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Condom Effectiveness for Reducing Transmission of Gonorrhea and Chlamydia: The Importance of Assessing Partner Infection Status

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This analysis examined the importance of differential exposure to infected partners in epidemiologic studies of latex condom effectiveness for prevention of sexually transmitted infections. Cross-sectional, enrollment visit data were analyzed from Project RESPECT, a trial of counseling interventions conducted at five publicly funded US sexually transmitted disease clinics between 1993 and 1997. The association between consistent condom use in the previous 3 months and prevalent gonorrhea and chlamydia (Gc/Ct) was compared between participants known to have infected partners and participants whose partner infection status was unknown. Among 429 participants with known Gc/Ct exposure, consistent condom use was associated with a significant reduction in prevalent gonorrhea and chlamydia (30% vs. 43%; adjusted prevalence odds ratio = 0.42, 95% confidence interval: 0.18, 0.99). Among 4,314 participants with unknown Gc/Ct exposure, consistent condom use was associated with a lower reduction in prevalent gonorrhea and chlamydia (24% vs. 25%; adjusted prevalence odds ratio = 0.82, 95% confidence interval: 0.66, 1.01). The number of unprotected sex acts was significantly associated with infection when exposure was known (p for trend < 0.01) but not when exposure was unknown (p for trend = 0.73). Restricting analyses to participants with known exposure to infected partners provides a feasible and efficient mechanism for reducing confounding from differential exposure to infected partners in condom effectiveness studies.

chlamydia; contraceptive devices, male; gonorrhea; HIV infections; sexual behavior; sexually transmitted diseases

Abbreviations: Gc/Ct, gonorrhea/chlamydia; HIV, human immunodeficiency virus; STD, sexually transmitted disease; STI, sexually transmitted infection.

Although latex condoms have been recommended for prevention of sexually transmitted infections (STIs), including human immunodeficiency virus (HIV), for many years (1, 2), this recommendation has recently been questioned because of concerns about condom effectiveness against STIs other than HIV (3, 4). Latex condoms cover the shaft of the penis, thereby acting as a physical barrier to direct genital contact with preejaculatory fluid and semen; genital lesions on the glans and shaft of the penis; and penile, cervicovaginal, and anal discharges. When used properly,

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condoms should effectively protect against STIs transmitted through semen or genital secretions (e.g., gonorrhea, chlamydia, trichomoniasis, hepatitis B, and HIV) (5). Laboratory studies indicate that condoms provide an effective mechanical barrier to a wide range of STIs (6–11). In addition, epidemiologic studies show that condoms are highly effective against sexually transmitted HIV infection. Prospective and retrospective studies among persons in relationships with HIV-infected partners consistently demonstrate condoms to be effective in preventing transmission (12, 13). Similarly designed studies of herpes simplex virus type 2 also show promising results (14).

By contrast, epidemiologic studies suggest that condoms offer highly variable protection against STIs other than HIV, such as gonorrhea and chlamydia (15–31), where protection would be expected. This inconsistency was highlighted in a recent scientific review of the evidence for condom effectiveness (32). Discrepancies between in vitro and biologic evidence suggesting condom effectiveness and the inconsistent results of epidemiologic studies can be largely attributed to study design limitations (5, 32–42).

The inability to distinguish which participants have sex partners who are infected is a key limitation of most condom effectiveness studies (5, 32, 36–38, 40, 43, 44). Unlike studies of incurable STIs (e.g., HIV and herpes simplex virus type 2), in which the infection status of partners is known, most studies of curable STIs involve participants who have partners of unknown infection status. In all likelihood, many participants were never exposed to STIs and contributed no useful information for studying condom effectiveness. Among participants who were exposed, however, STI exposure could have varied across condom-use groups. Because persons may use condoms based on their perceived risk of infection (e.g., using condoms with partners perceived as more likely to be infected with STI and not with those perceived as safe) (36, 37, 44–46), condoms may be used more frequently with infected than with uninfected partners, leading to confounding (47). Prospective designs that adjust for surrogate markers for partner STI exposure (e.g., multiple partners) may help minimize this difference (35); however, these markers still cannot ensure that condom users and nonusers are similarly exposed to infected partners. Uncontrolled confounding could explain why condoms do not appear as protective against STIs in studies in which researchers do not know the infection status of partners as they do in studies in which partners are known to be infected. As a result, most studies have likely underestimated the protective effect of condoms against curable STIs.

For curable STIs, such as gonorrhea and chlamydia, prospective cohort studies of persons in relationships with infected partners would be unethical, since infected persons must be promptly treated for these infections. Retrospective (case-control, cross-sectional, and cohort) studies of persons with infected partners would be ethical, but, to our knowledge, these designs have not been used in condom effectiveness research for curable STIs.

We evaluated the importance of knowing partner infection status for assessing condom effectiveness against gonorrhea and chlamydia by conducting a secondary, cross-sectional analysis of enrollment visit data from Project RESPECT, a large study of HIV counseling interventions. We compared condom effectiveness estimates obtained from the subgroup of study participants known to have infected partners at entry with corresponding effectiveness estimates obtained from participants whose partners were of unknown infection status, the situation typifying most condom effectiveness studies.

MATERIALS AND METHODS

Study population

We analyzed enrollment visit data from Project RESPECT, a multisite randomized controlled trial of HIV/sexually transmitted disease (STD) client-centered counseling among male and female clients attending publicly funded STD clinics in five US cities (Baltimore, Maryland; Newark, New Jersey; Denver, Colorado; San Francisco, California; and Long Beach, California) between 1993 and 1997 (48). Eligible participants were heterosexual, HIV negative, aged 14 years or older, English speaking, and sexually active during the preceding 3 months. At enrollment, participants received a full diagnostic examination for STIs and completed a structured behavioral questionnaire that assessed their sexual activity and condom use during vaginal and anal intercourse during the preceding 3 months. Gonorrhea was defined as a positive culture for *Neisseria gonorrhoeae* or, for males, gram-negative intracellular diplococci on a Gram stain from a urethral swab. Chlamydia was defined as a positive *Chlamydia trachomatis* polymerase chain reaction (PCR) of urine for males or endocervical samples for females. The protocol was reviewed and approved by the institutional review board at each site.

We used the "reason for clinic visit" at study entry to distinguish participants who had partners infected with gonorrhea or chlamydia ("known Gc/Ct exposure") from participants whose partners were of unknown infection status for gonorrhea and chlamydia ("unknown Gc/Ct exposure"). Participants with known Gc/Ct exposure presented a written slip of paper given to them by their partner or health department indicating that they had been a sexual contact to gonorrhea or chlamydia; alternately, they informed clinic staff that they were told this information by their partner or health department. The remaining participants, who attended the clinic for other reasons, were classified as having unknown Gc/Ct exposure. This latter group closely resembles the population used to assess condom effectiveness against curable infections in most studies (where partner infection status is not known).

Analysis

We based case definitions on researchers' knowledge of Gc/Ct exposure for participants in each group. For persons with known Gc/Ct exposure, we defined *cases* as participants diagnosed with the same STI (either gonorrhea or chlamydia) as their infected partner; this definition increased the likelihood that infection was acquired from (or transmitted to) the partner who referred them to the clinic. *Controls* were participants referred by an infected partner

but who did not have the same STI as their infected partner. For persons with unknown Gc/Ct exposure, we defined *cases* as participants diagnosed with either gonorrhea or chlamydia and *controls* as participants who were not.

We assessed condom effectiveness through two separate measures based on the number of acts of intercourse in the preceding 3 months during which condoms were or were not used: 1) consistent condom use (binary variable: 100 percent use vs. less than 100 percent use) and 2) the number of acts of unprotected intercourse (ordinal variable: 0, 1–10, or >10 unprotected sex acts). Although these two measures are related, the number of unprotected sex acts better accounts for differences in coital frequency between condom-use groups and permits evaluation of dose-response associations (35–37, 49, 50).

We used unconditional multivariable logistic regression (51) to evaluate the association between prevalent gonorrhea and chlamydia at the initial visit and a recent history of consistent condom use. Separate models were developed for participants according to whether we could distinguish Gc/Ct exposure. A hierarchic backward elimination approach was used to develop the final regression model in each group. Prevalence odds ratios with 95 percent confidence intervals were used to compare the odds of infection at the initial visit between consistent users and inconsistent users or nonusers, adjusting for known risk factors associated with STI: sex, age (≤25 vs. >25 years), race/ethnicity (non-Hispanic Black race vs. other race/ethnicity), education (high school or less vs. more than high school), study site, and report of a main partner, a new partner, and number of partners (>1 vs. 1) in the previous 3 months. Models evaluating the prevalence odds of gonorrhea and chlamydia between consistent users and inconsistent users or nonusers in each participant group were also adjusted for the number of sex acts to account for differences in coital frequency. Models evaluating the prevalence odds of gonorrhea and chlamydia based on the number of unprotected sex acts in each participant group were also adjusted for the number of sex acts protected by condoms. We included this variable to allow for the possibility that these STIs were acquired during either protected or unprotected sex, although we hypothesized that only unprotected sex would be associated with infection.

All regression models for both participant groups initially contained the potential confounding factors described above as well as product terms between consistent condom use (or number of unprotected acts) and each factor to assess interaction effects; however, none of the product terms was statistically significant, and these terms were subsequently removed from the model. We tested whether associations between consistent condom use and prevalent infection differed statistically between groups of participants with known versus unknown Gc/Ct exposure by including an interaction term between group and condom use in a model predicting infection that contained all study participants.

We used the prevalence odds ratio to provide an unbiased estimate of the incidence density ratio, assuming that this population is stationary and that duration of STI is not related to condom use (52, 53). All statistical analyses were conducted by using SAS, version 8.02 software (SAS Institute, Inc., Cary, North Carolina). An alpha level of 0.05 was considered statistically significant, and all statistical tests were two tailed.

RESULTS

Of 5,758 Project RESPECT participants, analyses were restricted to 4,743 (82 percent) who received both a diagnostic examination for STIs and completed a behavioral questionnaire at enrollment. Of 1,015 participants (18 percent) excluded from analysis, 946 had been assigned to the control arm in Project RESPECT and were not required to complete an enrollment visit questionnaire, 28 had missing questionnaires, and 41 completed a questionnaire but were missing information on their reason for the visit, condom use, or frequency of sexual activity.

Of the 4,743 participants, 429 (9 percent) had known Gc/Ct exposure, having been referred to the STD clinic because they were sexual contacts of partners infected with gonorrhea (n = 234) or chlamydia (n = 195). Females accounted for 170 (73 percent) contacts referred because of exposure to gonorrhea, while males accounted for 142 (73 percent) contacts referred because of exposure to chlamydia. Altogether, 205 contacts received written notice of their exposure to these STIs, and 224 contacts were notified in person by their partner or health department. Of all 429 contacts, 207 (48 percent) received a diagnosis of gonorrhea or chlamydia; for most (n = 179, 86 percent), this diagnosis was the same as that of their infected partner (85 had gonorrhea only, 50 had chlamydia only, and 44 had both).

For 4,314 (91 percent) participants, Gc/Ct exposure was unknown. Seeking a full examination was the most common reason for a visit (n = 3,656), followed by sexual contact with partners infected with STIs other than gonorrhea or chlamydia (e.g., HIV, syphilis, or unknown STI) (n = 572), other reasons (n = 76), and HIV testing (n = 10). Overall, 1,082 (25 percent) participants with unknown Gc/Ct exposure received a diagnosis of gonorrhea or chlamydia at their initial visit (517 had gonorrhea only, 444 had chlamydia only, and 121 had both).

Participants with known exposure differed from participants with unknown exposure (table 1). In general, participants with known exposure were significantly more likely to be female, Black, younger, and less educated than participants with unknown exposure. Participants for whom exposure status was known were also significantly more likely to have main partners and less likely to have occasional and new partners than were participants for whom exposure was unknown, regardless of sex (not shown). Only the number of partners did not differ between the two groups.

For all participants, the prevalence of Gc/Ct was approximately twofold higher among those who were male, Black, aged ≤25 years, less educated, and not from San Francisco compared with their counterparts (table 2). The adjusted prevalence odds of having Gc/Ct was approximately 20 percent lower among 663 participants who reported consistent condom use than among 4,080 participants who did not. Participants with known contact with a partner infected with gonorrhea or chlamydia were twice as likely to be diagnosed with these STIs than were participants without such contact.

TABLE 1. Characteristics of sexually transmitted disease clinic patients in Project RESPECT at enrollment, by knowledge of partner infection status, United States, 1993–1997*

Characteristic	Participants with known Gc/Ct† exposure						Participants with unknown Gc/Ct exposure					
	Male (*n* = 206)		Female (*n* = 223)		Total (*n* = 429)		Male (*n* = 2,470)		Female (*n* = 1,844)		Total (*n* = 4,314)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Race/ethnicity												
White	37	18.1	31	13.9	68	15.9	406	16.4	424	23.0	830	19.2
Black	123	60.0	151	67.7	274	64.0	1,603	64.9	934	50.7	2,537	58.8
Other	45	21.9	41	18.4	86	20.1	461	18.7	484	26.3	945	22.0
Age (years)												
≤25	131	63.6	137	61.4	268	62.5	1,128	45.7	1,054	57.2	2,182	50.6
>25	75	36.4	86	38.6	161	37.5	1,342	54.3	790	42.8	2,132	49.4
Educational level												
High school or less	145	70.4	182	81.6	327	76.2	1,707	69.4	1,323	71.9	3,030	70.4
More than high school	61	29.6	41	18.4	102	23.8	754	30.6	518	28.1	1,272	29.6
Site												
Baltimore, Maryland	35	17.0	60	26.9	95	22.1	496	20.1	295	16.0	791	18.3
Denver, Colorado	53	25.7	50	22.4	103	24.0	451	18.3	627	34.0	1,078	25.0
Long Beach, California	45	21.8	59	26.5	104	24.2	401	16.2	369	20.0	770	17.8
Newark, New Jersey	40	19.4	35	15.7	75	17.5	610	24.7	267	14.5	877	20.3
San Francisco, California	33	16.0	19	8.5	52	12.1	512	20.7	286	15.5	798	18.5
Had main partner												
Yes	181	87.9	208	93.3	389	90.7	1,811	73.3	1,617	87.7	3,428	79.5
No	25	12.1	15	6.7	40	9.3	659	26.7	227	12.3	886	20.5
Had occasional partner												
Yes	99	48.1	76	34.1	175	40.8	1,477	59.8	682	37.0	2,159	50.0
No	107	51.9	147	65.9	254	59.2	993	40.2	1,162	63.0	2,155	50.0
Had new partner												
Yes	97	47.3	85	38.3	182	42.6	1,305	53.0	775	42.4	2,080	48.5
No	108	52.7	137	61.7	245	57.4	1,157	47.0	1,053	57.6	2,210	51.5
No. of sex partners												
1	97	47.1	139	62.3	236	55.0	1,077	43.6	1,168	63.3	2,245	52.0
>1	109	52.9	84	37.7	193	45.0	1,393	56.4	676	36.7	2,069	48.0

* Totals may differ because of missing information.
† Gc/Ct, gonorrhea/chlamydia.

Condom effectiveness against prevalent gonorrhea or chlamydia varied markedly depending on whether participants were sexual contacts of persons with these infections (table 3). Among participants with known exposure, consistent condom use was associated with a 58 percent reduction in Gc/Ct prevalence after adjustment for demographic and behavioral characteristics (adjusted prevalence odds ratio = 0.42, $p < 0.05$). By contrast, among participants with unknown exposure, consistent condom use was associated with an 18 percent reduction in Gc/Ct prevalence in multivariable analyses adjusted for other factors (prevalence odds ratio = 0.82, $p = 0.06$). Similar differences in condom effectiveness estimates were found between the two groups when analyses were stratified by sex or either infection; however, these analyses were limited by small sample sizes, and the results were not statistically significant (not shown). Although the odds ratio for the protective effect of consistent condom use among participants with known exposure was nearly 50 percent lower than that among participants with unknown exposure, this difference did not attain statistical significance at the alpha = 0.05 level ($p = 0.10$).

The association between the number of unprotected sex acts and prevalent Gc/Ct also differed according to whether participants were sexual contacts for these infections (table 4). Among participants with known Gc/Ct exposure, the odds of prevalent infection increased significantly with number of unprotected sex acts (χ^2 test for linear trend = 10.3, $p < 0.01$). Compared with participants reporting no

TABLE 2. Demographic and behavioral predictors of prevalent gonorrhea or chlamydia infection among sexually transmitted disease clinic patients, Project RESPECT, United States, 1993–1997

Characteristic	No.	% Gc/Ct*	Crude POR*	95% CI*	Adjusted POR†	95% CI
Consistent condom use						
Yes	663	24.1	0.86	0.71, 1.04	0.79	0.64, 0.97
No	4,080	27.0	1.0		1.0	
Sex						
Male	2,676	31.9	1.90	1.66, 2.18	1.80	1.55, 2.10
Female	2,067	19.7	1.0		1.0	
Race/ethnicity						
Black	2,811	34.5	3.00	2.59, 3.46	2.10	1.75, 2.51
Other	1,929	15.0	1.0		1.0	
Age (years)						
≤25	2,450	32.4	1.88	1.65, 2.15	1.92	1.66, 2.22
>25	2,293	20.3	1.0		1.0	
Educational level						
High school or less	3,357	30.9	2.29	1.96, 2.68	1.65	1.38, 1.96
More than high school	1,374	16.3	1.0		1.0	
Site						
Baltimore, Maryland	886	35.3	3.49	2.73, 4.47	2.04	1.55, 2.68
Denver, Colorado	1,181	19.7	1.57	1.22, 2.02	1.59	1.23, 2.05
Long Beach, California	874	26.4	2.30	1.78, 2.96	1.82	1.40, 2.37
Newark, New Jersey	952	38.8	4.05	3.17, 5.16	2.32	1.79, 3.03
San Francisco, California	850	13.5	1.0		1.0	
Contact with infected partner						
Yes	429	41.7	2.14	1.75, 2.61	2.20	1.77, 2.74
No	4,314	25.1	1.0		1.0	
No. of partners in the past 3 months						
>1	2,262	31.0	1.55	1.36, 1.76	1.17	0.99, 1.37
1	2,481	22.5	1.0		1.0	
Main partner in the past 3 months						
Yes	3,817	24.7	0.62	0.53, 0.72	0.74	0.62, 0.88
No	926	34.6	1.0		1.0	
New partner in the past 3 months						
Yes	2,262	29.7	1.34	1.18, 1.53	1.32	1.13, 1.56
No	2,455	23.9	1.0		1.0	

* Gc/Ct, gonorrhea/chlamydia; POR, prevalence odds ratio; CI, confidence interval.

† Prevalence odds ratio for Gc/Ct for participants with that characteristic compared with those without that characteristic, adjusted for all variables listed in the table as well as the total number of sex acts reported in the past 3 months.

unprotected acts, participants reporting 1–10 unprotected acts and participants reporting >10 unprotected acts had adjusted relative odds of infection of 2.0 and 3.8, respectively. When exposure was unknown, however, the odds of prevalent infection did not increase significantly with the number of unprotected acts (χ^2 test for linear trend = 0.12, $p = 0.73$). The difference in the strength of the dose-response associations between the number of unprotected acts and prevalent infection for participants for whom Gc/Ct exposure could be distinguished and participants for whom it could not was statistically significant ($p < 0.01$).

We also examined the association between prevalent Gc/Ct and consistent condom use by restricting analyses to participants with other surrogate markers for partner infection status used in previous studies (33). Condom use was protective against prevalent Gc/Ct across all surrogate markers, yet point estimates varied little regardless of whether we included the entire study population or restricted

TABLE 3. Association between consistent condom use in the previous 3 months and prevalent gonorrhea/chlamydia, by knowledge of partner infection status, Project RESPECT, United States, 1993–1997

Consistent condom use	Participants with known Gc/Ct* exposure (n = 429)				Participants with unknown Gc/Ct exposure (n = 4,314)			
	No.	% Gc/Ct	Adjusted POR*,†	95% CI*	No.	% Gc/Ct	Adjusted POR	95% CI
Yes	33	30.3	0.42	0.18, 0.99	630	23.8	0.82	0.66, 1.01
No	396	42.7	1.0		3,684	25.2	1.0	

* Gc/Ct, gonorrhea/chlamydia; POR, prevalence odds ratio; CI, confidence interval.

† Prevalence odds ratio for Gc/Ct for participants reporting consistent condom use in the past 3 months compared with those not reporting consistent condom use in the past 3 months, adjusted for sex, age, race/ethnicity, education, site, and the number of sex partners, having a new partner, having a main partner, and total number of sex acts during the past 3 months.

the population to participants with multiple sex partners, participants with a new sex partner, participants with a perceived high-risk partner, or participants with all three surrogate markers (table 5). The strongest protective effect for consistent condom use remained for participants who reported sexual contact with an infected partner.

DISCUSSION

Our results indicate that self-reported, consistent condom use is associated with a reduced risk of gonorrhea and chlamydia. We believe that results of previous studies suggesting little or no effect for condoms may be related, in part, to difficulties measuring STI exposure in partners. We found that consistent condom use was more protective against gonorrhea and chlamydia simply by distinguishing participants whom we knew were exposed to these infections from participants whom we did not.

Exposure to infection is often difficult to measure in epidemiologic studies (47, 54, 55); however, valid estimates of condom effectiveness can be obtained only when users and nonusers are similarly exposed to infected partners. If persons use condoms more frequently with risky partners than with less-risky partners, estimates of condom effectiveness will be biased toward observing no protective effect simply because of the increased exposure to infection. In a cohort study in which condom effectiveness is 90 percent, for example, if condom users are twice as likely as nonusers to encounter an infected partner, the risk ratio measure for condom effectiveness would double from 0.10 to 0.20; consequently, apparent condom effectiveness would decrease from 90 percent to 80 percent. In reality, condom users may be several times more likely than nonusers to have infected partners, and the underestimate of condom effectiveness in most studies may be quite large.

TABLE 4. Association between number of unprotected and protected sex acts in the previous 3 months and prevalent gonorrhea/chlamydia, by knowledge of partner infection status, Project RESPECT, United States, 1993–1997

	Participants with known Gc/Ct* exposure (n = 429)						Participants with unknown Gc/Ct exposure (n = 4,314)					
	No.	% Gc/Ct	Crude POR*	95% CI*	Adjusted POR†	95% CI	No.	% Gc/Ct	Crude POR	95% CI	Adjusted POR†	95% CI
No. of unprotected sex acts												
>10	209	46.9	2.03	0.87, 4.83	3.78	1.48, 9.72	1,683	22.0	0.91	0.73, 1.12	1.13	0.87, 1.45
1–10	187	38.0	1.41	0.60, 3.38	2.03	0.82, 5.01	2,001	28.0	1.25	1.01, 1.53	1.25	0.99, 1.58
0	33	30.3	1.0		1.0		630	23.8	1.0		1.0	
p for trend					0.001						0.73	
No. of protected sex acts												
>10	60	36.7	0.78	0.43, 1.43	1.15	0.58, 2.28	695	24.8	1.10	0.90, 1.36	0.99	0.77, 1.26
1–10	188	42.6	1.00	0.66, 1.51	1.36	0.84, 2.20	2,000	26.9	1.23	1.06, 1.44	0.97	0.81, 1.16
0	181	42.5	1.0	1.0	1.0		1,619	23.0	1.0		1.0	
p for trend					0.47						0.63	

* Gc/Ct, gonorrhea/chlamydia; POR, prevalence odds ratio; CI, confidence interval.

† Logistic regression models for participants with known and unknown Gc/Ct exposure included the following terms: sex, age, race/ethnicity, education, site, and the number of sex partners, having a new partner, having a main partner, and the number of sex acts protected by and not protected by condoms in the previous 3 months.

TABLE 5. Association between consistent condom use in the previous 3 months and prevalent gonorrhea/chlamydia, when restricted to different surrogate markers for partner infection status, Project RESPECT, United States, 1993–1997

Marker for having an infected partner	No.	Adjusted POR*	95% CI*
Entire study population	4,743	0.79	0.64, 0.97
Multiple sex partners	2,262	0.79	0.58, 1.06
New sex partner	2,262	0.70	0.52, 0.92
Perceived high-risk partner	2,154	0.73	0.55, 0.96
All three previous risk markers	948	0.64	0.42, 1.00
Sexual contact to infected partner	429	0.42	0.18, 0.99

* POR, prevalence odds ratio; CI, confidence interval.

The need to distinguish infected from uninfected partners when assessing the association between behaviors and curable STI has been underscored by others (33, 37, 38, 43, 49); however, we are not aware of any studies that have directly assessed the effect of differential exposure to infected partners between condom users and nonusers on the association with infection. Some studies (16, 23, 24, 30) include no multivariable analyses and do not adjust for differences in STI exposure. Others adjust for this difference during analysis using surrogate markers for having an infected partner, such as the number of partners, prior STI diagnoses, the type or perceived risk of partners, or several of these behaviors concurrently (15, 26, 28, 29, 39, 46). However, such surrogate measures are likely insufficient to adjust for exposure to infected partners and have met with mixed success. In our analysis, neither adjusting for these markers (table 2) nor restricting analyses to participants with these markers reduced confounding as much as restricting analyses to participants with known exposure to infected partners (table 5).

A few studies have accounted for differential exposure to infected partners during the design. In the most rigorous study to date (20), investigators prospectively evaluated gonorrhea in 537 uninfected sailors who had had intercourse with sex workers during a 4-day liberty in the Far East. None of the sailors who reported "regular" use of condoms acquired gonorrhea in contrast to 10.2 percent of sailors who did not, a difference that was even greater when nongonococcal urethritis was included as an additional study outcome (56). Given the brief follow-up period and exposure to the same pool of sex workers, this design increased the likelihood that all sailors experienced the same level of STI exposure regardless of their condom use, thus leading to unbiased estimation of condom effectiveness.

The present study sought to minimize differences in exposure to infected partners by restricting analyses to participants who were known sexual contacts of infected patients. Although transmissibility of curable STIs has been estimated among contacts of infected patients (57–59), to our knowledge condom effectiveness has not been estimated by using this type of approach. Restricting our study population to contacts of infected patients increased the likelihood that all participants had sex with an infected partner, regardless of their condom use, and thus reduced confounding. Therefore, we incorporated the key design element of studies that demonstrate the strongest protective effects for condoms against curable STIs (20) and incurable STIs (12–14): a high likelihood that exposure to infected partners did not vary across condom-use groups.

Our findings are strengthened by the observation that the odds of prevalent infection increased with the number of unprotected sex acts when participants had infected partners but not when partner infection status was unknown. If condoms work, STI acquisition should be related to the number of unprotected acts with an infected partner but not to the number of acts in which condoms were used or to the number of unprotected acts with an uninfected partner. Consistent with this hypothesis, we observed these associations only when analyses were restricted to known contacts to these infections.

These study findings support others' recommendations (35–37, 49, 50) to assess condom use with the number of unprotected acts instead of the percentage of acts protected by condoms. The two measures are identical when assessed dichotomously within a sexually active cohort since persons who are "consistent condom users" have zero acts of unprotected sex and persons who are "inconsistent users" or "nonusers" have at least one unprotected act. However, when risk of infection increases with increasing exposure to infected partners (as in Project RESPECT), lumping unprotected sex into a dichotomous variable will obscure the underlying dose-effect association. In this case, where multiple categories of unprotected sex are appropriate, using the absolute number of unprotected acts is preferable to using the proportion of acts in which condoms were used since the latter is noninformative regarding overall levels of STI exposure. Measuring condom use as the proportion of sex acts in which condoms were used could weaken, or even reverse, a dose-response association with infection. We found evidence of this problem in Project RESPECT among participants with infected partners: infection was strongly associated with the number of unprotected acts but was not associated with the proportion of acts protected by condoms (not shown).

Our retrospective design for evaluating condom effectiveness against curable STIs is ethically permissible and offers several advantages. First, by using the participant's presentation of the contact slip (or verbal report) as evidence of having an infected partner, this design efficiently uses the existing STD clinic framework for partner notification to passively identify persons who have infected partners. Unlike previously conducted studies of incurable and curable STIs in persons with infected partners, active contact tracing of sex partners is not required because knowledge of the partner's infection is the precise reason that the participant came to the health department. Studies restricted to contacts of infected persons who are passively identified among all STD clinic attendees thus require fewer resources to implement and sustain in clinic-based settings. Second, studies of participants with infected partners are more efficient and may require smaller sample sizes than clinic-based studies that enroll participants without regard to partner

infection status. Recent recommendations reasonably suggest that studies of condom effectiveness against transmission of curable STIs should be powered to detect small-to-modest effect sizes when partner infection status is unknown (35); however, our analyses suggest a larger effect size for condoms when participants had partners who were infected. Third, our finding of different associations between consistent condom use (and number of unprotected sex acts) and infection between groups of participants with known versus unknown Gc/Ct exposure within Project RESPECT is further strengthened by the fact that both groups were recruited into the study by using the same eligibility criteria, were interviewed by using identical questionnaires, and did not receive their STD test results until after their interview had been completed.

Our findings are subject to some limitations. First, although we identified participants who had a known-infected partner, we could not determine whether participants had had intercourse while the partner was infected and whether this varied by condom-use status. Second, for participants reporting multiple partners, we could not distinguish which partner was diagnosed with STD; however, further analyses of participants reporting only one partner (whom we presumed was likely infected) suggested the strongest associations between condom use and the number of unprotected sex acts and infection (not shown). This finding suggests that inclusion of data from partners unlikely to be infected dilutes the association between condom use and infection. Third, our results likely overestimate the proportion of consistent users with infection among both participants with known exposure and those with unknown exposure. Infections in consistent condom users could have resulted from condom-use reporting error (31, 40), laboratory error (60), problems with condom use (e.g., breakage, slippage, or incomplete use) (35, 41, 42), or the inability to distinguish whether infection occurred before or during the recall period; however, we could not assess the effect of these problems from enrollment visit data in Project RESPECT.

Fourth, among participants who were infected sexual contacts of persons diagnosed with gonorrhea or chlamydia, we could not distinguish the origin of infection. Although the directionality of transmission may be easier to determine for certain subgroups (e.g., monogamous women whose partners have other partners) (58), we could not assess this factor in our analysis because of small sample sizes. Finally, our population of participants who had infected partners was likely overrepresented with participants who were condom "failures." If condoms work, persons who used condoms effectively would be unlikely to either transmit or acquire infection and thus would be unlikely to be included in our study population; our sample of sexual contacts likely contained only the most ineffective of condom users. Taken together, these limitations likely bias our results toward showing no protection for condoms against gonorrhea or chlamydia. Our finding that condoms reduced the risk of these infections thus provides only a minimum estimate of condom effectiveness; the true level of protection is likely greater.

Although laboratory studies consistently indicate that condoms should prevent STIs, the protective effect of condoms against curable STIs is likely underestimated in most epidemiologic studies because of the lack of information on partner infection status. By restricting our study population within Project RESPECT to sexual contacts of infected patients instead of the entire clinic population, we greatly minimized this difference. This type of methodology (that distinguishes persons with infected partners from persons with partners of unknown infection status) may have many other potentially important applications for future STI research beyond examination of condom effectiveness. For example, studies of contacts of infected patients could be used to help researchers better understand the complex (and often paradoxical) associations between behavioral and biologic outcome measures often observed in intervention trials, an issue well described by others (36, 46). Such studies could be used to distinguish whether factors apparently associated with STI (e.g., age, gender, race, lack of circumcision, vaginal douching, use of contraceptives (other than condoms)) are true risk factors for (or preventive mechanisms against) STI or perhaps simply markers for having an infected partner. Similarly, given that the infection status of partners is known for a subset of persons, this type of methodology could potentially be used to examine the per-act transmissibility of various STIs for which, with the exception of HIV, existing data are quite limited.

Cross-sectional studies restricted to persons who present to STD clinics because they were sexual contacts of infected patients could be further enhanced by including sex partners of patients who were diagnosed with STI but who presented to the STD clinic for reasons other than being a sexual contact of an infected partner. (In Project RESPECT, we found that 25 percent of participants who attended the STD clinic for "other reasons" were diagnosed with gonorrhea or chlamydia.) The sex partners of these participants, following routine notification of their potential exposure by the patient (or health department), could constitute a study population analogous to the current one if sex partners were passively identified and approached for enrollment as they presented to the STD clinic. This new study population would be likewise resource efficient and cost-effective to identify and could be enrolled on a continuing basis. This population of sex partners, if paired with the population of infected index patients who initially attended the STD clinic, would offer additional advantages to investigators, including the ability to assess the congruence of self-reported sexual histories between sex partners and, potentially, to evaluate the effectiveness of different approaches to partner notification to elicit sexual contacts to the clinic.

Our study results indicate that knowledge of partner infection status is critical when evaluating condom effectiveness for prevention of gonorrhea and chlamydia. Consistent condom use likely provides greater protection against transmission of these STIs than previously reported in the literature, a finding that holds important implications for public health recommendations and practice.

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