Sexually transmitted infections among persons who did not have sex: Possible sources of error in a controlled trial.

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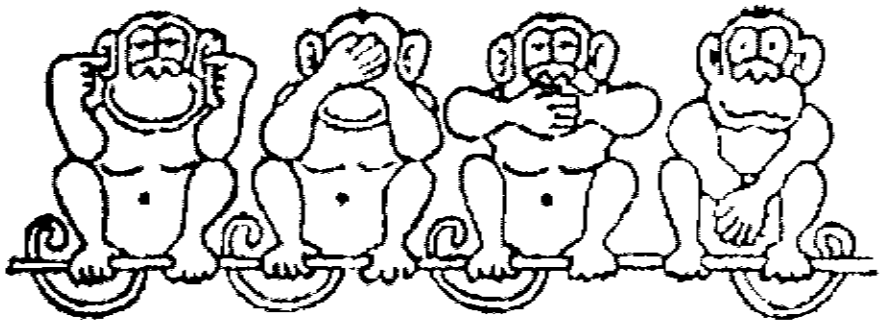
Introduction:

During follow-up in a prevention trial, 64 persons acquired an STI during a time when they said they were not having sex.



How did that happen???

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Methods:

Study data:
- Secondary analysis of RESPECT-2, an HIV prevention trial.
- STD clinic patients in Newark, Denver, and Long Beach.
- Computer-assisted interviews, exams, and lab tests for *C. trachomatis*, *N gonorrhoeae*, and *T vaginalis* at baseline, 3, 6, 9, and 12 months.
- Analysis restricted to participants tested for infections before and after an interval in which they reported having no sex partners.
- We calculated the incidence of new infections associated with different patient characteristics.

Possible Errors:
- Test problem:
  Sensitivity: Infections most likely in first follow-up interval.
  Specificity: Test specificities are reportedly 95-99%, so many positives could be False positives. If so, they would be randomly distributed.
- Inaccurate history
  Same risk factors for infection among persons who did vs did not have sex.
- Treatment failure
  New infections in interval following treatment for an infection.

Lab tests:

C. trachomatis and *N. gonorrhoeae* were nucleic acid amplification tests (NAATs) on urine. Long Beach and Newark used ligase chain reaction (LCR; LCx Uriprobe [*C. trachomatis*, 93.1/97.1] and [*N. gonorrhoeae*, 97.5/98.3], Abbott Diagnostics Division, Abbott Park, IL) (15, 16). Denver used polymerase chain reaction initially (PCR; Cobas Amplicor [*C. trachomatis*, 93.4/96.7] and [*N. gonorrhoeae*, 97.1/98.1], Roche Diagnostic Systems, Inc., Branchburg, NJ) (17, 18), then after 18 months strand displacement amplification (SDA; BDProbeTec ET [*C. trachomatis*, 90.7/96.6] and [*N. gonorrhoeae*, 96.0/98.8], BD Diagnostic Systems, Sparks, MD) (19).

T. vaginalis was considered positive if either wet mount or culture were positive. Culture of vaginal swabs used InPouch (sensitivity 82.4) or Diamond's medium (sensitivity 87.8); specificity for both culture methods is nearly 100% (20).

Results:

% Infected during Intervals when they had No sex and when they had Sex

Characteristic	*N gonorrhea*		*C trachomatis*		*T vaginalis*	
	No sex n=16	Sex n=133	No sex n=27	Sex n= 228	No sex n=21	Sex n=125
Total	1.6	2.2	2.3	3.7	3.9	4.2
Sex						
Male	1.9	2.4	2.6	3.4	na	
Female	1.0	1.9	2.2	4.0	4.0	4.2
Age						
15-25	1.2	2.5	3.7*	4.9	2.0	3.6
26-39	1.6	1.7	1.1	2.3	6.2**	5.1
Race						
Black	1.7	3.0	2.3	4.3	5.6	7.7
White	0.4	1.5	2.2	1.8	3.2	1.4
Hispanic	2.3	1.1	2.9	4.1	2.3	1.9
Other	0.8	1.4	2.5	4.1	0.0	2.5
Site						
Denver	1.9	2.3	2.6	4.0	4.3	3.7
Long Beach	0.0	1.2	1.9	3.1	2.1	2.4
Newark	2.1	2.9	2.6	3.9	4.9	8.0
Study interval						
3 months	2.9	2.3	3.3	4.3	3.4	5.5
6 months	1.8	2.6	2.2	4.0	3.4	4.2
9 months	0.7	1.2	2.4	3.1	4.0	4.2
12 months	0.4	2.5	1.7	3.3	4.6	2.8
Infected at baseline						
yes	2.2	4.7	5.7*	5.7	9.3**	9.1
no	1.1	1.4	1.5	3.1	2.0	2.7
Infected previous interval						
yes	9.5**	8.5	6.6	8.3	4.4	12.3
no	1.1	1.9	2.2	3.4	3.9	3.6

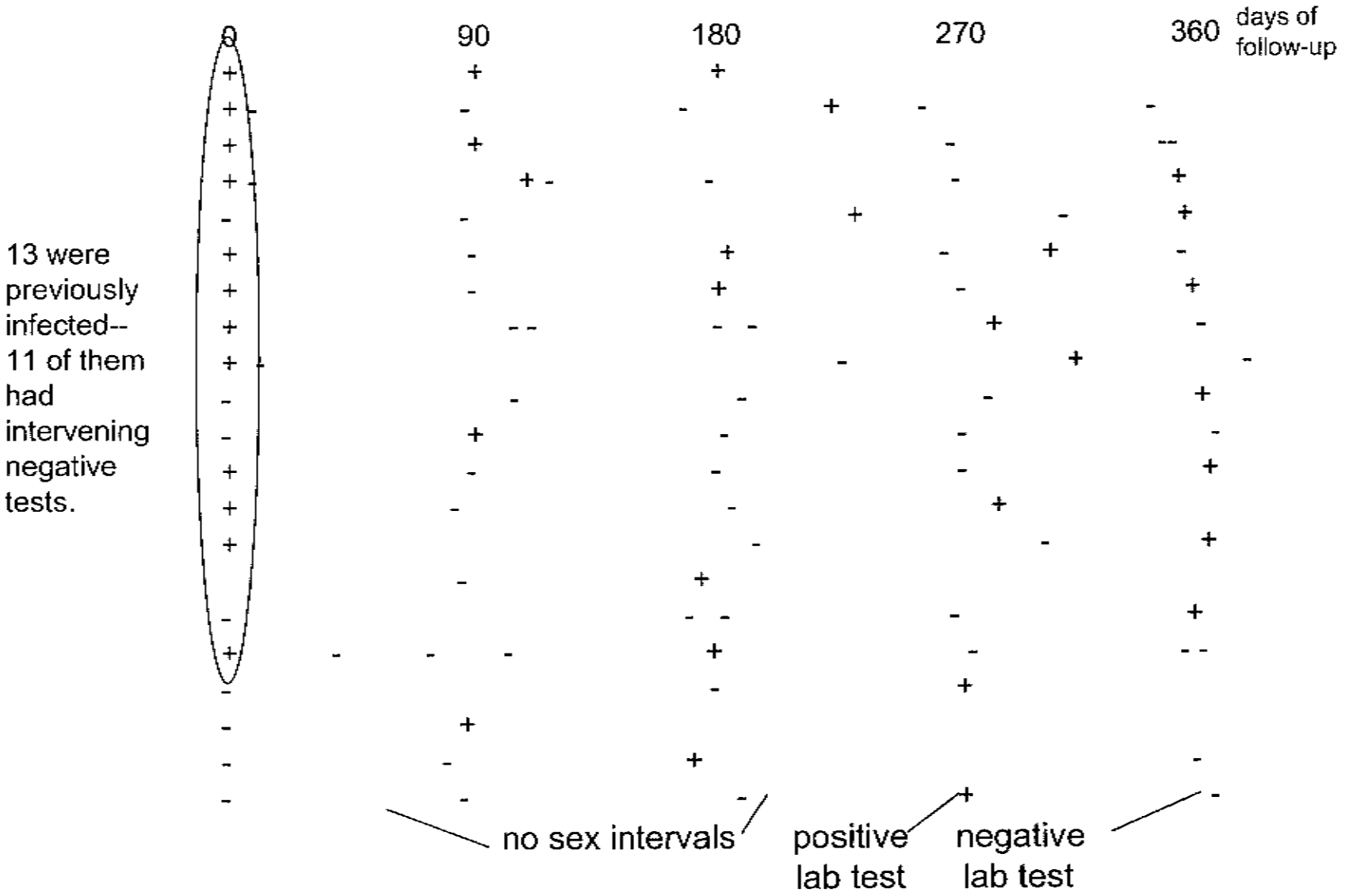
* p< 0.05 ** p< 0.01

Wow, same high incidence of *T vaginalis* for women having/not having sex!

Biggest risk for *T vaginalis*— having infection at baseline

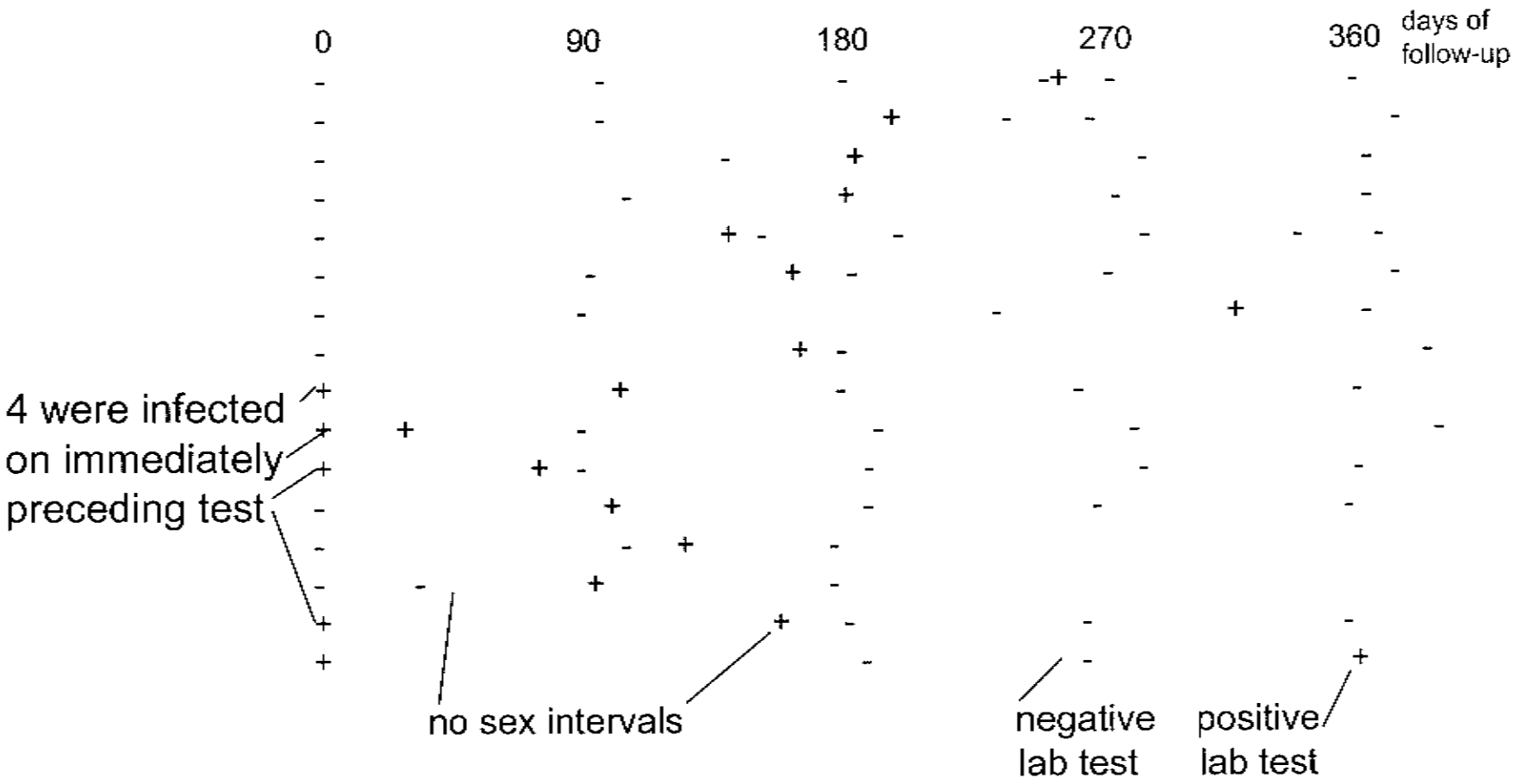
Over all, Similar risk factors for persons having/not having sex suggests # partner histories were inaccurate.

21 acquired *T vaginalis* during intervals when they were not having sex



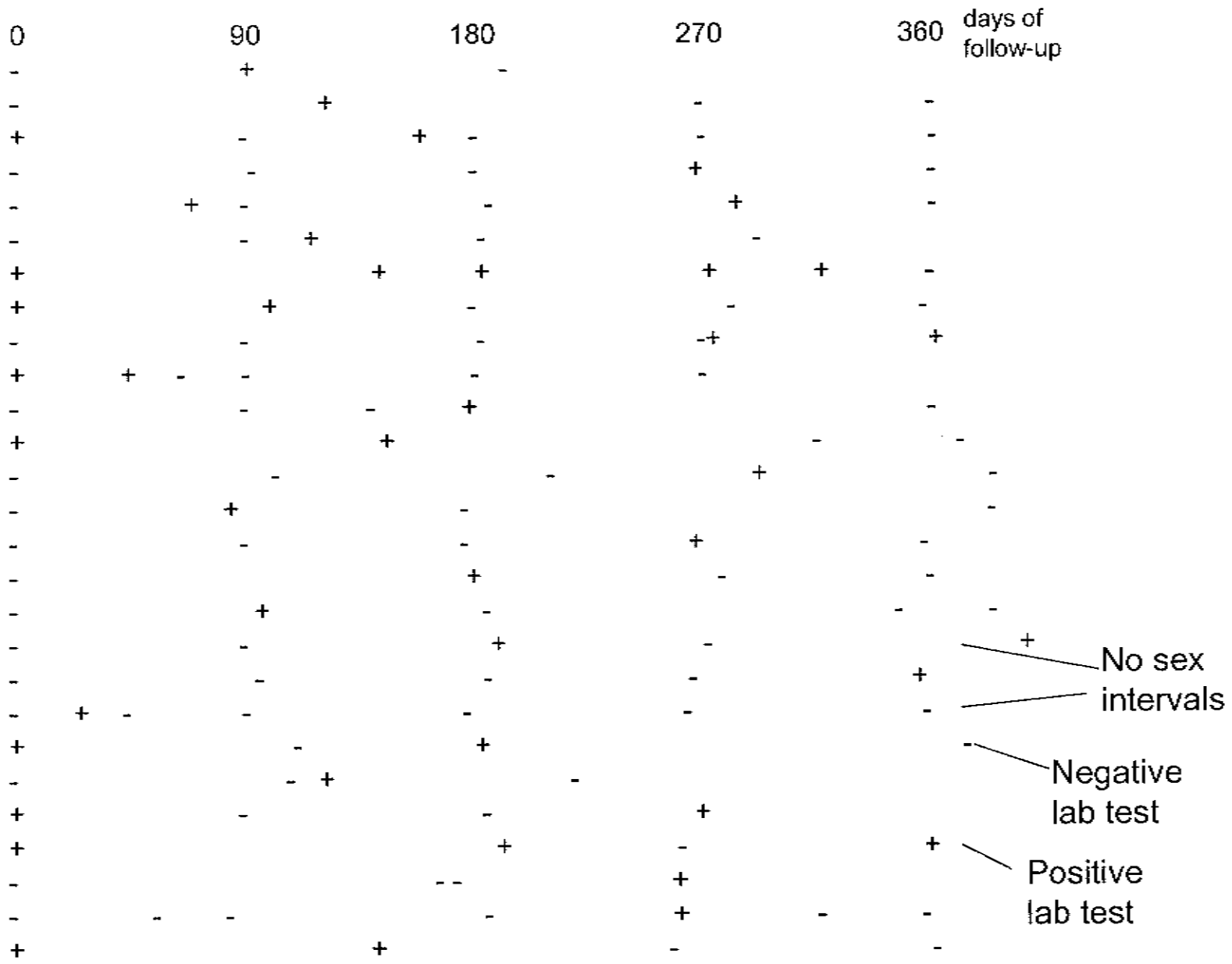
Infection often recurred after a negative test. Did treatment make infection non-detectable by culture for a few months without curing?

16 acquired *N gonorrhea* during intervals when they were not having sex



Possible treatment failure or inaccurate history for 4 persons; others may be inaccurate history or false positive lab tests.

27 acquired *C trachomatis* during intervals when they were not having sex



Probable mix of inaccurate histories, false positive lab tests.

Conclusions:

1. *T vaginalis:* often recurred months after treatment, during intervals when women were not having sex, and after intervening negative cultures. Much more common in *older* women, and women with baseline infection.
   Suggests treatment can make *T vaginalis* non-detectable by culture for months without curing.
   More research needed!

2. *N gonorrhea* and *C trachomatis* show evidence of history errors and non-specific tests.
   When prevalence is low, confirm positive lab tests.

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NEW SEXUALLY TRANSMITTED INFECTIONS AMONG PERSONS WHO DID NOT HAVE SEX: POSSIBLE SOURCES OF ERROR IN A CONTROLLED TRIAL

Poster (P-529)

Presented at the 17th International Society for Sexually Transmitted Disease Research (ISSTDR) Meeting, 27 July -- 1 August 2007, Seattle, Washington, USA

ABSTRACT

OBJECTIVE: In a recent large STI prevention trial 64 patients acquired gonorrhea (GC), chlamydia (CT), or trichomonas (TV) during an interval in which they reported having no sex. We wanted to identify errors that led to this paradoxical situation.

METHODS: Prior to data analysis we listed types of errors and how they would influence the data. 1) Test specificities are reportedly 95-99%, so many positives could be false positives and they would be randomly distributed. 2) Errors in sex behavior histories would manifest as infections among persons reporting no sex who have the same characteristics as all infected persons in RESPECT 2 (differences by age, race, infection at baseline). 3) Test sensitivity errors would manifest in the first follow-up interval, and 4) treatment failure would manifest in intervals following treatment; these were not expected to be major contributors. Data were reviewed for evidence of each of these possible sources of error. In RESPECT-2, patients from STD clinics in Newark, Denver, and Long Beach had computer-assisted interviews, exams, and lab tests at baseline, 3, 6, 9, and 12 months. Tests were nucleic acid amplification tests for GC and CT, and culture for TV (women only). This analysis was restricted to participants tested for infections before and after an interval in which they reported having no sex partners. We calculated the incidence of new infections associated with different patient characteristics.

RESULTS: The 64 infections occurred among 668 persons who reported no sex during 1125 three-month intervals. Tests were more likely to be positive for TV (4.0%) than for GC (1.4%, $p<0.01$), or CT (2.4%, $p=0.1$). Although this number of errors is compatible with test specificities of 96-98.6%, the infections were not randomly distributed. Relative risks (RR) for infection among persons who did not have sex and among all persons were: for GC, persons infected vs uninfected at baseline (2.2 [no sex], 3.1 [all persons]), blacks vs whites (4.3, 2.3); for CT, infected vs uninfected at baseline (3.8, 2.1), age <25 vs >25 (3.4, 2.1); and for TV, infected vs uninfected at baseline (4.6, 3.6), blacks vs whites (1.8, 5.3), and women <25 vs >25 (0.3, 0.6). Only gonorrhea was significantly associated with having infection in the previous interval (RR 6.8) but there were only 4 such infections among persons who reported no sex.

CONCLUSIONS: Infections among persons who reported no sex were associated with the same risk factors identified for all study participants, suggesting there were errors their sex histories. False positives also likely occurred, and could have been reduced by confirmatory testing. Treatment failure may have occurred in a few cases.