

## GYNECOLOGY

# Over-screening for chlamydia and gonorrhea among urban women age $\geq 25$ years

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**OBJECTIVE:** The purpose of this study was to determine the prevalence of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) in older women who are at increased risk of sexually transmitted infections (STIs) based on community STI prevalence. Additionally, we explored the associations between STI risk factors and CT/NG to determine the percentage of women who were over-screened.

**STUDY DESIGN:** We conducted a retrospective chart review of women  $\geq 25$  years old who were either tested or screened for CT/NG during a gynecology visit at an urban teaching institution. Pregnancy and HIV infection were exclusion criteria. Descriptive statistics, univariate analyses, and logistic regression were performed.

**RESULTS:** Of 658 eligible women, the median age of those positive for CT/NG was 30 years (range, 26–41 years). Chlamydia and gonorrhea prevalence was 1.7% (11/658 women) and 0.3% (2/658 women), respectively. All positive results were captured by testing women of any age who reported symptoms or an STI exposure and by screening women who were  $\leq 40$  years old. After adjustment of data for age, we

found that symptomatic women were 3 times more likely to test positive for CT/NG (adjusted odds ratio, 3.4; 95% confidence interval, 1.1–10.3) and that STI-exposed women were 10 times more likely to test positive for CT/NG (adjusted odds ratio, 10; 95% confidence interval, 1.9–52.5). In asymptomatic non-STI-exposed women, nonmonogamous relationship ( $P = 1.0$ ), abnormal examination results ( $P = 1.0$ ), and previous STI ( $P = .35$ ) were not associated with CT/NG. Over-screening occurred in 21% of women (141/658), all of whom were menopausal, had a hysterectomy, or were  $>40$  years old.

**CONCLUSION:** CT/NG prevalence among older women was low, even in a community of high STI prevalence. More than 20% of women could have avoided CT/NG evaluation without impacting the detection of positive results in our clinic cohort. Over-screening occurred among asymptomatic, non-STI-exposed women who were menopausal, had a hysterectomy, and were  $>40$  years old.

**Key words:** chlamydia, gonorrhea, older women, screening

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There are an estimated 2.8 million chlamydia infections and 820,000 gonorrhea infections annually in the United States.<sup>1,2</sup> The United States Preventive Services Task Force (USPSTF) recommends annual screening of all women  $<25$  years old and women  $\geq 25$  years old who are at increased risk for acquiring sexually transmitted infections (STIs).<sup>3</sup> Women are considered at increased risk of STI acquisition if they engage in high-risk

sexual behaviors (ie, report new or multiple current sexual partners, exchange sex for money or drugs, use condoms inconsistently, or have sex while under the influence of alcohol or drugs). Additionally, USPSTF states that black women may be at increased risk of chlamydia and gonorrhea, irrespective of age or sexual behaviors, in communities of high STI prevalence; therefore, annual screening can be considered.

*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infections can lead to significant acute and chronic morbidity among reproductive-aged women, including pelvic inflammatory disease, infertility, ectopic pregnancies, and chronic pelvic pain.<sup>4</sup> Physicians and other health care providers play a critical role in STI prevention, particularly secondary prevention through screening. However, CT/NG screening without an indication in older women, other than living in communities of high STI prevalence, might lead to significant health care expenditures while yielding minimal clinical benefit. Furthermore, the clinical implications of untreated asymptomatic infections in nonreproductive aged women are likely different than in women of younger, reproductive ages.

Studies have demonstrated that health care providers under-screen young women, while perhaps over-screening older women. Using a commercial

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claims database of >34 million patients, Tao et al<sup>5</sup> found that 65% of CT/NG tests were performed among women 25-44 years old. Within this older age group, only 56% of tests were prompted by symptoms or pregnancy. It is unclear whether the remaining 44% were screened unnecessarily, because this study did not analyze patient-level clinical data.

Given the lack of patient-level data among older women who live in high STI prevalent areas and the lack of direct evidence for guideline committees to recommend a specific age to stop screening, we sought to determine the prevalence of CT/NG in women  $\geq 25$  years old, with and without symptoms, who were examined at a gynecology clinic located in a community with high STI prevalence. In addition, we explored associations between STI risk factors and CT/NG to determine the percentage of women who were overscreened.

## MATERIALS AND METHODS

We conducted a cross-sectional study of women  $\geq 25$  years old who were tested for CT/NG in an outpatient gynecology resident clinic at Johns Hopkins Hospital in Baltimore, MD. Because of Baltimore's high STI prevalence, our gynecology clinic follows the USPSTF recommendations that all patients, irrespective of age or symptoms, be tested for CT/NG (cotesting) annually. A list of consecutive clinic patients who were examined from Jan. 1, 2009, to Dec. 31, 2010, was obtained from the billing department and compared with a list of CT/NG test results that had been generated by the laboratory during that time frame. Electronic medical records were reviewed, and data were collected and entered into a database by 2 authors (J.A.J. and J.S.C.). To ensure data integrity, 1 author (J.S.C.) reviewed 10% of completed entries. We used a standardized data collection form to collect demographic and clinical information (ie, age, race, marital status, signs, and symptoms at time of visit). If a patient had multiple gynecology clinic visits over the time frame, only data from the initial visit that had both a clinical note

and CT/NG test result were used for data abstraction. Women who were pregnant or infected with HIV were excluded because the screening guidelines for these populations can differ from a healthy gynecologic population.<sup>5,6</sup> Other exclusion criteria included patients with incomplete records (either missing CT/NG test result or clinical note) and patients with equivocal CT/NG test results. The Johns Hopkins University Institutional Review Board determined that the study met criteria for exempt review.

Chlamydia rates in Baltimore during 2009 and 2010 were 1221.3 and 1329.1 per 100,000 population, respectively, which are more than twice the national rates of 586.7 in 2009 and 610.6 in 2010.<sup>7,8</sup> Gonorrhea rates in Baltimore during 2009 and 2010 were 449.7 and 509.7 per 100,000 population, respectively, which are 4-5 times the national rates of 98.1 in 2009 and 100.2 in 2010. Clinic prevalence of CT and NG were obtained from reports that were submitted to the City of Baltimore. The clinic prevalence of CT and NG for all ages, which ranged from 13-69 years, was 6.4% and 1.9%, respectively. The prevalence of CT and NG for women <25 years old was 11.6% and 3.7%, respectively. Cervicovaginal secretions that were collected by the provider during pelvic examination were sent to the Hopkins Clinical Laboratory Core for analysis with a nucleic acid amplification test (NAAT; APTIMA Combo 2 Assay; Hologic Gen-Probe Incorporated, San Diego, CA). Results are available through the electronic medical record and maintained in a database within the laboratory.

## Definitions

*Testing* was defined as NAATs performed in women who reported genitourinary symptoms (ie, irregular bleeding; urinary urgency, frequency, or dysuria; discolored or foul smelling vaginal discharge, or vaginal irritation/itching); *screening* was defined as NAATs performed in women without genitourinary symptoms. Abnormal speculum examination findings included cervical motion tenderness, cervical friability, and

uterine tenderness. History of an STI included patients who reported ever being diagnosed with chlamydia, gonorrhea, trichomoniasis, genital herpes, or syphilis. Because the year of previous STI diagnosis was not recorded consistently in the medical records, there is a possibility that some of these infections were remote or further removed from the time of the study clinic visit.

## Data analysis

CT and NG tests were grouped and analyzed as 1 unit (CT/NG). Continuous variables were summarized by mean  $\pm$  standard deviation or median with corresponding interquartile range. Differences between categorical variables were evaluated with the Fisher exact test. A Student *t* test with unequal variance was used for evaluation of continuous variables that followed a normal distribution. Nonnormal continuous variables were analyzed with a Wilcoxon rank sum test. All reported probability values were 2-tailed, and a value of  $< .05$  was considered significant. Associations between STI risk factors and CT/NG test positivity were assessed with logistic regression models to calculate unadjusted odds ratios (ORs), adjusted ORs (aORs) that were controlled for age, and the corresponding 95% confidence intervals (CIs). Age was selected as a covariate a priori because younger age has been shown to be associated with CT/NG.<sup>8</sup> The models were not adjusted for other risk factors because of the low frequency of positive CT/NG events. Additionally, we categorized women into 2 groups based on the presence or absence of symptoms and/or reported STI exposure. This categorization allowed us to analyze the data for women with symptoms and/or STI exposure who were tested separately from those women without symptoms or women with STI exposure who were screened. Testing all women, regardless of age, is accepted generally; however, the routine screening of older women is debatable.<sup>3</sup> Inconsistent or no use of barrier contraception and number of sexual partners were not included, because these variables rarely were documented in the medical record. All

analyses were performed with STATA statistical software (version 12; Stata-Corp, College Station, TX).

## RESULTS

There were 720 nonpregnant, HIV-negative women who ranged in age from 25-69 years and who were evaluated during the 2-year timeframe of the study. Sixty-two patients were excluded because of missing documentation (either clinical note or test result), which left 658 eligible patients (91.3%). Approximately 2% of patients (13/658) had positive CT/NG test results, all of which were among black women. Specifically, the prevalence of CT and NG was 1.7% and 0.3%, respectively.

In 2009, 268 tests were performed, and 3 women tested positive (1%); in

2010, 372 tests performed, and 10 women (2.7%) tested positive. The difference between year of testing was not statistically significant ( $P = .16$ ). Thirty-three percent of women were 25-30 years old; 35% of the women were 31-40 years old; and 32% of the women were  $\geq 41$  years old (Figure). Younger age was associated with a positive CT/NG test ( $P = .046$ ). The oldest patients who tested positive (total of 2) were 41 years old, both of whom reported genitourinary symptoms during their clinic visits. Other demographic and clinical characteristics are presented in the Table.

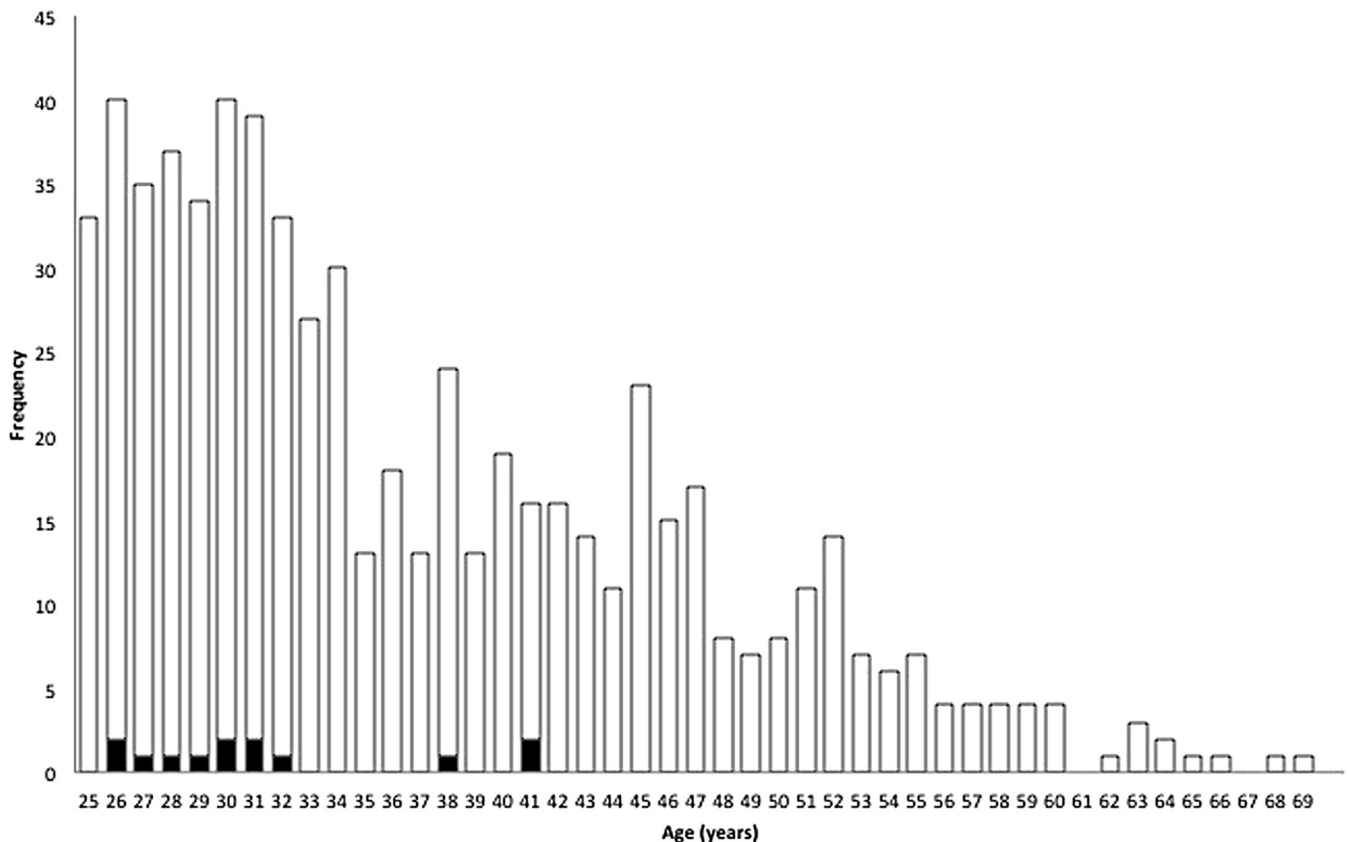
### Symptomatic women with or without an STI exposure

There were 198 women (30.1%) who reported either genitourinary symptoms

or reported an STI exposure; 9 of these patients (4.5%) tested positive for CT/NG. Symptoms alone were reported in 190 of 658 patients (29%); 7 of these patients (3.7%) tested positive for CT/NG. These symptomatic women were 3 times more likely to test positive for CT/NG compared with asymptomatic women (crude OR, 2.9; 95% CI, 0.98–8.9;  $P = .055$ ; adjusted OR, 3.4; 95% CI, 1.1–10.3;  $P = .03$ ). In addition, suspected STI exposure alone was reported in 8 of 658 patients (1.7%), and 2 of these STI exposed patients (25%) tested positive for CT/NG. STI-exposed women were 10 times more likely to test positive for CT/NG compared with women who did not report an STI exposure (crude OR, 10.5; 95% CI, 2.1–53;  $P = .004$ ;

FIGURE

### Frequency of *Chlamydia trachomatis*/*Neisseria gonorrhoeae* tests by age



The open columns indicate negative for *Chlamydia trachomatis*/*Neisseria gonorrhoeae*; the closed columns indicate positive for *Chlamydia trachomatis*/*Neisseria gonorrhoeae* (N = 658 women).

CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*.

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TABLE

## Demographic characteristics of participants by chlamydia/gonorrhea result

Demographic	Total (n = 658), n (%)	Chlamydia or gonorrhea result, n (%)		P value
		Positive (n = 13)	Negative (n = 645)	
Year of clinic visit, n (%)				.16
2009	286 (43.5)	3 (23.1)	283 (43.9)	
2010	372 (56.5)	10 (76.9)	362 (56.1)	
Age, y <sup>a</sup>	34 (29–43)	30 (28–32)	34 (29–44)	.046
Black race, n (%)	610 (92.7)	13 (100)	597 (92.6)	.61
Single (not married), n (%)	592 (90.2)	12 (92.3)	580 (90.2)	1.0
Ever pregnant, n (%)	620 (94.2)	13 (100)	607 (94.1)	1.0
Monogamous, n (%)	643 (97.7)	11 (84.6)	632 (98)	.033
Sexually transmitted infection exposed, n (%)	13 (2)	2 (15.4)	11 (1.7)	.025
Previous sexually transmitted infection, n (%)	347 (52.7)	5 (38.5)	342 (53.0)	.40
Symptomatic, n (%)	190 (28.9)	7 (53.9)	183 (28.4)	.045
Current hormonal contraception use, n (%)	106 (16.1)	3 (23.8)	103 (16)	.45
Menopausal, n (%)	76 (11.6)	0	76 (11.8)	.38
Hysterectomy, n (%)	24 (3.7)	0	24 (3.7)	1.0
Tobacco use, n (%)	263 (40.0)	5 (38.5)	258 (40.0)	1.0
Illicit drug use, n (%)	120 (18.9)	2 (15.4)	118 (18.1)	1.0

<sup>a</sup> Data are given as median (interquartile range).

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adjusted OR, 10; 95% CI, 1.9–52.5;  $P = .006$ ).

### Asymptomatic women without an STI exposure

There were 460 asymptomatic women who did not report an STI exposure; 4 of these patients (0.87%) tested positive for CT/NG. Eleven patients (2.4%) requested STI screening because they were not in mutually monogamous relationships, and none of these patients tested positive for CT/NG. Twenty-nine patients (6.3%) had abnormal speculum examination findings; however, none of these patients tested positive for CT/NG. Previous STI was reported in 240 women (52%), and some women reported more than one previous STI. Chlamydia was reported by 142 women (59%), gonorrhea was reported by 84 women (35%), trichomoniasis was reported by 93 women (39%), genital herpes was reported by 40 women (17%), and syphilis was reported by 16 women (7%). One of these asymptomatic patients

(0.42%) who reported a previous STI tested positive for CT/NG; she reported previous chlamydial infection and trichomoniasis. Nonmonogamous relationship ( $P = 1.0$ ), abnormal speculum examination findings ( $P = 1.0$ ), and personal history of an STI ( $P = .35$ ), irrespective of proximity of infection diagnosis, were not associated significantly with a positive CT/NG test in asymptomatic, non-STI-exposed women. Three women who did not report any risk factors and who tested positive for CT/NG were all  $\leq 40$  years old.

### Over-screening

We sought to determine which clinical variables, if present, would allow detection of all positive CT/NG tests and, if absent, potentially would avoid over-screening. Symptoms, STI exposure, and younger age were important clinical variables. All positive test results were captured by testing women who reported symptoms or who reported an STI exposure ( $n = 9$ ) and by screening

women who were  $\leq 40$  years old ( $n = 4$ ). Therefore, 21% of women 141 of 658 could have avoided CT/GC evaluation without impacting the detection of positive results in our clinic population. Over-screening occurred among women who were menopausal or had a hysterectomy ( $n = 54$ ), and who were  $> 40$  years old ( $n = 87$ ).

### COMMENT

The prevalence of CT and NG in our cohort was low despite the high rate of STIs in Baltimore during the same time period. Our findings suggest that most nonpregnant women who are  $\geq 25$  years old are not at high-risk for CT/NG infection, despite increased community STI prevalence. Furthermore, we found that over-screening occurred in  $> 20\%$  of the women in our cohort.

Previous studies have investigated the performance of universal STI testing in a general population of older women. Moller et al<sup>9</sup> found that 25% of all CT tests were performed on asymptomatic

women >30 years old, in whom the CT prevalence was just above 1%. Furthermore, compared with symptom-related testing, Paavonen et al<sup>10</sup> demonstrated that universal testing is only cost saving if the CT prevalence is >3.9%. Our analysis yielded a 2% prevalence of CT/NG combined, which falls below this threshold, and more closely approaches that of the study of Moller et al. Screening older patients for CT/NG is likely to increase in the United States because of the Affordable Care Act, which requires health insurance plans to cover recommended preventive services such as CT/NG screening.<sup>11</sup> Thus, more targeted testing among women from older age groups not only may prove more cost-effective but also represents an opportunity for health care savings and less resource wastefulness.

Interestingly, personal history of an STI was not associated with a positive CT/NG test in asymptomatic, non-STI-exposed women. It is possible that a patient's self-report of STI history was inaccurate or that clinical documentation of this history was flawed in the medical record. Because we included remote infections in this definition, it is also conceivable that positive behavioral changes over the patient's lifespan attenuated any underlying association.

None of the patients who reported menopause or had a hysterectomy (eg, including removal of the cervix) tested positive for CT/NG. A likely explanation is the relatively distant, or lack of, columnar epithelial cells that are infected preferentially by CT and NG in the female lower genital tract.<sup>12</sup> As a woman ages, the columnar epithelium regresses into the cervical canal and results in less exposure to infected seminal secretions. Conversely, adolescents are more likely to have ectropion or everted columnar epithelium onto the ectocervix. This age-related anatomic difference predisposes younger women to greater STI acquisition.<sup>13</sup> However, it is also possible that the lack of positive CT/NG test results among menopausal women or women who had a hysterectomy is consistent with older age, as previous data have shown that older women engage in less risky sexual behaviors compared with

younger women.<sup>3</sup> There have been case reports of symptomatic CT or NG infection among women after hysterectomy with removal of the cervix.<sup>14</sup> Although these organisms were detected with the use of vaginal swabs, they were most likely derived from close anatomic sites (ie, urethra or Bartholin's gland), which are also comprised of columnar epithelium.<sup>15</sup> Nevertheless, most of the complications of STIs (such as pelvic inflammatory disease, infertility, and ectopic pregnancies) affect a woman's reproductive capabilities. Thus, women who are menopausal or have had a hysterectomy are less susceptible to cervical infections on account of both biologic and behavioral changes and are potentially less impacted by the associated long-term sequelae.

Because the optimal age to cease screening is not known, we found that providers did not stop routine screening of women after a specific age. Although there is a lack of evidence, USPSTF states that it is reasonable to stop routine screening at menopause or at 55 years of age in sexually active women who are at increased risk only because of demographic reasons (ie, race, ethnicity, geographic location).<sup>3</sup> Because reproductive capacity ends at an average age of 41 years in the United States, complications of untreated CT/NG, such as infertility and ectopic pregnancy, should be less of a concern.<sup>16</sup> Given the lack of positive CT/NG in asymptomatic women who were >40 years old in our study, these data suggest that the USPSTF's proposed age cutoff of 55 years may be too high in certain clinical settings. However, additional research is needed to determine the degree to which other individual patient-level factors (eg, frequency of sexual activity, number of partners, risky sexual behaviors) are more predictive of CT/NG infections among older women compared with population-level determinants (ie, community prevalence). Such investigation would help to further refine screening practices that are specific to older women.

Our study has several limitations. First, it is a chart review from a single institution's gynecologic population.

Because it was not prospective in data collection, clinical examination findings (eg, vaginal discharge, mucopurulent cervicitis) were not recorded routinely and systematically. Furthermore, inconsistent clinical documentation prohibited us from examining associations between a positive CT/NG test result and other important behavioral risk factors, such as inconsistent condom use, multiple or new sexual partners, young age of sexual partners, transactional sex, or commercial sex work. Complete sexual behavioral information may have allowed us to better identify a subset of older women who are most at risk of infection and most likely to benefit from STI screening. Additionally, because of the infrequent positive CT events, we had to limit the number of covariates in our regression model. As such, there may be other significant covariates that we could not identify and appropriately adjust for in the analysis. However, the low frequency of positive CT/NG underscores the finding that not all older women should be screened for CT/NG, even in high prevalence regions. Finally, generalizability is somewhat limited as health care-seeking women may not be fully representative of all women in an urban low-income setting.

In conclusion, we estimated 20% of the women who received gynecologic evaluation in our clinic cohort were over-screened. Our findings confirm that it is sound clinical practice to test for CT/NG in women of any age who exhibit genitourinary symptoms or report an STI exposure, because almost 5% of the study patients tested positive for CT/NG. However, despite the well-established inverse relationship between age and CT/NG prevalence,<sup>8</sup> health care providers routinely screen older women.<sup>17</sup> A successful intervention to reduce CT over-screening among older women has been implemented in federally funded clinics; however, it is not known whether this intervention could be applied successfully to other health care settings.<sup>18</sup> Our data, although limited, suggest that providers should adhere to the USPSTF guidelines that recommend against screening

asymptomatic, non-STI-exposed women who are menopausal. Asymptomatic women who had a hysterectomy, including removal of the cervix, should also not be screened because cervical columnar epithelium is absent; however, they should continue to be tested if symptomatic, because the urethra can become infected. The optimal age to cease routine screening has yet to be established. We found that screening women who were  $\leq 40$  years old captured positive CT/NG tests, but this age cutoff might not be appropriate for other gynecologic clinics. Over-screening older women and even those with high STI prevalence among younger age cohorts has the potential to increase direct and indirect health care costs: from false-positive test results and unnecessary treatment to patient anxiety and subsequent relationship issues. Our findings support the need for additional research on the clinical benefits and potential harms of chlamydia and gonorrhea screening among older women. ■

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