Selective Screening for Chlamydial Infection In Women: A Comparison of Three Sets of Criteria

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Selective screening has been associated with marked declines in the prevalence of chlamydial infection, the most common bacterial sexually transmitted disease (STD) in the United States. A comparison of the performance of different selective screening criteria in three groups of family planning and STD clinic clients shows that criteria recommended by the Centers for Disease Control and Prevention performed well overall, detecting 88–89% of infections by screening 58–74% of women. Criteria based on age alone performed best among low-risk clients with a low prevalence of chlamydial infection, particularly when all women younger than age 25 were screened (sensitivity, 84–92%); the age-based criteria still required screening only 59–71% of all women. Selective screening criteria should be based on age, risk profile and chlamydia prevalence in specific clinical settings, and should be reevaluated as chlamydia prevalence declines.

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Infection with *Chlamydia trachomatis* is the most prevalent bacterial sexually transmitted disease (STD) in the United States,[1] and may be asymptomatic in nine out of 10 infected women.[2] Asymptomatic infections often result in delayed treatment, which increases the risk of upper reproductive tract infections and damage,[3] as well as transmission to sex partners. While universal screening of sexually active women for chlamydia has been endorsed as the surest way of detecting asymptomatic disease,[4] it is costly; thus, several selective screening approaches have been promoted.[5]

A randomized trial of selective screening for chlamydial infection in a large health maintenance organization showed that women who were screened had a reduced incidence of pelvic inflammatory disease.[6] However, optimal screening criteria are not always clear, particularly in settings where chlamydia prevalence is low—as is the case for some family planning providers. The increasing integration of STD services into family planning settings requires the development and evaluation of risk-assessment tools that are appropriate for these populations.[7]

When resources allocated for the prevention and control of chlamydial disease were expanded in 1993,[8] the Centers for Disease Control and Prevention (CDC) issued revised guidelines for selective screening for chlamydial infection in women.[9] However, the performance of these guidelines in predicting chlamydial infection has not been compared in population-based studies with that of criteria based on young age or behavioral risk.

In this article, to make such a comparison, we use data from the Region X Chlamydia Project, which has coordinated chlamydia screening for approximately 500 family planning and STD clinics in Alaska, Idaho, Oregon and Washington (U.S. Public Health Service Region X) since 1988. As part of the project, more than 600,000 women have been tested for chlamydia over that time, with an associated dramatic decline in chlamydia prevalence in the Pacific Northwest.[10]

Three periods of universal screening were conducted among women visiting health providers serving populations with low and moderate levels of chlamydia prevalence. Among these women, we retrospectively compared the performance of the CDC's selective screening criteria to the effectiveness of criteria based on young age and risk behavior.

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Methods

Study Groups

The study population consisted of three groups of women screened for chlamydial infection in the Pacific Northwest since 1990. All women undergoing pelvic examination for any indication were tested for *C. trachomatis* infection, regardless of signs or symptoms. The first group consisted of 11,142 women who were evaluated during 1990 at any of 10 clinics providing family planning services in Washington state. The second group includes 19,762 women seen during 1993 at 13 STD clinics in the four states of Region X. The third group consists of 6,315 women evaluated at 10 family planning clinics in Seattle and King County during 1994.

For all three groups, clinicians directly recorded clients' age, race and behavioral risks on a standardized data collection form at the time of evaluation. Behavioral risks included the women's report of having had a new sex partner in the preceding 30 days, having had more than two partners in the preceding 60 days or having a male partner with symptoms of urinary infection (defined as difficult or painful urination or urethral discharge). For the 1990 family planning clinic and 1993 STD clinic groups, women's "usual method of contraception" was recorded as being hormonal or barrier (with the latter defined as either condom or diaphragm), but information on temporal patterns of use was not requested. For participants interviewed in 1994, only condom use at last intercourse was recorded.

Screening Criteria

Three sets of selective screening criteria were analyzed:

•*CDC recommendations*. In addition to inflammation of the cervix as indicated by a discharge (mucopurulent cervicitis) and age younger than 20 as indications for screening sexually active women, the CDC guidelines recommend testing for chlamydia among women aged 20–24 if they have had a new sex partner or more than one partner in the preceding 90 days

or if they are using barrier contraceptives inconsistently. Among women aged 25 or older, testing is recommended for those reporting a new partner or multiple partners only if they are also inconsistent users of barrier methods.

• *Region X criteria*. According to guidelines derived from a previous analysis of data from the Region X Chlamydia Project,[11] chlamydia testing should be performed if a woman is younger than 21 or if she has such behavioral risks as a new partner in the preceding 30 days, more than two partners in the preceding 60 days or a male partner with STD symptoms (e.g., urethral discharge or painful urination).

• *Age-based criteria alone*. To analyze the performance of age alone as a screening criterion, we assessed age both as a continuous variable (19–30 years of age) and as a categorical variable (using cutoffs of younger than 21 and younger than 25) in the three groups.

Diagnosis and Analysis

For all study participants, cervicitis was diagnosed on the basis of either mucopurulent cervical discharge or sustained bleeding induced by the passage of an endocervical swab. (Among the STD clinic clients, in addition to either of these two criteria, a diagnosis of cervicitis was made if more than 10 polymorphonuclear leukocytes were visible per high-power field on endocervical Gram stain.) Specimens were obtained from the endocervical canal with a dacron swab in family planning clients and with either cytobrush or dacron swab in STD clients.

Laboratory methods for the detection of chlamydia differed for the three study groups, depending on clinic type and geographic locale. All clinics continued to use the standard diagnostic test for their setting; no special training was implemented in this regard. A direct fluorescent antibody test was used in the 1990 family planning clinic group; the test was considered positive if more than two elementary bodies were present.[12] Among women in the STD clinic group, 59% were tested using a commercial enzyme immunoassay,[13] 19% using a DNA probe test (GenProbe),[14] 19% using cell culture and 3% using the direct fluorescent antibody test. Cell culture was used for all women in 1994 family planning clinic group.*

Statistical analysis was performed using SPSS software. All differences between categorical variables were assessed using chi-square analysis. We calculated the proportion of infected women identified by the criteria (known as criteria sensitivity) and the proportion of women meeting the criteria who were infected (the positive predictive value). We also used respondent-operator curves (derived with ROC Analyzer Software) to compare the relationship between the percentage of infections detected (sensitivity) and the percentage of uninfected women screened.

Results

Table 1 shows the demographic, behavioral and clinical characteristics of the study participants. Chlamydia prevalence was 6.6% among both the 11,142 family planning clients tested in 1990 and the 19,762 STD clients tested in 1993, with a 95% confidence interval of 6.2%–7.0%. Among the 6,315 family planning clients tested in 1994, chlamydia prevalence was 3.3%, with a 95% confidence interval of 2.9%–3.7%. The women in the 1990 group were younger than those in the other two groups and were predominantly white; the 1993 and 1994 groups were more racially diverse, and the latter group had the highest proportion of women of Asian and Pacific Island origin.

Table 1. Percentages and means showing characteristics of female clients at family planning or sexually transmitted disease (STD) clinics, by type of clinic and year, Pacific Northwest region, 1990–1994

Characteristic	Family planning clinics		STD clinics, 1993
	1990	1994	
	(N=11,142)	(N=6,315)	(N=19,762)
% positive for chlamydia	6.6	3.3	6.6
Mean age (in yrs).	22.3	24.2	25.2
Age range	12–52	11–66	12–81
Race/ethnicity			
White	87.2	72.6	73.2
Black	1.2	9.2	12.3
Hispanic	9.2	7.5	6.5
Native American	0.9	1.4	3.3
Asian/Pacific Islander	1.5	9.3	3.0
Other/unknown	0.0	0.0	1.7
% with new sex partner*	11.3	10.0	35.4
% with >2 sex partners†	2.4	3.4	25.7
% with symptomatic sex partner‡	1.0	2.2	22.5
% with any of above risks	13.5	14.7	70.1
% using barrier contraceptive§	15.9	22.6	18.3
% with cervicitis	9.0	1.8	20.4

*In past 60 days. †In past 30 days. ‡Defined as male sex partner with a urethral discharge or dysuria (as reported by the female client). §For clients tested in 1990 and 1993, defined as use of condom or diaphragm as usual contraceptive method; for clients tested in 1994, defined as use of condom at last intercourse.

The STD clients were more likely to report all behavioral risks and were more frequently diagnosed with cervicitis than were the two groups of family planning clients. Compared with the family planning clients seen in 1990, those seen in 1994 were less likely to be infected with chlamydia ($p<.001$), were less likely to be white ($p<.001$), were more likely to report having used barrier contraceptives ($p=.006$) and were less frequently diagnosed with cervicitis ($p=.003$).

The proportion of women reporting any behavioral risk was similar in both groups of family planning clients. (While barrier contraceptive use was significantly higher in the 1994 group, this variable reflects only condom use at last intercourse, rather than the woman's "usual method of contraception," as in the other two groups.)

The performance of the selective screening criteria in the three groups is described in Table 2 (page 160). The screening criteria recommended by the CDC performed comparably in all three populations, detecting 88–89% of all chlamydia by screening 58–74% of women.

The Region X criteria performed best among the STD clients (sensitivity of 94% from screening 77% of clients) and worst in the 1990 group of family planning patients (sensitivity of 72% from screening 52% of clients). All of these criteria reduced the proportion of women tested when compared with the CDC criteria, especially in the 1994 group.

Using an age cutoff of younger than 25 detected 84–92% of infections. This criterion performed best in the 1994 family planning group, among whom the proportion of women tested was reduced by more than 40%.

As shown in Figure 1 (page 160), the sensitivity of criteria based on age alone increased consistently up to a plateau at age 28–29 in all groups. Age-based criteria performed better among the 1994 family planning clinic clients (the group with the lowest prevalence) at all age cutoffs. All but four of the 210 chlamydia-infected women in that group (98.1%) would have been detected using an age cutoff of younger than 29.

Using an age cutoff of younger than 21

*Enzyme immunoassay, the direct fluorescent antibody test and DNA probe tests were done according to manufacturers' specifications. Cell cultures were performed in a single reference laboratory at the University of Washington; specimens were inoculated into sucrose-phosphate transport media (0.2 M) and stored at 4° C for up to 48 hours before inoculation onto cyclohexamide-treated McCoy cells in microtiter plates. Growth of chlamydia was detected with fluorescein-labeled monoclonal antibody (see: W. E. Stamm et al., "Detection of Chlamydia trachomatis Inclusions in McCoy Cell Cultures with Fluorescein-Conjugated Monoclonal Antibodies," *Journal of Clinical Microbiology*, **17:**666–668, 1983).

Table 2. Measures of performance of chlamydia screening, by criteria study group, according to type of clinic and year

Measure and criteria study group	Family planning clinics		STD clinics
	1990 (N=11,142)	1994 (N=6,315)	1993 (N=19,762)
CDC criteria			
% of women meeting criteria	74	58	67
Criteria sensitivity	89	88	89
% reduction in tests	26	42	33
Positive predictive value	8.0	5.0	8.9
% infected with chlamydia (among unscreened)	2.7	0.9	2.1
Region X criteria			
% of women meeting criteria	52	46	77
Criteria sensitivity	72	82	94
% reduction in tests	48	54	23
Positive predictive value	9.2	5.9	8.2
% infected with chlamydia (among unscreened)	3.8	1.0	1.8
Age <25 alone			
% of women meeting criteria	71	59	56
Criteria sensitivity	87	92	84
% reduction in tests	29	41	44
Positive predictive value	8.0	5.0	10.0
% infected with chlamydia (among unscreened)	3.0	0.7	2.5

was uniformly insensitive, with the highest sensitivity (77%) among the family planning clinic clients tested in 1994, and did not reduce the number of women requiring screening relative to the CDC criteria.

Many of the chlamydial infections missed by selective screening criteria occurred among women older than 20 who reported no barrier method use and who had neither other risk behaviors nor cervicitis. Lack of barrier contraceptive use was most important as a risk marker among the 1990 family planning clients: Twenty percent of chlamydial infections in this group occurred among women aged 20–24 whose only reported risk factor was using not having used barrier contraceptives. In addition, 49–64% of chlamydial infections missed by the most sensitive selective screening criteria for each study group occurred among women older than 24 who reported "no barrier contraceptive use" as their only risk.

Figure 2 shows a respondent-operator curve depicting the relationship between the "true positive rate" (i.e., the percentage of infections detected, or the sensitivity of the screening criteria) and the "false positive rate" (i.e., the percentage of uninfected women who were screened).* When the slope of the curve is less than 1.0, the percentage of women tested is higher than the percentage of infections detected, which is undesirable. A perfect screening mechanism would be represented by an upside down "L" shape, which has an area equal to 1.0. The larger the area under the curve is, the more close is the fit to the ideal shape, and thus the more ideal the screening mechanism is.

In general, the curves depicted in Figure 2 confirm that age cutoffs for screening for chlamydial infection in our study groups performed best in both groups of family planning clients, whose respondent-operator curves had similar areas (p=.14). The area under the curve for the STD clients, however, was significantly smaller than the areas of the 1990 and 1994 family planning client groups (p<.001 and p=.004, respectively). In other words, at each age cutoff, the false positive rate was higher among the STD clinic clients than among the family planning clinic clients.

We can also estimate the tradeoff between sensitivity and specificity by comparing the age cutoffs at which the slope of each curve becomes less than 1.0; this occurs at younger ages for both family planning client groups (approximately 22 years) than for STD client groups (approximately 23.5 years), again supporting the use of age cutoffs as more appropriate for the family planning clients in our analysis than for the STD clinic population.

Discussion

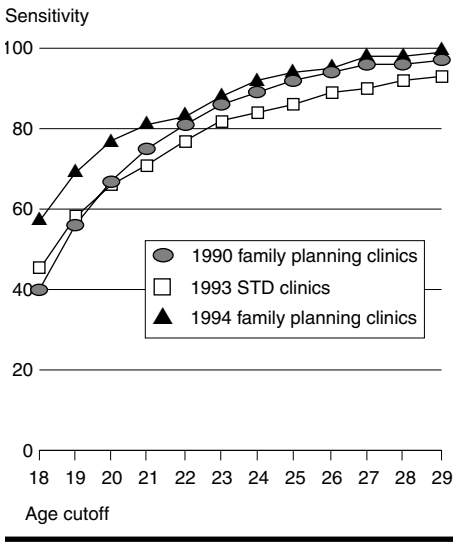
In this comparison of selective screening criteria for chlamydial infection in three large, diverse groups of women, the CDC's recommendations performed consistently well, detecting 88–89% of all chlamydial infections by screening 58–74% of women. Criteria based on young age alone (i.e., younger than age 21) were the least sensitive, demonstrating at best a sensitivity of 77% among low-risk, low-prevalence family planning clients. It was only in this group where screening all women younger than 25 was more sensitive than using the CDC criteria, and required the same proportion of women to be screened.

In general, criteria based solely on age performed best for family planning clients when the age cutoff included women up to age 27; the sensitivity was 92–94%, and 59–71% of all women had to be screened. With an age cutoff of younger than 25 among family planning and STD clients with moderate chlamydia prevalence (6.6%), age-based criteria were less sensitive in detecting infection than the CDC recommendations. The performance of Region X criteria (based on age younger than 21 or any behavioral risk) was directly related to the frequency of reported risk behavior in the groups assessed—i.e., was most sensitive in STD clients, who reported behavioral risk factors 70% of the time.

The extent to which selective screening criteria reduce the proportion of women screened depends in part on the population under study and in part on the components of the criteria. In our study, selective screening was most effective at reducing the number of low-risk, low-prevalence family planning clients tested; however, the positive predictive values for all three criteria were lowest in this group. In the two groups with moderate prevalence (6.6%), the CDC criteria afforded only a modest reduction in the number of women screened (26–29%), but they reduced by 42% the number of family planning clients screened in the low-prevalence group. Among STD clinic clients, the cutoff of age younger than 25 reduced the number of clients screened considerably (44%), but at the expense of criteria sensitivity.

These analyses suggest that the balance between optimizing criteria sensitivity and reducing the number of tests performed needs to be individualized to the population under consideration. For STD clinic clients, incorporating some measure

Figure 1. Sensitivity of chlamydia screening, by age cutoff for screening, according to study group



*The false positive rate indicates the extent to which women not infected with chlamydia were mistakenly identified as such by the screening criteria. It is calculated as 1.0 minus the specificity of the criteria, which is defined as the proportion of uninfected women who did not meet the screening criteria.

of behavioral risk (as in the CDC or Region X guidelines) seems appropriate. For family planning client populations with modest prevalence (about 6%), either the CDC or age-based criteria work well; for family planning populations with low prevalence (about 3%), age-based criteria would appear to be the best choice.

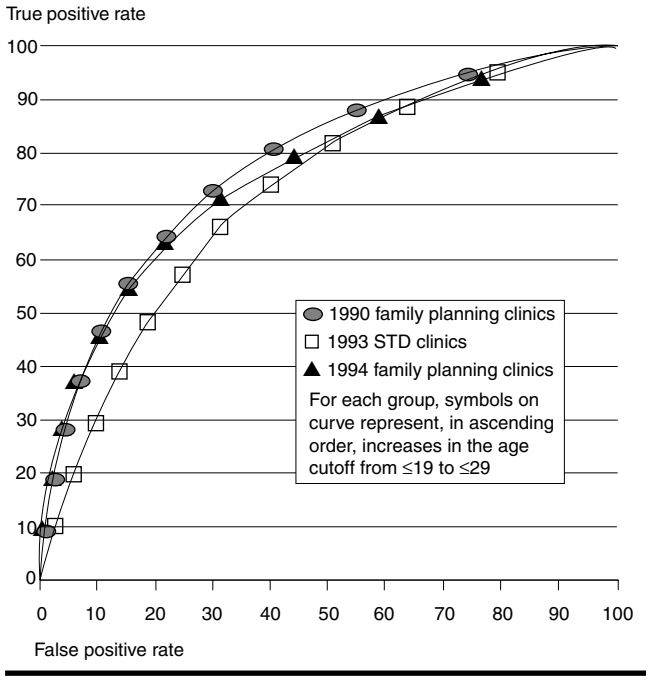
Among the criteria assessed, only the CDC criteria include behavior related to barrier method use as an indication for screening. Although a previously reported multivariate analysis demonstrated no independent association between chlamydial infection and lack of barrier contraceptive use,[15] the latter measure contributed substantially to the superior performance of the CDC criteria in these groups. In all study groups, including "inconsistent barrier contraceptive use" in the screening criteria increased criteria sensitivity, largely by enhancing the detection of chlamydia among women older than 20 who reported only this risk.

The usefulness of clients' contraceptive history may relate in part to the clinical setting; data collected at dedicated family planning clinics may be more reliable than those collected in STD or combined family planning–STD clinic settings. This suggests that information on barrier contraceptive use may be an important adjunct to selective screening decisions, particularly in family planning clinics. Similarly, reports of risk behavior may have more validity in STD clinics, and may have contributed to the performance of the risk-based criteria among the STD clinic clients.

The fact that criteria based on age alone performed better than more extensive criteria among the family planning clients tested most recently deserves comment. A decade of widespread screening for chlamydial infection in family planning and STD clinics in the Pacific Northwest may be having a measurable impact on the epidemiology of this disease. Particularly at family planning clinics, most of this screening has been selective and has targeted women who have clear risk factors (such as young age and behavioral risks). The result may have been to shift the burden of infection to women whose increased risk of infection is not as easily characterized by the standard markers of young age and behavioral risks.

If the prevalence of chlamydial infection is declining due to widespread screening, more inclusive selective screening criteria based on age (e.g., younger than 25) may prove to be a more sensitive means of detecting chlamydial infection. In fact, in an analysis of 148,560 female adolescents seen in the Region X Chlamydia Project, the authors concluded that no additional factors beyond young age could predict chlamydial infection well enough to be routinely included in screening criteria.[16] Among 19,547 women attending family planning or STD clinics in the northeastern United States, young age performed well relative both to risk criteria incorporating behavioral indices and to the CDC screening recommendations.[17]

Figure 2. Relationship between true positive rate of chlamydia screening criteria and false positive rate for screening criteria, by age cutoff for screening, according to year and clinic type



Our study has several limitations. First, the method of detecting *C. trachomatis* differed among the three groups. Since the nonculture tests are only 70–90% as sensitive as culture tests, infections detected by culture may have differed from those detected by the direct fluorescent antibody test—e.g., in organism burden or in inflammatory response. This inconsistency in testing methodology would be of most concern in the comparisons between the family planning clients seen in 1990 and 1994.

However, the decline in chlamydia prevalence from 1990 to 1994 in Region X parallels that seen in similar populations, and there would be little reason to expect that the risk factors of the women whose infection was detected by the direct fluorescent antibody test (especially with the cutoff used in this study—more than two elementary bodies) would differ from those whose infection was detected by culture. Also, the sensitivities of the direct fluorescent antibody test and of enzyme immunoassay are comparable to that of cell culture.[18] Nonetheless, the prevalence of disease in the study groups in which nonculture tests were used was probably underestimated.

Second, the sensitivity of all of the diagnostic tests used in our study is now known to be 10–30% lower than that of amplified DNA probes such as ligase chain reaction and polymerase chain reaction.[19] The performance of selective screening criteria should be assessed in settings in which these newer tests have been employed.

Third, only the STD clinic group included Gram stain of endocervical secretions in the criteria for cervicitis; this could have affected the performance of the CDC criteria, which include cervicitis. The fact that the CDC criteria performed comparably in all three groups makes this unlikely, however. We have also previously shown that the additional sensitivity afforded by cervicitis alone as part of a selective screening approach is minimal (1–4%), and that the majority of women with chlamydia detectable by selective screening criteria can be identified by age and behavioral risk alone.[20]

Finally, data on contraceptive use were not collected in a uniform manner across study groups: Some clinics assessed condom use at last intercourse and others measured condom use as the usual method of contraception. However, the relative contribution of information on barrier contraceptive use to the performance of selective screening criteria was remarkably stable across groups, suggesting its general usefulness in whatever form it is obtained.

While the performance of selective screening criteria in a specific setting is strongly affected by clients' risk profile and disease prevalence, the single most important criterion in selective screening of women in any setting should be age. Many clinicians are inclined to screen for chlamydial infections based primarily on risk history, yet the result of this practice is that the majority of infections remain undetected. For populations with low or

moderate chlamydia prevalence, our findings support the practice of selectively screening all women younger than 25 and all women 25–29 years of age who do not consistently use barrier contraceptives; however, we also find the CDC criteria to be a sensitive means of detecting chlamydial disease in these groups.

In choosing selective screening criteria, factors other than the criteria's sensitivity should be considered, such as characteristics of the client population, the ratio of staff to clients, the costs of the diagnostic tests and the general ease with which criteria can be implemented. Changes in chlamydia prevalence, and prevalence in specific locales, must also be taken into account. Our results confirm previous observations of changes in the performance of selective screening criteria as chlamydia prevalence declines,[21] and we recommend that selective screening criteria be reevaluated periodically.

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