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## Effect of Rectal Douching/Enema on Rectal Gonorrhoea and Chlamydia Among a Cohort of Men Who Have Sex with Men on HIV Pre-Exposure Prophylaxis

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### Abstract

**INTRODUCTION**—Rectal douching/enema (RD) is a common practice among men who have sex with men (MSM) in preparation for sex. RD can break down the rectal mucosal barrier and potentially affect the rectal microbiome, however, it is unclear if this is associated with acquiring rectal infections (RI) with either rectal gonorrhoea (NG) and/or chlamydia (CT).

**METHODS**—From 2013–2015, 395 adult HIV-uninfected MSM were enrolled in a randomized controlled study for pre-exposure prophylaxis (PrEP) adherence with routine sexual risk survey and testing. Using data from this cohort, baseline differences by RI were assessed using Pearson's Chi-square and Wilcoxon-Mann-Whitney test. Association between RD and RI was modelled using multivariable logistic regression adjusted for potential confounders (sexual behaviour, substance use, and age) selected a priori. Effect modification by number of male partners and sensitivity analysis to rule out reverse causality were also conducted.

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AH and SM conducted statistical analysis.

All authors interpreted data, reviewed drafts and approved final version.

**Competing Interest:** None declared.

**Data Sharing:** Data can be available at request to corresponding author.

**Ethical Approval:** All participants were consented prior to participating.

**RESULTS**—Of 395 participants, 261 (66%) performed RD and 133 (33%) had at least one NG/CT RI over 48 weeks. Number of condomless anal receptive sex (med:4,  $p<0.001$ ), male partners (med:6,  $p<0.001$ ), and substance use (any of methamphetamine/hallucinogens/dissociative/poppers) ( $p<0.001$ ) were associated with increased odds of RI. Controlling for potential confounders, odds of prevalent RI were 3.59 ( $p<0.001$ , 95% CI 1.90–6.78) and incident RI 3.87 ( $p=0.001$ , 95% CI 1.78–8.39) when douching weekly or more compared to not douching. MSM with more than six male partners had 5.41 ( $p=0.002$ , 95% CI 1.84–15.97) increased odds of RI when douching weekly or more compared to not douching.

**CONCLUSION**—Rectal hygiene with RD is a common practice (66%) among HIV-uninfected MSM on PrEP in this study, which increases the odds of acquiring rectal NG and/or CT independent of sexual risk behaviour, substance use and other factors. This suggests interventional approaches targeting rectal hygiene products and practices could reduce sexually transmitted infections.

## INTRODUCTION

Close to a million people were infected with chlamydia, gonorrhoea, syphilis and/or trichomoniasis globally in 2016<sup>1</sup>, all of which are curable. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are two common types of sexually transmitted infections (STIs) which facilitate transmission of human immunodeficiency virus (HIV)<sup>23</sup>. In the United States, chlamydia and gonorrhoea rates have been increasing and men who have sex with men (MSM) have been disproportionately affected by both STIs and the HIV epidemic<sup>4</sup>.

While the association between vaginal douching, HIV and STIs have been well studied<sup>5–8</sup>, evidence is conflicting for an association between rectal douching/enema (RD) and acquisition of HIV<sup>9–11</sup>, chlamydia<sup>12–15</sup>, and gonorrhoea<sup>15–17</sup>. Most RD studies have been in HIV-infected populations with limited data for risk associated with HIV-uninfected MSM and none on MSM on pre-exposure prophylaxis (PrEP). Introduction of PrEP as prevention for HIV has raised concerns regarding unintended negative consequences of increased STIs<sup>18, 19</sup>.

RD is the act of cleansing the rectum using a device to insert liquid into the rectum before anal receptive sex (ARS) and can be a potential risk for STIs. In a 2014 study by Noor and Rosser of 4,992 MSM, most commonly cited reasons for douching included cleanliness, request of sex partner, advice by friend and to prevent STIs<sup>11</sup>. Studies have also demonstrated an association of RD with breakdown of rectal mucosal barrier leading to increased risk of HIV and lymphogranuloma venereum (LGV)<sup>12, 20, 21</sup>. While condomless anal receptive sex (cARS) has been associated with high prevalence of HIV/STI among MSM<sup>22</sup>, it is unclear if douching is associated with acquiring rectal infections (RI) with gonorrhoea or non-LGV chlamydia. In a recent cross-sectional study surveying RD and sharing douching equipment among MSM, no significant association was found between RD and RI after adjusting for risk factors, although frequency of douching was not included in the analysis<sup>15</sup>. To further test the hypothesis that RD is independently associated with RI, we used prospective cohort data from the California Collaborative Treat Group randomized control trial (Daily Text Messages To Support Adherence to PrEP In At-Risk for HIV

Individuals: The TAPIR Study) on PrEP adherence of high risk HIV-uninfected MSM to analyse if RD behaviour predicted prevalent and incident rectal gonorrhoea and/or rectal chlamydia, adjusting for differences in sexual risk behaviour, substance use and other factors.

## METHODS

### Study Setting

Data for this secondary analysis were obtained from sexual risk surveys and STI testing conducted for the TAPIR study enrolling from February 2013 to February 2015 at four Southern California medical centres (University of California, San Diego; University of Southern California; Harbor-University of California Los Angeles; and Long Beach Health Department). Subjects were followed for a minimum of 48 weeks ending in February 2016. Four hundred and thirty-five individuals screened for the study, 398 participants were eligible to enrol and 324 participants completed week 48 visit. Institutional review boards at each of the participating institutions approved the TAPIR study (NCT01761643).

### Eligibility Criteria

English or Spanish speaking MSM or transgender woman without HIV infection aged 18 years or older at increased risk of HIV were eligible to participate in the main study. This analysis was limited to 395 MSM enrolled (Supplementary Figure 1). HIV-uninfected status was confirmed by a negative 4<sup>th</sup> generation antigen-antibody assay or an antibody assay in addition to HIV nucleic acid amplification test (Procleix). Persistent elevated risk of HIV infection was assessed by meeting one or more of the following criteria: 1) At least one HIV-infected sexual partner for 4 weeks; 2) No condom use during anal intercourse with 3 male sex partners who are HIV-infected or of unknown HIV status during the last 3 months; or 3) No condom use during anal sex with 1 male partner plus an STI diagnosis during the last 3 months. All participants were prescribed tenofovir disoproxil fumarate (TDF) combined with emtricitabine (FTC) for PrEP and received comprehensive preventive care per the Centers for Disease Control and Prevention guidance for PrEP<sup>23</sup>.

### Study Measures

Douching frequency in the past 30 days was collected only at baseline with the following question, “In the past month, how frequently have you performed rectal douching or enema (cleaning out your rectum or colon)?” Response options were: “Never, once/twice, less than weekly, about weekly, more than once a week, do not know, and prefer not to answer.” Solution of RD was assessed by asking: “For rectal colonic cleansing in the past month what do you use?” Multiple response options were: “Nothing, soapy water, plain water, saline, mineral oil, do not know, prefer not to answer.” Participants were also asked if they used oral agents such as “polyethylene glycol-oral, oral colonic cleanser, other oral colonic cleanser” to promote bowel evacuation. For analytical purposes, responses on the frequency of douching were categorized as: 1) Never douching, 2) Douching weekly or more, and 3) Douching less than weekly. Responses on solution were dichotomized a priori to “Water only” and “Water and/or other solutions.”

Rectal chlamydia and gonorrhoea screening assessments were conducted using Hologic Aptima Combo2 and rectal swabs at baseline for all participants and weeks 4, 12, 24, 36 and 48 for most during follow-up. Participants with new STI diagnoses were notified and referred to their provider or local sexually transmitted disease clinic for treatment. The main outcome for this analysis was at least one RI by either chlamydia and/or gonorrhoea at any time point from baseline to week 48. Participants with multiple infections over 48-week period were counted once.

Study visits occurred at baseline and weeks 4, 12, 24, 36, and 48, and questionnaire responses were captured using a computer assisted self-report survey. Baseline data included sociodemographic characteristics (monthly income, education, age, race, ethnicity, employment and relationship status), HIV risk factor and antibiotic use. Risk behaviour on drug abuse (more than one drug at a time) and multiple substance use were collected every visit for past three months. Use of methamphetamines (e.g., crystal meth, ice, glass), hallucinogens (e.g., LSD, mushrooms, acid), dissociative (e.g., PCP, angel dust, ketamine) and/or poppers were combined into one substance use variable to collectively control for drugs associated with increased sexual risk.<sup>24</sup> Participants answering “yes” to sex in the past three months were asked “How many male sexual partners have you had in past 3 months?” Participants answering “yes” to ARS, as defined as “their penis in you, sometimes referred to as being a ‘bottom’” were also asked, “How frequently did you use condoms with (these) partners in the past 3 months when having anal receptive (their penis in you) sex?” Response options were: “Never, Rarely, Sometimes, Often or Always.” MSM answering “yes” to sex with anyone in the last month were asked to list “Number of unprotected anal receptive (their penis in you) acts.” Only MSM engaging in ARS were included in the models.

### Statistical Analysis

Baseline characteristics of 395 MSM with and without RI were summarized and compared using Pearson’s chi-squared or Fisher’s exact test for categorical variables and T-test and Wilcoxon Mann-Whitney test for continuous variables. Primary analysis on the effect of RD on RI by 48 weeks included 384 MSM and was conducted using a multivariable logistic regression adjusted for age, number of cARS, number of male sexual partners, use of antibiotics and substance use selected a priori based on causal structure of confounding<sup>25, 26</sup>. For analytical purposes, the median number of partners over 48 weeks was transformed to log base two to adjust for skewness and ease of interpretability. A sensitivity analysis was conducted to compare odds of incident cases (RI free at baseline and at least one positive test between weeks 4–48) with prevalent cases (at least one positive test between weeks 0–48) of RI to rule out reverse causality. A secondary analysis testing for effect modification by number of male sexual partners on RI was conducted by fitting interaction terms between RD and median number of male sexual partners (log 2 transformed) to the regression model. A p-value less than 0.05 was considered statistically significant. Goodness of fit and model selection was assessed using standardized Pearson residuals, likelihood ratio test, Hosmer Lemeshow and Akaike information criterion (AIC)/Bayesian information criterion (BIC) (Supplementary Tables 1-2, Supplementary Figures 2-3). Data management and statistical analysis was conducted using STATA 14.2, College Station, TX: StataCorp LP.

## RESULTS

### Sample Characteristics

Mean age of 395 participants was 35 years, ranging from 19 to 64 years. Mean age of MSM with RI was 33 years (SD 9), five years younger than MSM without a RI ( $p<0.001$ ). Majority of participants were non-Hispanic (70%) and White (71%), with fewer African Americans (17%), and Asian or other racial identity (5%). Participants were generally well educated with majority having college or some college level education (71%). Most participants were either employed or working part-time (81%) and were single (65%) for relationship status.

### Rectal Infection

One hundred and thirty-three of 395 participants (33%) had a RI over 48 weeks, majority with rectal chlamydia (81%), and less commonly with rectal gonorrhoea (41%). Twenty-two percent of participants with RI were infected with both rectal gonorrhoea and chlamydia. Among 133 participants with RI, 55 (41%) had a RI at baseline, 78 (59%) were RI free at baseline, but had a RI between weeks 4–48 (incident cases). Majority of incident cases were rectal chlamydia infections (81%), with fewer rectal gonorrhoea (37%), and 18% with rectal gonorrhoea and chlamydia.

### Sexual, Drug Use and Douching Behaviour

Frequency of condom non-use for ARS was significantly associated with RI ( $p<0.017$ ). Only 9% of participants without RI reported never using a condom for ARS compared to 15% of participants with a RI. Overall, participants with RI at baseline had higher: 1) Number of cARS (median 1, IQR 0–5 vs. median 0, IQR 0–2;  $p<0.001$ ); 2) Number of male sexual partners (median 8, IQR 5–10 vs. median 5, IQR 3–10;  $p=0.001$ ), and 3) Substance use (74% vs. 52%,  $p<0.001$ ).

Total of 261 (66%) of 395 MSM reported RD at baseline, 81% MSM with RI were douching compared to 59% without a RI. While the majority of MSM used a water solution for douching/enema, 32% of MSM who douched used a combination of water and/or other solutions. Proportion of participants douching less than weekly in the past month were similar between MSM with and without RI (36% and 33%, respectively); however, 47% of MSM with RI douched more than weekly in the past month compared to 23% without any RI ( $p<0.001$ ). Sociodemographic, sexual and behavioural risk factors are summarized by RI status in Table 1.

### Primary Analysis

Compared to not douching, douching less than weekly and weekly or more per month increased odds of RI to 1.97 (95% CI 1.11–3.49) and 4.57, (95% CI 2.58–8.09), respectively. Other factors associated with increased unadjusted odds of RI were: Substance use (OR 2.83, 95% CI 1.59–5.03), median number of male partners (OR 1.45, 95% CI 1.23–1.72), and number of cARS (OR 1.02, 95% CI 1.01–1.04). Controlling for age, number of cARS, number of male partners, use of antibiotic and substance use, MSM douching weekly or more had increased adjusted odds (aOR) of 3.59 (95% CI 1.90–6.78) for RI compared to not

douching. Douching less than weekly was no longer significantly different than not douching with aOR of 1.75 (95% CI 0.96–3.20) (Table 2).

### Sensitivity Analysis

Comparing RD to predict incident with prevalent RI, incident cases had slightly greater aOR 3.87 (95% CI 1.78–8.39,  $p=0.001$ ) compared to prevalent aOR 3.59 (95% CI 1.90–6.78,  $p<0.001$ ) for participants douching weekly or more (Figure 1). Odds of RI when douching less than weekly remained similar (aOR 1.78, 95% CI 0.83–3.84,  $p=0.142$  vs. aOR 1.75, 95% CI 0.96–3.20,  $p=0.070$ ) when comparing incident with prevalent RI, respectively. Considering prevalent rectal gonorrhoea and rectal chlamydia cases individually, aOR of rectal gonorrhoea was 2.11 (95% CI 0.84–5.26,  $p=0.110$ ) and rectal chlamydia was 1.73 (95% CI 0.91–3.29,  $p=0.093$ ), when douching less than weekly. Adjusted odds of rectal gonorrhoea and rectal chlamydia increased to 3.56 (95% CI 1.43–8.85,  $p=0.006$ ) and 3.01 (95% CI 1.55–5.85,  $p=0.001$ ), respectively, when douching weekly or more.

### Effect Modification

The effect of douching on RI was modified by the median number of male sexual partners in the past three months ( $p<0.05$ ). Comparing MSM by median number of partners,  $\leq 6$  versus  $>6$ , aOR of RI was 0.99 (95% CI 0.45–2.18,  $p=0.988$ ) and 3.99 (95% CI 1.40–11.41,  $p=0.010$ ), respectively, when douching less than weekly compared to not douching. Significant increased odds are observed when douching weekly or more between MSM with  $\leq 6$  median number of partners (aOR 2.83, 95% CI 1.23–6.50,  $p=0.014$ ) compared to  $>6$  median number of partners (aOR 5.41, 95% CI 1.84–15.97,  $p=0.002$ ). This effect can be visualized by plotting the predicted probability of RI when douching at any frequency against median number of male sexual partners (Figure 2). The probability of RI ranges from 20–24% as the number of male sexual partner increase from 1 to 100 if not douching, while the probability of RI increases from 18% with one partner to 77% with 100 partners when douching at any frequency.

## DISCUSSION

Our study found douching is common among MSM seeking PrEP in Southern California and the odds of RI increases to 3.59 when douching at least weekly and to 5.41 for MSM with more than six male sexual partners. Like other behavioural studies on douching in Europe<sup>15, 17</sup> and the United States<sup>14, 27</sup>, we found douching to be popular among MSM engaging in ARS. We also had a high prevalence of RD (261 of 395, 66%), slightly higher than the prevalence of 14–53% found in previous studies<sup>10, 15, 16, 28, 29</sup>. Our cohort had a high prevalence of RI (133 of 395, 34%) with rectal chlamydia cases (27%) twice the prevalence of rectal gonorrhoea cases (14%).

Unlike other cross-sectional<sup>11, 14, 17</sup> and case control<sup>12, 30</sup> studies reporting an association between douching and RI, our cohort included HIV-uninfected MSM on PrEP followed prospectively and systematically tested for RI. Our results are higher than that of Heiligenberg et al where the adjusted odds of acquiring chlamydia or gonorrhoea were 2.4 (95% CI 1.3–4.4) among HIV-infected participants reporting enema use before sex<sup>16</sup>. While



they did not control for number of cARS, it is lower than the aOR 3.59 (95% CI.190–6.78) in our HIV-uninfected MSM population.

Similar to other studies, individuals in our study used tap water or soap for douching<sup>14, 15</sup>. Previous research show type of solution to alter the rectal mucosa. In a repeated measure double blind study by Schmelzer et al, mucosal irritation by rectal biopsies after each enema by type of solution were compared<sup>20</sup>. Epithelium loss was found in rectal biopsies after soapsuds and tap water enemas, but not polyethylene glycol-electrolyte solution enemas in 24 healthy volunteers. We did not find any significant association between RI and douching with water compared to douching with water and/or other solutions but may have had limited power to detect this. Further research is needed to explore the effects of different douching solutions on the rectal mucosa among HIV-uninfected MSM and implications for prevention of STIs/HIV.

Strengths of our study include lab-confirmed routine testing for rectal gonorrhoea and chlamydia for all participants and control for high-risk behaviours, especially substance use associated with ARS, collected systematically over 48-weeks. The behavioural data collected by self-report using computer assisted self-interview made it less susceptible to interviewer and social bias, although recall bias may remain. The multivariate analysis was restricted to participants engaging in ARS as this group is at highest risk for RI. We conducted a sensitivity analysis to further examine incident RI and rule out concerns on reverse causality, such as douching because of exposure or known status of a STI. Results of the sensitivity analysis showed approximately the same increased odds when douching weekly or more with incident cases (aOR 3.87, p=0.001) as prevalent cases (aOR 3.59, p<0.001). Considering associations between douching weekly or more and prevalent rectal gonorrhoea or rectal chlamydia cases separately, aOR for rectal gonorrhoea was slightly higher (3.56, p=0.006) compared to aOR of rectal chlamydia (3.01, p=0.001).

This study had several limitations including information on the frequency of douching, which was only available for 30 days prior to baseline. As changes in any frequency of douching was not captured, we assumed douching behaviour tended to be consistent over time<sup>10</sup>. In addition, we did not collect information on the type of douching equipment, sharing behaviours, lubricant use, onset of douching and timing of douching (pre- or post-sexual activity) and previous STI, all of which remain as unmeasured confounders. Since gonorrhoea and chlamydia testing were conducted at assigned visit dates only, there was potential for undetected cases occurring between study visits. Finally, the results from this study were based on MSM at high risk for HIV seeking PrEP shortly after approval of TDF-FTC for this indication, and thus only representative of high-risk population.

Our study shows RD is a common practice among HIV-uninfected MSM on PrEP which increases the odds of acquiring rectal gonorrhoea and/or chlamydia. Furthermore, odds of RI may be increased with higher frequency of douching and increasing number of male sexual partners. It is frequently observed a previous STI is a risk factor for detecting prevalent STI. Within the conceptual framework of a microbiome and STI occurrence, this could be related to persistent susceptible microbiome or a change in the microbiome related to the STI or its treatment. Individuals may also be douching as a possible mitigating strategy for future

STIs. Further research is needed to distinguish whether the increased odds are attributed to a change in the rectal microbiome or related to rectal trauma or local inflammation. This would be an important step to support development of rectal hygiene products to preserve the mucosal integrity and microbiome. In a population where behavioural prevention strategies like condom use are inconsistently accepted, STI prevention through modifications of current practices could be achieved by education on rectal hygiene frequency or possibly douche composition, if an alternative product was developed. These prevention strategies could lower biological transmission and acquisition risks in addition to PrEP and antiretrovirals to control for the HIV and STI epidemic.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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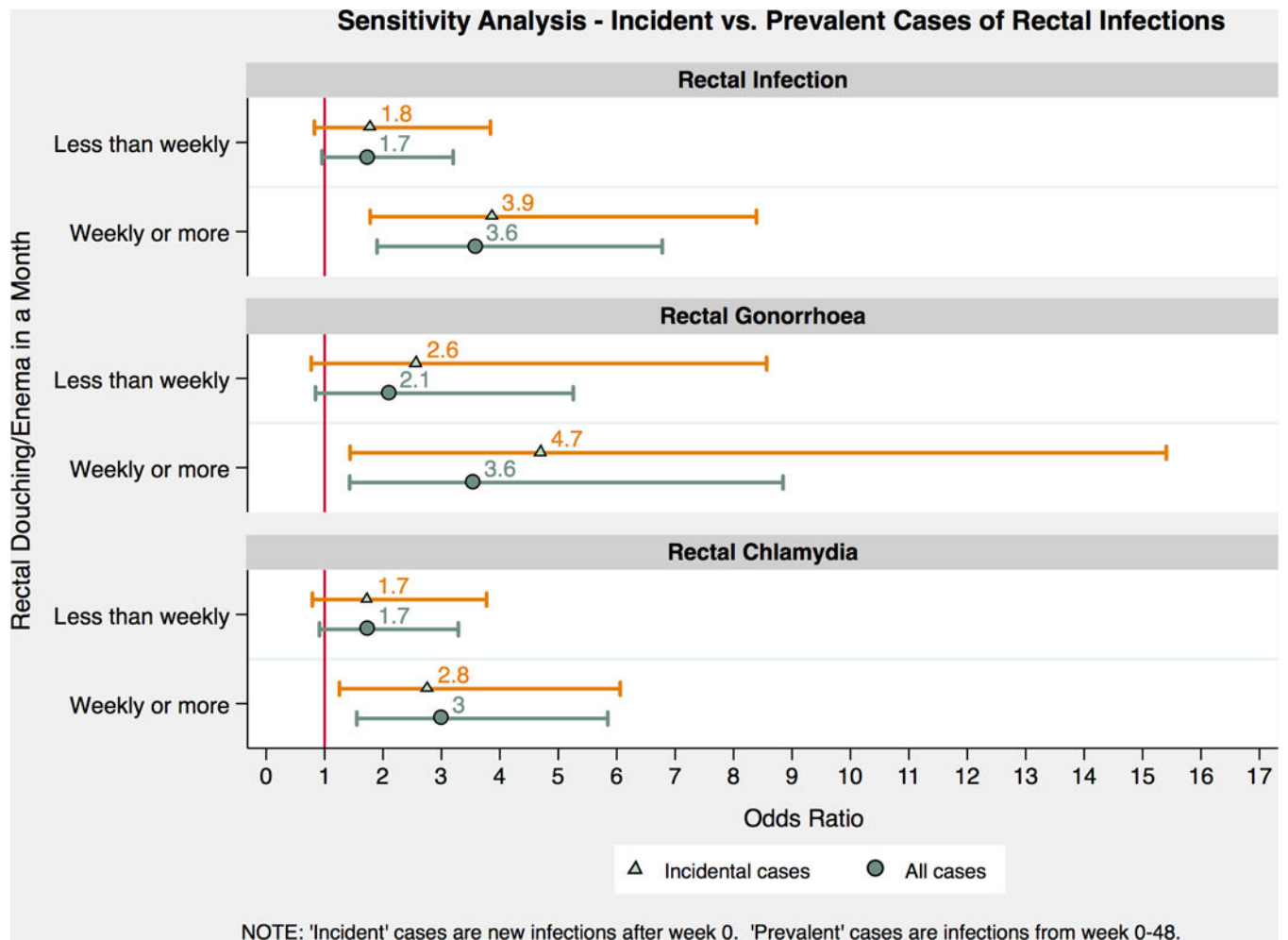


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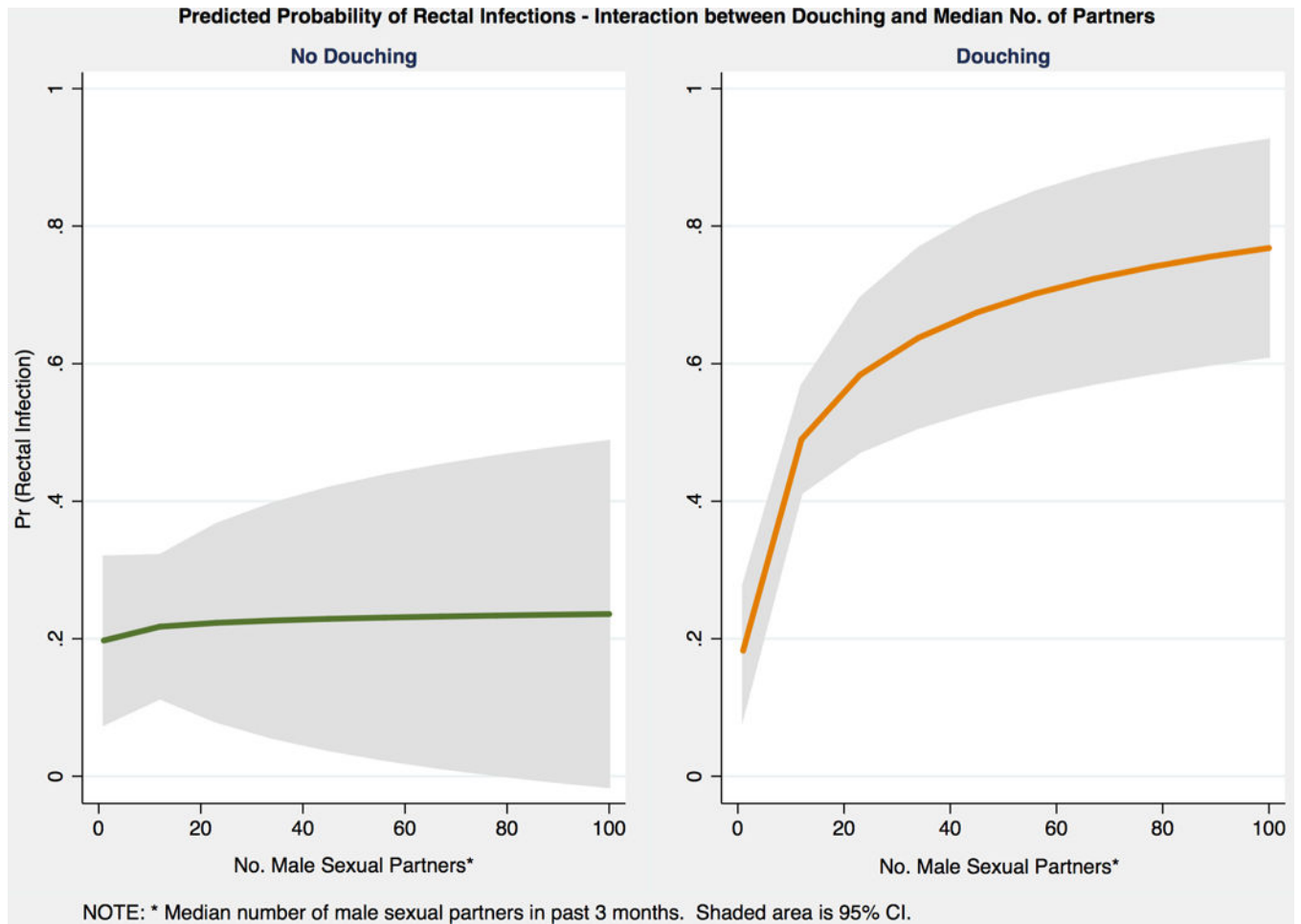
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**Key Messages:**

- Rectal douching/enema is common among men who have sex with men (MSM), but unclear if it contributes to higher risk of sexual infection.
- Among MSM in southern California, 66% practiced rectal douching/enema and 33% had at least one case of rectal gonorrhoea and/or chlamydia over 48 weeks.
- Adjusted odds of rectal gonorrhoea and/or chlamydia increases by 3.59 when douching weekly or more and by 5.41 among MSM with more than six partners.
- Rectal hygiene products could be used as interventional approaches to reduce sexually transmitted diseases.



**Figure 1.** Sensitivity analysis comparing odds of incident versus prevalent cases of rectal infections, rectal gonorrhoea and rectal chlamydia. Incident cases are new infections after week 0, marked in triangles. Prevalent cases are infections from week 0 to 48, marked in circles.



**Figure 2.** Predicted probability of rectal infections by interaction between douching and median number of male sexual partners in the past three months. The 95% CI is shaded in grey.

**Table 1.**

Baseline socio-demographic, sexual and behavioural characteristic of HIV-uninfected MSM on PrEP by rectal infection.

	Rectal Infection				P
	No (N=262)		Yes (N=133)		
	n*	%**	n*	%**	
<i>DEMOGRAPHICS</i>					
Household Monthly Income Before Tax					0.25
<\$1000	27	10%	8	6%	
\$1,000-\$1,999	27	10%	22	17%	
\$2,000-\$2,999	38	15%	22	17%	
\$3,000-\$3,999	31	12%	13	10%	
\$4,000-\$7,999	72	28%	30	23%	
>\$8,000	26	10%	17	13%	
Employment					0.31
Employed	161	62%	87	66%	
Part-time	46	18%	26	20%	
Unemployed	48	18%	19	15%	
Retired/Disabled	5	2%	0	0%	
Relationship Status					0.37
Committed	91	35%	37	28%	
Separated	7	3%	4	3%	
Single	163	62%	92	69%	
Education Level					0.23
High school or less	26	10%	8	6%	
Some college	89	34%	58	44%	
College	90	34%	42	32%	
Some graduate/Adv	57	22%	25	19%	
Age (yrs), mean (SD)	37	±9	33	±9	<0.001
Race					0.036
White	186	71%	94	77%	
African American	48	18%	17	14%	
Asian/Other	8	3%	11	9%	
Ethnicity					0.043
Hispanic	68	26%	48	36%	
Not Hispanic	191	73%	85	64%	
<i>SEXUAL AND RISK BEHAVIOURS</i>					
Drug Abuse	50	19%	36	27%	0.063
Alcohol Use	214	82%	110	84%	0.68
Marijuana Use	116	45%	72	55%	0.053



	Rectal Infection				
	No (N=262)		Yes (N=133)		P
	n*	%**	n*	%**	
Tobacco Use	83	32%	54	41%	0.069
HIV Risk Factor					0.906
MSM	249	95%	128	96%	
Heterosexual	2	1%	0	0%	
Both	11	4%	5	4%	
No. Male Partners, median (IQR) <sup>+</sup>	5	3–10	8	5–10	0.001
Rectal Douching <sup>++</sup>					<0.001
Never	104	40%	24	18%	
Less than Weekly	94	36%	44	33%	
Weekly or More	60	23%	63	47%	
Cocaine Use	38	15%	22	17%	0.57
Heroin Use	14	5%	2	2%	0.1
Substance Use	137	52%	98	74%	<0.001
Antibiotic Use <sup>+</sup>	71	27%	39	29%	0.69
Condom Non-use for ARS <sup>+</sup>					0.017
Never	24	9%	20	15%	
Rarely/Sometimes	63	24%	60	45%	
Always/Often	85	32%	39	29%	
No. cARS, median (IQR) <sup>++</sup>	0	0–2	1	0–5	<0.001
Douching Solution <sup>++</sup>					0.623
Water and/or Other	51	19%	32	24%	
Water Only	106	40%	76	57%	

Substance Use = Any of Methamphetamine/Hallucinogen/Dissociative/Popper

MSM = Men Who Have Sex with Men

ARS = Anal Receptive Sex

cARS = Condomless Anal Receptive Sex

\* Mean/median for continuous variables.

\*\* Standard deviation/interquartile range for continuous variables.

<sup>+</sup> Past 3 months at baseline.

<sup>++</sup> Past month at baseline.

**Table 2.**

Adjusted/unadjusted odds of rectal infection among HIV-uninfected MSM on PrEP performing rectal douching and/or enema.

	Rectal Infection						
	Total (N=384) n (%)	Unadjusted OR			Adjusted OR*		
		OR	95% CI	p	aOR	95% CI	p
Rectal Douching/Enema							
Never	125 (33%)	-	-	-	-	-	-
Less than weekly	138 (36%)	1.97	1.11–3.49	0.020	1.75	0.96–3.20	0.070
Weekly or more	121 (31%)	4.57	2.58–8.09	<0.001	3.59	1.90–6.78	<0.001
Substance Use							
No	92 (24%)	-	-	-	-	-	-
Yes	292 (76%)	2.83	1.59–5.03	<0.001	1.97	1.06–3.67	0.033
Number of Male Sexual Partners** (med/IQR)	6 (3–10)	1.45	1.23–1.72	<0.001	1.33	1.10–1.60	0.003
Number cARS (med/IQR)	4 (0–16)	1.02	1.01–1.04	<0.001	1.01	0.99–1.02	0.093
Age (yrs) (mean/SD)	35 (±9)	0.96	0.93–0.98	0.001	0.95	0.92–0.98	<0.001
Antibiotic Use							
No	274 (71%)	-	-	-	-	-	-
Yes	110 (29%)	1.09	0.68–1.73	0.726	0.82	0.49–1.38	0.455

Substance Use = Methamphetamine/Hallucinogen/Dissociative/Popper

cARS = Condomless Anal Receptive Sex

\* Adjusted for age, number of condomless anal receptive sex, log<sub>2</sub> median number of male sexual partners, use of antibiotics and substance use.

\*\* Log<sub>2</sub> transformed median number of partners in past three months.