15.0% of men in our sample said they took a dual role during sex with other men.

The overall HIV seroprevalence in the sample was 18.6%. Overall, the MSM in our sample began having sex with men when they were relatively young—56.9% reported first having sex with a man before they turned 18 years old and 97.5% of the men had their first homosexual experience by the age of 20. Over one fifth of the sample (22.2%) reported having given money or a gift for sex, and another 65.4% having received money or a gift in exchange for sex with another man. Anal sex with a man during the previous week was reported by 76.4% of the sample. Just over half of the sampled men reported UAI always or often and the other half only sometimes or never.

More than two thirds of the sample reported ever consuming alcohol (64.8%). The overall percent of non-drinkers (35.2%) was similar to the percent of Muslim in the sample (32%), however, 53% of the Muslim MSM reported drinking. This was lower than the 73.0% drinking rate among Hindu MSM.

Sex Position, Circumcision, Marital Status, and HIV

Figure 1 displays the percent HIV positive along with 95% confidence intervals for the percentage within sub-groups defined by sexual position, marital status, and circumcision for the 387 MSM in our sample. This allows one to visually compare the effect of each explanatory variable on HIV seroprevalence rate across groups defined by the other two factors. Because of limited sample sizes within these sub-groups, comparisons are hypothesis generating and do not reflect statistically significant associations between groups. Trends in HIV seroprevalence based upon circumcision and marital status are evident. In order to explore these findings, we conducted multivariate analyses of HIV risk among the receptive MSM separately.

Table 2 Behavioral characteristics of men who have sex with men in Hyderabad India ($n = 387$)

Characteristic (N) ^a	%
Sex position (386)	
Receptive	64.5
Dual	15.0
Insertive	20.5
Age at first sex with man (362)	
12–14 years	8.3
15–17 years	48.6
18–20 years	40.6
Over 20 years	2.5
Ever pay money or gift for sex (379)	
No	77.8
Yes	22.2
Ever receive money or gift for sex (382)	
No	34.6
Yes	65.4
Last anal sex with man (368)	
1–2 days	15.8
3–7 days	60.6
>7 days	23.6
Unprotected anal intercourse (381)	
Sometime/never	50.9
Always/often	49.1
Lubricant use (359)	
Sometime/never	83.6
Always/often	16.4
History of alcohol use (369)	
No	35.2
Yes	64.8
Frequency of alcohol use (200) ^b	
Daily	15.0
4 or more times a week	19.5
2 to 3 times a week	22.0
2 to 4 times a month	28.5
Once a month	15.0
STI diagnosed in last 6 months (313)	
No	73.2
Yes	26.8
Currently with an STI (323)	
No	84.5
Yes	15.5
Frequency of cleaning under foreskin/penis (228)	
Everyday	48.2
2–4 times a week	4.8
Once a week	25.9
1 or less a month	21.1
When is foreskin/penis cleaned (270)	
After sex	0.7

Table 2 continued

Characteristic (<i>N</i>) ^a	%
After sex/bathing	14.1
Bathing	85.2
HIV status (387)	
Negative	81.4
Positive	18.6
CD4 Count (43) ^c	
<200	27.9
200–350	37.2
350–500	23.3
>500	11.6

^a Numbers non-missing. Variable totals may not equal sample total due to missing data

^b Participants with history of any alcohol use (*n* = 200)

^c For HIV infected participants who received CD-4 testing (*n* = 43)

Factors Associated with HIV Seroprevalence

Table 3 presents results of bivariate analysis and multiple logistic regression models of HIV seroprevalence for a set of demographic, biological, and behavioral risk factors.

Age was significantly related to HIV status, with men in their twenties having lower rates of HIV (AOR 0.23, 95% CI 0.05–0.97) compared to men younger than 20. The association between education and infection was not statistically significant in the bivariate model, however, there was a clear linear negative trend in the sample between these variables—the lower the level of education attained, the higher the HIV seroprevalence.

Sex position was strongly related to HIV in our sample, with seroprevalence among MSM who were exclusively receptive partners in anal sex over triple the rate found among the insertive only and dual MSM. Insertive only men had the lowest prevalence compared to receptive only men (AOR 0.13, 95% CI 0.03–0.55), though dual MSM were also low compared to insertive only men (AOR 0.16, 95% CI 0.03–0.80).

A recent finding in studies of MSM in India is that married MSM are more likely to be HIV infected than unmarried men [17, 23], with marriage referring to opposite-sex marriage. We find a similar pattern in our sample in bivariate analysis where married men were more likely to be infected than unmarried men. This finding may be explained in part by the collinearity between age and marital status as discussed earlier, and the fact that both age and marital status are related to HIV among the MSM in our sample. Based on the regression results, non-circumcision and UAI were the strongest predictors of HIV infection. MSM who were circumcised were much less

Table 3 Bivariate and multiple logistic regression for factors associated with HIV infection in men who have sex with men in Hyderabad, India (*n* = 387)

Characteristic	HIV %	Bivariate		Multivariable	
		OR	95% CI	OR	95% CI
Age category					
Less than 20 years	20.8	1.00 (ref)	–	1.00 (ref)	–
20–24 years	12.4	0.54	0.17–1.69	0.23	0.05–0.97 [†]
25–29 years	13.4	0.59	0.20–1.76	0.23	0.06–0.99 [†]
More than 29	29.5	1.60	0.55–4.62	0.76	0.17–3.32
Education					
Primary (<6)	28.6	1.00 (ref)	–	1.00 (ref)	–
Secondary (6–10)	19.5	0.61	0.29–1.29	1.63	0.52–5.05
Higher (11–12)	14.9	0.44	0.17–1.10	1.00	0.24–4.10
College (>12)	7.5	0.20	0.05–0.79 [†]	0.86	0.07–10.09
Sex position					
Receptive	24.9	1.00 (ref)	–	1.00 (ref)	–
Dual	7.6	0.25	0.10–0.60 [‡]	0.16	0.03–0.80 [‡]
Insertive	6.9	0.22	0.08–0.64 [‡]	0.13	0.03–0.55 [‡]
Circumcision					
Uncircumcised	22.8	1.00 (ref)	–	1.00 (ref)	–
Circumcised	11.3	0.43	0.24–0.79 [‡]	0.17	0.07–0.46
Marriage status					
Divorced/unmarried	14.6	1.00 (ref)	–	1.00 (ref)	–
Married	28.0	2.28	1.35–3.86 [‡]	2.32	0.90–5.99
Last time sex with man					
1–2 days	27.6	1.00 (ref)	–	1.00 (ref)	–
3–7 days	20.1	0.66	0.34–1.29	0.56	0.19–1.64
>7 days	9.2	0.27	0.11–0.67 [‡]	0.09	0.02–0.49 [‡]
Unprotected anal intercourse					
Sometime/never	9.8	1.00 (ref)	–	1.00 (ref)	–
Always/often	27.3	3.45	1.96–6.25	5.10	2.12–12.35
Lubricant use					
Sometime/never	21.0	1.00 (ref)	–	1.00 (ref)	–
Always/often	5.1	0.20	0.06–0.67 [‡]	0.39	0.08–1.96
Alcohol use					
No	11.5	1.00 (ref)	–	1.00 (ref)	–
Yes	22.2	2.19	1.18–4.06 [†]	0.81	0.33–1.99
STI symptoms					
None	12.1	1.00 (ref)	–	1.00 (ref)	–
Any	24.6	2.36	1.31–4.23 [‡]	1.60	0.72–3.57

Values reflective of only those participants for whom we have complete data

[†] *P* < 0.05

[‡] *P* < 0.01

^{||} *P* < 0.001

likely to be infected than men who were uncircumcised (AOR 0.17, 95% CI 0.07–0.46), while those who reported UAI always or often versus sometimes or never had much greater odds of infection (AOR 5.10, 95% CI 2.12–12.35).

A number of measures of HIV risk related to sexual practices were associated with HIV seroprevalence, including recency of sexual contact with a male partner. Men who reported their last anal intercourse was more than 1 week before the interview were significantly less likely to be infected than men who had had sex in the previous one to 2 days (AOR 0.09, 95% CI 0.02–0.49). Lubricant use, alcohol use and reporting of an STI were each statistically associated with HIV infection in bivariate analysis, but lost significance in the multivariable analysis model, respectively (AOR 0.39, 95% CI 0.08–1.96; AOR 0.81, 95% CI 0.33–1.99; AOR 1.60, 95% CI 0.72–3.57). Interestingly, in separate models (data not shown) circumcised men were more likely to engage in UAI, (AOR 2.06, 95% CI 1.16–3.66) and more likely to have had sex with a man in the past 1–2 days when compared to the group in the last 3–7 days (AOR 3.42, 95% CI 1.49–7.87).

Multivariate Analysis of Factors Associated with HIV Among Receptive Only Men

Almost two thirds of the MSM in the sample define themselves as exclusively the receptive partner in anal sex with other men. As we have seen, they have a higher rate of HIV than the other men in our sample, 24.9% compared to 14.5% for insertive and dual MSM combined ($P < 0.01$). While from a physiological and biological perspective we would not expect to find a protective effect of circumcision for MSM who take the receptive role in anal intercourse, the lower HIV rates among circumcised receptive men found in Fig. 1 led us to examine the effect of circumcision along with other risk factors for HIV among the receptive men in our sample.

Table 4 presents two logistic regression models for HIV status of the receptive men for whom we have complete data. The first model includes socio-demographic and sexual practice variables that were associated with HIV status in bivariate analyses, including education, marital status, circumcision, sexual behavior (recency of sex, UAI, use of lubricants, STI symptoms) and alcohol use. Age was also included in this model although it was not significant at the 0.05 level. Religion was not included because of its high collinearity with circumcision. In this model, age, circumcision, UAI, and recency of sex had a statistically significant association with HIV seroprevalence. A backwards selection process was then used to identify those variables that were the strongest independent predictors of HIV seroprevalence, which were used to produce the final

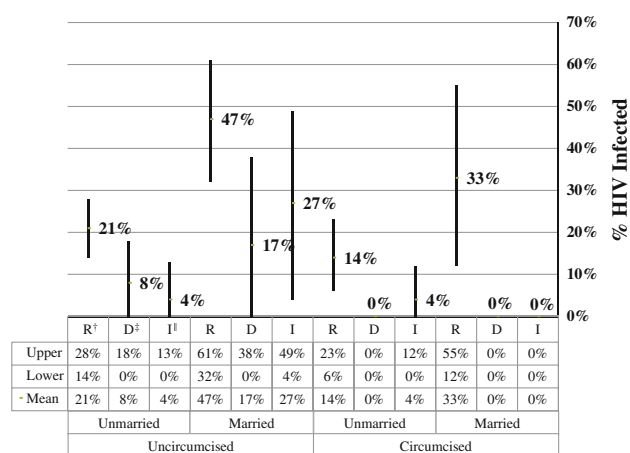


Fig. 1 Representation of sexual position, circumcision status, marital status, and HIV seroprevalence amongst Indian MSM in Hyderabad ($n = 387$)*. *Percentages represent number of HIV infected individuals of respective sex position meeting marital status and circumcision condition. [†]R Receptive. [‡]D Dual. [§]I Insertive. The magnitude of the confidence intervals is largely a function of the varying sub-group sizes; the smaller the group the larger the standard error and therefore the confidence interval. Non-overlapping confidence intervals between two groups indicate a difference in their percentages that is significant at the 0.05 level. Large absolute differences found here, even those that do not achieve significance at the 0.05 level, seem worth noting as possibly important trends found in this sample

model. This led to the exclusion of education, marital status, alcohol use, and STI symptoms.

In the final model, all variables were significant at the 0.05 level except lubricant use. Following the pattern seen in men across sex position, both circumcision and UAI were significant indicators of HIV infection. The odds of HIV seroprevalence among circumcised men was slightly less than one third that of uncircumcised men after controlling for all other variables in the model (AOR 0.30, 95% CI 0.12–0.76). Receptive MSM who did not report sex with a man in the previous week were less likely to be HIV infected compared to receptive MSM who reported sex within the previous 2 days (AOR 0.08; 95% CI 0.01–0.60). Receptive MSM who reported UAI often or always also were more likely to be HIV infected when compared to MSM who practiced UAI sometimes or never (AOR 5.65; 95% CI 2.40–13.33) in the final model.

Discussion

In this study of 387 Indian MSM with 18.6% HIV seroprevalence, male circumcision was strongly associated with decreased HIV infection amongst study participants overall, and surprisingly this trend endured within the receptive only MSM. Additionally, there was a complex relationship between sex position, marital status and

Table 4 Factors associated with prevalent HIV infection amongst receptive men who have sex with men in Hyderabad, India ($n = 249$)

Characteristic	Adjusted odds of HIV infection with Initial multiple logistic regression model		Adjusted odds of HIV infection with Final multiple logistic regression model	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Age	1.09	1.01–1.19 [†]	1.12	1.04–1.20 [‡]
Education				
Primary (< 6)	1.00 (ref)	–	–	–
Secondary (6–10)	0.97	0.30–3.16	–	–
Higher (11–12)	0.67	0.15–2.97	–	–
College (> 12)	0.60	0.04–8.42	–	–
Circumcision				
Uncircumcised	1.00 (ref)	–	1.00 (ref)	–
Circumcised	0.22	0.08–0.61 [‡]	0.30	0.12–0.76 [†]
Marital Status				
Divorced/unmarried	1.00 (ref)	–	–	–
Married	1.88	0.70–5.02	–	–
Last time Sex with man				
1–2 days	1.00 (ref)	–	1.00 (ref)	–
3–7 days	0.61	0.19–1.95	0.63	0.21–1.87
>7 days	0.09	0.01–0.65 [†]	0.08	0.01–0.60 [†]
Unprotected Anal Intercourse				
Sometimes/never	1.00 (ref)	–	1.00 (ref)	–
Always/often	5.05	2.00–12.50	5.65	2.40–13.33
Lubricant Use				
Sometimes/never	1.00 (ref)	–	1.00 (ref)	–
Always/often	0.19	0.02–1.63	0.16	0.02–1.35
Alcohol Use				
No	1.00 (ref)	–	–	–
Yes	0.63	0.23–1.71	–	–
STI Symptoms				
None	1.00 (ref)	–	–	–
Any	2.08	0.87–4.99	–	–

Values reflective of only receptive participants for whom we have complete data

[†] $P < 0.05$

[‡] $P < 0.01$

^{||} $P < 0.001$

circumcision status, with marital status associated with greater rates of HIV infection in some sub-populations including receptive only MSM. Unlike most other studies of MSM and circumcision, our sample was drawn from a population with strong sex position identification, with

only 15% of the sample reporting a dual (or versatile) sex position. One of the strengths of this sample was the mixture of circumcised and uncircumcised MSM. Almost two thirds (63.1%) of the sample was uncircumcised, and the remaining one third was circumcised. How are we to interpret the relationship between circumcision status and HIV seroprevalence amongst MSM in the sample, particularly amongst the receptive only sub-sample?

Evidence for the protective role of circumcision against HIV acquisition amongst heterosexual men [24–26] propels questions of whether this protective effect is also possible for MSM. Studies of circumcision as protective against HIV acquisition among MSM have yielded mixed results, with no evidence of a relationship in most Western settings [6, 27], with the exception of findings among insertive only MSM in one Western setting [3]. However, in resource restricted settings, a few studies have suggested that circumcision does have some protective effect [4, 5]. While there appears to be a trend towards a protective effect of circumcision among insertive only and versatile MSM in our data, the sample was not large enough for model convergence, given lower rates of insertive only partners and rates of HIV seroprevalence. What is striking from our data is the previously unreported finding of lower HIV seroprevalence among circumcised receptive only MSM.

It is hard to imagine a physiological or biological mechanism which would explain circumcision's observed protective effect against HIV in receptive MSM. Certainly, variation in behavior or other socio-demographics could explain these findings; for example, alcohol use was more common among uncircumcised men. However, our analyses demonstrated that behaviors traditionally associated with higher risk of HIV infection (e.g., UAI, recency of sex) were more common among circumcised men. This increased risky sex behavior among Indian circumcised men has also been described in a recent large population based study [28]. This suggests that our findings, as well as other findings of an association between circumcision and HIV status [29], might be even larger if sex behavior between circumcised and uncircumcised men in India was similar.

A potential explanation could be one of the most common patterns of interaction found in social and sexual networks which accounts for the selection of network partners who share similar characteristics—homophily [30]. This phenomenon has been postulated to explain higher seroprevalence rates of HIV among African American MSM, and may also provide an explanation for the lower rates of HIV among circumcised receptive only MSM in India [10]. The selection by receptive men of sexual partners who are also circumcised, and who therefore may have lower rates of HIV than sexually active

uncircumcised men, may result in a lower risk of being exposed to and becoming infected with HIV. In the present study, there were no data to directly measure partner characteristics and the extent of homophily in selection of partners. However, this social phenomena is widespread and evident in sexual networks of MSM in other settings [28, 29]. The significant effect of circumcision on HIV status among receptive MSM found in the multiple logistic regression models even when controlling for other variables such as marital status, recency of sex, UAI, use of lubricants, alcohol use and STI symptoms, suggests the importance of further research specifically focused on the effects of social networks, with particular attention paid to the social characteristics of sex partners.

Homophily based on circumcision may or may not operate directly on the basis of a preference for physical characteristics, including characteristic appearance of the genitals. In our sample, circumcision is highly correlated with religion. Receptive partners who are Muslim may be more likely to select their sexual partners from among insertive and versatile MSM who are also Muslim (or vice versa). Finally, sex behavior can vary based upon circumcision status. In a landmark sex survey in the United States, masturbation was found to be more common among circumcised heterosexual men, although this difference varied across race and ethnic categories [31]. In some settings masturbation has been posited as a potential HIV prevention strategy found to be associated with lower reported high-risk behaviors [32, 33], and future research could explore this and other sexual behaviors (e.g., oral sex) as they relate to circumcision status.

Our study had several limitations. First, the sample was drawn from MSM visiting drop-in centers and therefore unlikely to well represent the general MSM population. However, this is consistent with previous studies in this setting [17, 32], and this population is one with high HIV seroprevalence and thus target of ongoing government HIV prevention programs. Second, because the data is cross-sectional we are unable to determine whether sexual behavior as reported is influenced by HIV serostatus. While it is likely that some sex behaviors change after HIV diagnosis in this setting, sex position in India is strongly tied to identity [11] and would be unlikely to change following new HIV diagnosis. Thirdly, circumcision is self-reported and not observed. As in previous research in India where circumcised status was directly observed [18], circumcision status in our study was highly correlated with Muslim religion. While some Hindus may obtain circumcision for medical or other non-cultural reasons [33], this component was also limited in our study. Fourth, our sample size limited several sub-group analyses, however, we were able to run a final model on the largest group—receptive only MSM. Finally, we did not collect

information on non-marital female sex partners. There is evidence that sex with female partners is associated with higher HIV seroprevalence among MSM [17], however, such analyses have not included sex position in the context of sex with men, and it is less likely for receptive only MSM to assume an insertive role with non-spousal female sex partners. As previously described, sex position reflects a role identity for MSM [11] and further research is required to determine how this identity might vary within the context of MSM extra-marital female sex partnering patterns [16].

As previously suggested, dramatic differences in alcohol use between Muslim and Hindu MSM, with Hindu MSM (who are much less likely to be circumcised) reporting higher rates of alcohol use in the previous 6 months, could potentially explain our finding of HIV seroprevalence differences between circumcised and uncircumcised MSM. Other sexual partnering and positioning patterns could also explain differences in circumcision status, including higher rates of Muslims taking only an insertive role. Most observational studies of circumcision and HIV serostatus suggest that any findings may be due to residual confounding of unmeasured factors [34]. However, many of these factors were controlled for in our models, with no significant change to the point estimate of the protective effect of circumcision in the final model. Other potential explanations for our finding include misclassification of receptive MSM and thus inclusion of insertive or dual men in this category, as this data was gathered by self-report. However, this is unlikely given the strong sex identity in this setting [11] and traditionally lower rates of versatile positioning than in western settings [1, 16]. While there are some examples of anal sex between traditionally receptive partners [35], this evidence is mostly anecdotal and limited to more westernized regions within India, and has not been systematically analyzed.

In sum, we found a significant inverse association between circumcision and HIV seropositivity among MSM, persisting within the subcategory of receptive only MSM, when we control for other factors associated with HIV status. Biologic or physiologic mechanisms of the index participant are unlikely to explain this effect. Alternatively, homophily, or the selection of network partners who share similar characteristics, may provide an explanation for the lower rate of HIV among receptive only MSM. The selection by circumcised receptive men of sexual partners who are also circumcised, and who have lower rates of HIV than insertive uncircumcised men, may make for a lower risk of being exposed to and becoming infected with HIV. These findings suggest a potential need to disaggregate HIV prevention efforts in order to focus on those MSM most at risk for infection in India, acknowledging that circumcision as a prevention intervention may

be difficult to implement in this setting [33]. Additionally, further research is needed to more thoroughly describe MSM social networks, specifically pertaining to the social characteristics of sexual partners. Our finding that biological circumcision status operates in conjunction with other important social structural factors to influence risk of HIV infection underscores the importance of social and sexual network analyses in this context.

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