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Receptive anal sex contributes substantially to heterosexually-acquired HIV infections among at-risk women in Twenty US Cities: results from a modelling analysis

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Abstract

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Problem: Receptive anal intercourse (RAI) is more efficient than receptive vaginal intercourse (RVI) at transmitting HIV, but its contribution to heterosexually-acquired HIV infections among at-risk women in the US is unclear.

Method of study: We analysed sexual behaviour data from surveys of 9,152 low-income heterosexual women living in 20 cities with high rates of HIV conducted in 2010 and 2013 as part of US National HIV Behavioral Surveillance. We estimated RAI prevalence (past-year RAI) and RAI fraction (fraction of all sex acts (RVI and RAI) at the last sexual episode that were RAI among those reporting past-year RAI) overall and by key demographic characteristics. These results and HIV incidence were used to calibrate a risk-equation model to estimate the population attributable fraction of new HIV infections due to RAI (PAF_{RAI}) accounting for uncertainty in parameter assumptions.

Results: RAI prevalence (overall: 32%, city range: 19-60%) and RAI fraction (overall: 27%, city-range: 18-34%) were high overall and across cities, and positively associated with exchange sex. RAI accounted for an estimated 41% (uncertainty range: 18-55%) of new infections overall (city range: 21-57%). Variability in PAF_{RAI} estimates was most influenced by uncertainty in the estimate of the per-act increased risk of RAI relative to RVI and the number of sex acts.

Conclusions: RAI may contribute disproportionately to new heterosexually-acquired HIV infections among at-risk low-income women in the US, meaning that tools to prevent HIV transmission during RAI are warranted. Number of RVI and RAI acts should also be collected to monitor heterosexually-acquired HIV infections.

Keywords

Anal sex; HIV; women; sexual behaviour; heterosexual; United States

Introduction

Current evidence suggests that penile-anal intercourse (receptive anal intercourse, RAI) increases the risk of HIV acquisition per sex act by up to 18-fold compared to one act of penile-vaginal intercourse (receptive vaginal intercourse, RVI)[1,2]. Previous modelling studies suggested that even if 5-10% of all heterosexual sex acts are RAI this may reduce the effectiveness of HIV interventions that are only efficacious for RVI, such as daily or long-lasting vaginal microbicides, by up to 50%[3,4].

Recent systematic reviews suggest RAI is commonly practised by women across a variety of populations and contexts throughout their lifetime[5,6]. For example, 2-36% of South African women and 20-24% of sexually active women under 25 years old worldwide report ever engaging in RAI[5,6]. National surveys in the US and UK indicate that around 12 and 11% of women aged 18-59 years respectively engaged in RAI over the previous year[7-9]. RAI prevalence among women may also have increased since the 1990s[8,10,11], even doubling in places[8,10]. Women reporting RAI often also report other practices such as exchange sex[12], high numbers of sexual partners and more frequent sex acts[13,14], substance use[12,13,15,16], coerced sex[17] and low condom use[14,18] associated with increased risk of acquiring sexually transmitted infections (STI), including HIV. Nevertheless, RAI has, until recently, been sidelined from receptive partner-controlled HIV prevention and product innovation both for

men who have sex with men (MSM) and women[19-22]. Understanding the epidemiological context of RAI among heterosexual women and its contribution to HIV and other STI, is necessary to tailor prevention messaging and product development, such as rectal microbicides[23,24].

In the US, heterosexual transmission accounted for 24% of all adult and adolescent HIV infections diagnosed in 2017; whilst MSM and people who inject drugs (PWID) accounted for 70% and 6% of cases[25]. Black/African American (henceforth, Black) and Hispanic/Latino (henceforth, Hispanic) populations are disproportionately affected by HIV[26]. In 2017, the HIV diagnosis rates (per 100,000) for adult and adolescent Black and Hispanic women were respectively 15 and 3 times the rate for White women[25]. The Centers for Disease Control and Prevention (CDC) established the National HIV Behavioral Surveillance (NHBS), a comprehensive system for conducting behavioural surveillance among people at high risk for HIV infection in the U.S. and identifying risk factors (including RAI) associated with infection[27,28].

Using NHBS data from low-income women at increased risk of HIV infection living in 20 US cities, we 1) describe RAI practices across key demographic and risk factor groups among women reporting heterosexual intercourse in the past year and 2) use these results to inform a mathematical model and estimate the annual fraction of new heterosexually-acquired HIV infections that are due to RAI among at-risk women in the NHBS sample overall and in 20 cities.

Methods

Data used

NHBS has conducted independent serial cross-sectional behavioural surveys among heterosexual women (NHBS-HET) living in high HIV prevalence metropolitan statistical areas (MSAs) every three years since 2007[26,27]. To derive average estimates for 2010 and 2013, our analysis combines the data from 20 MSAs included in the 2010 and 2013 study cycles. The 2007 cycle was excluded from this analysis due to differences in the sampling methods. Detailed data collection procedures have already been described[26,29]. In short, participants were recruited through respondent driven sampling (RDS)[30]. Recruitment prioritised women with household income below the federal poverty guidelines[31] or with no more than high school education. Individuals aged 18-60 years were eligible to participate if they lived in a participating MSA, could complete the survey in English or Spanish, provided informed consent and reported at least one episode of sexual intercourse (RVI or RAI) with an opposite-sex partner during the previous year. As our analysis focused on heterosexually-acquired HIV, we excluded the minority of women who reported injecting drugs in the previous year (2010: N=165 excluded, 3.4%; 2013: N=192 excluded, 4.0%) or who only reported oral intercourse during their most recent sexual episode (2010: N=74 excluded, 1.6%; 2013: N=76 excluded, 1.6%).

The survey was administered through face-to-face interviews (FTFI) to collect demographic information (e.g. age, race/ethnicity, marital status) and self-reported sexual behaviour over the previous 12 months (e.g. RAI, number and type of male partners, condom use,

exchanging sex for money or drugs) as well as characteristics of their last sexual episode (e.g. whether participants practised RVI and/or RAI, condom use during RVI and RAI, partner type: main, casual or exchange partner, partner's HIV status, and partner's race - 2013 cycle only). Questions were the same across cycles apart from the question about sex work (in the 2010 cycle the definition of exchange sex included exchanging money or goods with either main or casual partners but in the 2013 cycle exchange sex included only casual partners). No information on number of sex acts per unit time or per partners was available. Health departments from participating cities obtained local institutional review board approval before initiating each cycle[26,29].

Statistical analyses

In this study, the level of RAI in the population was characterised by: 1) RAI prevalence, the proportion of women reporting RAI with at least one partner in the past-year, and 2) RAI fraction, the fraction of all acts (RVI and RAI) at last sexual episode that were RAI among those reporting RAI in the past year. We calculated RAI prevalence and RAI fraction estimates stratified by key demographic and risk factors (age, race/ethnicity, exchange sex and partner type), overall and by city for the two cycles combined. We also used two binary outcome variables measuring 1) whether or not women practised RAI in the past-year (RAI and non-RAI women respectively); 2) among sex acts of RAI women at last sexual episode, whether or not the sex act was RAI. Bivariate and stratified analyses, using chi-squared and Mantel-Haenszel tests respectively,[32] compared both outcomes across the levels of demographic and risk factors except for condom use during the last sexual episode across which only RAI prevalence was compared; two-sample t-test tested differences in the mean annual number of partners. Stratification controlled for city and additionally for each of the factors in turn. Among RAI women, bivariate and stratified analyses compared condom use at last vaginal sex with condom use at last anal sex. Partner's race/ethnicity was excluded from analyses as it was only collected in one cycle. We treated the data as a convenience sample; we report unadjusted and stratified odds ratios as well as 95% confidence intervals and p-values based on normal approximation. We report estimates and confidence intervals unadjusted for network size or clustering of RDS recruitment chains because these were used to derive prior ranges for parameters in the risk equation model and in model sensitivity analyses and not to make inferences about the wider population of low-income heterosexual women at risk of HIV. These intervals are therefore likely to be narrower than if recruitment-chain clustering was accounted for. This decision was taken because in sensitivity analyses quadrupling the standard error did not affect our model predictions of the PAF.

Risk-equation model

We developed a Bernoulli risk-equation model of HIV incidence in at-risk women[33]. The model was stratified by demographic and risk factors (noted j with J groups) to estimate the annual cumulative risk of HIV acquisition ($CIR_{i,j}$) over multiple independent sex acts per partnership among women practising and not practising RAI (noted i=1,2)(Equation 1). The model was used to estimate HIV risk overall and separately by age (J=2 groups: 18-24, 25-60 years old), race/ethnicity (J=4 groups: Hispanic, Black, White, Other), exchange sex (J=2 groups: not exchanging sex, exchanging sex), or city (J=20 groups) and finally by exchange sex within city (details in supplement tables 1&2, parameter ranges for exchange

sex within city available on request). $CIR_{i,j}$ depends on the annual number of sexual partners ($m_{i,j,k}$) of type "k" (i.e. main or casual) for women in groups ij, the probability that a male partner j' is HIV infected ($p_{j'}$), the annual number of sex acts per partnership of type k ($n_{i,j,k,}$), the fraction of sex acts which are RAI ($fa_{i,j,k}$), the probability of using a condom during RVI ($fcv_{i,j,k}$) and RAI ($fca_{i,j,k}$) per partner type, condom efficacy in reducing HIV transmission during one RAI or RVI act (e_c), HIV transmission probability per RVI (β), and the relative risk of HIV infection during RAI compared to RVI (RR_{RAI}). For each factor, the overall HIV risk is the average of the cumulative incidences over the J groups weighted by relative group size and RAI status ($F_{i,j}$) (Equation in supplement A).

$$CIR_{i,j} = 1 - \prod_{k=1}^{2} \Big[(1 - p_{j'}) + p_{j'}(1-\beta)^{n_{i,j,k} * (1 - fa_{i,j,k}) * (1 - fcv_{i,j,k})}(1 - (1 - e_c)\beta)^{n_{i,j,k} * (1 - fa_{i,j,k}) * fcv_{i,j,k}}(1 - \beta \cdot RR_{RAI})^{n_{i,j,k} * fa_{i,j,k} * (1 - fca_{i,j,k})}(1 - \beta \cdot RR_{RAI}(1 - e_c))^{n_{i,j,k} * fa_{i,j,k} * fca_{i,j,k}}\Big]^{m_{i,j,k}} \quad \text{Equation 1}$$

Parameter assumptions and model calibration

Uniform ranges of plausible values were specified for each parameter (i.e. prior parameter range) based on the unadjusted 95% CI of the estimates from NHBS data (overall and by demographic or risk group) when available and sourced from the literature otherwise (Table 1, supplement tables 1 and 2). The HIV transmission probability per unprotected receptive vaginal intercourse (RVI) and the increase in HIV acquisition risk during RAI (RR_{RAI}) were based on meta-analyses of observational studies[2,34,35]. Given the uncertainties in these estimates, we assumed wider ranges, varying RR_{RAI} between 2-18[1,2,34-36] (supplement E) and the transmission probability per RVI between 0.0004-0.002. HIV prevalence of heterosexual male partners was derived from published data on male participants of NHBS-HET[37]. As no information on number of sex acts per partnership type ($n_{i,j,k}$) was directly available from NHBS-HET surveys, we specified and independently sampled wide prior ranges for both RAI and non-RAI populations, and obtained posterior estimates of these parameters at the fitting stage (see below). Empirical estimates of overall HIV incidence rate and the incidence risk ratio for RAI vs non-RAI women were available from a cohort study (HPTN-064[38,39]) conducted in 2009-2010 in a comparable study population in 5 of 20 NHBS-HET sites.

At the fitting stage, we simultaneously sampled prior parameter ranges using Latin-hypercube sampling[40] to generate 10,000 parameter sets that were used to produce model predictions of the annual cumulative HIV incidence risk ($CIR_{i,j}$). Predicted cumulative incidence risk estimates were converted to annual incidence rates to be comparable with data observed in 2010 from HPTN-064[41] (supplement C). We retained entire parameter sets if predicted rates and risk ratio fell within the 95%CI of HPTN-064 HIV incidence rate[39] and incidence risk ratio[38], and if the total number of sex acts in a year across all partnerships and

the ratio of sex acts reported by RAI women and non-RAI women generated by the model agreed with available data from similar US populations and other sources (prior parameter ranges in table 1; details in supplement parts A, B). Given the lack of city-specific HIV incidence data, we estimated it by applying a scaling factor, to the HPTN-064 incidence rate estimates, based on 2013 HIV diagnosis rate among adults for each city (details in supplement C). The resulting sets of fitting parameters define the baseline scenario in our modelling analysis.

Modelling analysis

For each retained parameter set, we derived two population attributable fraction (PAF) estimates measuring the fraction of heterosexually-acquired HIV infections in a year among women due to 1) RAI only (PAF_{RAI}) and 2) RAI as well as the higher risk behaviours reported by women practising RAI ($PAF_{RAI+Beh}$). PAF_{RAI} compares the cumulative incidence between the baseline scenario where $RR_{RAI}>1$ ($CIR_{RR>1}$) and a counterfactual where $RR_{RAI}=1$ ($CIR_{RR=1}$), i.e. where per act risk during RAI is assumed to be the same as during RVI. $PAF_{RAI+Beh}$ compares the CIR between the baseline scenario and a second counterfactual where $RR_{RAI}=1$ and where the risk behaviours of RAI women (i.e. condom use and number of sexual partners) are set to the same level as non-RAI women.

We report the median PAF and 10th-90th percentile uncertainty intervals (80%UI). We conducted an uncertainty analysis first to assess which parameter most influenced the variation across overall PAF estimates using Pearson's correlation coefficients. Second, we conducted a more general sensitivity analysis using wider parameter ranges and fitting only on the incidence rate and incidence risk ratio (as opposed to fitting additionally to the number of acts and act ratio). The first and second analysis help determine which additional and new data to prioritise for collection in the context of the NHBS study and in settings where little data is available, respectively.

Although our analysis focused on heterosexual transmission, we also assessed the potential influence of HIV transmission by needle-sharing on PAF_{RAI} estimates (see detailed methods in supplement D). We explored scenarios where we assumed that HIV incidence rate among PWID was the same, twice or five times larger than among women who do not inject (NIDU).

All analyses were conducted in R version 3.4.0[42] using R-studio version 1.0.143[43].

Results

Study sample

Women had a mean age of 37 years, 24% were under 25 years old, 73% were Black, 41% reported having had only main partners in the last year, and 23% reported exchanging sex. HIV prevalence was 3% overall and similar between women who did or did not practise RAI in the past year (OR=0.99, 95%CI 0.77-1.29). Apart from race/ethnicity, other city-level demographic and risk factor patterns were broadly similar to overall patterns. In all but four cities (Denver, Los Angeles, San Diego and San Juan) the percentage of Black women was

at least 60%. In these four cities, the percentage of Hispanic women was greater than 40% (Supplement figures 1a-d).

How common is RAI?

Table 2 summarises the RAI prevalence and RAI fraction of the sample participants by demographic characteristics for both study cycles combined. Overall, RAI prevalence was 32% (95%CI 31-33%). RAI prevalence was high even among 18-19 year olds (22%), but higher among older women (>31%)(Table 2). RAI prevalence was higher among Hispanics (35%) and Whites (37%) than Blacks (31%) (p=0.003) and among women reporting only casual (41%) or reporting exchange sex partners (53%) in the past year than women with only main partners (19%) or no exchange partners (26%) but consistent across marital status (Table 2).

RAI prevalence was consistently high across cities, ranging from 18% in New Orleans (95%CI 16-22%) to 60% in San Juan (95%CI 55-65%; Figure 1 and Supplement table 2). Among 18-19 year olds RAI prevalence varied substantially across cities (mean ranges: 6% in Miami to 61% in San Juan) and was lower than among 25-29 year olds in 5 cities; prevalence differed less among 25-29 year olds and older age groups; supplement figure 2a). Across cities with at least 10 participants RAI prevalence ranged between 18-50% among Blacks, 15-60% among Hispanics, 14-69% among Whites, and 20-64% among Other races/ethnicities (supplement figure 2b). In all cities, RAI prevalence was higher among women who had casual-only and main-and-casual partners over the past year than women who had main partners only (supplement figure 2c) and was higher among women exchanging sex than women who did not (supplement figure 2d).

How frequently is RAI practised?

A quarter (27%, 95%CI 25-28%) of the sex acts during the most recent sexual episode of RAI women were RAI (Table 2). Similarly, a quarter of unprotected sex acts were unprotected RAI (27%, 95%CI 26-29%) (results not shown). The RAI fraction ranged between 24% among 18-19 year olds to 30% in 40-60 year olds (p=0.05), 19% among White women to 27% among Hispanic women (p=0.28) and was consistent across marital status (26-28%, p=0.67). The RAI fraction was higher in women exchanging sex (30%, OR=1.28, 95%CI 1.10-1.47, p<0.001) than women not exchanging sex (25%) (Table 2).

Across cities, the RAI fraction varied between 18% (95%CI 12-25%) in Denver and 34% (95%CI 29-39%) in San Juan. Patterns of RAI fraction by age group, race/ethnicity and exchange sex within cities resembled the overall patterns (though comparisons across cities were limited by small numbers) (data not shown).

Differences in sexual behaviours reported by women reporting/not reporting RAI in the past year

Table 3 describes the sexual behaviours of RAI and non-RAI women. RAI women reported higher numbers of sexual partners (mean difference=6.7, 95%CI 4.7-8.7), were more likely to report casual partners at last sex (OR=1.91 95%CI 1.74-2.10), report a partner with unknown/positive HIV status (OR=1.71 95%CI 1.56-1.88), but were less likely to report

condoms with main or casual partners at last RVI (e.g. OR=0.44, 95%CI 0.38-0.50) and hardly changed after stratifying by city (Table 3). Stratification by age group, race/ethnicity, exchange sex produced similar results (not shown). There was only weak evidence that RAI women used condoms less often during last RAI than last RVI (mhOR=0.80, 95%CI 0.61-1.05), (Table 3).

Predicted fraction of heterosexually acquired HIV infections due to RAI

The model suggests that RAI independently contributed two-fifths of all annual heterosexually-acquired HIV infections among this at-risk sample, i.e. PAF_{RAI} = 41% (80%UI:18-55%) (Figure 2A). The $PAF_{RAI+Beh}$ reflecting the contribution of RAI and riskier sexual behaviours of RAI women was only 2percentage points higher (43%, 80%UI:17-63%) (Figure 2A).

Across cities, PAF_{RAI} ranged from 21% (80%UI:7-39%) in Denver to 57% (80%UI:30-70%) in San Juan reflecting the RAI prevalence across cities (Figure 2B). PAF_{RAI} estimates did not differ substantially by age group, or race/ethnicity (supplement figure 3) reflecting limited differences in RAI prevalence and RAI fraction between groups. However, PAF_{RAI} was substantially greater for women exchanging sex than women not exchanging sex overall (median: 57% vs 31%) and across all cities (ranges=exchange: 30-64%; not exchange: 15-56%) apart from Dallas (PAF_{RAI}: exchange similar to not exchange ~30%) (Figure 2A, supplement figure 4).

Uncertainty and Sensitivity analyses

First in our uncertainty analysis, RR_{RAI} (correlation=0.89) and the total number of RVI acts among non-RAI women (correlation=0.28) were the parameters that were most associated with the variation in PAF_{RAI} estimates (Figure 3A). PAF_{RAI} 80% uncertainty interval estimates increased from 20-30% to 43-58% if RR_{RAI} increased from 5 to more than 15, respectively (Figure 3B) and decreased from 28-55% to 15-51% if number of vaginal acts increased from 50 to 150 (Figure 3C). Second, in our more general sensitivity analysis with wider parameter ranges the correlation with RR_{RAI} was substantially lower (correlation=0.59) and RAI prevalence and RAI fraction became more influential (correlation=0.35, −0.27 respectively) followed by HIV prevalence among male partners (Figure 3D).

Finally, we assessed the influence of transmission due to needle-sharing among PWID on our PAF_{RAI} estimates. Assuming 100% of infections among PWID come from injecting behaviours, the PAF_{RAI} due to RAI would range from 39% (UI:17-52%), 37% (UI:16-49%), 32% (UI:14-43%) if the HIV incidence rate among PWID was the same, twice as large, and five times larger than in NIDU.

Discussion

Our results suggest that approximately one in three low-income women at increased risk for HIV infection in the US NHBS sample practised RAI at least once a year, overall. RAI was commonly practised across cities (~1 in 2 to ~1 in 5), including by young women (18-19 years old). Women who practised RAI in the past year did so frequently (overall

approximately one RAI/unprotected RAI in 4 sex acts/unprotected sex acts), which means that in the whole sample of women (reporting and not reporting RAI), about 1 in 10 of all sex acts/unprotected sex acts were RAI/unprotected RAI. Women practising RAI also reported riskier sexual behaviours than non-RAI women: more sexual partners annually and lower condom use with main and casual sexual partners, even though condom use was universally low.

Despite only 11% of all unprotected acts being unprotected RAI, RAI alone may contribute to 41% (80% UI: 18-55%; city range: 21%−57%) of heterosexually-acquired incident HIV infections annually among low-income women in the NHBS sample, due primarily to the high risk of HIV transmission during RAI. The higher sexual risk behaviour of women practising RAI had a negligible impact on the PAF. The PAF_{RAI} was even higher among women exchanging sex (overall: ~60%, city range: 30%−64%) partly because RAI prevalence was the highest and about twice as large among women who exchanged sex (overall and across cities) than among women who did not. Even though younger and Black women tended to report lower RAI prevalence than older or White and Hispanic women, there were no major differences in PAF estimates by age or race/ethnicity given the relatively small differences in RAI prevalence and no difference in the fraction of last sex acts that were RAI across these groups.

RAI prevalence among low-income women in this study is higher overall and across all ages than general populations[7], but comparable to other at-risk populations[13] in the US. Our estimates of prevalence among18-19 year old women are consistent with recent review estimates among youth (20-24%)[5] and adds to growing evidence of a wide (and widening) sexual repertoire among adolescents in the US[44,45] and elsewhere[5,46,47]. Similar to our findings, other studies among at-risk and general populations also found Black women were less likely than White women to report lifetime[14,48,49] or recent RAI[12] and yet others observe no differences[13,50]. While our results do not exclude RAI as a HIV risk factor for Black women, other factors driving risk such as partner concurrency[50] and the sexual network may be more influential[51]. Our results are consistent with findings from other studies that women who practise RAI tend to report higher numbers of sexual partners[50], exchange sex[12,50,52] and lower condom use during vaginal and anal sex[48,50].

We know of three other mathematical models predicting the contribution of RAI to different heterosexual epidemics: two from Africa[53,54] and one from the US[55]. Our estimates are slightly higher than O'Leary et al's[55] transmission dynamics model predictions for a nationally representative population of 13-64 year old US women over one year (PAF:28%) but are comparable to estimates for 18-34 year old women who have higher RAI prevalence (PAF:40%)[55]. Their model also accounts for transmission risk through injection drug use. Our estimates are more comparable when we account for HIV infection risk from needle sharing (32-39%). The remaining differences can be partly explained because the two models use different prior ranges for sensitive model parameters; O'Leary et al. use data from general populations with higher condom use, lower RAI prevalence and RAI fraction than reported by women in the NHBS survey[55].

Strengths and limitations

Our analysis has several strengths and some limitations chiefly due to shortcomings in data. We report for the first time about 4 in 10 new heterosexually-acquired HIV infections among a specific population of low-income women at increased risk of HIV infection in the US may be due to RAI despite a minority of all unprotected sex acts being unprotected RAI. We benefited from detailed high quality sexual behaviour data from multiple cities, which allowed us to account for parameter uncertainties and for detailed differences in the sexual behaviour of women reporting and not reporting RAI, across different demographic and risk groups and twenty different cities. We were able to draw on a comparable study (HPTN-064) to provide estimates of HIV incidence and the relative risk of RAI to calibrate the model[38,39]. While, we cannot exclude the possibility of reporting biases of RAI from FTFI which can produce lower estimates for sensitive behaviours than more confidential methods[56], NHBS estimates were similar to those from HPTN-064 which used more confidential methods (RAI prevalence:38%). Our analysis likely reflects the average behaviour prevailing over the 2010-2013 period rather than a specific year. Prior parameter ranges were derived from confidence intervals of estimates that were unadjusted for RDS design. However, this did not impact our modelling results since our PAF and UI estimates were very similar even after quadrupling standard errors (i.e. prior parameter ranges) in additional sensitivity analyses (results not shown). The lack of impact is because the main source of uncertainty in PAF estimates was due to uncertainty in estimates of the biological increased risk of RAI compared to RVI. Although the range for this parameter was informed by pooled estimates from systematic literature reviews, it remains uncertain because it is based on few studies[1,2,34-36]. We did not have data on the number of RVI and RAI acts (used to estimate the total number of sex acts and the fraction of sex acts that are RAI). Instead, we approximated the fraction of acts that were RAI using the fraction of RAI at the last sexual episode, which could be biased due to over- or under-reporting of certain practices at last sex. Our range for the RAI fraction is slightly higher but overlaps the confidence intervals of an estimate from a 1999 study among STI clinic attendees[13] and is comparable with estimates from general populations[55]. The total number of sex acts were informed from the literature and calibrated by model fitting. Our uncertainty analysis suggested that, while this was not the most important source of uncertainty in PAF estimates, it was still influential, meaning that questions on the number of protected and unprotected RAI and RVI acts would be valuable additions to future NHBS cycles. Our past year PAF estimates may underestimate the contribution of RAI to HIV transmission at a population-level since these estimates do not account for onwards transmissions from women to their male partners, and so on. Nevertheless, our results are consistent with a transmission dynamic modelling study[55].

Our extensive sensitivity analyses demonstrate the robustness of our findings and show that RAI contributes at least a third of infections even when infections from injecting drug use are accounted for. This estimate assumes all HIV infections among PWID in NHBS were due to injection practices and that the incidence rate among PWID was five times greater than the incidence rate among NIDU. These estimates are conservative because a fraction of infections among PWID are likely sexual[57-59], and available studies suggest HIV incidence rates among PWID may be about twice those observed among higher-risk heterosexuals[60].

Even though our estimates are not representative of all low-income women at increased risk of HIV in the US, this population is historically underserved for prevention and care[26,61,62] and are a priority population for HIV prevention[27,28].

Public Health Implications

Our analysis highlights RAI as a key risk factor for HIV acquisition among women across a range of demographic and risk groups. This finding can usefully inform HIV prevention strategies among heterosexual women at increased risk for HIV infection in the US as well as future data collection. The consistently high prevalence of RAI in young women across cities is particularly concerning because it is often coerced[17,63,64] which could further elevate the per-act HIV risk[49,65-67]. Although, women who engage in RAI also have higher risk practices, our results suggest that the greatest risk is due to the elevated transmission efficiency during RAI. These findings imply that vaginal microbicides or rings with no efficacy against rectal transmission may have limited utility for this population and, together with our observations of consistent low condom use, support the value of pre-exposure prophylaxis drugs with systemic activity. Finally, our larger sensitivity analysis suggested HIV studies wishing to evaluate RAI in contexts where no data exist should prioritise RAI prevalence and RAI fraction, agreeing with previous recommendations[66]. Despite the importance of RAI to heterosexual HIV transmission, key data to estimate its contribution to HIV epidemics such as the frequency of RAI sex acts are missing. The extent that RAI is underreported and imprecisely measured[5,68] in different contexts and subgroups affects the accuracy of our estimates of RAI practices across populations and our estimates of its contribution to HIV epidemics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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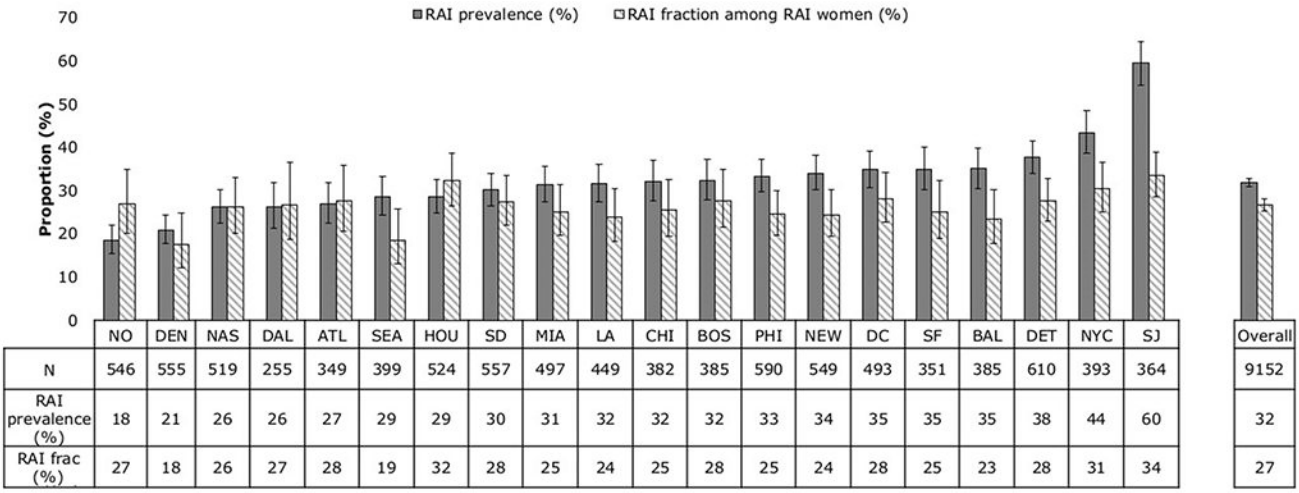


	NO	DEN	NAS	DAL	ATL	SEA	HOU	SD	MIA	LA	CHI	BOS	PHI	NEW	DC	SF	BAL	DET	NYC	SJ	Overall
N	546	555	519	255	349	399	524	557	497	449	382	385	590	549	493	351	385	610	393	364	9152
RAI prevalence (%)	18	21	26	26	27	29	29	30	31	32	32	32	33	34	35	35	35	38	44	60	32
RAI frac (%)	27	18	26	27	28	19	32	28	25	24	25	28	25	24	28	25	23	28	31	34	27

Figure 1.

RAI prevalence and RAI fraction overall and across cities, NHBS-HET combined 2010 and 2013 cycles. City abbreviations: NO New Orleans, DEN Denver, NAS Nassau, DAL Dallas, ATL Atlanta, SEA Seattle, HOU Houston, SD San Diego, MIA Miami, LA Los Angeles, CHI Chicago, BOS Boston, PHI Philadelphia, NEW Newark, DC Washington DC, SF San Francisco, BAL Baltimore, DET Detroit, NYC New York City, SJ San Juan, Puerto Rico.

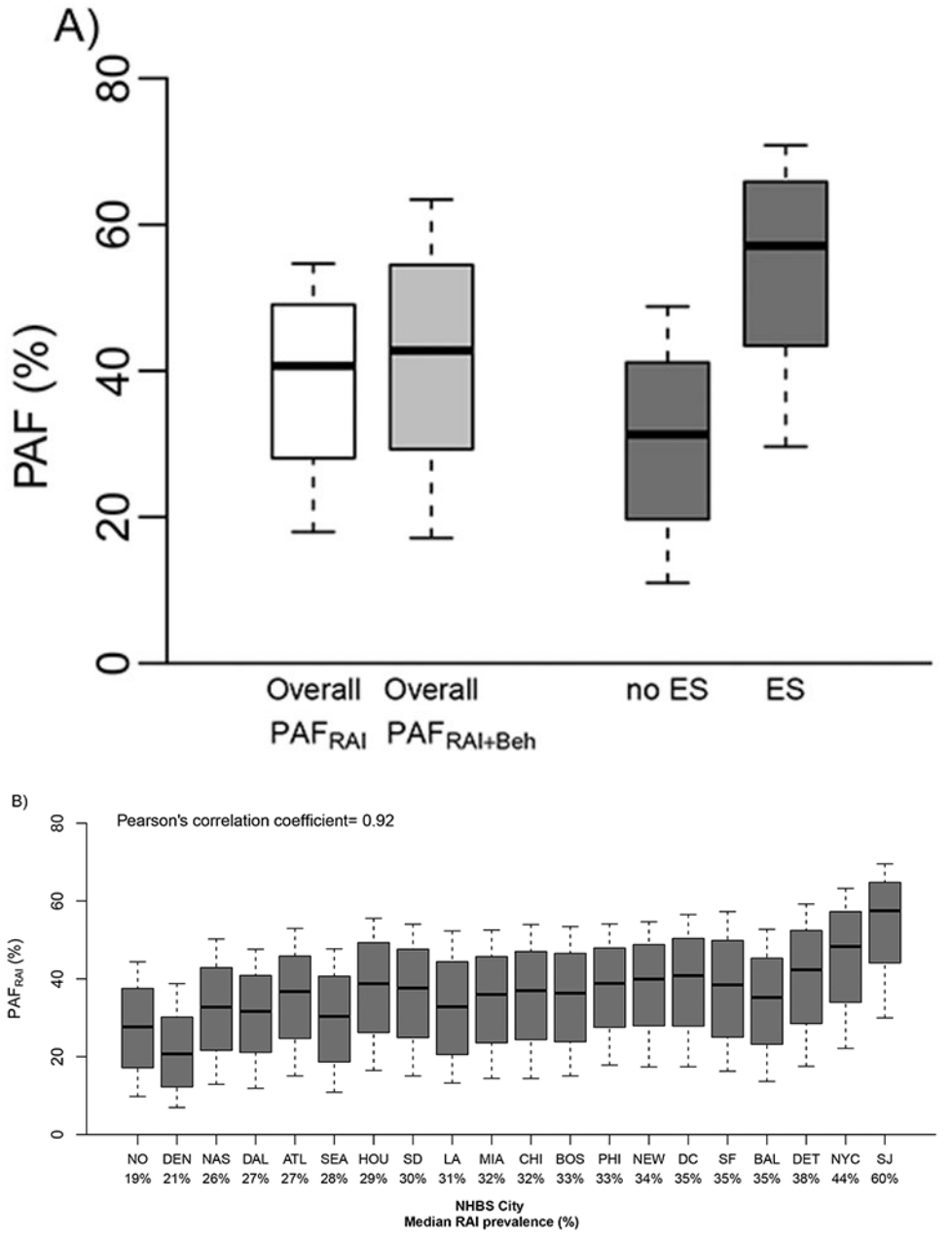
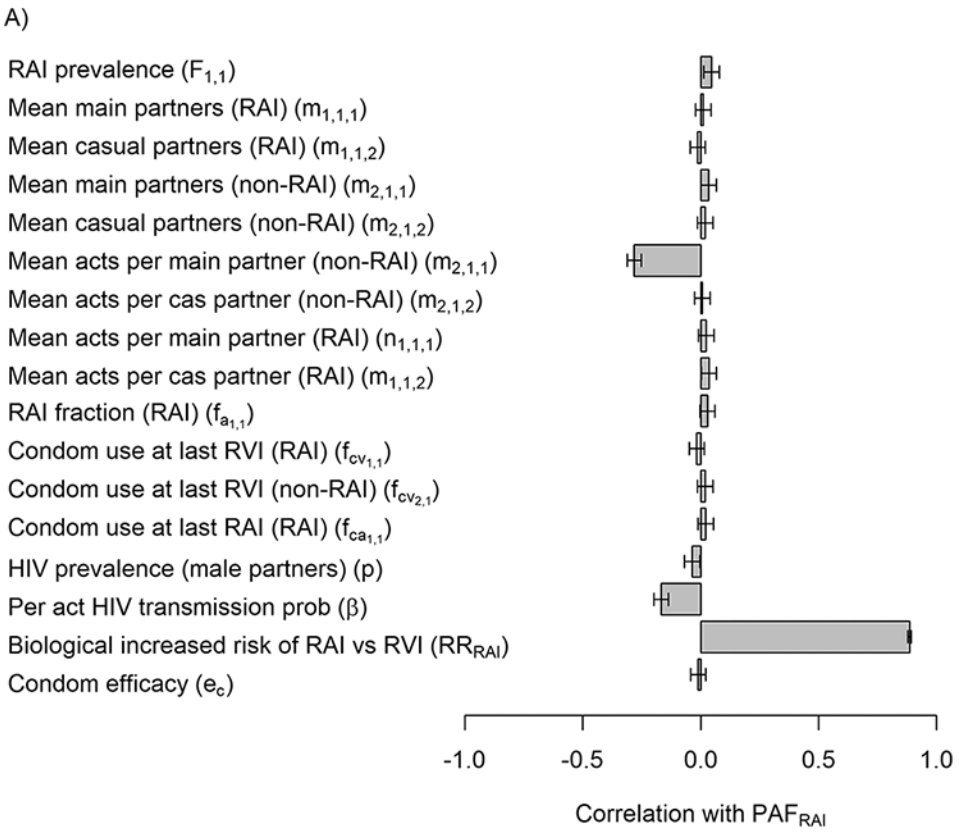
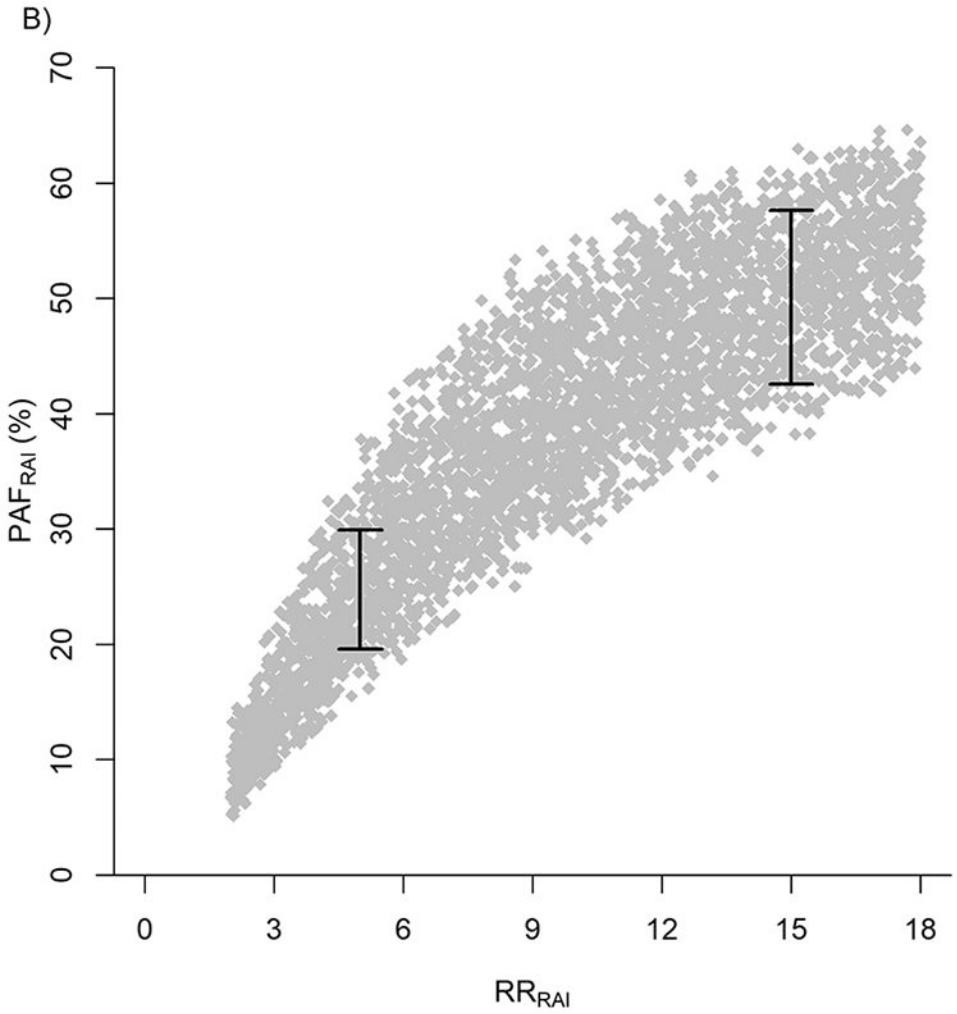
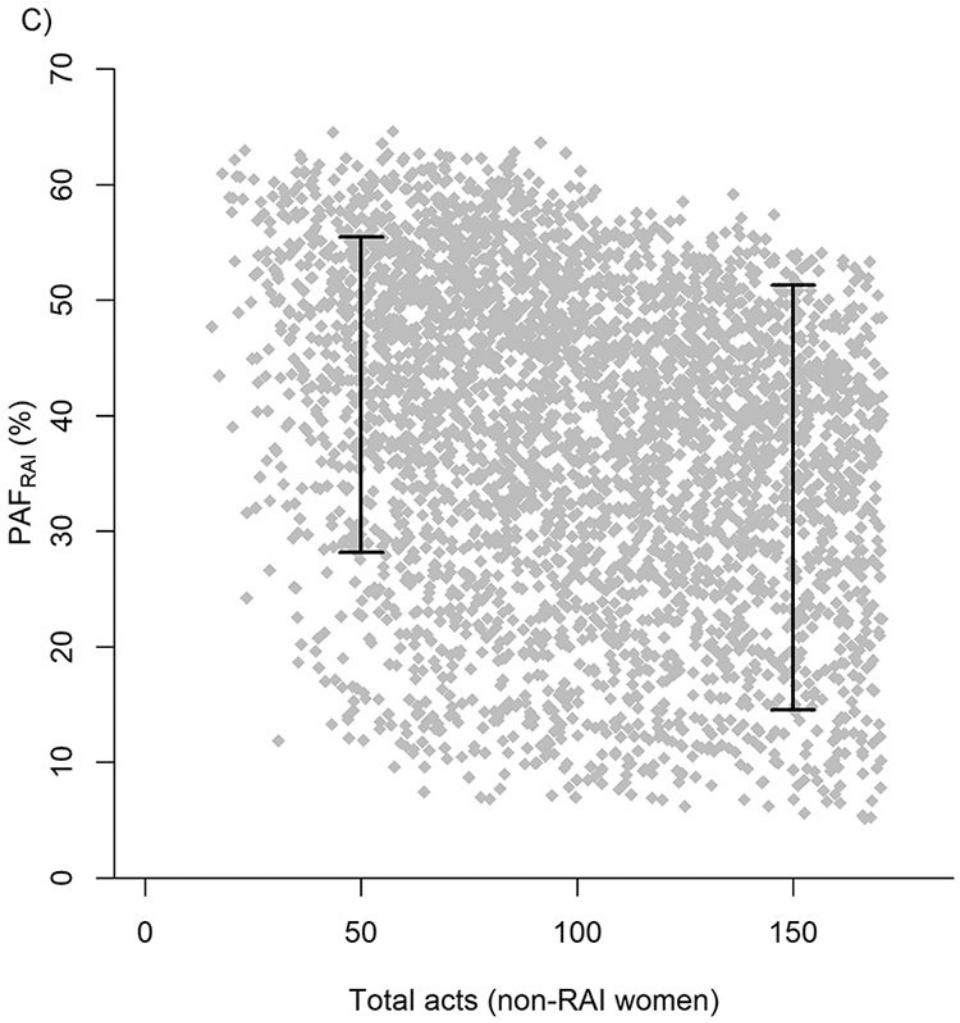


Figure 2.

A) Model estimates of the contribution of RAI to new annual HIV infections due to RAI alone (PAF_{RAI}) and due to RAI and riskier behaviours of RAI women ($PAF_{RAI+Beh}$) overall and among those who do (ES) and do not exchange sex (No ES). b) PAF_{RAI} in 20 US cities. Boxplots (median, and 10-90th percentiles) are shown in ascending order of city-specific median past-year RAI prevalence (Pearson's correlation coefficient between RAI prevalence and median PAF across cities). City abbreviations are as in figure 1.







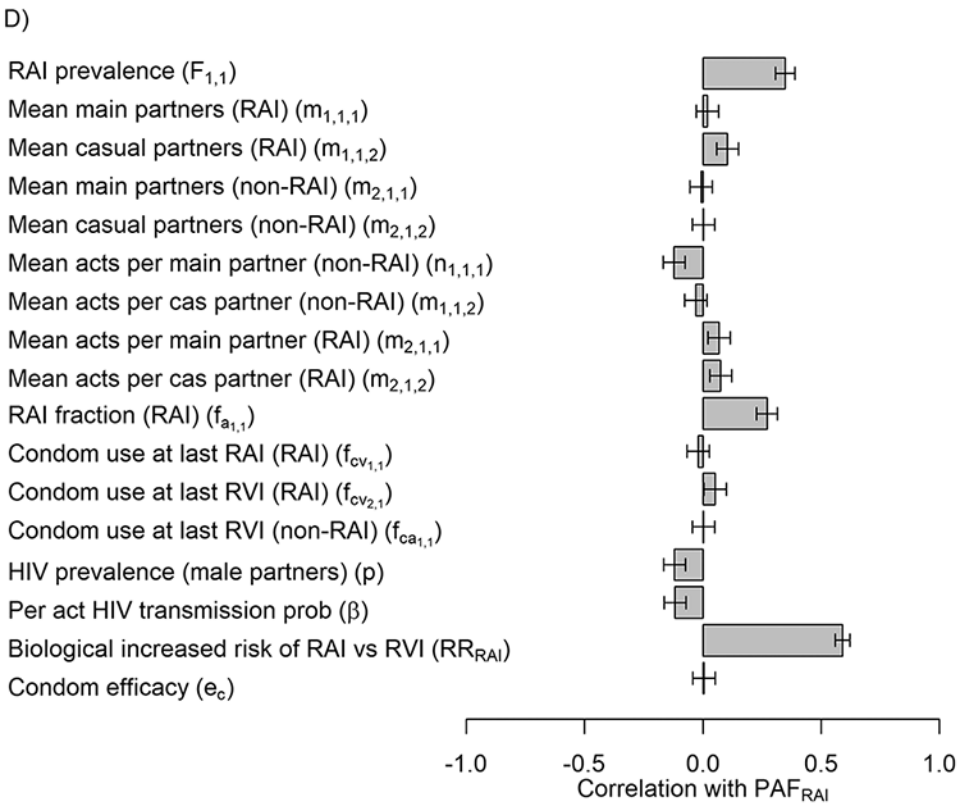


Figure 3.

In A) Tornado plot showing the correlation between uncertainty in PAF_{RAI} overall model (J=1) and key model parameters from NHBS-HET analysis. Input parameter ranges for each of the parameters are shown in table 1. In B&C) Scatter plots of the most influential parameters (endpoints represent 80%UI): RR_{RAI} (in B), total number of acts among non-RAI women (in C). In D) Tornado plot showing correlation of PAF_{RAI} variability with wider ranges of variables taken from the minimum and maximum values across cities.

Table 1.

Model parameters and their ranges for the overall model

Parameter (for individual in RAI group i=1,2 and overall model J=1)		Parameter ranges				Source
Symbols	Description	RAI (i=1)		Non-RAI (i=2)		
		Main partners (k=1)	Casual partners (k=2)	Main partners (k=1)	Casual partners (k=2)	
$F_{i,1}$	Fraction of the population	0.31-0.33		0.67-0.69		Table 2
$m_{i,1,k}$	Annual number of partners of type k	1.3-1.5	7.2-10.0	1.1-1.1	2.1-2.6	Table 3
$n_{i,1,k}$	Number of sex acts per year of per partner type k	0-150	0-3	0-150	0-3	13,69
$f_{a_j,1,k}$	Fraction of sex acts that are anal among RAI women (RAI fraction) with partner of type k	0.23-0.26	0.28-0.32	0	0	Table 2
$f_{cv_j,1,k}$	Fraction of vaginal sex acts that are protected by condoms with partner of type k	0.06-0.08	0.11-0.15	0.12-0.14	0.21-0.24	Table 3
$f_{ca_j,1,k}$	Fraction of anal sex acts that are protected by condoms with partner of type k	0.07-0.11	0.04-0.08	0	0	Table 3
p'_1	HIV prevalence in male partners of subgroup j'=1	1.3-2.7%				37
β	Male to female HIV transmission probability per unprotected vaginal act	0.0004-0.002				34,35
RR_{RAI}	Increased risk of HIV acquisition through RAI compared to RVI	2-18				1,2,34,35
e_c	Condom efficacy per act	0.8-1				70,71
Fitting data						
Annual HIV incidence		0.14-0.74%				39
Incidence risk ratio		0.3-8.7				38
Total sex acts per year across all partners		1-170		1–170		Supplement table 3 13,69
Ratio of total acts across all partnerships for RAI women to the total acts across all partnerships for non-RAI women		0.5-3		0.5-3		Supplement table 3 72,73

Table 2.

Receptive anal intercourse (RAI) prevalence and RAI fraction among women by demographic characteristics and past year sexual behaviours, combined NHBS-HET study cycles 2010 and 2013.

	Sexual behaviour in the past year among all women in study population					Last sexual episode among women who reported RAI in the past year				
Characteristics	**RAI prevalence % (95% CI)**	**RAI women (RAI in the past year) N (%)**	**Non-RAI women (No RAI in the past year) N (%)**	**OR (95%CI)**	**p-value**	**RAI fraction % (95%CI)**	**RAI acts[1] N_{acts} (%)**	**RVI acts[1] N_{acts} (%)**	**OR (95 %CI)**	**p-value**
Overall	31.9 (30.9-32.8)	2924 (100)	6228 (100)	NA		26.7 (25.3-28.1)	1045 (100)	2870 (100)	NA	
Demographics										
Age					<0.001					0.050
18-19	22.4 (19.4-25.7)	148 (5.1)	512 (8.2)	1.00		23.6 (18.1-30.1)	45 (4.3)	146 (5.1)	1	
20-24	31.7 (29.3-34.0)	483 (16.5)	1042 (16.7)	1.60 (1.30-1.98)	<0.001	25.6 (22.3-29.1)	162 (15.5)	471 (16.4)	1.12 (0.76-1.63)	0.570
25-29	33.0 (30.5-35.6)	424 (14.5)	860 (13.8)	1.71 (1.37-2.12)	<0.001	26.1 (22.7-29.9)	147 (14.1)	416 (14.5)	1.14 (0.78-1.68)	0.485
30-39	36.0 (33.8-38.2)	676 (23.1)	1203 (19.3)	1.94 (1.58-2.39)	<0.001	24.0 (21.3-27.0)	212 (20.3)	670 (23.3)	1.03 (0.71-1.48)	0.889
40-60	31.4 (29.9-32.9)	1193 (40.8)	2611 (41.9)	1.58 (1.30-1.92)	<0.001	29.1 (27.0-31.4)	479 (45.8)	1166 (40.6)	1.33 (0.94-1.89)	0.107
Race/ethnicity					0.003					0.278
Black	31.1 (30.0-32.2)	2079 (71.1)	4613 (74.1)	1.00		26.7 (25.1-28.4)	741 (70.9)	2034 (70.9)	1	
Hispanic	35.0 (32.8-37.3)	607 (20.8)	1127 (18.1)	1.20 (1.07-1.34)	0.002	27.7 (24.8-30.8)	231 (22.1)	603 (21.0)	1.05 (0.88-1.25)	0.570
White	37.2 (31.7-43.1)	102 (3.5)	172 (2.8)	1.32 (1.02-1.69)	0.033	19.4 (13.4-27.2)	24 (2.3)	100 (3.5)	0.66 (0.42-1.04)	0.069
Other	30.0 (25.9-34.4)	133 (4.5)	311 (5.0)	0.95 (0.77-1.17)	0.633	27.0 (21.0-33.9)	48 (4.6)	130 (4.5)	1.01 (0.72-1.43)	0.939
Marital status					0.187					0.665
Married/cohabiting	31.0 (28.7-33.4)	468 (16.0)	1042 (16.7)	1.00		26.3 (24.6-28.1)	648 (62.0)	1815 (63.2)	1	
Never married	31.7 (30.5-32.9)	1,845 (63.1)	3,982 (63.9)	1.03 (0.91-1.17)	0.641	26.6 (23.3-30.2)	167 (16.0)	461 (16.1)	1.01 (0.83-1.24)	0.886
Other	33.7 (31.5-35.9)	611 (20.9)	1,204 (19.3)	1.13 (0.98-1.31)	0.102	27.9 (25.0-31.1)	230 (22.0)	594 (20.7)	1.08 (0.91-1.29)	0.368
Past year sexual behaviours						**Last-sex[3]**				
Partner type					<0.001					
Main only	18.8 (17.6-20.1)	707 (24.2)	3054 (49.0)	1.00		24.5 (22.8-26.3)	577 (55.2)	1780 (62.0)	1	
Main and casual partners	41.3 (39.8-42.9)	1628 (55.7)	2311 (37.1)	3.04 (2.74-3.37)		NA	NA	NA	NA	

	Sexual behaviour in the past year among all women in study population					Last sexual episode among women who reported RAI in the past year				
Characteristics	**RAI prevalence % (95% CI)**	**RAI women (RAI in the past year) N (%)**	**Non-RAI women (No RAI in the past year) N (%)**	**OR (95%CI)**	**p-value**	**RAI fraction % (95%CI)**	**RAI acts[1] N_{acts} (%)**	**RVI acts[1] N_{acts} (%)**	**OR (95 %CI)**	**p-value**
Casual only	40.6 (38.1-43.1)	589 (20.1)	863 (13.9)	2.95 (2.58-3.37)		30.0 (27.8-32.4)	468(44.8)	1090 (38.0)	1.32 (1.15-1.53)	<0.001
Exchange sex[2]					<0.001					0.001
No	26.0 (25.0-27.0)	1848 (63.2)	5264 (84.5)	1.00		24.9 (23.2-26.6)	601 (57.5)	1817 (63.3)	1	
Yes	52.7 (50.6-54.9)	1075 (36.8)	964 (15.5)	3.18 (2.87-3.52)	<0.001	29.7 (27.4-32.0)	444 (42.5)	1052 (36.7)	1.28 (1.10-1.47)	<0.001

All P-values are derived from the chi-squared statistic, 95% confidence interval using the Wilson interval and 95% confidence intervals for odds ratios are estimated using normal approximation (Wald).

NA = not available

[1]Number of acts defined as the sum of anal or vaginal acts reported by RAI women at last their sexual episode

[2]Definition changed across rounds: in 2010 the definition of women exchanging sex included women who had any exchange partners in the last year; in 2013 the definition of women exchanging sex included women who had only casual exchange partners in the last year.

[3]By definition this refers to acts with main or casual sexual partners at last sexual episode.

Table 3.

Differences in sexual risk behaviours between women who reported receptive anal intercourse (RAI) and did not (non-RAI) in the past-year, combined NHBS-HET study cycles 2010 and, 2013.

Sexual risk behaviours	**RAI women N=2924**		**Non-RAI women N=6228**		**Mean difference[1] (95% CI)**	**p-value**
Behaviours in past 12 months	**Mean (N)**	**95%CI**	**Mean (N)**	**95%CI**		
Number of partners						
All partners	10.2	7.7-12.7	3.5	3.0-3.9	6.7 (4.7-8.7)	<0.0001
Main partners	1.4	1.3-1.5	1.1	1.1-1.1	0.3 (0.1-0.4)	<0.0001
Casual partners	8.6	7.2-10.0	2.3	2.1-2.6	6.3 (4.8-7.7)	<0.0001
Last-sex partner characteristics	**N**	**%**	**N**	**%**	**OR (95%CI)**	**mhOR[2] (95% CI)**
Partner type						
Main partner	1805	61.8	4704	75.6	ref	ref
Casual partner	1115	38.2	1520	24.4	1.91 (1.74-2.10)	1.84 (1.67-2.02)
Partner HIV status						
Negative	941	32.2	2792	44.9	ref	ref
Unknown/positive	1979	67.8	3431	55.1	1.71 (1.56-1.88)	1.68 (1.53-1.85)
Condom use during last sexual episode	**N**	**%**	**N**	**%**	**OR (95%CI)**	**mhOR[2] (95% CI)**
Condom use – at last RVI						
All partners						
UVI	2605	90.8	5054	81.2	ref	ref
Condom protected RVI	264	9.2	1170	18.8	0.44 (0.38-0.50)	0.46 (0.40-0.53)
Main partners						
UVI	1657	93.1	3984	84.7	ref	ref
Condom protected RVI	123	6.9	720	15.3	0.41 (0.34-0.50)	0.43 (0.35-0.53)
Casual partners						
UVI	948	87.1	1070	70.4	ref	ref
Condom protected RVI	141	12.9	450	29.6	0.35 (0.29-0.44)	0.38 (0.31-0.47)
Condom use - by RAI women (all partners)			-	-		
UVI	2605	90.8	-	-		
Condom protected RVI	264	9.2			ref	ref
UAI	970	92.8	-	-		
Condom protected AI	75	7.2			0.76 (0.58-1.00)	0.80 (0.61-1.05)

Note. RAI, receptive anal intercourse; UVI, unprotected vaginal intercourse; UAI, unprotected anal intercourse; RVI, receptive vaginal intercourse

[1] T-tests stratified for age, exchange sex, race/ethnicity produced similar results, not shown (with some exceptions where there was weaker evidence for a difference in main partners among Hispanic and Other racial/ethnic women and for main and casual partners among White women, p>0.05). Evidence for a difference in main partners was only observed in San Diego (p=0.02); there was evidence for a difference in casual partners in all but 4 cities (Baltimore, Denver, San Juan, Seattle).

[2] Mantel-Haenszel OR stratified for city (adjustments for age, exchange sex, race/ethnicity produced similar results, not shown)