

High Incidence of New Sexually Transmitted Infections in the Year following a Sexually Transmitted Infection: A Case for Rescreening

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Background: Studies show 11% to 15% of women treated for *Chlamydia trachomatis* are reinfected 3 to 4 months after treatment, suggesting the need for rescreening. There is little information on infections among men, infections with *Neisseria gonorrhoeae* or *Trichomonas vaginalis*, or long-term follow-up.

Objective: To determine the incidence of new sexually transmitted infections during the year after a visit to a sexually transmitted disease (STD) clinic and associated risk factors.

Design: Secondary analysis of data from a randomized, controlled trial (RESPECT-2).

Setting: 3 urban STD clinics.

Patients: Sexually active patients enrolled in an HIV prevention counseling trial.

Measurements: Patient characteristics at the initial visit; behaviors during follow-up; and new infections with *C. trachomatis*, *N. gonorrhoeae*, or *T. vaginalis* (women only) detected during 4 scheduled return visits and any other interim visits.

Results: 2419 persons had 8129 three-month follow-up intervals. Among 1236 women, 25.8% had 1 or more new infections (11.9% acquired *C. trachomatis*, 6.3% acquired *N. gonorrhoeae*,

and 12.8% acquired *T. vaginalis*); among 1183 men, 14.7% had 1 or more new infections (9.4% acquired *C. trachomatis*, and 7.1% acquired *N. gonorrhoeae*). Black persons and those with sexually transmitted infections at baseline were at highest risk for recurrent infection (adjusted odds ratio, 2.5 and 2.4, respectively). For persons infected at baseline, the risk for infection was high at 3 and 6 months (16.3 per 100 three-month intervals) and remained high at 9 and 12 months (12.0 per 100 three-month intervals). Most (67.2%) infections were diagnosed during study-related visits, and 66.2% of these patients reported no symptoms.

Limitations: Because patients were recruited from STD clinics, results may not be generalizable.

Conclusions: Men and women who receive diagnoses of *C. trachomatis*, *N. gonorrhoeae*, or *T. vaginalis* infections should return in 3 months for rescreening because they are at high risk for new asymptomatic sexually transmitted infections. Although single-dose therapy may adequately treat the infection, it often does not adequately treat the patient.

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In 1985, the Centers for Disease Control and Prevention (CDC) treatment guidelines recommended that persons infected with *Neisseria gonorrhoeae* should return for a “test of cure” to be sure that the antibiotics had cured the infection (1). With new medications, treatment failure became rare, and by 1989, the guidelines suggested testing 1 to 2 months after treatment to detect treatment failure and reinfection (2). By 1993, the guidelines stated only that a test of cure was not recommended for *N. gonorrhoeae* (3). Test of cure has been unnecessary for *Chlamydia trachomatis* after treatment with first-line drugs, but infections detected among women several months after treatment have suggested that rescreening might be effective for detecting reinfection (3). Recent studies have found that 11% to 15% of women treated for *C. trachomatis* were infected when retested 3 to 4 months after treatment, possibly due to treatment failure, reinfection from an untreated partner, or infection from a new partner (4–6). New infections are often asymptomatic. One study with scheduled follow-up visits found that 62% of new *C. trachomatis* infections in men and in women were asymptomatic or unrecognized and would therefore probably be missed without rescreening (7). Untreated *C. trachomatis* infections can persist for years (8) and put infected women at risk for complications of asymptomatic pelvic inflammatory disease (9). In addition,

transmission from asymptomatic persons may be responsible for most new infections in a community (10).

The CDC has recommended that health care providers consider advising women with diagnoses of *C. trachomatis* infection to have another *C. trachomatis* test in 3 months—not as a test of cure but as a test for reinfection (11). We wondered whether men might also benefit from retesting, whether retesting should be expanded to include persons with *N. gonorrhoeae* or *Trichomonas vaginalis* infections (12), and whether there were other factors that clinicians could use to recommend retesting. We analyzed data from a large prevention counseling trial (13) that included baseline and 4 scheduled follow-up visits of patients in 3 sexually transmitted disease (STD) clinics to determine the

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Editors' Notes 565
Summary for Patients I-44

Web-Only

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incidence of new sexually transmitted infections during the year after a visit to the clinics.

METHODS

A multicenter randomized, controlled trial of HIV prevention counseling with a rapid HIV test or a standard HIV test (RESPECT-2) was conducted in 3 public STD clinics in Denver, Colorado; Long Beach, California; and Newark, New Jersey. Primary analyses and detailed methods are described elsewhere (13). Briefly, eligible clients were those who came to the clinics for a full diagnostic examination for sexually transmitted infections, were HIV-negative at enrollment, reported having vaginal or anal sex in the preceding 3 months, and were 15 to 39 years of age. At the initial visit, participants were counseled, examined, and tested for sexually transmitted infections and HIV infection. Outcomes were measured at 13-week intervals, scheduled 3, 6, 9, and 12 months from the date of enrollment. Before each follow-up visit, study staff mailed a reminder letter to each participant and made a reminder telephone call. When participants did not keep appointments, staff mailed additional reminder letters and made additional telephone calls to reschedule the visit as needed. Participants who were due for a study follow-up visit were screened for sexually transmitted infections and were interviewed if they visited the clinic any time from 1 week before the due date up to 12 weeks after the due date. Participants were given \$25 for completing each follow-up visit. This amount was later increased to \$50 in an attempt to improve retention rates.

Participants were tested for *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* infections at enrollment, at each quarterly follow-up visit, and at other visits not related to the study that occurred during the 12-month follow-up period (interim visits). An incident sexually transmitted infection was defined as a positive laboratory result either preceded by a negative result for the same infection or detected more than 14 days after provision of antibiotics effective against that infection. Testing was done in the local laboratories used by each clinic. Tests for *C. trachomatis* and *N. gonorrhoeae* infections were done on urine specimens by using nucleic acid amplification tests. The sensitivity and specificity values from the package inserts for these tests are cited here; the exact values are difficult to establish because there is no gold standard for identifying infected patients (14). The Long Beach and Newark clinics used ligase chain reaction (LCx Uriprobe, Abbott Diagnostics Division, Abbott Park, Illinois); the sensitivity and specificity for *C. trachomatis* were 93.1% and 97.1%, respectively, and the sensitivity and specificity for *N. gonorrhoeae* were 97.5% and 98.3%, respectively (15, 16). The Denver clinic used polymerase chain reaction initially (Cobas Amplicor, Roche Diagnostic Systems, Inc., Branchburg, New Jersey); the sensitivity and specificity for *C. trachomatis* were 93.4% and 96.7%, respectively, and the

Context

The Centers for Disease Control and Prevention recommends that women treated for *Chlamydia trachomatis* infection return in 3 months for evaluation of reinfection.

Contribution

When data from the RESPECT-2 trial were used, these investigators found that among patients treated for sexually transmitted infections, 25.8% of women and 14.7% of men acquired 1 or more new infections with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Trichomonas vaginalis* during 1 year of follow-up. Approximately 66% of reinfections were asymptomatic.

Implications

Successful treatment of incident cases of sexually transmitted infections is unlikely to eliminate a reservoir of infection in the community. Physicians need to perform ongoing surveillance on men and women and encourage lifestyle changes in patients with reinfection.

—The Editors

sensitivity and specificity for *N. gonorrhoeae* were 97.1% and 98.1%, respectively (17, 18). Eighteen months later, however, this clinic changed to using strand displacement amplification (BDProbeTec ET, BD Diagnostic Systems, Sparks, Maryland); the sensitivity and specificity for *C. trachomatis* were 90.7% and 96.6%, respectively, and the sensitivity and specificity for *N. gonorrhoeae* were 96.0% and 98.8%, respectively (19). *Trichomonas vaginalis* was cultured by using the InPouch TV test (BioMed Diagnostics Inc., San Jose, California) or modified Diamond medium as the culture medium. The sensitivity has been estimated at 82.4% for the InPouch TV test and 87.8% for Diamond medium; specificity for both culture methods is nearly 100% (20). Cultures were done by using vaginal swab specimens from women. At follow-up visits, vaginal swabs were collected by the participant (Denver and Long Beach) or by a clinician (Newark), depending on local clinic policy. Behavioral data were collected by using Audio Computer-Assisted Self-Interview technology at enrollment and at each scheduled study follow-up visit. For most questions, a uniform 3-month recall period was used, regardless of the time since the most recent study visit.

Because previous work has shown that most new infections are asymptomatic, we limited our analysis to participants who returned for testing and therefore could be classified as “infected” or “not infected.” Return visits with testing and interviews were scheduled every 3 months, and most participants returned within 2 weeks of their scheduled time. However, some participants also returned before their scheduled visit because of concern about a possible infection. Those who returned early were tested for sexually transmitted infections and were told to return for their scheduled visit for the interview and repeated testing. All

Table 1. Percentage of Participants Testing Positive for a Sexually Transmitted Infection during 3-Month Intervals, by Demographic and Behavioral Characteristics*

Characteristics	<i>Chlamydia trachomatis</i> Infection		<i>Neisseria gonorrhoeae</i> Infection		<i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infection	
	Value (95% CI), %	Adjusted Odds Ratio (95% CI)	Value (95% CI), %	Adjusted Odds Ratio (95% CI)	Value (95% CI), %	Adjusted Odds Ratio (95% CI)
Interval						
1 (n = 2140)	4.2 (3.3–5.0)	1.3 (0.9–1.8)	2.4 (1.8–3.1)	1.0 (0.7–1.5)	6.3 (5.3–7.4)	1.2 (0.9–1.6)
2 (n = 2095)	4.0 (3.2–4.9)	1.2 (0.9–1.7)	2.6 (1.9–3.3)	1.1 (0.7–1.7)	6.0 (5.0–7.0)	1.2 (0.9–1.5)
3 (n = 1968)	3.2 (2.4–4.0)	1.0 (0.7–1.4)	1.3 (0.8–1.9)	0.6 (0.3–0.9)	4.3 (3.4–5.2)	0.8 (0.6–1.1)
4 (n = 1926)	3.1 (2.3–3.9)	1	2.2 (1.6–2.9)	1	4.9 (3.9–5.8)	1
Sex						
Female (n = 4260)	3.9 (3.3–4.5)	1.2 (0.9–1.6)	1.9 (1.5–2.4)	0.8 (0.6–1.1)	5.4 (4.7–6.1)	1.0 (0.8–1.2)
Male (n = 3869)	3.3 (2.7–3.9)	1	2.4 (1.9–2.9)	1	5.4 (4.7–6.1)	1
Age						
15–25 y (n = 4422)	4.8 (4.2–5.4)	2.2 (1.7–2.9)	2.5 (2.0–3.0)	1.4 (1.0–2.0)	6.7 (5.9–7.4)	1.8 (1.4–2.2)
26–39 y (n = 3707)	2.3 (1.8–2.7)	1	1.8 (1.3–2.2)	1	3.9 (3.3–4.5)	1
Race						
Black (n = 4105)	4.1 (3.5–4.7)	2.0 (1.3–3.1)	3.0 (2.5–3.5)	2.0 (1.2–3.4)	6.6 (5.9–7.4)	1.9 (1.3–2.8)
Hispanic (n = 1464)	4.0 (3.0–5.0)	1.9 (1.2–2.9)	1.3 (0.7–1.9)	0.9 (0.5–1.7)	4.9 (3.8–6.1)	1.5 (1.0–2.2)
Other (n = 803)	3.8 (2.5–5.1)	1.8 (1.1–2.9)	1.3 (0.5–2.0)	1.1 (0.5–2.2)	4.5 (3.1–6.0)	1.4 (0.9–2.2)
White (n = 1757)	2.1 (1.5–2.8)	1	1.3 (0.8–1.9)	1	3.3 (2.5–4.2)	1
Site						
Long Beach (n = 2386)	2.9 (2.2–3.5)	0.9 (0.6–1.2)	1.0 (0.6–1.4)	0.5 (0.3–0.9)	3.7 (2.9–4.4)	0.7 (0.5–1.0)
Denver (n = 3209)	4.0 (3.3–4.7)	1.3 (0.9–1.8)	2.3 (1.8–2.9)	1.3 (0.9–1.9)	5.8 (5.0–6.7)	1.2 (0.9–1.7)
Newark (n = 2534)	3.9 (3.1–4.6)	1	3.0 (2.3–3.7)	1	6.5 (5.5–7.5)	1
Infection at baseline						
Yes (n = 1827)	6.1 (5.0–7.2)	1.8 (1.3–2.3)	4.6 (3.6–5.5)	2.6 (1.9–3.7)	9.8 (8.5–11.2)	2.1 (1.7–2.6)
No (n = 6302)	2.9 (2.5–3.3)	1	1.5 (1.2–1.8)	1	4.1 (3.6–4.6)	1
New partner†						
Yes (n = 3452)	5.1 (4.3–5.8)	1.6 (1.2–2.2)	2.7 (2.2–3.3)	1.1 (0.8–1.6)	7.3 (6.4–8.2)	1.4 (1.1–1.8)
No (n = 4622)	2.5 (2.0–2.9)	1	1.7 (1.3–2.0)	1	3.9 (3.3–4.4)	1
Number of partner†						
0 (n = 1246)	2.5 (1.6–3.3)	1.1 (0.7–1.7)	1.5 (0.8–2.1)	0.9 (0.5–1.5)	3.7 (2.6–4.7)	1.0 (0.7–1.4)
1 (n = 4656)	2.9 (2.4–3.3)	1	1.6 (1.3–2.0)	1	4.3 (3.7–4.8)	1
2–4 (n = 1975)	5.9 (4.8–6.9)	1.7 (1.3–2.3)	3.5 (2.7–4.3)	1.9 (1.3–2.7)	8.7 (7.5–10.0)	1.8 (1.4–2.3)
≥5 (n = 197)	4.6 (1.7–7.6)	1.2 (0.6–2.3)	3.6 (1.0–6.3)	1.6 (0.7–3.6)	7.2 (3.6–10.9)	1.2 (0.7–2.2)

*Persons are counted only once for each type of infection per 3-month interval but can contribute up to 4 intervals. Odds ratios are adjusted for all of the variables in the table. NA = not applicable.

† Totals do not add up to 8129 because of missing values.

test results from interim visits between 2 interviews were associated with behaviors reported during the next scheduled interview after the interim tests. Study interviews were conducted the first time the participant returned during the scheduled follow-up time (visit 1, 84 to 174 days; visit 2, 175 to 265 days; visit 3, 266 to 356 days; and visit 4, 357 to 448 days). Test data from participants who missed interviews were grouped in the analysis with their next interview. We excluded data from visits that occurred after participants missed 2 consecutive follow-up interviews. Men who reported having sex with men in the baseline interview were also excluded because of the small sample size. Person-years at risk were calculated by using the time between interviews. Participants could contribute up to 4

intervals of observation. Those who had multiple infections with the same organism in the same interval were only counted as having 1 infection, but if an infection recurred in a different interval it was counted again.

We looked for 2 types of risk factors for infection. First, we looked for characteristics that clinicians could identify during a clinic visit that might predict infection at a subsequent visit. These factors included demographic characteristics, past risk behaviors, and infections detected during that visit. Second, we looked at events that might occur during follow-up that would alert patients to a need to return for testing for sexually transmitted infections. These factors included acquiring a new partner or having sex with more than 1 partner.

Table 1—Continued

Trichomonas vaginalis Infection		Chlamydia trachomatis, Neisseria gonorrhoeae, or Trichomonas vaginalis Infection	
Value (95% CI), %	Adjusted Odds Ratio (95% CI)	Value (95% CI), %	Adjusted Odds Ratio (95% CI)
5.2 (3.8–6.6)	1.6 (1.0–2.6)	8.3 (7.2–9.5)	1.3 (1.1–1.7)
5.4 (4.0–6.8)	1.8 (1.2–2.8)	8.1 (7.0–9.3)	1.3 (1.0–1.7)
4.4 (3.1–5.7)	1.4 (0.9–2.3)	6.3 (5.2–7.4)	1.0 (0.8–1.3)
3.2 (2.1–4.2)	1	6.1 (5.1–7.2)	1
4.6 (3.9–5.2)	NA	8.9 (8.1–9.8)	1.8 (1.5–2.2)
NA	NA	5.4 (4.7–6.1)	1
3.6 (2.9–4.4)	0.6 (0.5–0.9)	8.1 (7.3–8.9)	1.3 (1.1–1.6)
5.9 (4.8–7.0)	1	6.2 (5.5–7.0)	1
7.9 (6.6–9.1)	4.7 (2.4–9.3)	9.6 (8.7–10.5)	2.5 (1.8–3.5)
1.9 (0.9–2.9)	1.2 (0.5–2.8)	5.6 (4.4–6.8)	1.5 (1.0–2.1)
2.0 (0.8–3.2)	1.6 (0.7–3.8)	5.6 (4.0–7.2)	1.5 (1.0–2.2)
1.5 (0.7–2.3)	1	3.9 (3.0–4.8)	1
2.2 (1.4–3.1)	0.6 (0.4–0.9)	4.6 (3.8–5.5)	0.7 (0.6–1.0)
3.8 (3.0–4.7)	1.1 (0.8–1.7)	7.5 (6.6–8.5)	1.3 (1.0–1.7)
8.3 (6.6–9.9)	1	9.4 (8.3–10.5)	1
10.0 (8.1–11.9)	3.0 (2.1–4.2)	14.2 (12.6–15.8)	2.4 (2.0–2.9)
2.8 (2.2–3.4)	1	5.2 (4.7–5.8)	1
6.3 (5.1–7.5)	1.3 (0.9–1.9)	9.6 (8.6–10.6)	1.4 (1.2–1.8)
3.4 (2.6–4.1)	1	5.4 (4.7–6.0)	1
4.2 (2.6–5.8)	1.1 (0.7–1.7)	5.7 (4.4–7.0)	1.1 (0.8–1.5)
3.8 (3.0–4.5)	1	5.9 (5.2–6.6)	1
6.0 (4.4–7.6)	1.5 (1.1–2.2)	10.7 (9.3–12.1)	1.7 (1.4–2.1)
15.4 (6.6–24.2)	3.2 (1.5–6.7)	11.7 (7.2–16.2)	1.7 (1.1–2.7)

Multivariate analysis of factors associated with sexually transmitted infection included serial measures for each participant. We performed unconditional logistic regression using generalized estimating equations, which accounted for within-participant correlations of repeated measures (21). Because this method assumes that missing data are missing completely at random, we assessed the relationship between missing visits and response variables for all 2419 participants included in our study. We found no statistically significant association, which supports the assumption that the data were missing completely at random (22). Three time-varying covariates were involved in models, so an independence working correlation matrix was used to avoid potential bias (23, 24). Unstructured, exchangeable,

and autoregressive correlation structures were also used to build models. The 4 models provided very similar results, so we show only the results of the unstructured correlation matrix.

To assess the number of infections that were detected during the scheduled screening visits, we counted all infections diagnosed in the four 21-day periods surrounding the dates that the participants were told to return for their examinations. Data on symptoms were only available for the 4 visits when a questionnaire was administered. We assessed the number of infections that were diagnosed during a questionnaire visit at which the participants reported they had no symptoms and their only reason for the visit was RESPECT-2. Women were considered symptomatic if they responded “yes” when asked whether they had “pain when you urinate (pee),” “discharge from your vagina,” “pain when you have sex,” or “itching in your genital area” (for *T. vaginalis* infections only). Men were considered symptomatic if they responded “yes” when asked whether they had “pain when you urinate (pee)” or “drip or discharge from your penis.”

Statistical Analysis

All statistical analyses were performed by using SAS, version 9.1 (SAS Institute, Cary, North Carolina). Confidence intervals for proportions were usually calculated by using the asymptotic method; exact confidence limits were calculated when the numerator times the proportion was less than 5 or the denominator was less than 40.

Role of the Funding Source

This secondary analysis of RESPECT-2 data was done without additional funding.

RESULTS

From February 1999 through December 2000, 9457 clients were assessed, 7587 were eligible, and 3342 (44.0%) agreed to participate. After we excluded additional persons who were discovered to be ineligible, 3297 participants were assigned to the rapid- or standard-test groups. Of participants enrolled in RESPECT-2, 2868 (87.0%) returned for at least 1 follow-up visit. After we excluded men who reported having sex with men and visits that occurred after participants missed 2 consecutive follow-up visits, 2419 participants had 8129 follow-up intervals.

Among 1236 women, 319 (25.8%) had at least 1 new infection, including 147 (11.9%) who acquired 163 *C. trachomatis* infections, 78 (6.3%) who acquired 80 *N. gonorrhoeae* infections, and 158 (12.8%) who acquired 180 *T. vaginalis* infections. Of the 1183 men, 174 (14.7%) had at least 1 new infection, including 111 (9.4%) who acquired 127 *C. trachomatis* infections and 84 (7.1%) who acquired 92 *N. gonorrhoeae* infections. Several baseline characteristics were associated with acquiring a new infection during follow-up (Table 1). A new infection with *N. gonorrhoeae* or *C. trachomatis* was more common for younger women,

Table 2. Percentage of Participants Testing Positive during Follow-Up among Those with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Trichomonas vaginalis* at Baseline Compared with Those without Infection at Baseline*

Baseline Infection and Sex of Participants	Visit (Infection), n	<i>Chlamydia trachomatis</i> Infection (95% CI), %	<i>Neisseria gonorrhoeae</i> Infection (95% CI), %	<i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infection (95% CI), %	<i>Trichomonas vaginalis</i> Infection (95% CI), %	<i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> , or <i>Trichomonas vaginalis</i> Infection (95% CI), %
Female						
<i>Chlamydia trachomatis</i> alone (n = 94)	3 (84)	10.7 (4.1–17.3)	3.6 (0.7–10.1)	13.1 (5.9–20.3)	3.8 (0.8–10.7)	13.1 (5.9–20.3)
	6 (80)	10.5 (3.6–17.4)	0.0 (0.0–4.7)	10.5 (3.6–17.4)	1.3 (0.0–7.2)	11.3 (4.3–18.2)
	9 (81)	6.3 (1.0–11.7)	6.3 (1.0–11.7)	11.4 (4.4–18.4)	2.7 (0.3–9.6)	13.6 (6.1–21.0)
	12 (82)	3.7 (0.8–10.3)	1.2 (0.0–6.6)	4.9 (1.3–12.0)	1.3 (0.0–7.0)	6.1 (0.9–11.3)
<i>Neisseria gonorrhoeae</i> alone (n = 39)	3 (30)	0.0 (0.0–11.9)	3.6 (0.1–18.4)	3.5 (0.1–17.8)	14.8 (4.2–33.7)	16.7 (5.6–34.7)
	6 (33)	3.1 (0.1–16.2)	9.4 (2.0–25.0)	9.4 (2.0–25.0)	3.5 (0.1–17.8)	9.1 (1.9–24.3)
	9 (28)	3.9 (0.1–19.6)	7.7 (1.0–25.1)	11.5 (2.5–30.2)	11.1 (2.4–29.2)	21.4 (8.3–41.0)
	12 (28)	10.7 (2.3–28.2)	10.7 (2.3–28.2)	17.9 (6.1–36.9)	16.0 (4.5–36.1)	25.0 (10.7–44.9)
<i>Trichomonas vaginalis</i> alone (n = 119)	3 (100)	4.3 (1.2–10.5)	5.4 (0.8–10.0)	9.5 (3.6–15.4)	16.5 (8.9–24.1)	23.0 (14.8–31.3)
	6 (104)	3.0 (0.6–8.4)	4.0 (1.1–9.8)	6.9 (2.0–11.9)	18.5 (10.6–26.4)	21.2 (13.3–29.0)
	9 (102)	3.0 (0.6–8.6)	0.0 (0.0–3.7)	3.0 (0.6–8.6)	12.5 (5.9–19.1)	13.7 (7.1–20.4)
	12 (102)	4.0 (1.1–10.0)	2.0 (0.3–7.1)	5.1 (0.7–9.4)	6.9 (2.0–11.9)	11.8 (5.5–18.0)
Multiple infections (n = 60)	3 (51)	4.1 (0.5–14.0)	10.2 (1.7–18.7)	14.3 (4.5–24.1)	17.8 (6.6–29.0)	25.5 (13.5–37.5)
	6 (53)	5.7 (1.2–15.7)	7.6 (2.1–18.2)	9.4 (1.6–17.3)	22.7 (10.3–35.1)	24.5 (12.9–36.1)
	9 (52)	7.8 (2.2–18.9)	0.0 (0.0–7.1)	7.8 (2.2–18.9)	6.8 (1.4–18.7)	13.5 (4.2–22.7)
	12 (49)	6.3 (1.3–17.2)	4.2 (0.5–14.3)	8.3 (2.3–20.0)	13.3 (3.4–23.3)	20.4 (9.1–31.7)
None (n = 924)	3 (835)	3.8 (2.5–5.2)	1.2 (0.5–2.0)	4.8 (3.3–6.3)	2.9 (1.7–4.1)	7.2 (5.4–8.9)
	6 (811)	4.5 (3.1–6.0)	1.8 (0.9–2.7)	5.7 (4.1–7.3)	3.3 (2.0–4.6)	8.3 (6.4–10.2)
	9 (787)	3.1 (1.9–4.4)	0.7 (0.1–1.2)	3.5 (2.2–4.8)	3.1 (1.9–4.4)	6.1 (4.4–7.8)
	12 (768)	2.2 (1.1–3.2)	1.5 (0.6–2.4)	3.2 (2.0–4.5)	1.8 (0.8–2.7)	4.4 (3.0–5.9)
Male						
<i>Chlamydia trachomatis</i> alone (n = 133)	3 (112)	9.8 (4.3–15.3)	2.7 (0.6–7.6)	11.6 (5.7–17.5)		
	6 (106)	5.7 (1.3–10.2)	2.9 (0.6–8.2)	7.6 (2.5–12.6)		
	9 (97)	4.2 (1.2–10.3)	4.1 (1.1–10.2)	7.2 (2.1–12.4)		
	12 (91)	4.4 (1.2–11.0)	2.2 (0.3–7.7)	5.5 (0.8–10.2)		
<i>Neisseria gonorrhoeae</i> alone (n = 82)	3 (68)	9.0 (2.1–15.8)	14.9 (6.4–23.5)	22.1 (12.2–31.9)		
	6 (70)	4.3 (0.9–12.0)	4.3 (0.9–12.0)	8.6 (2.0–15.1)		
	9 (65)	1.6 (0.0–8.4)	3.1 (0.4–10.7)	4.6 (1.0–12.9)		
	12 (65)	9.4 (2.2–16.5)	7.7 (1.2–14.2)	16.9 (7.8–26.0)		
<i>Chlamydia trachomatis</i> and <i>Neisseria gonorrhoeae</i> (n = 31)	3 (25)	8.0 (1.0–26.0)	12.0 (2.6–31.2)	20.0 (6.8–40.7)		
	6 (26)	16.0 (4.5–36.1)	19.2 (6.6–39.3)	30.8 (14.3–51.8)		
	9 (23)	13.6 (2.9–34.9)	4.4 (0.1–22.0)	17.4 (5.0–38.8)		
	12 (20)	15.0 (3.2–37.9)	5.0 (0.1–24.9)	20.0 (5.7–43.7)		
None (n = 937)	3 (835)	2.7 (1.6–3.8)	1.3 (0.5–2.1)	4.0 (2.6–5.3)		
	6 (812)	2.3 (1.2–3.4)	2.1 (1.1–3.1)	4.2 (2.8–5.6)		
	9 (733)	2.3 (1.2–3.4)	1.0 (0.3–1.7)	3.3 (2.0–4.6)		
	12 (721)	2.2 (1.2–3.3)	2.1 (1.0–3.1)	4.2 (2.7–5.6)		

*A few persons were not tested for all infections. The number actually tested is used as the denominator for each infection. Multiple infections at baseline for women include *C. trachomatis* and *N. gonorrhoeae* (n = 16), *N. gonorrhoeae* and *T. vaginalis* (n = 12), *C. trachomatis* and *T. vaginalis* (n = 25), and all 3 infections (n = 7).

whereas *T. vaginalis* was more often diagnosed among older women (age 26 to 39 years). Black participants were at higher risk than those from other ethnic groups for any infection and were at particularly high risk for *T. vaginalis* infection. *Chlamydia trachomatis* and *T. vaginalis* infections were also more common among Hispanic participants and those of other races or ethnicities than among white participants. New infections were most common in participants from Newark, followed by those from Denver, then those from Long Beach. On univariate analysis (odds ratios not shown), the strongest association with acquiring a new infection was seen for having an infection at baseline (odds ratio, 3.0). Participants who received a diagnosis of a sex-

ually transmitted infection at baseline had a new infection diagnosed in 14.2% of the follow-up intervals.

Behaviors during follow-up also predicted acquisition of a new infection. New infection was more common among participants who had a new partner (odds ratio, 1.9) or had more than 1 partner (odds ratio, 2.0) than in those without these behaviors. Such behaviors had similar effects on risks for *N. gonorrhoeae*, *C. trachomatis*, and *T. vaginalis* infections.

Multivariate analysis, controlling for all the variables in Table 1, produced odds ratios that were similar to the unadjusted odds ratios (only the adjusted odds ratios are shown). There were statistically significant increases in risk

for new infection with *C. trachomatis*, *N. gonorrhoeae*, or *T. vaginalis* during follow-up for participants who were young, black, or Hispanic compared with those who were white; for participants from Newark or Denver compared with those from Long Beach; and for participants who had infections at baseline, had a new partner during the interval, and had more than 1 partner during the interval. The largest increases in risk were for participants who were black (adjusted odds ratio, 2.5) and those who had a sexually transmitted infection at the baseline visit (adjusted odds ratio, 2.4).

Most (62.5%) of the new infections were diagnosed within a 3-week period surrounding the dates for the scheduled follow-up visits, but this varied by sex and infecting organism. For women, the percentages of infections diagnosed within the 3 weeks surrounding the scheduled visit were 55.0% for *N. gonorrhoeae*, 71.2% for *C. trachomatis*, and 70.0% for *T. vaginalis*. For men, the percentages of infections diagnosed within the 3 weeks surrounding the scheduled visits were 48.9% for *N. gonorrhoeae* and 55.1% for *C. trachomatis*.

Most (432 [67.2%]) infections were diagnosed at a time when the participants said they were visiting the clinic for the RESPECT-2 study and 286 (66.2%) participants reported having no symptoms suggestive of these infections. The percentages, by organism, of infections that were diagnosed when the reason for the clinic visit was the RESPECT-2 study and the participant was asymptomatic were 36.3% (*N. gonorrhoeae*), 49.1% (*C. trachomatis*), and 43.3% (*T. vaginalis*) for women and 39.1% (*N. gonorrhoeae*) and 49.6% (*C. trachomatis*) for men.

New infections diagnosed at 3 months were not always related to the infection diagnosed at the initial visit (Table 2). A new *C. trachomatis* infection at 3 months was more likely for women with *C. trachomatis* infection alone at the initial visit (10.7%) than for those with *N. gonorrhoeae* (0%) or *T. vaginalis* (4.3%) infections or those without infection (3.8%). However, new *N. gonorrhoeae* infections were equally common for women with initial diagnoses of *C. trachomatis* infection alone (3.6%), *N. gonorrhoeae* infection alone (3.6%), or *T. vaginalis* infection alone (5.4%) compared with those without infection (1.2%). A new *T. vaginalis* infection was more likely for women with initial diagnoses of *T. vaginalis* (16.5%) or *N. gonorrhoeae* (14.8%) infections than for those with initial diagnoses of *C. trachomatis* infection alone (3.8%) or those without infections (2.9%). Among men, a new infection with *C. trachomatis* was similarly likely for those with initial diagnoses of *C. trachomatis* infection alone (9.8%) or *N. gonorrhoeae* infection alone (9.0%) compared with those without infection (2.7%). However, a new *N. gonorrhoeae* infection was more common in men with an initial diagnosis of *N. gonorrhoeae* infection alone (14.9%) than for those with *C. trachomatis* infection alone (2.7%) or those without infection (1.3%).

Among the 265 women infected at baseline who were

retested, 19.6% had a new infection detected in the 3-month interval (1 of every 5.1 participants tested). Among the 205 men with infections at baseline, 16.1% (1 of every 6.2 participants retested) had a new infection detected in the 3-month interval. For participants with infections at baseline, new infections were slightly more common during the 3- and 6-month intervals (16.3 per 100 three-month intervals) than during the 9- or 12-month intervals (12.0 per 100 three-month intervals). However, the risk for acquiring a new infection remained high throughout the 4 follow-up intervals. Among women with *N. gonorrhoeae* infection alone at baseline, a new infection was diagnosed in 25.0% during the final interval. Among men with *N. gonorrhoeae* infection at the baseline visit, *N. gonorrhoeae* or *C. trachomatis* infections were diagnosed in 16.9% during the final interval.

DISCUSSION

Women who received diagnoses of *C. trachomatis*, *N. gonorrhoeae*, or *T. vaginalis* infections were all at high risk for new asymptomatic infections with all of these organisms. Similarly, men receiving diagnoses of *C. trachomatis* or *N. gonorrhoeae* infections were at high risk for new asymptomatic infections with either organism. Participants with an infection were at highest risk for having that same infection within 3 months. Although all infections were treated with highly effective single-dose therapy, some of the infections may have been related to treatment failure and others may have been due to lack of partner treatment. However, the increased risk for infections persisted throughout all four 3-month follow-up periods, and participants with 1 infection also were generally at high risk for the other infections. This suggests that persons with 1 of these sexually transmitted infections may be part of a sexual network that places them at continued risk for all such infections.

Earlier studies have assessed the risk for new infection following the diagnosis of a sexually transmitted infection, but study designs often made interpretation difficult. In Baltimore, Maryland, the risk for returning to the clinic with *N. gonorrhoeae* infection was 4.3 per 100 person-years after this infection was diagnosed (25). In San Diego, California, the risk for returning with *N. gonorrhoeae* or *C. trachomatis* infections was 6.1 per 100 person-years for persons who had these infections at baseline compared with 1.1 per 100 person-years for those without a sexually transmitted infection at baseline (26). These studies underestimate the risk because participants who were not tested were included in the denominator and were assumed to be not infected; thus, most asymptomatic infections would have been missed.

Studies that limited analysis to persons who were retested found a much higher likelihood of infection. In Denver, the risk for new *C. trachomatis* infection was 23.6 per 100 person-years for participants with *C. trachomatis*

infections at baseline and 10.0 per 100 person-years for those without such infections at baseline (12). Similarly, in Birmingham, Alabama, the new infection rate with *C. trachomatis* was 23.3 per 100 person-years for participants with *C. trachomatis* infection at baseline and 9.6 per 100 person-years for those without this infection at baseline (27). These studies might overestimate risk if only symptomatic participants returned to the clinic and were included in the study and those without subsequent symptoms were excluded. On the other hand, these studies might underestimate risk because those who were tested only once or twice in 3 years may have had infections that were not diagnosed.

A few studies have scheduled rescreenings to eliminate selection bias caused by testing only the persons who decided to return. One *C. trachomatis* treatment trial found a recurrence and reinfection rate of 4.6% 1 month after women were treated (28). A large cohort study of women with *C. trachomatis* infections found that 6.3% were infected at 1 month and another 7.1% were infected at 4 months (4). The pilot phase for a partner-treatment trial rescreened women for *C. trachomatis* infection an average of 17 months after their diagnosis, and 11.5% to 25.5% per 100 person-years had *C. trachomatis* infection again (29). A large partner-treatment trial for women with *C. trachomatis* infection found that 5% to 7% were reinfected at 1 month and an additional 11% to 12% were reinfected at 4 months (5). Another partner-treatment trial found similar infection rates when men and women were retested 3 to 19 weeks after treatment. Infection with *N. gonorrhoeae* was detected among 3% to 11% of those who had *N. gonorrhoeae* infection at baseline, and *C. trachomatis* infection was detected among 11% to 13% of patients who had *C. trachomatis* infection at baseline (6). These studies provide the best estimates for infection rates, but retesting was limited to participants with infections at baseline and follow-up was limited to a few months.

Many of the new infections in our study were asymptomatic and were detected only because of scheduled follow-up visits. Other recent studies have shown that sexually transmitted infections are more often asymptomatic than was appreciated in the past. One study estimated that persons in New Orleans, Louisiana, were never symptomatic for 45% of *N. gonorrhoeae* infections and 77% of *C. trachomatis* infections (30). Lack of symptoms was the reason for lack of treatment for 86% of cases of untreated *N. gonorrhoeae* infections and 95% of cases of untreated *C. trachomatis* infections. Because they are less likely to be treated, persons with asymptomatic infections are more likely to transmit infections than are those with symptomatic infections. Among men in Colorado Springs, Colorado, an estimated 20% of *N. gonorrhoeae* infections were asymptomatic, but contact tracing suggested they accounted for nearly half of the transmissions to women (10). Similarly, 43% of *C. trachomatis* infections were

asymptomatic and men with asymptomatic infections accounted for 58% of transmissions to women (10).

This high rate of new asymptomatic infections suggests that persons who have an infection should be advised to return for rescreening in 3 months. Telling infected persons to return for rescreening lets them know they are at high risk for reinfection and may motivate them to get their partners treated and take other steps to reduce their risk. By rescreening women, clinicians can detect and treat asymptomatic infections that may cause asymptomatic pelvic inflammatory disease, ectopic pregnancy, and infertility. Rescreening visits could be brief, perhaps involving only leaving a urine specimen or self-collected vaginal swab. However, even with brief visits, patients may be reluctant to return, and methods to improve rescreening are needed (31). Retesting rates may increase if patients are given a choice of returning to the clinic or mailing a specimen (32). Packaging and mailing costs for self-collected specimens are less than \$4 (33).

From a public health perspective, persons who are reinfected are probably part of the core group responsible for maintaining disease in the community (26). Persons found to be reinfected could receive extra attention to ensure that all of their partners are treated and to try to identify why they were reinfected. They could also receive additional counseling about their ongoing risk, the importance of consistent and correct use of condoms, and the value of having future partners tested before beginning a sexual relationship. Thus, identifying and treating persons who have repeated infections and their partners will probably prevent more infections in the community than will treating the average infected person.

One strength of our study is that it included scheduled rescreening for patients with and without a baseline infection. This provided reliable estimates of the absolute and relative risk for new infection for these groups. Another strength is that we assessed risk every 3 months for a year, which has shown that the high risk for infection persists for at least a year. A weakness of our study is that all of our patients were recruited from STD clinics, so the results may not be generalizable to patients in other settings. Several other reinfection studies also enrolled patients from such clinics (12, 25–27). However, 1 large study found that reinfection rates were similar for patients enrolled from STD clinics, emergency departments, family planning or community clinics, and offices of private practitioners (6). A second weakness is that we did not do confirmatory testing for participants who had positive or negative results, so we cannot estimate the specificity or sensitivity of our tests. Recent studies of the sensitivity and specificity of urine tests for *C. trachomatis* and *N. gonorrhoeae* infections suggest that a substantial number of false-negative and false-positive results may occur during follow-up (34). Reported test sensitivity was particularly low for women with *N. gonorrhoeae* infections, so our reinfection estimates may be low.

The persistent high risk for new sexually transmitted infections during follow-up suggests that continuing care for persons with diagnoses of infections would benefit the patient and the community. Patients with any of these infections should be advised to return in 3 months for rescreening because they are at high risk for a new asymptomatic infection. The risk for new infection decreased over time but remained high 1 year after the initial diagnosis, suggesting that additional screening may be appropriate beyond 3 months. Modeling has suggested that semiannual screening for *C. trachomatis* infection for previously infected 15- to 29-year-old females is a cost-effective approach (35). Further research is needed to determine the optimal rescreening strategy. Although single-dose therapy may adequately treat the infection, it often does not adequately treat the patient.

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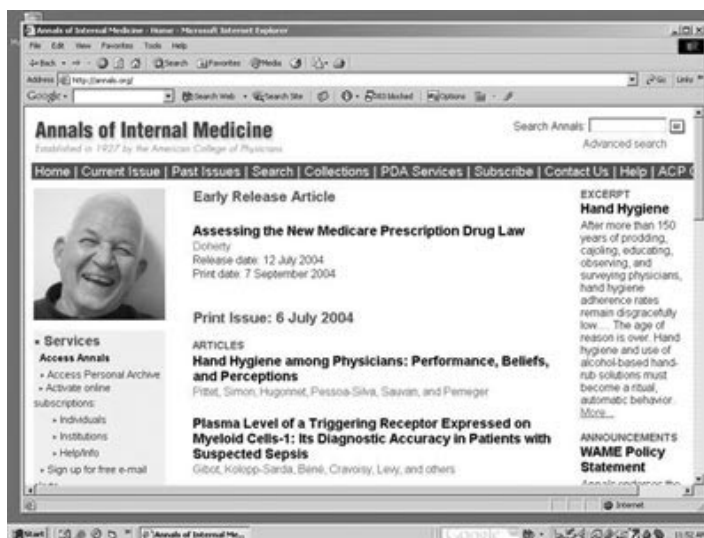
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