

# Screening and Syndromic Approaches to Identify Gonorrhea and Chlamydial Infection among Women

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*The standard diagnostic tools to identify sexually transmitted infections are often expensive and have laboratory and infrastructure requirements that make them unavailable to family planning and primary health-care clinics in developing countries. Therefore, inexpensive, accessible tools that rely on symptoms, signs, and/or risk factors have been developed to identify and treat reproductive tract infections without the need for laboratory diagnostics. Studies were reviewed that used standard diagnostic tests to identify gonorrhea and cervical chlamydial infection among women and that provided adequate information about the usefulness of the tools for screening. Aggregation of the studies' results suggest that risk factors, algorithms, and risk scoring for syndromic management are poor indicators of gonorrhea and chlamydial infection in samples of both low and high prevalence and, consequently, are not effective mechanisms with which to identify or manage these conditions. The development and evaluation of other approaches to identify gonorrhea and chlamydial infections, including inexpensive and simple laboratory screening tools, periodic universal treatment, and other alternatives must be given priority. (STUDIES IN FAMILY PLANNING 2000; 31[1]: 55-68)*

Evidence that some reproductive tract infections (RTIs) enhance human immunodeficiency virus (HIV) transmission (Laga 1992) has concentrated public health efforts on the prevention and treatment of these conditions. Among the most serious RTIs are two sexually transmitted infections (STIs), gonorrhea and chlamydial infection. In pregnancy, these are associated with prematurity, intrauterine growth retardation (Barnes 1979; Hauth et al. 1995; Hillier et al. 1995), ophthalmia neonatorum (causing blindness), and stillbirth (chlamydial infection only) (Martin et al. 1982; Brunham et al. 1984). Risk of pelvic inflammatory disease (PID) increases significantly in the presence of chlamydial or gonococcal (CT/GC) infection (Westrom 1980; Westrom and Mardh 1984 and 1990; Faúndes et al. 1998), particularly with transcervical events

such as abortion, IUD insertion, and giving birth (Ory 1978; Plummer et al. 1987; Westrom and Mardh 1984). Without treatment, PID can lead to infertility, ectopic pregnancy, chronic pelvic pain, recurrent infection, and death.

The World Health Organization (WHO) estimates that, globally, 333 million new cases of curable sexually transmitted infections occur annually (WHO et al. 1996). With an annual incidence of 62 million and 89 million new cases, respectively, gonorrhea and chlamydial infections constitute 45 percent of this burden (Gerbase et al. 1998). Sub-Saharan Africa is estimated to have the highest prevalence of gonorrhea and chlamydial infection, followed by South and South East Asia and Latin America and the Caribbean. Rates are substantially lower in North America and Western Europe (Gerbase et al. 1998). The prevalence of these conditions is 50 percent to 300 percent higher among women than among men. In Africa, Asia, and Latin America, the prevalence of chlamydial infection ranges from 4 percent to 7 percent, and gonorrhea ranges from 1 percent to 3 percent among women, compared with 3 percent to 5 percent and less than 1 percent to 2 percent, respectively, among men (Gerbase et al. 1998). Women

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are more likely than men to contract gonorrhea or chlamydial infection during sexual intercourse with an infected partner (Donovan 1993); this likelihood is particularly true of adolescent girls (Shafer and Sweet 1990; Brookman 1990). This finding may account for the gender differences in prevalence, although these differences may also be attributable partially to differences in treatment and duration of infection.

In response to the call for comprehensive approaches to reproductive health services emanating from the International Conference on Population and Development held in Cairo in 1994, family planning services have paid particular attention to the identification and management of sexually transmitted infections. Clinicians, program managers, and policymakers recognized that integration of these services could be problematic because standard laboratory diagnosis of gonorrhea and chlamydial infection is usually beyond the financial and technical capacity of resource-constrained health systems in developing countries, particularly at the primary-care and dispensary level.

Simple diagnostic tests work well for some STIs, including bacterial vaginosis, trichomoniasis, and candidiasis, although even these are still unavailable at most peripheral sites (Celum et al. 1994). More sophisticated tests requiring laboratory facilities, culture media, an incubator, an enriched carbon dioxide environment, careful and temperature-controlled handling in transport to a laboratory in situations where incubators are not locally available, and a trained technician are needed to diagnose cervical infections caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.<sup>1</sup> Even the validity of standard tests declines under less than optimal conditions (Wentworth et al. 1991; Alary et al. 1998).

The high prevalence and consequences of RTIs stimulated service providers, policymakers, and researchers to develop simpler tools that could be feasibly implemented to address immediately the identification and treatment of gonorrhea and chlamydial infections without diagnostic tests. Traditionally, screening tools are used to minimize the number of (more expensive) standard diagnostic tests performed while maximizing the identification of infections by identifying a group of people with a higher-than-average prevalence of infection than the total population. Individuals with a positive screening test are routinely referred for standard diagnosis and given treatment as appropriate. Simple screening tools for STIs have been developed by researchers and clinicians as substitutes for diagnosis, to provide clinicians with a system whereby they can assume cervical infection exists and to provide immediate treatment for the presumed infection. Eliminating

subsequent referral for standard diagnosis and treatment has been argued to reduce costs, potential loss to follow-up, and complications of further transmission during the interim between initial presentation and definitive diagnosis. Screening tests should not be used as substitutes for standard diagnosis, however, when the ability of the tool to identify individuals correctly as infected or uninfected is poor. Screening is not cost-beneficial if it identifies most individuals as infected and results in almost universal treatment.

Screening tools to identify gonorrhea and chlamydial infection in women were developed by the World Health Organization (WHO) and implemented in their original or, as recommended by WHO, locally modified versions by governmental and nongovernmental family planning and primary health-care clinics around the world before receiving adequate evaluation. Subsequent research indicates that clinical flowcharts for genital ulcers in men and women perform adequately as tools to manage cases of early syphilis and chancroid infection (Vuylsteke and Meheus 1996; Ryan and Holmes 1995; Adler 1996; van Dam et al. 1998). Researchers have questioned the ability of inexpensive simple screening tools to identify and manage gonorrhea and chlamydial infections among women, however (Dallabetta et al. 1998). A substantial body of literature now exists on the usefulness of screening tools for identifying cervical infections.

## Methods

This review assesses the ability of tools using sociodemographic and behavioral risk factors, algorithms, clinical flow charts, risk scoring, and simple laboratory screening tests to identify gonorrhea and chlamydial infection in women in developing countries. The screening tools that have been evaluated for diagnosis of women's conditions and presented in this paper were tested for their usefulness as substitutes for diagnosis using standard epidemiologic criteria for evaluating the validity of screening tools (Mausner and Kramer 1985). The most important criteria for evaluating the usefulness of screening tools are sensitivity (the proportion of women correctly identified as having the condition) to ensure that most women requiring treatment will get it; specificity (the proportion of women correctly identified as not being infected); and their associated false-positive rate (the proportion of women identified as having the condition when they do not) to minimize the number of women receiving inappropriate treatment (Copeland et al. 1977; Cochrane and Holland 1969). The false-positive rate is directly associated with the prevalence of the condition

(Galen 1979; Vecchio 1966), because misclassification is common when the prevalence of a condition is lower than 20 percent (Mausner and Kramer 1985). The formulas for these indices are provided in the footnotes of all tables presenting these estimates.

The odds ratio (OR) is frequently calculated for test efficiency—the proportion of infected and noninfected people correctly identified (as demonstrated by Bayes’ theorem, Fleiss 1981)—but is inadequate to demonstrate the usefulness of screening tests. Galen (1979) has demonstrated that the sum of sensitivity and specificity must be greater than 100 percent if the ability of the test to identify infected and uninfected people is better than chance. Comparing the screening test to chance, however, is perhaps most useful to determine if the test is ineffective. A poor test will have a high efficiency if the prevalence of the condition is low as long as it classifies the majority of people as uninfected. Screening is not justified where the prevalence of infection and false-positive rates are high, because this situation will result in identifying and treating the majority of people screened as infected. Clearly, if the screening tool identifies few or no infected women, or if it identifies many infected individuals at the cost of incorrectly identifying many more uninfected women as infected, its usefulness as a basis for treatment to reduce the prevalence of the condition is limited.

One of the papers reviewed illustrates this point (see Table 1). Vuylsteke et al. (1993) conducted a study in an antenatal clinic in Zaire where the prevalence of gonorrhea and chlamydial infection was moderate (7 percent). Using multiple indices in a scoring system, the odds ratio of women’s being correctly classified as having gonorrhea or chlamydial infection (test efficiency) was highly statistically significant ( $p < 0.001$ ), because most women (94 percent) did not have gonorrhea or chlamydial infection, and most women without infection were correctly identified (specificity = 74 percent). Seventy-two percent of

those with gonorrhea or chlamydial infection were correctly identified (sensitivity). The sum of sensitivity and specificity was greater than 100 percent. This scoring system missed identifying 28 percent of women requiring treatment and incorrectly identified more than five times as many uninfected as infected women as requiring treatment, however. The researchers’ conclusion that this risk score was not sensitive and specific enough to use as a proxy for diagnosis of infection is clearly accurate.

Peer-reviewed published validation studies of screening tools for chlamydial infection and gonorrhea among women were identified through computer searches of PopLine and MedLine from 1985 through 1998. Articles were identified using the following key words: chlamydia, gonorrhea, sexually transmitted infections, reproductive tract infections *or* cervicitis; *and* screening, diagnosis, case finding, case management, prevalence, risk, algorithm, syndromic *or* flowcharts. The computer search was limited to studies published in English, Spanish, or French. No published studies were found between 1985 and 1989. Unpublished literature and presentations at selected conferences during those years were also compiled. Studies were included based on their methodological soundness, availability of adequate data in the report to calculate sensitivity and false-positive rates,<sup>2</sup> and the use of standard diagnostic tests to confirm cervical infection.<sup>3</sup>

Thirty-two studies presented in 29 articles met these criteria (see Appendix Table 1). The studies were conducted in different environments, including antenatal, family planning, and maternal–child health clinics (generally with samples of moderate prevalence, <20 percent combined gonorrhea and chlamydial infection). Some studies were conducted with samples of higher prevalence (≥20 percent combined gonorrhea and chlamydial infection), generally in STD clinics or with groups of female sex workers. Two studies were conducted in samples of the general population with moderate prevalence. Most were conducted in urban areas, but some used rural samples. Some of these studies tested tools that were recommended by WHO or in national guidelines, whereas others constructed their own algorithms or risk scores using variables found to be associated with infection in their sample. Some studies actually implemented screening tools, whereas others simulated their application. Symptomatic and asymptomatic women were included in most studies, although some analyses were limited to women with specific symptoms.

Most of the reviewed studies included women with gonorrhea or chlamydial infection, whereas others included women with only one of these conditions. Some

**Table 1** Usefulness of a multivariate scoring system for a population with moderate prevalence of chlamydial infection or gonorrhea

Scoring system results	Has chlamydial infection or gonorrhea	Does not have chlamydial infection or gonorrhea	Total
Positive	True positives (TP): 54	False positives (FP): 288	TP+FP = 342
Negative	False negatives (FN): 21	True negatives (TN): 797	TN+FN = 828
Total	TP+FN = 75	FP+TN = 1,085	1,160

**Notes:** Prevalence of chlamydial infection or gonorrhea = (75) / 1,160 = 6.5 percent. Sensitivity = 54 / (75) = 72.0 percent. Specificity = 797 / (1,085) = 73.5 percent. False-positive rate = 288 / 342 = 84.2 percent. Positive predictive value = 54 / (342) = 15.8 percent. Negative predictive value = 797 / (828) = 96.3 percent. Test efficiency = (54 + 797) / 1,160 = 73.4 percent. Log odds ratio and 95 percent confidence intervals for test efficiency = 8.89 (5.32, 14.84),  $p < 0.001$ .

**Source:** Vuylsteke et al. (1993).

analyzed their data stratified by these conditions, and combining these data was not possible, generally, because the characteristics of women with both conditions were not adequately specified. The analyses presented are based on bivariate associations, because multivariate analyses, which are important in identifying causal relationships, do not define how, pragmatically, clinicians can take into account multiple variables to identify infection unless algorithmic flow charts or risk scores are created. Such algorithms and risk scores have been analyzed here for their bivariate associations with infection.

Estimates of the sensitivity, specificity, false-positive rate, positive predictive value (100 percent–FPR) and test efficiency (where not reported) were computed for each variable. To facilitate interpretation and use of the data, meta-analyses were conducted by a simple unweighted (that is, weighted by proportion of subjects studied) pooling of samples from all studies within each specified risk factor or type of tool. (Results of pooled data where each study was given an equal weight were similar to the analyses weighted by proportion of total subjects studied.) Linear regression analyses of the effects of prevalence and sample size on sensitivity, false-positive rate, and test efficiency showed virtually no effect of sample size, but demonstrated variation by prevalence of gonorrhea or chlamydial infection. To reduce the dissimilarity of the samples that might affect the results differentially, these analyses were stratified by the prevalence of gonorrhea and chlamydial infection (moderate <20 percent, high ≥20 percent).<sup>4</sup> If a study tested more than one algorithm or risk-scoring tool or presented separate results for gonorrhea and chlamydial infection, only the one with the best test efficiency was included to give the greatest chance to the highest screening utility while avoiding over-representation of any single study.

## Results

The meta-analyses of individual risk factors (Table 2) and symptoms and signs (Table 3) thought to be associated with chlamydial and gonorrhea infections show that these criteria, used independently, generally have poor sensitivity and high false-positive rates. In populations with moderate prevalence (an average of between 5 percent and 7 percent), less than half of infected women were identified by symptoms, signs, or risk factors other than lack of condom use, which classified 15 times more women for unnecessary than for necessary treatment. The sensitivity of risk factors, such as being unmarried or having multiple partners in a specified period, is generally higher (45 percent to 90 percent) in

groups with high prevalence than in those with moderate prevalence (12 percent to 69 percent), but sensitivities are similar between groups with high and with moderate prevalence for symptoms and signs. Vaginal discharge, as a symptom or sign, is often a key criterion for symptomatic management approaches, although it generally identified fewer than half of those needing treatment. Based on symptoms and signs, it incorrectly identified 8 to 11 percent and 1.5 percent times as many women as were infected in moderate and high-prevalence samples, respectively. In general, the false-positive rates are lower in groups with higher prevalence than in those with lower prevalence (59 percent to 71 percent versus 77 percent to 92 percent), because more people have the infection and fewer people can be classified incorrectly as not having the infection. The overall test efficiency of individual risk factors, symptoms, or signs, however, is generally <75 percent even in groups with high prevalence and is too poor to be used as a substitute for diagnosis or as a basis for treatment.

The variable with the highest test efficiency, having a symptomatic partner, shows that approximately 12 percent of infected women would be treated and about 3.5 times as many women would receive unnecessary treatment using this strategy in a population with moderate GC/CT prevalence (average 6 percent). False-positive rates for the two studies conducted in a general population (nonclinical setting with an average prevalence of around 5 percent) that measured only chlamydial infection had sensitivities ranging from 3 percent to 6 percent and false-positive rates between 94 percent and 96 percent.<sup>5</sup> If this criterion were to be used in nonclinical settings, only 6 percent of women would receive treatment, but approximately 23 times as many women would be treated incorrectly as correctly. In the four studies conducted in clinical settings, 11 percent of infected women attending these clinics were correctly identified and three times as many women would have been inappropriately treated (94 false positives versus 30 true positives).

### *Simple Lab Screening Tests*

Leukocyte esterase dipstick (LED) and polymorphonuclear leucocytes (PMN) screening tests generally identified a minority of the women requiring treatment (31 percent to 52 percent) and misidentified many women who were not infected as requiring treatment (42 percent to 48 percent false-positive rates in the groups with high prevalence and 89 percent to 90 percent in those with moderate prevalence, respectively, as shown in Table 4).

**Table 2** Meta-analysis of risk factors for chlamydial infection and gonorrhea among women

Index—risk factors	Study prevalence of GC/CT (percent)	Number of GC/CT cases	True positives	False negatives	True negatives	False positives	Total sample	Sensitivity (percent)	Specificity (percent)	Positive predictive value (percent)	False-positive rate (percent)	Test efficiency (percent)	Number of studies in meta-analysis
<b>Moderate prevalence</b>													
Young age	6.81	985	427	558	8,704	4,765	14,454	43.35	64.62	8.22	91.78	63.17	16
Unmarried	6.99	870	293	577	8,734	2,838	12,442	33.68	75.48	9.36	90.64	72.55	14
>One partner in a specified period	7.25	829	190	639	9,780	826	11,438	22.92	92.21	18.70	81.30	87.17	14
Partner symptomatic	6.47	316	38	278	4,441	127	4,884	12.03	97.22	23.03	76.97	91.71	6
No condom use	6.83	696	480	216	2,356	7,131	10,183	68.97	24.83	6.31	93.69	27.85	9
Oral contraceptive use	5.05	410	116	294	6,120	1,593	8,123	28.29	79.35	6.79	93.21	76.77	6
IUD use	5.19	507	86	421	7,512	1,748	9,767	16.96	81.12	4.69	95.31	77.79	7
<b>High prevalence</b>													
Young age	30.06	1,542	693	849	2,578	1,009	5,129	44.94	71.87	40.72	59.28	63.77	8
Unmarried	28.99	619	520	99	347	1,169	2,135	84.01	22.89	30.79	69.21	40.61	2
>One partner in a specified period	28.64	754	638	116	489	1,390	2,633	84.62	26.02	31.46	68.54	42.80	2
No condom use	31.03	879	502	377	784	1,170	2,833	57.11	40.12	30.02	69.98	45.39	5
Oral contraceptive use	35.00	239	214	25	50	394	683	89.54	11.26	35.20	64.80	38.65	1

n = sample size. Moderate prevalence = <20 percent. High prevalence ≥20 percent.

Formulas: Prevalence = (true positive + false negative) / n; sensitivity = true positive / (true positive + false negative); specificity = true negative / (true negative + false positive); false-positive rate = false positive / (true positive + false positive); positive predictive value = true positive / (true positive + false positive) or 100 percent – false-positive rate; test efficiency = (true positive + true negative) / n.

Acronyms: GC = gonorrhea; CT = chlamydial infection.

**Table 3** Meta-analysis of symptoms and signs of chlamydial infection and gonorrhea among women

Index	Study prevalence of GC/CT (percent)	Number of GC/CT cases	True positives	False negatives	True negatives	False positives	Total sample	Sensitivity (percent)	Specificity (percent)	Positive predictive value (percent)	False-positive rate (percent)	Test efficiency (percent)	Number of studies in meta-analysis
<b>Symptoms</b>													
<b>Moderate prevalence</b>													
Vaginal discharge	8.44	689	205	484	5,824	1,654	8,167	29.75	77.88	11.03	88.97	73.82	12
Vaginal itch	6.70	419	165	254	3,863	1,509	5,791	39.38	71.91	9.86	90.14	69.56	7
<b>High prevalence</b>													
Vaginal discharge	33.01	1,056	313	743	1,688	455	3,199	29.64	78.77	40.76	59.24	62.55	6
Vaginal itch	32.44	618	217	401	835	452	1,905	35.11	64.88	32.44	67.56	55.22	2
<b>Signs</b>													
<b>Moderate prevalence</b>													
Vaginal discharge	7.91	645	272	373	4,475	3,033	8,153	42.17	59.60	8.23	91.77	58.22	12
Malodorous discharge	8.17	379	116	263	3,232	1,027	4,638	30.61	75.89	10.15	89.85	72.19	6
Yellow-green vaginal discharge	9.01	410	97	313	3,295	844	4,549	23.66	79.61	10.31	89.69	74.57	7
Clumpy, thick or frothy vaginal discharge	6.30	200	91	109	2,029	948	3,177	45.50	68.16	8.76	91.24	66.73	4
Abdominal/lower abdominal pain	8.30	739	282	457	5,713	2,447	8,899	38.16	70.01	10.33	89.67	67.37	13
Mucopus	8.59	562	161	401	5,443	537	6,542	28.65	91.02	23.07	76.93	85.66	10
Cervical friability	6.29	393	97	296	4,746	1,107	6,246	24.68	81.09	8.06	91.94	77.54	9
Cervical ectopy	7.33	337	49	288	4,018	244	4,599	14.54	94.27	16.72	83.28	88.43	6
<b>High prevalence</b>													
Vaginal discharge	33.57	888	523	365	1,010	747	2,645	58.90	57.48	41.18	58.82	57.96	4
Malodorous discharge	24.90	93	41	52	180	101	374	44.09	64.06	28.87	71.13	59.09	1
Abdominal/lower abdominal pain	31.96	786	301	485	1,090	583	2,459	38.30	65.15	34.05	65.95	56.57	4
Mucopus	31.10	960	271	689	1,736	391	3,087	28.23	81.62	40.94	59.06	65.01	6
Cervical friability	29.55	1,254	297	957	2,472	518	4,244	23.68	82.68	36.44	63.56	65.25	6
Cervical ectopy	31.00	379	44	335	783	60	1,222	11.61	92.88	42.31	57.69	67.68	1

n = sample size. Moderate prevalence = <20 percent. High prevalence ≥20 percent.

Formulas: Prevalence = (true positive + false negative) / n; sensitivity = true positive / (true positive + false negative); specificity = true negative / (true negative + false positive); false-positive rate = false positive / (true positive + false positive); positive predictive value = true positive / (true positive + false positive) or 100 percent – false-positive rate; test efficiency = (true positive + true negative) / n.

Acronyms: GC = gonorrhea; CT = chlamydial infection.

**Table 4** Meta-analysis of simple laboratory tests for chlamydial infection and gonorrhea among women

Index—simple lab	Study prevalence of GC/CT (percent)	Number of GC/CT cases	True positives	False negatives	True negatives	False positives	Total sample	Sensitivity (percent)	Specificity (percent)	Positive predictive value (percent)	False-positive rate (percent)	Test efficiency (percent)	Number of studies in meta-analysis
<b>Moderate prevalence</b>													
Leucocytes	8.57	301	94	207	2,480	730	3,511	31.23	77.26	11.41	88.59	73.31	3
Polymorphonuclear leukocytes (PMNS)	6.18	423	222	201	5,254	1,949	6,841	52.48	72.94	10.23	89.77	80.05	7
<b>High prevalence</b>													
Leucocytes	31.41	332	138	194	625	100	1,057	41.57	86.21	57.98	42.02	72.19	2
Polymorphonuclear leukocytes (PMNS)	37.50	345	123	222	460	115	920	35.65	80.00	51.68	48.32	63.37	3

n = sample size. Moderate prevalence = <20 percent. High prevalence ≥20 percent.

Formulas: Prevalence = (true positive + false negative) / n; sensitivity = true positive / (true positive + false negative); specificity = true negative / (true negative + false positive); false-positive rate = false positive / (true positive + false positive); positive predictive value = true positive / (true positive + false positive) or 100 percent – false-positive rate; test efficiency = (true positive + true negative) / n.

Acronyms: GC = gonorrhea; CT = chlamydial infection.

### Algorithms and Risk Scoring

The studies reviewed included four categories of algorithms or risk scoring: (1) simple tools using signs and symptoms (individually or in combination) without a speculum exam; (2) tools using speculum exams (these tools include variables that require a speculum exam, such as endocervical mucopus or cervical friability individually or in combination with other variables that may or may not require a speculum exam); (3) tools that include combinations of risk factors or individual risk factors in combination with signs, symptoms, and/or simple laboratory tests. This category also includes assessments of the WHO algorithm and syndromic flowcharts; and (4) risk scoring based on risk factors, signs, and symptoms. Risk scores are derived by assigning weights to the presence of particular variables. A score is considered positive if it is equal to or higher than a cutoff point.

Meta-analyses of all these tools show better case identification in groups of high than in those with low prevalence (sensitivity 47 percent to 78 percent versus 28 percent to 54 percent), and lower false-positive rates (54 percent to 67 percent versus 82 percent to 90 percent, respectively), but have poor test efficiency in groups with high prevalence (55 percent to 62 percent, similar to chance, as shown in Table 5). These tools have better test efficiency (69 percent to 84 percent) in groups with lower prevalence, because they correctly identify many women as uninfected; however, they generally identify fewer than half of those infected and requiring treatment. The tools that correctly identify most individuals (algorithms using speculum exams or including risk factors with 82 percent to 84 percent test efficiency) are also the tools that correctly identify the lowest proportion of women requiring treatment. These same algorithms also incorrectly identify seven times as many women for treatment who do not require it as they identify correctly.

### Discussion

The data and the analysis presented here have limitations. Most of the studies that met the criteria for inclusion in the analysis selected all women identified in the data-collection period,<sup>6</sup> whereas criteria for selecting the particular clinic or community in which data were collected varied from study to study. Few clinic-based studies were conducted at more than one clinic. Nor do the data presented reflect a systematic sample of women in developing countries, and this may limit their generalizability. The point estimates of the sensitivity and specificity cannot be construed as generalizable. Results of analyses that include more studies will be more reliable than those based on fewer studies. Furthermore, the unweighted aggregation of data does not attempt to measure effect (the odds ratio) or to minimize the variance of effect by weighted analysis. Results from larger studies could, theoretically, influence the unweighted estimates disproportionately. Stratifying the unweighted pooled estimates of the screening criteria by prevalence alone attained substantially homogenous groups. When sensitivity was poor or false-positive rates high in one study, they were basically poor or high in the vast majority of studies.

The tools' usefulness was generally overestimated because they were often developed and tested in the same sample (and thus took advantage of associations found in the sample) and were used under better-than-normal conditions (where clinicians were likely to be well trained in their use).<sup>7</sup> The meta-analysis maximized the validity of multivariate algorithms, hierarchical flow charts, and individual risk factors by including only tests with the best efficiency for single studies that conducted evaluations of multiple-risk scores or algorithms. Therefore, although the data do not represent a systematic sample of women from developing countries, the find-

**Table 5** Meta-analysis of algorithms and risk scoring for chlamydial infection and gonorrhea among women

Index	Study prevalence of GC/CT (percent)	Number of GC/CT cases	True positives	False negatives	True negatives	False positives	Total sample	Sensitivity (percent)	Specificity (percent)	Positive predictive value (percent)	False-positive rate (percent)	Test efficiency (percent)	Number of studies in meta-analysis
<b>Algorithms without speculum exams</b>													
Moderate prevalence	8.08	264	111	153	2,128	876	3,268	42.05	70.84	11.25	88.75	68.51	4
High prevalence	30.80	547	258	289	712	517	1,776	47.17	57.93	33.29	66.71	54.62	3
<b>Algorithms using speculum exams</b>													
Moderate prevalence	5.53	560	154	406	8,179	1,383	10,122	27.50	85.54	10.02	89.98	82.33	8
High prevalence	34.12	633	388	245	765	457	1,855	61.30	62.60	45.92	54.08	62.16	5
<b>Algorithms using risk factors</b>													
Moderate prevalence	6.05	488	151	337	6,661	916	8,065	30.94	87.91	14.15	85.85	84.46	11
High prevalence	30.12	125	98	27	145	145	415	78.40	50.00	40.33	59.67	58.55	2
<b>Algorithms using risk scores</b>													
Moderate prevalence	9.22	657	357	300	4,840	1,628	7,125	54.34	74.83	17.98	82.02	72.94	12
High prevalence	32.74	702	529	173	772	670	2,144	75.36	53.54	44.12	55.88	60.68	3

n = sample size. Moderate prevalence = <20 percent. High prevalence  $\geq$ 20 percent.

Formulas: Prevalence = (true positive + false negative) / n; sensitivity = true positive / (true positive + false negative); specificity = true negative / (true negative + false positive); false-positive rate = false positive / (true positive + false positive); positive predictive value = true positive / (true positive + false positive) or 100 percent - false-positive rate; test efficiency = (true positive + true negative) / n.

Acronyms: GC = gonorrhea; CT = chlamydial infection.

ing that these screening tools have poor sensitivity and high false-positive rates is probably generalizable given that the data were collected and analyses conducted in a manner that would overestimate the tools' validity.

This review found little difference in the usefulness of simple screening criteria and algorithms or risk scores to identify gonorrhea and chlamydial infection among women. Multivariate algorithms or risk scores, signs, symptoms, and risk factors among women generally identify a minority of women with these infections, regardless of their prevalence. These strategies consistently identify many more women incorrectly than correctly as needing treatment. In addition, many have test efficiencies that are roughly equivalent to or worse than chance. In concurrence with many authors of the studies included in the meta-analysis, these approaches are found not to be efficient or cost-effective for identification of women with gonorrhea and chlamydial infection or for treatment of women with symptoms thought to be suggestive of these infections.

Decisions about what constitutes reasonable overtreatment depend on the seriousness of the infection and its sequelae, the cost, frequency, and number of people who would be overtreated, the adverse consequences of the medication, the psychological cost of being falsely labeled positive, and the risk of infecting others in light of the HIV/STI infection patterns and sexual behaviors of the population.

In the meta-analysis, the average sensitivity, specificity, and false-positive rate of all the screening tests analyzed was approximately 35 percent, 75 percent, and 90 percent, respectively, in groups with moderate prevalence (average 7 percent). If a clinic had an annual patient load of 1,000, a 10 percent prevalence of gonorrhea and

chlamydial infection, a sensitivity, specificity, and false-positive rate equivalent to that observed in groups with moderate prevalence in this analysis and saw each patient once per year, presumptive treatment would involve 35 of the 100 infected women and 225 of the 900 uninfected women. Clinics do not see only new patients; some infected women but many more uninfected women would be treated repeatedly over time. The associated costs of presumptive treatment include the costs of screening (clinicians' time, supplies, and simple tests) and the costs of spending time giving relatively ineffective care rather than reallocating that time for effective care.

Decisions regarding the appropriateness and effectiveness of strategies for gonorrhea and chlamydial infection control need to take into account factors beyond those presented in this review of screening tools to identify women with cervical infections. Development of simple, inexpensive, valid field diagnostics is a top priority for identifying and treating women with gonorrhea and chlamydial infection (Wasserheit 1989; Behets et al. 1995; Ryan et al. 1995; Mayaud et al. 1995; Vuylsteke et al. 1993; van Dam et al. 1998). Whether family planning and other health-care services will be able to afford even inexpensive diagnostic tests and appropriate treatment is unknown. No simple recommendation can be made that completely ameliorates the problem of our inability to diagnose and treat women with gonorrhea and chlamydial infection correctly. Clinicians should avoid spending time on ineffective care whenever possible, however, because that time can be better used providing effective care (such as provision of information and condoms), even if this care currently does not include the diagnosis and treatment of gonorrhea and chlamydial infection among women.

# Appendix

**Table 1** Studies included in the meta-analyses, by author and date, according to selected characteristics

Author/ date of publication/ country	Sample	GC and/or CT	Preva- lence of GC/CT <sup>a</sup>	Sample size <sup>a</sup>	Risk	Symptoms	Indices measured		Algorithms <sup>b</sup>
							Signs	Simple lab <sup>b</sup>	
Acosta-Cazares et al. 1996: Mexico (rural)	General clinic	CT	7.3	559	Age, married, >one partner, OC, IUD	—	Mucopus, friability	—	Any four genitourinary signs and symptoms (urinary symptoms, signs of cervical inflammation, cervical friability, mucopurulent cervical discharge)
Alary et al. 1998: Benin	PHC	GC or CT	7.8	192	—	—	—	—	Symptomatic vaginal discharge + lower abdominal pain + any two (< 21 years, single, > one partner in past year or new partner in past three months)
Behets et al. 1995: Jamaica	STD	GC or CT	31.9– 35.1 <sup>a</sup>	239– 724 <sup>a</sup>	Age, married	—	Mucopus	—	Cervical mucopus; cervical mucopus and asymptomatic partner. Score: Partner has urethral discharge (2); <21yrs (1); new or >one partner in last three months (1 each); not living with steady partner (1). If score is >2, treat for GC/CT. If score <2, examine with speculum for mucopus
Bourgeois et al. 1996: Gabon	ANC	GC or CT	13.5	192	Married, >one partner, condoms	Vaginal discharge	Vaginal, foul odor, yellow-green discharge, abdominal pain, friability	PMN	Reported symptom + clinical exam + speculum, age <25, marital status. Score >3: Age <25, vaginal discharge symptom, low back pain, yellow-green discharge, foul-smelling discharge, cervical discharge, cervical ulcer, cervical friability
Bourgeois et al. 1998: Gabon	ANC	GC or CT	11.8	505	—	—	—	—	Midwives' score at least 3: Age <25, single or cohabiting, vaginal discharge symptom, lumbar or pelvic pain, colored vaginal discharge, foul- smelling vaginal discharge
Braddick et al. 1990: Kenya	FP	GC or CT	15.7–16.2 <sup>a</sup>	173– 178 <sup>a</sup>	Married, >one partner	Vaginal discharge	Profuse, yellow-green, frothy discharge; abdominal pain; mucopus; friability	—	Clinical cervicitis and/or >one partner
Chout et al. 1995: Martinique	ANC	CT	26.6	1,411	Age, married, >one partner	—	Friability	—	—
Coetzee and Mathews 1998: South Africa	STD	GC or CT	27.3	161	Age	—	—	—	Women, < 25 years of age, sexually active, not pregnant, and premenopausal, reporting vaginal discharge and/or lower abdominal pain
Costello Daly et al. 1994: Kenya	FP	GC	3.2–3.3 <sup>a</sup>	3,965– 4,033 <sup>a</sup>	Age, married, >one partner, condoms, OC, IUD	—	—	—	Vaginal discharge or cervicitis. Unmarried and >one partner in past year and vaginal discharge/cervicitis
Costello Daly et al. 1998: Malawi	Outpatient clinic at hospital	GC or CT	19.5	550	Age, married, >one partner, partner symptomatic, condoms	Thick mucopus	Vaginal itch, foul odor, yellow-green discharge, mucopus/ cervical discharge/ blood on speculum	†10 WBCs on HPF wet mount	WHO risk score †2: Symptomatic partner, age <21, unmarried, >one partner in past three months.

Continued

**Appendix Table 1** (continued)

Author/ date of publication/ country	Sample	GC and/or CT	Prevalence of GC/CT <sup>a</sup>	Sample size <sup>a</sup>	Risk	Symptoms	Indices measured		Algorithms <sup>b</sup>
							Signs	Simple lab <sup>b</sup>	
Diallo et al. 1998: Côte d'Ivoire	FSW	GC or CT	35.0	683	Age, condoms, OC	Vaginal discharge, itch	Vaginal discharge, abdominal pain, mucopus, friability	±10 (cervical) WBCs on HPF	WHO generated: Speculum exam cervical mucopus or friability, and vaginal or cervical ±10 WBC/HPF. WHO generated: History and computed risk score (±2) two points each: age <20, vaginal discharge; one point each: price for sex £500 FCFA, duration as FSW £2years, number of clients †four/day, dysuria
Germain et al. 1997: Benin	FSW	GC or CT	48.4	366		Vaginal discharge	Vaginal discharge	PMN> 10 HPF (urine)	Algorithm: Speculum exam and vaginal wet mount, mucopus, yellow swab, vaginal leucocytes >10/field
Herrmann et al. 1996: Nicaragua	ANC, FP, general clinic	CT	4.3–5.0 <sup>a</sup>	863– 926 <sup>a</sup>	Age, married, OC IUD	—	Vaginal discharge, mucopus, cervical ectopy	—	—
Kapiga et al. 1998: Tanzania	FP	GC or CT	8.2	897	Age, married, >one partner, condoms, OC, IUD	Vaginal discharge	Vaginal discharge, mucopus, friability, cervical ectopy	PMN ‡25 ml	Vaginal discharge or dysuria Mucopus or friability Tanzanian flowchart Score >1: mucopus or friability
Kaufman et al. 1996: China (rural)	General population	GC, CT separate	5.4–6.1 (CT), 0.4 (GC)	1,572– 1,644	Partner symptomatic	Vaginal discharge, itch	Yellow-green/ bloody, thick vaginal discharge; foul odor, abdominal pain, friability	PMN >30 wet mount	All three signs: yellow, green or bloody discharge, thick discharge, and abnormal cervical exterior
Mayaud et al. 1995: Tanzania (rural)	ANC	GC or CT	8.4	964	Age, married >one partner	Vaginal discharge	Vaginal discharge, abdominal pain	PMN >10 HPF	S1 = reported vaginal discharge and/or genital itching S1 + abnormal vaginal discharge on exam S1+R1: Women with a risk score † a cut-off value, where R1= score based p£0.05 SES factors in logistic regression
Mayaud et al., 1998a: Tanzania (rural)	ANC	GC or CT	7.96–8.08 <sup>a</sup>	619–660 <sup>a</sup>	Age, married	—	—	LED >=3+	WHO: Vaginal discharge symptom + any two (<21 years old, single, new partner in last three months, >one partner in last three months) or partner has urethral discharge and/or dysuria in last month
Mayaud et al. 1998a: Tanzania (rural)	Outpatient clinic at hospital	GC or CT	11.00– 11.39 <sup>a</sup>	391–395 <sup>a</sup>	Age, married	—	—	LED >=3+	WHO: Vaginal discharge symptom + any two (<21 years old, single, new partner in last three months, >one partner in last three months) or partner has urethral discharge and/or dysuria in last month
Mayaud et al. 1998b: Tanzania (rural)	ANC	GC or CT	7.40	660	Age, married, >one partner, partner symptomatic, condoms, OC, IUD	—	Vaginal itch; foul odor; yellow-green/ bloody, frothy discharge; abdominal pain; cervical mucopus	>5–10 PMN/HPF	WHO risk score = one for each with odds ratio > 10: Age<25, polygamous marriage, never used contraceptives, >one partner in past three months, partner's symptom: discharge, yellow-green vaginal discharge, frothy vaginal discharge, PMNs/HPF, trichomonas infection

Continued

**Appendix Table 1** (continued)

Author/ date of publication/ country	Sample	GC and/or CT	Preva- lence of GC/CT <sup>a</sup>	Sample size <sup>a</sup>	Risk	Symptoms	Indices measured		Algorithms <sup>b</sup>
							Signs	Simple lab <sup>b</sup>	
Meda et al. 1997: Burkina Faso	ANC	GC or CT	4.7	645	—	—	—	—	Length of relationship with regular partner <three years and urine leucocyte esterase test (LET) positive
Moherdauí et al. 1998: Brazil	STD	GC or CT	15.0	334	—	—	Vaginal discharge	—	Symptom vaginal discharge + any two: < 20 years old, no steady partner, > one partner in three months + cervical mucopus, friability, erythema or ectopy
Ndoye et al. 1998: Senegal	FSW at STD	GC or CT	24.9	374	Age, condoms	Vaginal discharge	Vaginal discharge, foul odor, cervical mucopus, friability	Leuco- cytes > 10 on gram stain	—
Ronsmans et al. 1996: Turkey	General population	CT	4.9	695	Age, partner symptomatic, condom, OC, IUD	Profuse vaginal discharge, itch	Profuse vaginal discharge; foul odor; yellow- green, clumped discharge; abdominal pain; mucopus; friability; cervical ectopy	PMN >30/HPF	Reported profuse discharge and cervical ectopy. Reported discharge in husband and age <25
Ryan et al. 1998: Morocco	PHC, FP, STD	GC or CT	5.9–8.6 <sup>a</sup>	220– 1,112 <sup>a</sup>	Age, married, >one partner, partner symptomatic, condom, OC, IUD	—	—	—	Algorithm: chief complaint vaginal discharge without lower abdominal pain + risk: (symptomatic partner, age <21, single, >one partner, new partner in past three months) + (cervical mucopus or yellow discharge on speculum or bimanual exam) Algorithm: chief complaint vaginal discharge without lower abdominal pain + risk (symptomatic partner, age <21, single, >one partner, new partner in past three months)
Sánchez et al. 1998: Peru	FP and GYN	GC or CT	12.1– 14.8 <sup>a</sup>	324– 630 <sup>a</sup>	Age, >one partner, condoms	Vaginal discharge	Profuse vaginal discharge, yellow-green; abdominal pain, mucopus, friability, cervical ectopy	PMN squamous cells †1.3 in vaginal fluid	Algorithm: abnormal yellow vaginal discharge, lower abdominal pain + risk (£21 years, age at intercourse £15, never used condom, new partner within three months or partner with STD in last year); signs (ectopy, friability, cervical motion tenderness or moderate-severe adnexal tenderness); PMN†10 x 400 in cervical mucous
Schneider et al. 1998: South Africa	FP	GC or CT	13.8	247	Age, >one partner	Vaginal discharge	Abnormal vaginal discharge, abdominal pain	—	Vaginal discharge symptom, dysuria or abdominal pain, mucopus or friability Score >12: Age <25 (11 points), mucopus or friability (9 points)

Continued

**Appendix Table 1** (continued)

Author/ date of publication/ country	Sample	GC and/or CT	Preva- lence of GC/CT <sup>a</sup>	Sample size <sup>a</sup>	Risk	Symptoms	Indices measured		
							Signs	Simple lab <sup>b</sup>	Algorithms <sup>b</sup>
Thomas et al. 1994: Kenya	ANC	GC or CT	10/8	286– 291	Age, married, >one partner, condoms	Vaginal discharge, itch	Vaginal discharge, abdominal pain, mucopus, friability, cervical ectopy	—	R1+exam (each one point); Women with a risk score $\geq$ a cutoff value + abnormal vaginal discharge on exam, where R1= score based p $\leq$ 0.05 SES factors in logistic regression
Thongkrajai 1996; MCH/FP Thongkrajai and Pongsaa 1997: Thailand		GC	3.3–4.7 <sup>a</sup>	573– 791 <sup>a</sup>	Age, >one partner	Vaginal discharge, itch	Abdominal pain	Leuco- cytes 100 cell/ml	Score>8: Husband's frequency of working away from home; husband and wife living together in last three months; and lower abdominal pain. Scores of 11, 10, and 8 assigned, respectively
Vuylsteke et al. 1993: Zaire	ANC	GC or CT	6.5	1,160	Age, married, >one partner, condoms	Vaginal discharge, itch	Vaginal discharge, abdominal pain, mucopus, friability, cervical ectopy	>75 PMN/ml; >10 PMN HPF (vaginal)	Hierarchical algorithm: vaginal discharge, lower abdominal pain + speculum exam Score>28: single (5); >one partner in last year (10); <25 years old (14); 25–34 years old (11); reported vaginal discharge (1); lower abdominal pain (3); LED (10, 12, 15).
Vuylsteke et al. 1993: Zaire	FSW	GC or CT	31.0	1,222	Age, >one partner, condoms	Vaginal discharge, itch	Vaginal discharge, abdominal pain, mucopus, friability, cervical ectopy	—	Score>28: single (5); >one partner in last year (10); <25 years old (14); 25–34 years old (11); reported vaginal discharge (1); lower abdominal pain (3); LED (10, 12, 15).
Wi et al. 1998: Philippines (Manila)	FSW at STD	GC or CT	23.3	270	Age, condoms	Vaginal discharge	Abdominal pain, mucopus, friability	$\geq$ 20 PMN x 1,000 field on gram stain (cervical)	Any symptom of abnormal vaginal discharge, lower abdominal pain, abnormal vaginal bleeding, dyspareunia. Mucopus or cervical motion, uterine or adnexal tenderness
Wi et al. 1998: Philippines (Cebu)	FSW at STD	GC or CT	37.0	284	Age, condoms	Vaginal discharge	Abdominal pain, mucopus, friability	$\geq$ 20 PMN x 1,000 field on gram stain (cervical)	Any symptom of abnormal vaginal discharge, lower abdominal pain, abnormal vaginal bleeding, dyspareunia. Mucopus or cervical motion, uterine or adnexal tenderness

— = Not applicable. <sup>a</sup>Sample size and prevalence vary according to number of respondents (missing responses) and analyses. <sup>b</sup>Only algorithms included in meta-analyses are specified.

Sample: ANC = antenatal clinic; FP = family planning clinic; FSW = female sex worker; GYN = gynecology clinic/ward; MCH = maternal-child health-care clinic; PHC = primary health-care clinic; STD = sexually transmitted disease clinic. GC and/or CT conditions measured: CT = chlamydial infection; GC = gonorrhea. Separate = GC and CT could not be aggregated. Risk: IUD = Intrauterine device; OC = oral contraceptives. Simple lab: HPF = High-power field; PMN = polymorphonucleotides; WBC = white blood cell count. Algorithms: LET = leucocyte esterase test.

## Notes

- 1 Standard tests are: culture for gonorrhoea and culture with live cells for chlamydia. Because use of live cells makes chlamydia culture complex, other, less complicated tests are more commonly used for chlamydia diagnosis: direct fluorescent antibody (DFA) and enzyme immunoassay (EIA). More recently, polymerase chain reaction (PCR), and ligase chain reaction (LCR) have emerged as highly accurate screening tests that now are often used as alternative diagnostic tests for chlamydia, with better sensitivity than culture (Gray and Wawer 1996; Wawer et al. 1999).
- 2 Screening criteria numerators and denominators estimated from marginal data may reflect small errors that do not affect whole-percentage estimates.
- 3 Cervical chlamydia was diagnosed in these studies with culture, antigen detection enzyme immunoassay and confirmatory blocking antibody assay; enzyme immunoassay confirmed by direct fluorescent; enzyme immunoassay and ligase chain reaction; enzyme immunoassay and various polymerase chain reaction assays; and direct immunofluorescent assay. Gonorrhoea was diagnosed in most of these studies with culture or, rarely, with PCR assays.
- 4 The raw data are similarly presented and are available from the authors upon request.
- 5 Data not shown. The raw data upon which these calculations were based are available upon request from the first-listed author.
- 6 Some included all women with a particular symptom.
- 7 A program in the Philippines found that without ongoing facilitative supervision, service providers generally were unable or unwilling to implement the guidelines they had learned in the training (Costello 1998).

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