Accuracy of sexual behavior reporting using mobile apps: comparisons to clinic questionnaires and validation with biomarkers

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Objectives

Determine the feasibility of identifying vaginal and rectal HIV exposures to help identify subpopulations at highest risk of acquisition and improve the design of HIV prevention efficacy trials and public health interventions.

Define the feasibility of frequent sexual behavior assessments and mucosal self-collection.

Determine the differences between mobile-phone collected sexual behaviors and clinic-based CASI assessments

HVTN 915: Study conduct

Soweto, South Africa

50 sexually active women ages 18-25

Practicing frequent vaginal intercourse and using contraception during study

Daily SELF-Collection for 3 months

1) self-collected vaginal swabs daily

2) sexual behavior questionnaires via text messaging (SMS) daily

8 clinic visits for 3 months:

1) Clinician collected vaginal swabs
2) Clinic administered behavioral questionnaires
3) HIV testing and counseling

HVTN 915: Daily Mobile SMS based questionnaire

Phone with SurveyCTO App provided to participants for them to keep after the study ended

Phone locked with a password to provide privacy

Remember to complete your questionnaire!

Did you have sex between 7am yesterday and 7 am today?

Did you use condoms?

Did you collect your swab today?

What swab number did you use?

How much time had passed between sex and swab collection?

When did you collect your swab today?

Participants received 5min time credit for calls or texting every time they completed a questionnaire

HVTN 915: Facilitators for filling the daily questionnaire

Dietrich J et al.. PLoS ONE 15(4): e0231086.

Questions during clinic visit regarding SMS questionnaire (336 clinic visits)

1) 92% of participants found daily SMS reminders helpful in remembering to fill out the app

Others found helpful to

receive a call from staff

associate the questionnaire to other routine behaviors

2) Participants reported the phone time credit as a strong incentive to filling out the questionnaire

HVTN 915: Barriers filling the daily questionnaire

Dietrich J et al.. PLoS ONE 15(4): e0231086.

Questions during clinic visit regarding SMS questionnaire (336 clinic visits)

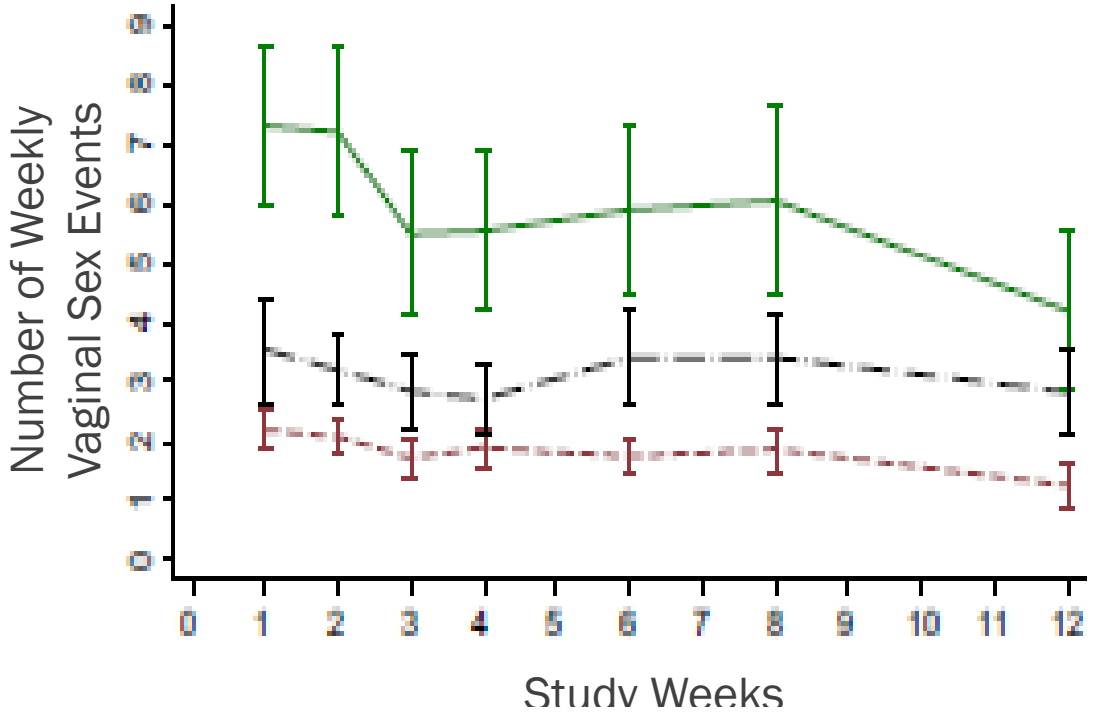
1) Participants reported not filling the questionnaire due to:
   - Forgetting 23.7%
   - Being too busy 18.6%
   - Inconvenient 15.7%
   - Misplaced the phone 6.8%
   - Lack of privacy 3.4%
   - Worry about partner finding out 3.4%

Additional focus groups (n=15) identified additional barriers such as:
- Difficulty charging the phone
- Weekends as most difficult time
- Expiration of monthly time credit
- Software/Hardware errors like daily reminders when people completed the survey.

High feasibility of the Mobile SMS based questionnaire

Of 4219 questionnaires received by the participant's phone
3486 answered by the participant (82% response rate)

Dietrich J et al. Sex and Behavior 2018



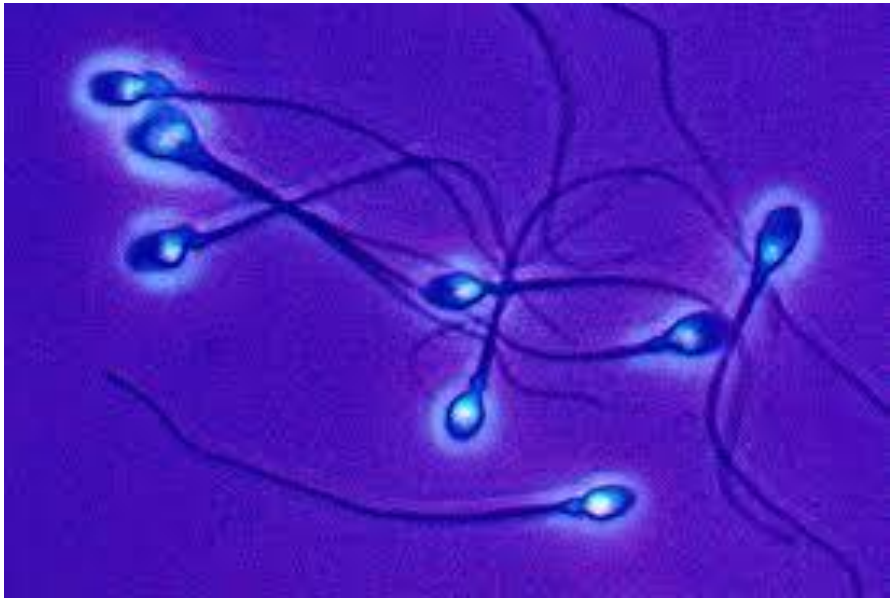
Daily mobile phone sex frequency

Average Weekly mobile phone sex frequency

In Clinic sex frequency

Sexual Activity reporting decayed over the study period

Validating the use of the mobile sex reporting with biomarkers of condomless vaginal sex



Glycogen
94% of swabs sampled the vagina

Quantifiler Duo Real Time PCR
SRY(Sex determining region Y)Human Male DNA

Lemos et al. J Acquir Immune Defic Syndr 2019;81:e39–e48

Mobile SMS sex reporting is validated with biomarkers of condomless vaginal sex

MOBILE APP REPORT VAGINAL SWAB TEST	CONDOM/ ABSTINENCE Swab number (%)	CONDOMLESS VAGINAL SEX Swab number (%)
SRY DNA POSITIVE	10 (6.2%)	20 (50%)
SRY DNA Negative	167 (89.4%)	19 (47.5%)

Fisher's Exact
p<0.0001

Comparing mobile sex reporting with clinic questionnaires

Did you have sex between 7am yesterday and 7 am today?

Did you have sex in the past 7 days?

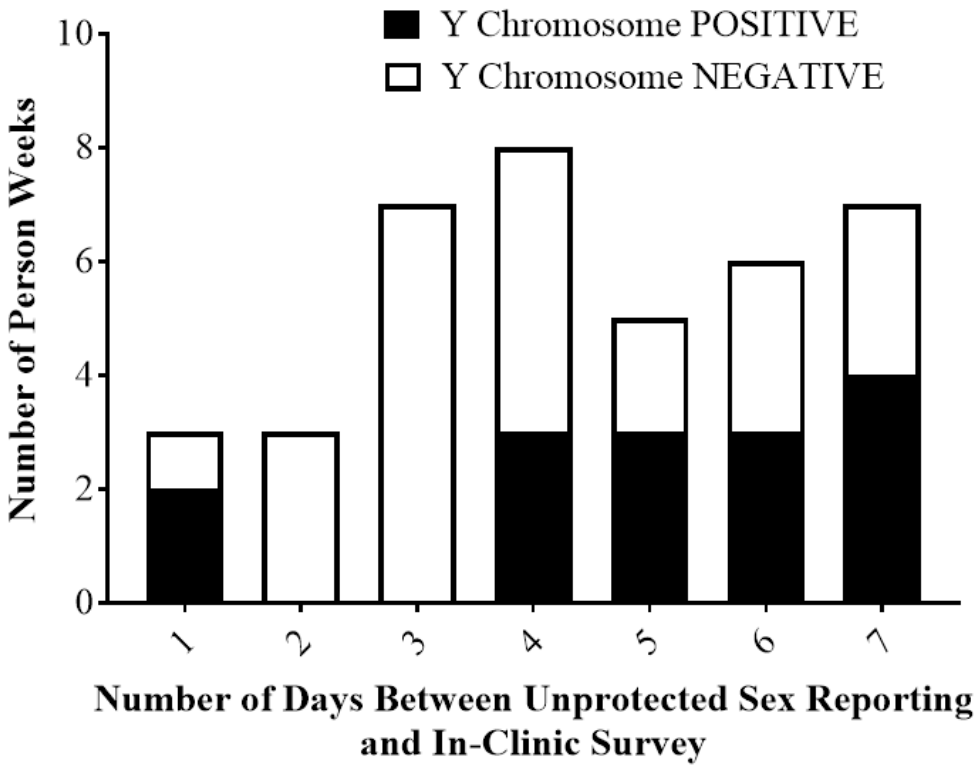
Condom usage reporting via mobile SMS is more accurate than clinic questionnaires

Yc-DNA detection in 77 swabs where the clinic report did not match mobile phone data

VAGINAL SWAB TEST	CONDOM/ ABSTINENCE reported in mobile SMS Swab number Per person weeks (%)	CONDOM/ ABSTINENCE reported at the clinic Swab number Per person weeks (%)
SRY DNA POSITIVE	2 2 (12.5%)	15 13 (61.9%)
SRY DNA Negative	36 14 (87.5%)	21 8 (38.1%)

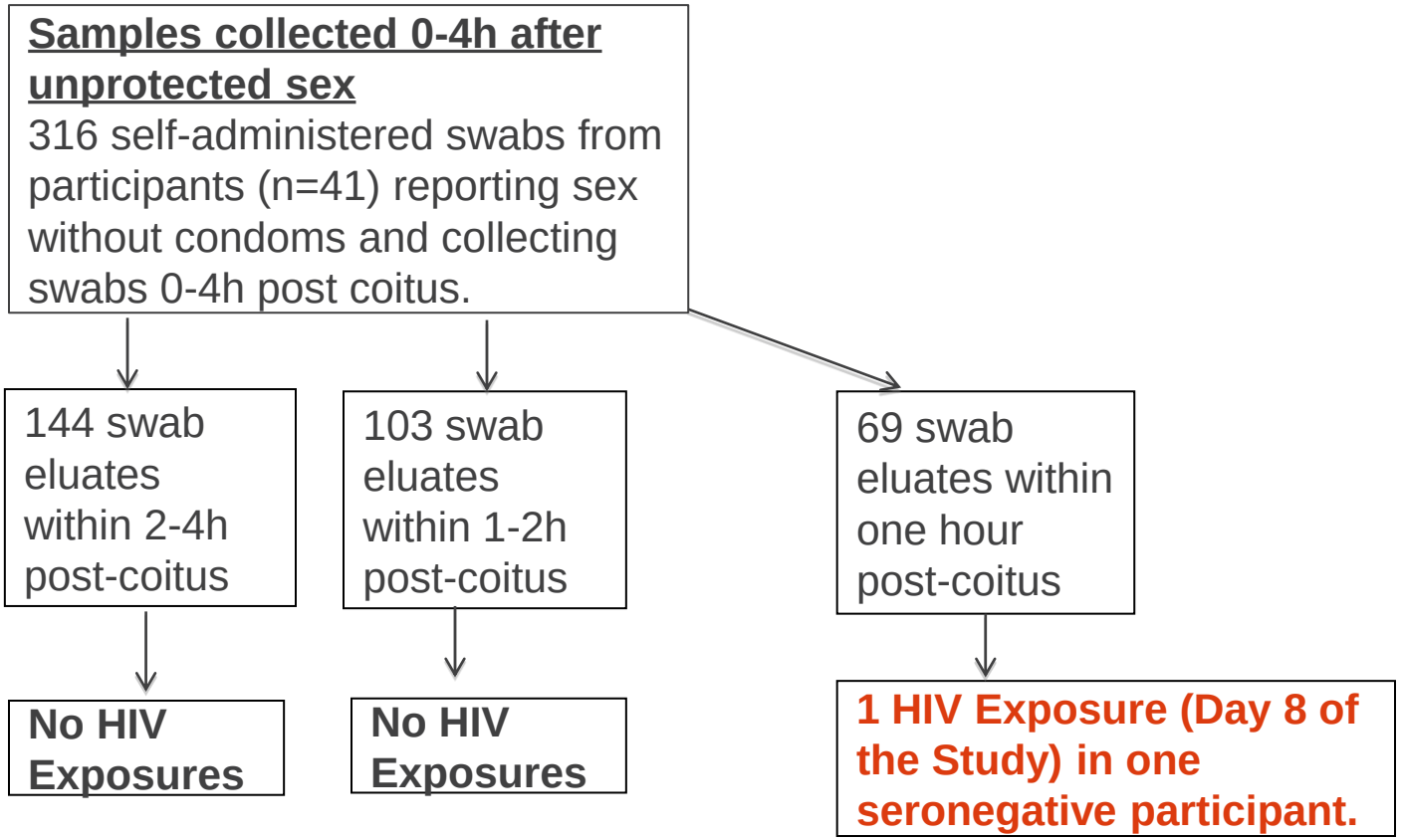
p=0.003

Daily Sex Reporting data appears less sensitive to long-term recall errors



Lemos et al. J Acquir Immune Defic Syndr 2019;81:e39–e48

HIV exposures in Vaginal Swabs detected early after sex



SexApp(eal) Study

30 Sexually MSM from NYC ages 18-50

2 sex partners with unknown status per month or

3 unprotected ARI per month

HIV negative

Daily SELF-Collection for 2 months

1) Daily (in morning) or per sex event (within 8h) self-collected rectal swabs (n=2)

2) Mobile-based sexual behavior questionnaires (6am previous day to 6am of swab collection day)

- 2 clinic visits

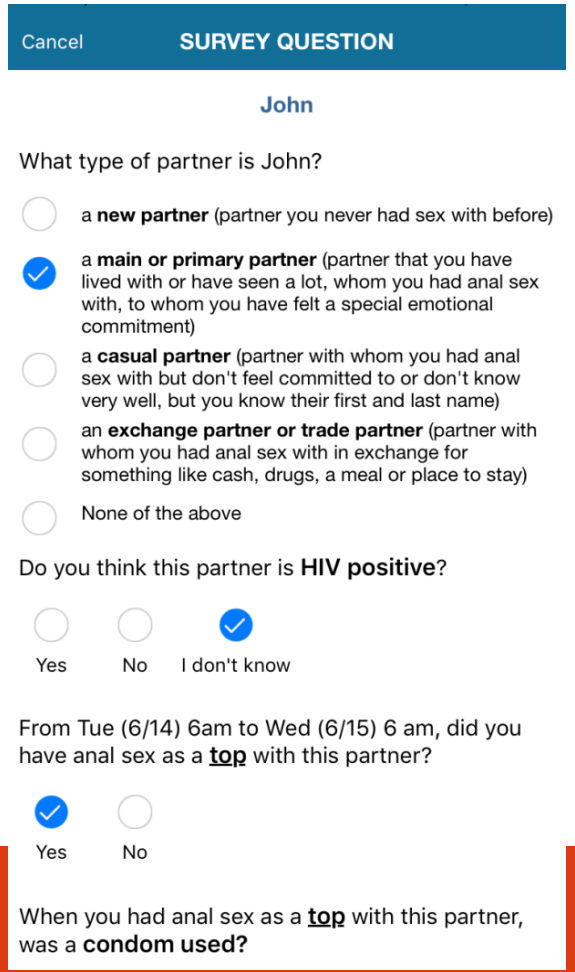
1) HIV test at month 0 an 2
2) Blood DNA
3) Clinic administered behavioral questionnaires
4) Swab return every 2 weeks

Sex App(eal)

Password protected App was installed in participant's own phone

Remember to complete your questionnaire!

Participants received Daily SMS reminders to complete the survey



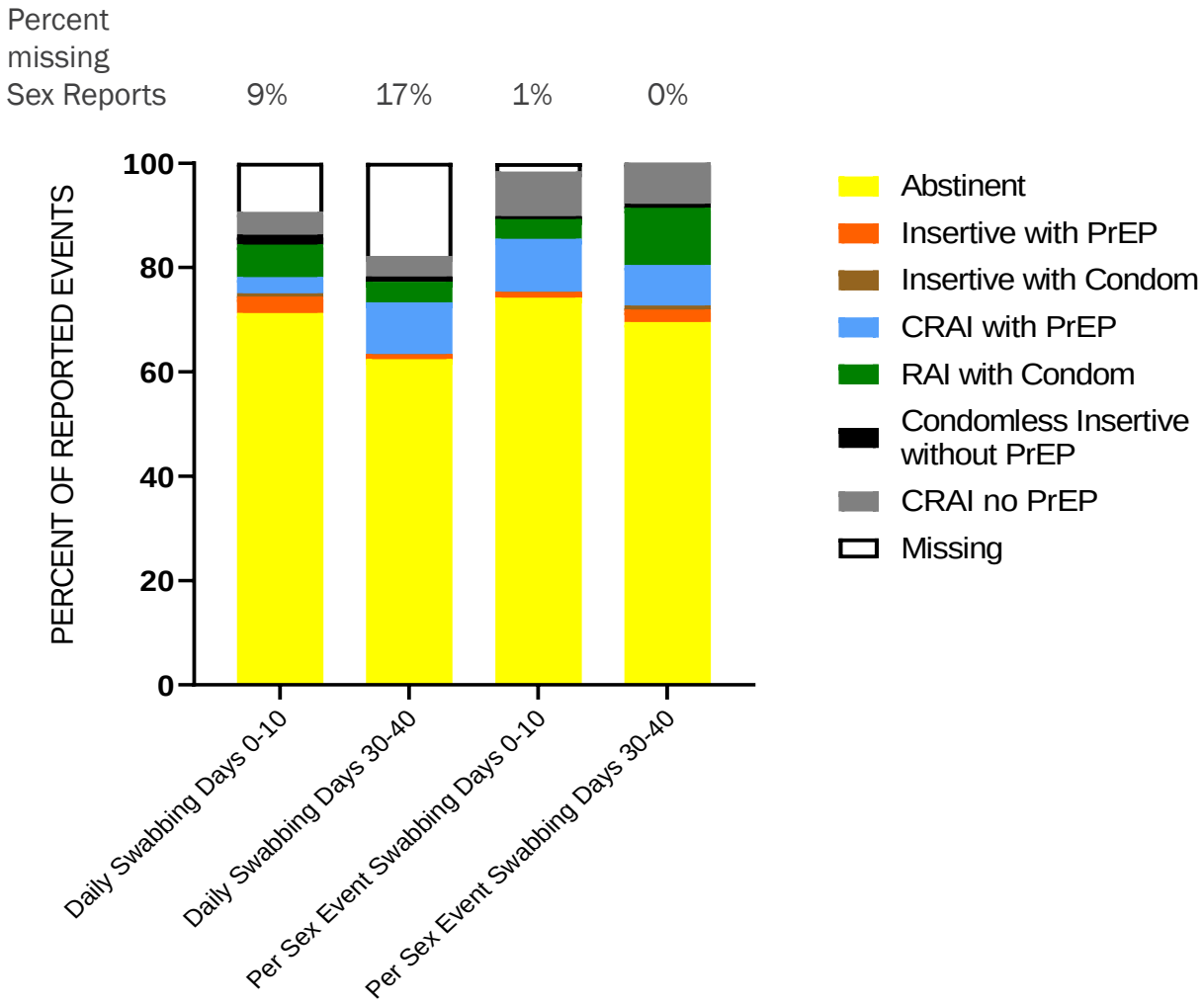
- Whether participant had anal sex (top or bottom) with a man or transwoman in past 24 hours (6am-6am)
- Number of partners
- Perceived HIV status of partner
- condom use
- Ejaculation of sperm in anus during sex
- Use of lubricant, enema, steroid/anti-inflammatory cream
- Bowel movement
- Whether rectal swab was collected for at least 15 seconds as instructed

Clinic surveys report increased proportions of Condomless Receptive Anal Intercourse

No differences in sexual behaviors at month 0 and 2 in the clinic questionnaire

Risk Behaviors	Daily swabbing			Per sex event swabbing			Sex App(eal) differences among study arms
	Sex App(eal)	Clinic		Sex App(eal)	Clinic		
	N (%)	N (%)	p-value	N (%)	N (%)	p-value	p-value
Number of anal sex reports in 2 months	119	59		162	120		
Reports of sex as a bottom (RAI)	83 (69.8%)	43 (72.9%)	Chi-square 0.663	157 (96.9%)	92 (76.7%)	Chi-square <0.001	Chi-square <0.001
Reports of sex as a bottom without condom (CRAI)	23 (19.3%)	32 (54.2%)	Chi-square <0.001	49 (30.3%)	50 (41.7%)	Chi-square 0.047	Chi-square 0.038
Number of participants reported having HIV positive partner(s)	4/15 (26.7%)	6/15 (40.0%)	Fisher's exact 1.00	4/15 (26.7%)	3/15 (20.0%)	Fisher's exact 1.00	Fisher's exact 0.559

Daily and Per-Sex Swab Collection Arms had differences in their Sex App(eal) reporting



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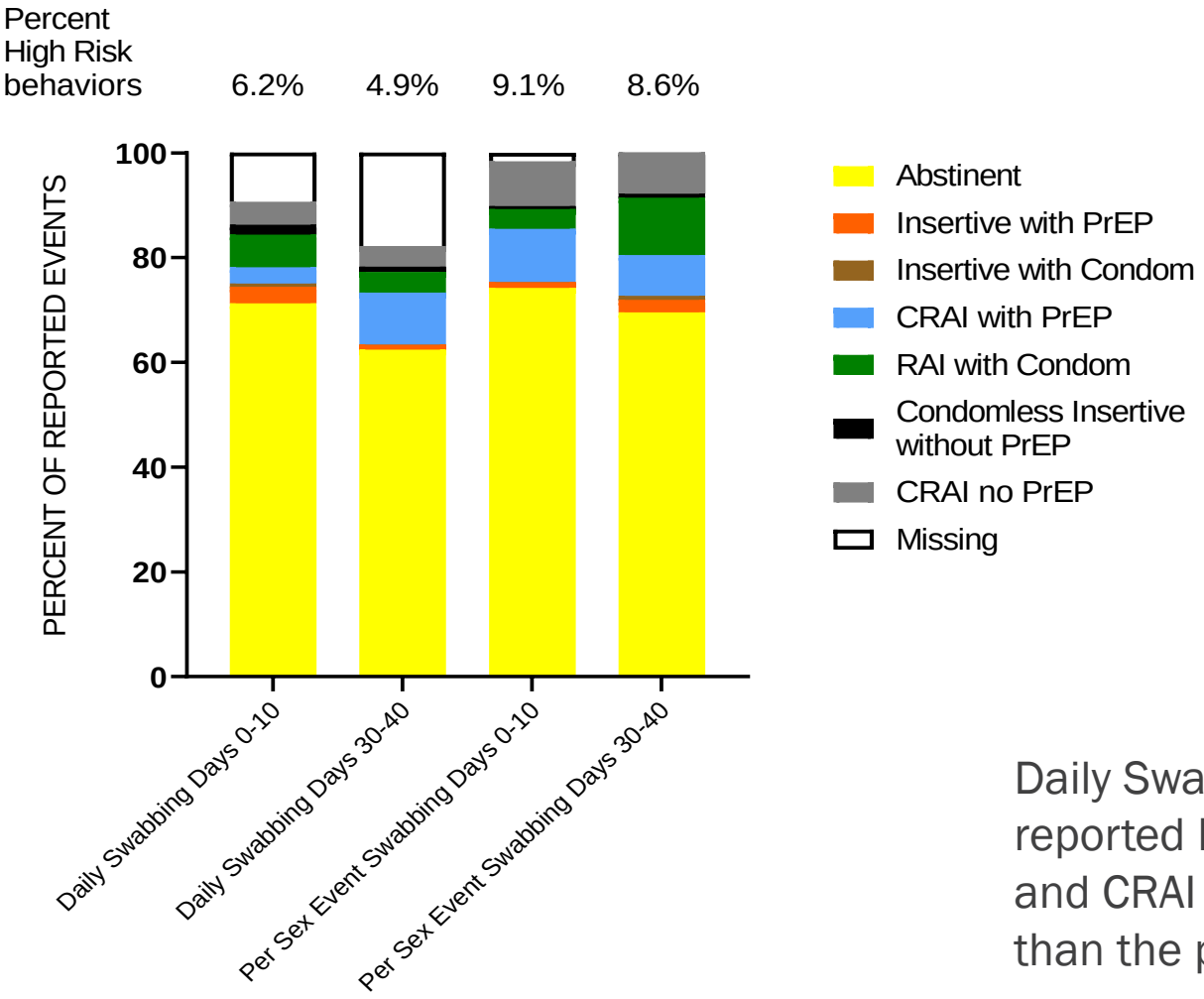


Daily Swabbing reported reported less RAI ($p<0.001$) and CRAI ($p<0.038$) than the per-sex-event arm

Despite more HIV-risk behaviors, adherence to rectal swabbing is higher in per-sex act arm

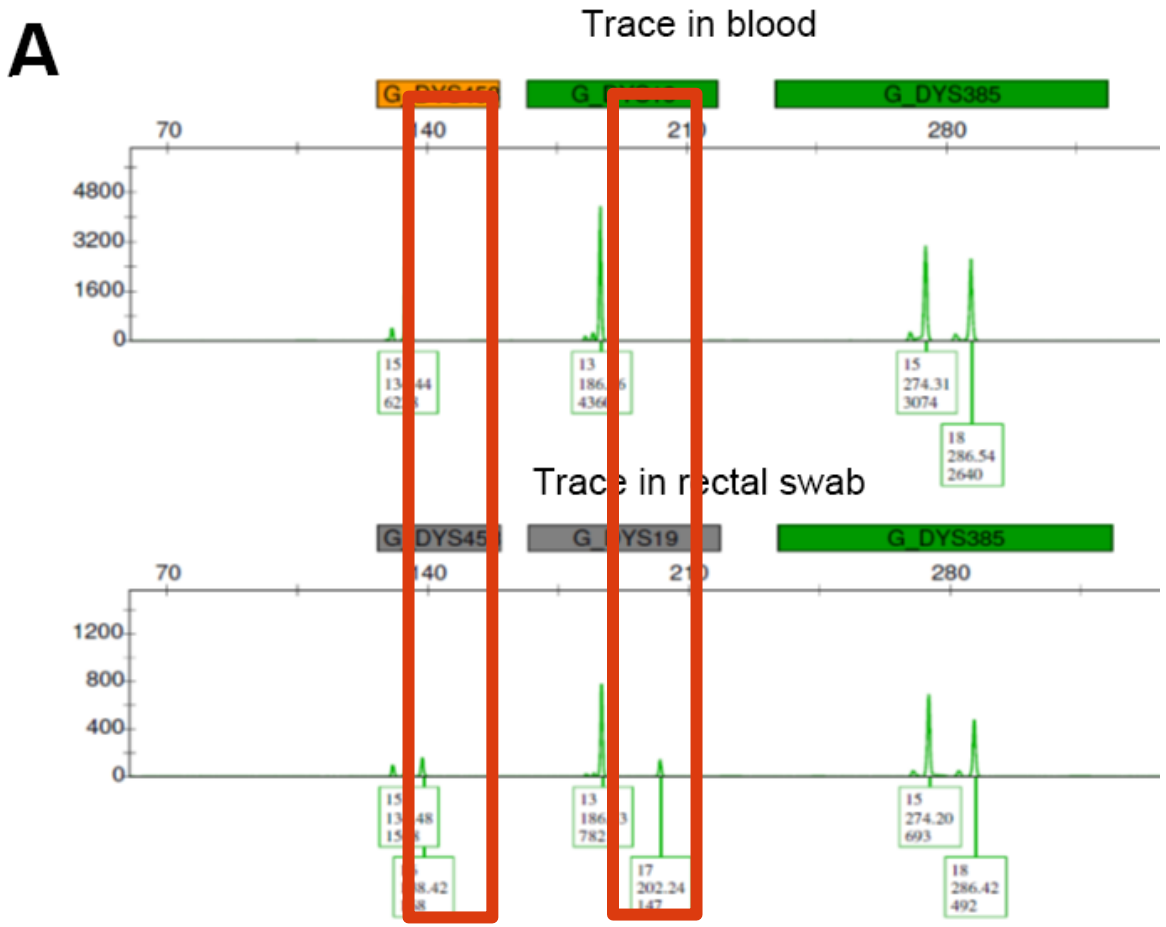
Human RPPH1 Ribonuclease P DNA	Human DNA +	Human DNA -	Total	Adherence
Daily	145	48	193	75.1%
Per Sex event	158	5	163	96.9%

Fisher's Exact test $p<0.0001$

Matching mobile sex reporting with biomarkers of condomless receptive anal sex

Insertive and receptive partner DNA cannot be distinguished based on the presence/absence of SRY

We used Y chromosome Single Tandem Repeat analysis to distinguish polymorphisms at 16 different sites of the Yc to identify mixtures



233 samples with sufficient Y chromosome including:

All episodes of CRAI (224)

Selected episodes of abstinence, protected RAI, or insertive sex (less than 48h from CRAI)

20 paired Blood Controls

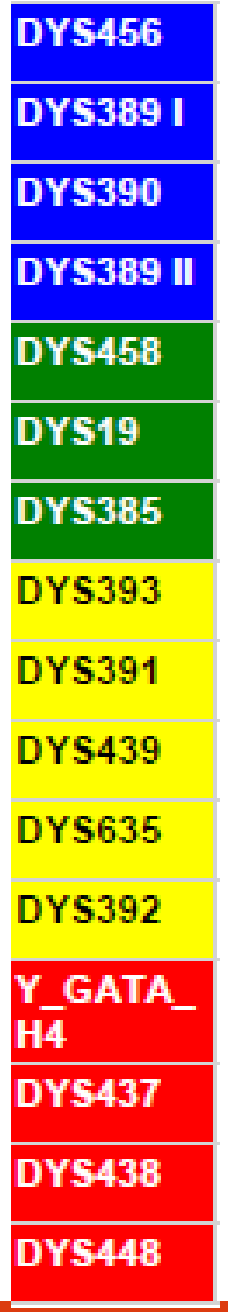
MIXTURES:

Episodes of unprotected RAI should have two or more YSTR polymorphisms at least 2 sites

IDENTICAL TO BLOOD:

Episodes of abstinence, insertive sex, or protected RAI should have only set of YSTR polymorphisms

(matching blood samples)



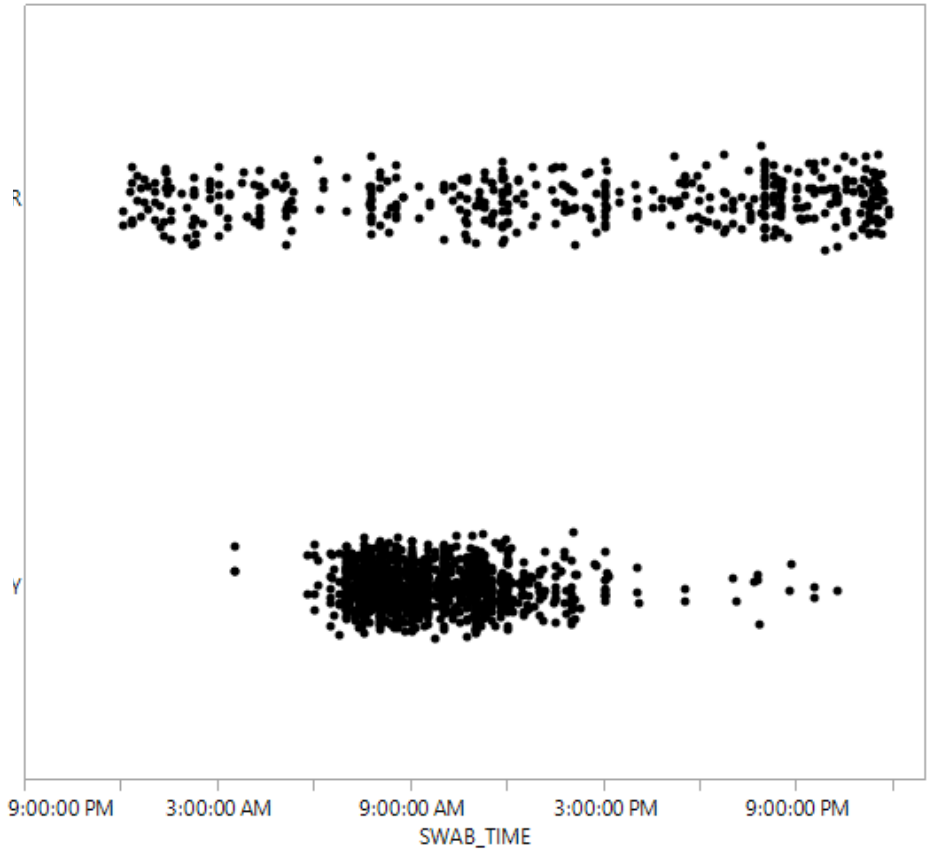
Multivariable model matching YSTR mixtures to mobile sex reporting

Factors Affecting detection of YSTR mixtures in reports of RAI		Odds Ratio	95% CI		p-value
			LOWER	UPPER	
Study Arm	Per Sex vs Daily arm	2.95	1.18	7.39	0.021
Sex App(eal) Sex Report	CRAI vs RAI with condoms	0.90	0.21	3.88	0.888
Lubricant use	No vs Yes	0.45	0.15	1.33	0.147
Enema between RAI and before swab collection	No vs Yes	0.50	0.21	1.18	0.113
Bowel movement after RAI and before swab collection	No vs Yes	0.47	0.16	1.39	0.174
Partner ejaculation during RAI event	No vs Yes	0.42	0.17	1.04	0.062

Per Sex Event Collection occurred throughout the day, likely associated with sexual activity

PER SEX EVENT N=439

DAILY N=1378



SWAB Collection Time

- Closer time of collection from sex event

- Not collected after sleeping (retrograde semen transport farther from the swabbing surface)

HIV exposures after CRAI

158 samples matched to CRAI (23 PTIDs)

Controls:
- 20 rectal swabs spiked with HIV+ semen (1 from each participant)
- 51 samples reporting RAI with condoms (n=11), abstinence (n=24), insertive sex (n=5), or missing sex report (n=11)

HIV Positive:
- 6 samples reporting CRAI

Participant 21 in Daily Arm taking PrEP
- 2 events with 2 different new partners (<200 copies/ml)
  - Participant reported CRAI and thought the partners were HIV negative
  - Other episodes of sex with those partners used condoms
  - YSTRs not tested

Participant 3 in Per-sex Event Arm taking PrEP:
- 1 event with new HIV positive partner (505 copies/ml)
  - Participant reported CRAI with an HIV+ partner, not knowing partner's meds or VL
  - YSTR mixture not found
  - Participant reported another CRAI event with that partner, but HIV was undetectable, and yield was too low for YSTR testing.
- 3 events with primary partner, HIV Positive (340 and <200 copies/ml)
  - Participant reported CRAI with an HIV+ partner who was not taking meds and had undetectable viral load
  - YSTR mixtures detected
  - There were 6 other reports of CRAI with that partner: 3 swabs had a YSTR mixture but no HIV DNA; 3 swabs were identical to blood in YSTR and negative for HIV DNA

HVTN 915 Conclusions

Daily sexual behavior reporting and vaginal self-swabbing among young South African Women was acceptable and feasible:

- 82% of daily SMS responses were completed in a 3-month period
- 93% sampled the vaginal compartment as indicated by glycogen detection.

Reports in the daily SMS mobile app were more accurate than 7-day clinic surveys

- More vaginal sex reported in the daily app
- 90% PPV of abstinence and condom use, correlating well with lack of SRY DNA
- less susceptible to the bias of a longer recall

This approach allowed to identify 1 episode of HIV exposures

- only when vaginal swabs are collected very soon after vaginal sex

SexApp(eal) Conclusions

Phone App sexual behavior and rectal self-swabbing was acceptable and feasible for MSM and TGW in New York City

75. 1% adherence to daily swabbing defined by presence of male DNA

96.1% adherence to per-sex event swabbing defined by presence of male DNA

Reports in the daily SexApp(eal) mobile app collected more RAI and RAI with condoms than reported at the clinic.

YSTR mixtures were more common in participants self-collecting in the per sex-event arm, and after ejaculation had taken place.

Sex App(eal) reporting and rectal swab collection allowed for the identification of 6 episodes of HIV exposures, in two men taking PreP

HVTN915 and Sex App(eal) Teams

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