Criterion-based screening for sexually transmitted infection: sensitivity, specificity, and predictive values of commonly used questions.

Précis:

Standard screening questions to identify increased likelihood of sexually transmitted infection are not useful in predicting the presence of infection.

Abstract: Background: Practice protocols that mandate pre-screening for sexually transmitted infection prior to insertion of an intrauterine device for contraception can pose obstacles for women seeking this highly effective method of birth control. Some practices screen for presumed risk factors for sexually transmitted infection in order to identify those who may be infected, or those in whom laboratory testing should be obtained. The value of such criterion-based screening is unclear.

Design: Data from a prospective observational trial of offering the copper intrauterine device for emergency contraception were used to assess the value of several screening questions in predicting the presence of sexually transmitted infection. Criteria evaluated were age under 25, history of a sexually transmitted infection, and having 2 or more sexual partners in the previous 3 months. The sensitivity, specificity, and likelihood ratio of both positive and negative tests, and positive and negative predictive values were calculated for three separate questions, as well as for combinations of these three questions.

Results: There were 197 women who received a copper intrauterine device for emergency contraception at the same time they were tested for sexually transmitted infection. In this sample, there were 8 cases of *Chlamydia trachomatis* identified, and no cases of *Neisseria gonorrhea*. The sensitivity of individual and combined questions in identifying those who were infected ranged from 0 to 88%; specificity ranged from 37-97%. The positive predictive values for single or combined screening questions were in the range of 4-6%. Likelihood ratios for both positive and negative tests did not change post-test likelihood of disease in any appreciable way.

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Conclusion: Standard screening questions used to identify sexually transmitted disease risk could presume infection in large numbers of uninfected women and are of little value in identifying the women who are truly infected.

INTRODUCTION

The most effective contraceptive methods are those that minimize the possibility of user error such as forgetting to take a pill, receive a repeat injection, or replace a patch. Emphasis on long-acting reversible contraception is seen as an important means for reducing unintended pregnancies and abortions. Intrauterine contraceptive devices (IUDs) are long-acting reversible contraceptive methods. The two types of IUDs available in the United States are the copper T 380A (brand name ParaGard) and the levonorgestrel intrauterine system (brand name Mirena). However these IUDs are only used by 5.5% of women using contraception in the United States.[1] Removing barriers to IUD use is an important step toward more widespread use of these methods. Indeed, a recent large cohort study of 10,000 women of reproductive age demonstrated that once appropriate information is given and financial and other barriers are removed, 56% of women will choose intrauterine contraception as a family planning method.[2]

The United States Medical Eligibility Criteria for Contraceptive Use[3] state that current purulent cervicitis or infection with *Chlamydia trachomatis* or *Neisseria gonorrhea* are contraindications to initiation of any intrauterine device. However these guidelines also point out that there is no evidence to support an increased risk of upper genital tract infection among women undergoing IUD insertion in the presence of a sexually transmitted infection (STI). A systematic review of observational studies demonstrated that women with asymptomatic infection with *N. gonorrhoea* or *C. trachomatis* who have an IUD inserted have a higher risk of salpingitis than do uninfected women having an IUD inserted, but the absolute risk of infection was low for both groups (0–5% for those with STIs and 0–2% for those without). [4] In another review, Grimes suggested that the risk was similar to that of infected women not having an IUD inserted, that development of salpingitis appears to be due to the presence of infection, not to the insertion of the IUD, and choice of inappropriate comparison groups has exaggerated the appearance of risk. [5]

Unfortunately it is unlikely that the clinical question of actual (as opposed to presumed) risk can ever be addressed in randomized trials, and surveys have shown that common prescribing practices continue to reflect the erroneous belief that intrauterine contraceptives are

appropriate only in a restricted set of circumstances. [6,7] For example, many local practice patterns continue to mandate pre-testing for current sexually transmitted infection before an IUD can be inserted. Such policies generally require two visits to obtain an intrauterine contraceptive method: one visit for assessment and screening, and a second visit for IUD insertion once a negative screening test has been returned. This two visit requirement creates barriers related to time, cost, and access for women who wish to obtain an effective contraceptive method. In addition, such protocols reduce opportunities to provide an excellent emergency contraceptive method, the copper intrauterine device.

Some authoritative clinical practice guidelines point to a paucity of data about the need for routine screening in women at low risk of STIs, and advise that, for women at higher risk, it is reasonable to screen at the time of insertion and treat if results are positive. [8] Categorization as to whether a woman is at low or higher risk of STI by predicting the likelihood of an infection from her history could eliminate the need for screening for some women and could increase opportunities for same day insertion.

Commonly cited criteria for STI risk include: less than 25 years of age, history of a sexually transmitted infection, and a history of more than one sexual partner in the prior 3 months. [8 9,10] The purpose of this study was to evaluate how well these characteristics could be used to predict sexually transmitted infection in sexually active women who chose the copper IUD as an emergency contraceptive method and planned to continue its use.

METHODS

This study was a secondary data analysis. Data were obtained from a previously reported prospective observational trial of women choosing the copper IUD for emergency contraception and the pilot study that preceded it.[11,12] The studies were approved by the University of Utah Institutional review board. In brief, study enrollment occurred at two family planning clinics in Utah during two distinct periods: from April 2008, to July 2008 and from November 2009 to July 2010. Women aged 18-30 years seeking emergency contraception were offered participation in a study comparing oral levonorgestrel pills to the copper IUD. Potential participants received scripted counseling on both methods that compared their efficacy rates as emergency contraceptives and the benefit of continuing highly effective contraception with the copper IUD for up to 10 years. Either method was provided to the woman without charge.

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The following exclusion criteria were employed in the original study: current pregnancy, pelvic inflammatory disease or a septic abortion within the past 3 months, infection with *C. trachomatis* or *N. gonorrhea* in the last 60 days, current sexual behavior suggesting a high risk for pelvic inflammatory disease (multiple sexual partners without the use of a barrier method for STI prevention), allergy to copper or Wilson's disease (for participants selecting copper IUD), allergy to levonorgestrel (for participants selecting the oral form of emergency contraception), and abnormalities of the uterus that distort the uterine cavity including leiomyomas, mucopurulent cervicitis, an IUD already in place, genital bleeding of unknown etiology, ovarian, cervical or endometrial cancer, or a small uterine cavity (<6 cm).

The women who chose the copper device had the device inserted at the time of their visit by a qualified provider. Testing for *C. trachomatis* and *N. gonorrhea* was done at the time of the insertion; specimens were sent to the laboratory as per clinic protocols. Those women whose tests were positive were recalled for treatment.

Data on common criterion-based screening for sexually transmitted infection risk were collected on all or most participants including history of prior STI, age < 25 years, and 2 or more sexual partners in the prior 3 months. Laboratory results for all women who requested immediate IUD insertion for emergency contraception were then compared to these data to determine the sensitivity, specificity and likelihood ratios of the screening questions, and the predictive values of the questions in identifying sexually transmitted infection. The three criteria were evaluated separately, and composite screening criteria, based on having two or more of the criteria, were also evaluated.

Screening test parameters evaluated were sensitivity, specificity, and positive and negative predictive values. These were calculated according to standard definitions (Table 1). Likelihood ratios are most commonly used in the setting of evaluating a diagnostic test, rather than a screening test. Nonetheless these were also calculated in the interest of providing a full picture of test performance.

INSERT TABLE 1 ABOUT HERE

RESULTS

A total of 605 women presented for emergency contraception during the original study, 57 for the pilot study and 548 for the prospective trial. Of these, 23 women from the pilot study and 176 women from the prospective trial requested and received the copper IUD at the time of

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the visit (n = 199). All women had STI testing at the time of insertion; there were 8 positive laboratory tests for *C. trachomatis* and none for *N. gonorrheae*. Two women had indeterminate or equivocal tests and did not return for re-test and follow-up; diagnosis was thus not available. The overall prevalence of STI in the evaluable sample was 4.1% (8/197). All women with positive tests were recalled for treatment. They were treated without removing the IUD; there were no cases of upper genital tract infection in this group. Demographic characteristics of the study sample are presented in Table 2.

INSERT TABLE 2 ABOUT HERE

Table 3 provides the results of the various screening questions according to whether or not the woman had a positive laboratory test for a STI. Table 4 presents the sensitivity, specificity, predictive values, and likelihood ratios for each question. Results were recalculated assuming that the two women with equivocal tests had positive tests and did not change these test parameters in any appreciable way.

INSERT TABLES 3 and 4 ABOUT HERE

DISCUSSION

This study attempted to quantify the usefulness of criterion-based screening, based on age, STI history, and number of sexual partners, in predicting which women presenting for an IUD will actually have a sexually transmitted infection. Criterion-based screening, if it proved to have good sensitivity, specificity, and predictive values, could facilitate on-demand IUD insertion and reduce costs of making multiple visits. Unfortunately these commonly used criteria had minimal usefulness in this regard.

Of the screening questions, only one (age <25) had a sensitivity of greater than 80% in correctly identifying women with *C. trachomatis*. As is often true however, this came at the expense of poor specificity (37%) and the false positive attribution of a likely STI to a large number of women who were in fact free of infection. Most of the single and combined questions had sensitivities below 50% (less than a 1 in 2 chance of being correct).

Specificity, or correct attribution of disease-free status to uninfected women, was in the 70% range or lower for single questions and in some cases lower even than 50%. Combining the questions provided specificities upward of 80-90%, but this came at the expense of sensitivity, which was reduced to 0 for some questions. Thus these combined questions

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indicated that all women with infection were falsely presumed to be negative for STI even though the risk of falsely labeling uninfected women as positive was low.

Positive predictive values in the range of 4-6% mean that the probability someone who answered positively to any of these screening questions had a minimal risk of actually being infected; indeed the prediction value was hardly different from the overall prevalence of STI in the women seeking IUDs in this sample (4%). Positive responses to the screening questions were of little value in actually predicting the presence of cervical infection, and had they been used as screening questions would have denied same day IUD insertion to anywhere from 25% to 65% of women requesting it. Negative predictive values were all above 95%, suggesting that negative response can provide some confidence that women are at low risk for STI and can have an IUD inserted without much concern about infection. Whether any of these predictive values are at a level deemed important to provide or deny IUD insertion on the day of the visit is likely a matter for provider or program preference or philosophy.

The positive predictive value of a screening test depends in large measure on the background prevalence or the a priori probability that a person actually has the condition of interest. Assuming that a 4% background prevalence of STIs seen here might be lower than in some other service programs in the United States, we used the sensitivity and specificity of these screening questions in a scenario of higher STI prevalence. In an artificially created sample of 200 women in which the prevalence of STI was set at 10%, the positive predictive value of the criterion related to a history of STI was between 9 and 10%; the positive predictive value of the criterion related to age was 13-14%, and the positive predictive value of the criterion related to number of sexual partners was 14-15%. Even in this scenario, the likelihood that someone with a positive test actually had an STI was only 1-2 out of every 10 women.

Likelihood ratios were similarly not useful. In general, likelihood ratios are applied to the pre-test probability of a condition (in this scenario, essentially the background prevalence of the condition in the community or sample in the setting of screening). Depending on whether the test is positive or negative, the likelihood ratio increases or decreases the post-test probability that a disease is actually present. A likelihood ratio for a positive test that is greater than 1 produces a post-test likelihood of having the condition that is higher than the pre-test likelihood (ie, a positive test is more likely to be seen in an infected person than in one who is uninfected). However, in the range of 1-2, which was the case for all of these questions and question combinations, likelihood ratios for positive tests have negligible effects in changing the post-test probability; even likelihood ratios between 2 and 5 will generate only small changes in the post-test likelihood that the disease is present. In order to moderately change the probability of the

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diagnosis given a positive test, a likelihood ratio should be between 5 and 10, and a ratio of 10 or more is needed to change the post-test probability in a large and conclusive way. None of these LRs for positive screening questions tests were high enough to change the post test probability in more than a small or negligible way.

Likelihood ratios for negative tests operate in a similar fashion. In the range of 1-0.5, likelihood ratios for a negative test result will have negligible effects in changing the post-test probability of the condition and between 0.5 and 0.2 they generate only small changes in the post-test probability. In order to be useful the likelihood ratio for a negative test should be between 0.2 and 0.1 to moderately change the probability of disease (given a negative test result), and less than 0.1 to change this probability in a large and conclusive way. Again, none of the likelihood ratios for negative responses to the single screening questions changed the post test probability in more than a small or negligible way. All of these changes in likelihood ratios can be visualized rather than calculated using an online nomogram from the Centre for Evidence Based Medicine: http://www.cebm.net/index.aspx?o=1161.

Morrison et al[13] evaluated several algorithms for their usefulness in predicting STI in women. The algorithms, based on criterion-based screening questions similar to ours, were developed from data collected from women in Kenya, and then tested in family planning clinic databases from Kenya, Jamaica and the United States. An unweighted algorithm that asked age, living with partner, education, bleeding between periods, number of sex partners, and condom use proved the most predictive. In the United States sample, the overall prevalence of STI was 5.7%; a score of 3 or more on the algorithm produced a post-test probability of 10-11% and had a LR of 2. The prevalence of STI in this sample was 1-2% higher than in our sample, but the performance of their algorithm was similar to the hypothetical scenario we created which postulated a background STI prevalence if 10%. It may be that adding more questions could improve the predictive value of criterion-based screening questions, but the questions asked in our study were the most likely to be routinely collected in our clinics. In the final analysis however, the post-test probabilities using Morrison's expanded criteria in a US based sample still did not exceed 11%, or about a 1 in 10 probability that a woman who tests positive on the criterion-based screen would actually have an STI. If IUD insertion is delayed for STI test results, potentially 9 of 10 women interested in an IUD would be denied their contraceptive method of choice unless they returned for another visit. Family planning programs and providers need to decide what level of probability of STI would be used to deny same day IUD insertion, before the practical usefulness of any of these algorithms can be determined.[13]

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The present study is limited by its location and convenience sample nature; all women were requesting emergency contraception and represent those willing to consider an IUD. This was a secondary analysis and eligibility criteria were established for the parent study, not specifically for this one. Thus those with current behavior suggesting a high risk for pelvic inflammatory disease (multiple sexual partners without the use of a barrier method for STI prevention) were excluded. The screening questions assessed were the ones that had been collected in the parent study, but also represent commonly cited screening criteria for STI risk. [3,4,5] While this sample is clearly self-selected on a number of parameters, and might be considered relatively low risk, it does represent a population of women interested in and potentially eligible for same day IUD insertion.

Removing barriers to IUD insertion will improve uptake of this long acting reversible contraceptive method, but providers need to be cautious about safety. If the same day IUD insertion is offered, the woman should be medically eligible according to practice standards set by the US Medical Eligibility Criteria for Contraceptive Use. [3] These standards state that initiation of the IUD is contraindicated in the presence of current infection with *C. Trachomatis* or *N. Gonorrhea*. However, these guidelines also acknowledge that there is no solid evidence that IUD insertion in women with these STIs increases their risk for pelvic inflammatory disease (PID) over the risk of PID in women with STIs who do not have an IUD inserted. Recognizing the small sample size in the current study, it is noted that those with positive tests were recalled for treatment without removing the IUD and there were no cases of upper genital tract infection in the group with positive tests. To reduce barriers to IUD insertion, authoritative guidelines state that STI testing can be done at the time of IUD insertion, and those women who test positive recalled for prompt treatment. [8] Should an infection be diagnosed, most authorities suggest there is no need to remove the IUD unless symptoms fail to improve or worsen on appropriate therapy. [14] Nelson[15] has criticized many of the published contraindications to IUD use found in product labeling and guidelines of specialty groups as being overly restrictive, and asserts that a condition should be listed as a contraindication only if the associated risk exceeds that of pregnancy. She further suggests that practices review their lists of contraindications to ensure they are evidence-based.

CONCLUSION

Requiring STI testing before scheduling an IUD insertion is an obstacle to delivering on-demand care. Attempting to triage testing based on categorizing women as being at low or high risk of STI according to commonly used screening questions is unlikely to be helpful. Negative

responses to screening questions such as those evaluated in this study may provide the clinician with some confidence that cervical infection is unlikely, but positive responses are not useful in identifying the presence of infection. In fact the use of such criterion-based screening may deny many healthy women on-demand access to an IUD. A rapid point of care STI test would better facilitate the STI screening process prior to IUD insertion. Data from a large group of women undergoing simultaneous STI screening and IUD insertion may provide additional information on infection risk in this setting.[16] Until we have such tests and information, however, screening and insertion can be done simultaneously, and is recommended by authoritative clinical guidelines.

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TABLE 1: Definitions of test parameters used in this study.

Sensitivity	The probability that a person with the target condition will have a positive test. This is calculated as the proportion of those with a sexually transmitted infection (as determined by laboratory testing) who had a positive criterion-based screening test. This is represented as all true positive tests (in the numerator) divided by all infected women (in the denominator).
Specificity	The probability that a person free of the target condition will have a negative test. This is calculated as the proportion of women without a sexually transmitted infection who had a negative criterion-based screening test. This is represented as all true negative tests (in the numerator) divided by all uninfected women (in the denominator).
Positive predictive value	The probability that someone with a positive criterion-based test actually has the target condition. This is calculated as the proportion of those with a positive criterion-based screening test who actually had a sexually transmitted infection (as determined by laboratory testing). This is represented as all true positive tests (in the numerator) divided by all positive tests (in the denominator). *Note that both sensitivity and positive predictive value have "true positive tests" in the numerators; the difference is the denominator on which the percent is calculated.*
Negative predictive value	The probability that someone with a negative criterion-based test result is actually free of the target condition. This is calculated as the proportion of women with a negative criterion-based screening test who did not have a sexually transmitted infection. This is represented as all true negative tests (in the numerator) divided by all negative tests (in the denominator). *Note that both specificity and negative predictive value have "true negative tests" in the numerators; the difference is the denominator on which the percent is calculated.*
Likelihood ratio for a positive test (LR+)	The likelihood that a positive test result would be seen in a person with the condition compared to the likelihood that the same result would be seen in a person without the condition. This is the ratio of true positives to false positives [sensitivity/(1-specificity)].
Likelihood ratio for a negative test (LR-)	The likelihood that a negative test result would be seen in a person with the condition compared to the likelihood that that same result would be seen in a person without the condition. This is the ratio of false negatives to true negatives [(1-sensitivity)/specificity].

Table 2: Demographic profile of 197 women requesting same day insertion of IUD for Emergency Contraception

Variable[a]	N (%)
Age<25 yrs	127 (65)
History of a previous STI	51 (26)
Reports 2 or more sexual partners in previous 3 months (n=175)	52 (30)
Race/Ethnicity (n = 162)	
White	135 (83)
Asian American	5 (3)
Native Alaskan/Pacific Islander	5 (3)
Native American	6 (4)
Black	2 (1)
Other	9 (6)
Hispanic Ethnicity	43 (27)
Annual Income (n = 194)	
< $20,000	127 (65)
$20,001 to $40,000	52 (27)
$40,001 to $60,000	10 (5)
$60,001 to $80,000	4 (2)
> $80,001	1 (1)
Insurance (n = 193)	
Private	71 (37)
Medicaid	13 (7)
None	109 (56)
Nulligravid (n = 190)	
Yes	86 (45)
No	104 (55)
Marital Status (n = 177)	
Single, never married	115 (65)
Married	17 (10)
Divorced	7 (4)
Separated	5 (3)

Widowed	0 (0)
Single, living with partner	33 (19)
Employment Status (n = 182)	
Full-time	70 (38)
Student	38 (21)
Unemployed	29 (16)
Homemaker	9 (5)
Part-time	36 (20)

[a]Numbers reflect missing data in some categories.

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TABLE 3: Results of screening question responses in relation to presence of confirmed current sexually transmitted infection

Screening Question	+ STI n	-STI n	Total n	% with Positive Screen who had STI
Positive History of STI	2	49	51	3.9%
Age under 25	7	120	127	5.5%
2 or more partners	3	49	52	5.8%
Age <25 AND history of STI	2	25	27	7.4%
Age <25 AND 2 or more partners	2	29	31	6.5%
History of STI AND 2 or more partners	0	13	13	0
Age <25 AND History of STI AND 2 or more partners	0	5	5	0

STI: Sexually Transmitted Infection

**missing data for some variables*

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Table 4: Sensitivity, specificity, predictive values, and likelihood ratios of screening questions in predicting current sexually transmitted infection

Screening question	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive value	LR of a positive test	LR of a negative test
History of STI	25%	74%	4%	96%	0.96	1.01
Age < 25	88%	37%	6%	99%	1.4	0.32
2 or more partners	43%	71%	6%	97%	1.5	0.8
Age <25 AND hx STI	25%	87%	7%	96%	1.9	0.86
Age <25 AND 2 or more partners	29%	83%	6%	96%	1.7	0.86
Hx STI AND 2 or more partners	0	93%	0	96%	-	1.08
Age <25 AND Hx STI AND 2 or more partners	0	97%	0	96%	-	1.03