NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC™)
GUIDELINE SYNTHESIS

SCREENING FOR AND MANAGEMENT OF CHLAMYDIAL INFECTION

Guidelines

1. American College of Preventive Medicine (ACPM). American College of Preventive Medicine practice policy statement. Screening for Chlamydia trachomatis. Am J Prev Med 2003 Apr;24(3):287-92. [82 references}
2. Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases (AGUM/MSSVD). 2002 national guideline for the management of Chlamydia trachomatis genital tract infection. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [42 references]
3. Centers for Disease Control and Prevention (CDC). Diseases characterized by urethritis and cervicitis. Sexually transmitted diseases treatment guidelines 2002. MMWR Recomm Rep 2002 May 10;51(RR-6):30-42.
4. Finnish Medical Society Duodecim (FMSD). Chlamydial urethritis and cervicitis. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 19. Various p.
5. Scottish Intercollegiate Guidelines Network (SIGN). Management of genital Chlamydia trachomatis infection. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2000 Mar. 26 p. (SIGN publication; no. 42). [176 references]
6. United States Preventive Services Task Force (USPSTF). Screening for chlamydial infection: recommendations and rationale. Am J Prev Med 2001 Apr;20(3S):90-4 [7 references]

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INTRODUCTION:

A direct comparison of APCM, AGUM/MSSVD, CDC, FMSD, SIGN, and USPSTF recommendations for chlamydial infection is provided in the tables, below. The comparison focuses on screening for and management of chlamydial infection in adults. CDC also discusses diagnosis and management of chlamydial infections in infants and children as well as other sexually transmitted diseases characterized by urethritis and cervicitis, such as those caused by Neisseria gonorrhoeae. These latter topics, however, are not addressed in this synthesis. Table 1 compares guideline scope.

Table 2 compares recommendations for screening and management. The evidence supporting the major recommendations is also identified, with the definitions of the rating schemes used by AGUM/MSSVD, FMSD, SIGN, and USPSTF included in the last row of Table 2. Literature references for certain recommendations provided by AGUM/MVSSD and FMSD are also listed in this table.

Table 3 compares the potential benefits and harms of implementing the guidelines recommendations.

Following the content comparison table and discussion, the areas of agreement and differences among the guidelines are identified.

Abbreviations used in the text and tables follow:

- ACPM, American College of Preventive Medicine
- AGUM/MSSVD, Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases
- CDC, Centers for Disease Control and Prevention
- C. trachomatis, Chlamydia trachomatis
- DFA, Direct fluorescent antibody
- EIA , Enzyme immunoassay
- ELISA, Enzyme-linked immunosorbent assay
- FMSD, Finnish Medical Society Duodecim
- GUM, Genitourinary medicine
- HIV, Human immunodeficiency virus
- LCR, Ligase chain reaction
- MPC, Mucopurulent cervicitis
- NAAT, Nucleic acid amplification techniques
- PCR, Polymerase chain reaction
- PHE, Periodic health examination
- SIGN, Scottish Intercollegiate Guidelines Network
- STDs, Sexually transmitted diseases
- USPSTF, U.S. Preventive Services Task Force

TABLE 1: SCOPE	
Objective	
ACPM (2003)	To present a practice policy statement on screening for Chlamydia trachomatis
AGUM/MSSVD (2002)	To present a national guideline for the management of Chlamydia trachomatis genital tract infection
CDC (2002)	• To assist physicians and other health-care providers in preventing and treating sexually transmitted diseases (STDs) • To present updated recommendations for the diagnosis, treatment, and prevention of STDs characterized by urethritis and cervicitis, including nongonococcal urethritis, mucopurulent cervicitis, chlamydial infection, gonorrhea, and gonococcal infections
FMSD (2004)	Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.
SIGN	• To present evidence-based recommendations for the

(2000)	prevention, diagnosis, treatment and management of chlamydial infection
	• To specifically address the following questions:
	  • In which circumstances should potential chlamydial infection be sought routinely in adults?
	  • What is the optimum management of patients identified as Chlamydia trachomatis positive?

USPSTF (2001)	• To make recommendations for screening for chlamydial infection • To update the 1995 recommendations contained in the Guide to Clinical Preventive Services, second edition
Target Population	
ACPM (2003)	• United States • Women and men who are sexually active, particularly females between the ages of 15 and 24 and all pregnant women
AGUM/MSSVD (2002)	• United Kingdom • Men and women with Chlamydia trachomatis genital tract infection
CDC (2002)	• United States • Sexually active women aged 25 years or younger and older women with risk factors for chlamydial infection (screening) • Men with urethritis definitely or possibly related to Chlamydia trachomatis infection • Women with mucopurulent cervicitis definitely or possibly related to Chlamydia trachomatis infection • Adolescents and adults with suspected chlamydial infection • Sex partners of individuals with diagnosed chlamydial infections Note: The guideline also targets individuals with other forms of nongonococcal urethritis and cervicitis; infants and children with chlamydial infection; adolescents and adults with gonococcal infection; individuals with quinolone-resistant Neisseria gonorrhoeae infection; and newborns, infants, and children with gonococcal infection.
FMSD (2004)	• Finland • Men and women with (or symptoms suggestive of) chlamydial urethritis or cervicitis (Diagnosis; Treatment;

	Management; Secondary Prevention) • Family planning clinic customers and, in general, women who see their physician to renew their contraceptive pill prescription (Screening) • Partners of patients diagnosed with chlamydial infections (Screening)

SIGN (2000)	• Scotland
	• Individual patients presenting with signs and symptoms of genital chlamydial infection
	• Asymptomatic patients in the following specific circumstances:
	  • All women undergoing termination of pregnancy
	  • All patients attending genitourinary medicine clinics
	  • All patients with another sexually transmitted infection, including genital warts
	  • Sexual partners of those with chlamydial infection
	  • Mothers of infants with chlamydial conjunctivitis or pneumonitis
	  • Semen and egg donors
	  • Sexual partners of those with suspected chlamydial infection
	  • Women younger than 25 years and sexually active (targeted for opportunistic testing)
	  • Women aged 25 years or older with two or more partners in the last year or a change of sexual partner in the last year (targeted for opportunistic testing)

USPSTF (2001)	• United States • All sexually active women aged 25 years and younger • Asymptomatic pregnant women aged 25 years and younger • Other asymptomatic women at increased risk for infection • Asymptomatic men • High-risk young men
Intended Users	
ACPM (2003)	Advanced Practice Nurses, Allied Health Personnel, Nurses, Physician Assistants, Physicians, Public Health Departments
AGUM/MSSVD (2002)	Physicians
CDC (2002)	Advanced Practice Nurses; Allied Health Personnel; Health Care Providers; Managed Care Organizations; Nurses; Physician

	Assistants; Physicians; Public Health Departments
FMSD (2004)	Health Care Providers; Physicians
SIGN (2000)	Physicians; Nurses; Nurse Practitioners; Physician Assistants; Allied Health Care Practitioners; Students
USPSTF (2001)	Physicians; Nurses; Nurse Practitioners; Physician Assistants; Allied Health Care Practitioners; Health Care Providers
Interventions and Practices Considered	
ACPM (2003)	Screening 1. Annual screening of high-risk women 2. Prenatal screening of all pregnant women 3. Testing of sexual partners of women who test positive for Chlamydia Diagnostic tests for chlamydial infection 1. Culture 2. Immunoassay, such as enzyme immunoassay (EIA) with positive confirmation, rapid office-based immunoassay, or direct immunofluorescent antibody (DFA) 3. Deoxyribonucleic acid (DNA) probe 4. DNA amplification, such as polymerase chain reaction (PCR), ligase chain reaction (LCR), or amplified DNA probe (strand displacement amplification) 5. Ribonucleic acid (RNA) amplification, such as transcription-mediated amplification (TMA) 6. Dipstick, such as leukocyte esterase with "trace cutoff"
AGUM/MSSVD (2002)	Diagnostic tests for chlamydial infection 1. Cell culture 2. DFA 3. EIA 4. Nucleic acid amplification techniques (NAAT) Treatment/Management 1. Antibiotics • Doxycycline • Azithromycin • Erythromycin • Deteclo

	• Ofloxacin • Tetracycline 2. Patient education 3. Partner notification 4. Follow-up and test of cure
CDC (2002)	Screening 1. Screening of sexually active adolescents and young adults during routine annual examinations 2. Annual screening of older women with risk factors 3. Prenatal screening of pregnant women, especially those < 25 years of age and those with multiple sex partners Diagnostic tests for chlamydial infection 1. Tissue culture for C. trachomatis 2. Nonculture tests (e.g., direct fluorescent antibody tests, enzyme immunoassays, and nucleic acid amplification tests) for C. trachomatis Treatment/Management 1. Antibiotics • Azithromycin • Doxycycline • Erythromycin base • Erythromycin ethylsuccinate • Ofloxacin • Levofloxacin • Amoxicillin 2. Sex partner notification and referral for examination and treatment 3. Follow-up to ensure that treatment has been effective and to detect possible reinfection, with patient instruction to abstain from sexual intercourse until treatment is completed
FMSD (2004)	Screening 1. Targeted and/or systematic screening for chlamydial infection 2. Tracing contacts and partner screening Diagnostic tests for Chlamydia infection 1. Assessment of clinical symptoms and signs

	2. Laboratory diagnostics • Gene amplification methods, such as PCR and LCR • First-void urine samples • As an alternative for women to first-void urine, analyses of samples from the urethra, cervix, or cornea of the eye by gene amplification methods • Chlamydial culture of swab from the urethra or cervix • Serology (chlamydial serology for chronic infections and immunoglobulin G [IgG] antibody titres) • Note: Immunological staining methods were considered but not recommended because of poor sensitivity Treatment/Management 1. Antibiotics • Azithromycin as the treatment of choice for chlamydial infection • Other alternatives: tetracycline or doxycycline, or erythromycin for pregnant women • Combination of antibiotics in pelvic infections 2. Testing of the permanent sexual partner of the index patient before treating partner 3. Post-treatment follow-up 4. Tracing the contacts of the patient
SIGN (2000)	Diagnostic tests for chlamydial infection 1. Cell culture 2. Antigen detection 3. DNA amplification tests (LCR or PCR) 4. Newer tests such as transcription-mediated amplification and strand-displacement amplification are considered Treatment/Management 1. Antibiotics • Azithromycin • Doxycycline • Lymecycline • Minocycline • Ofloxacin • Erythromycin • Amoxicillin • Doxycycline plus metronidazole (ofloxacin as an alternative to doxycycline; clindamycin as an alternative to metronidazole) • Oxytetracycline

	2. Follow up and test of cure 3. Partner notification 4. Health education
USPSTF (2001)	Screening for chlamydial infection in the general population, certain high-risk groups, and in pregnant women using the following laboratory tests 1. Cell culture 2. Antigen detection tests (DFA assay and EIA) 3. Non-amplified nucleic acid hybridization, or newer technologies based on amplified DNA assays (PCR, LCR, strand displacement assay, hybrid capture system, and transcription-mediated amplification of RNA)

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR CHLAMYDIAL INFECTION	
Screening — Population Groups to be Screened	
	Routine screening of asymptomatic general population
ACPM (2003)	No recommendations offered
AGUM/MSSVD (2002)	No recommendations offered
CDC (2002)	No recommendations offered
FMSD (2004)	No recommendations offered
SIGN (2000)	No recommendations offered
USPSTF (2001)	No recommendation can be made for or against routinely screening asymptomatic low-risk women in the general population for chlamydial infection. (C recommendation) The evidence is insufficient to recommend for or against routinely screening asymptomatic men for chlamydial infection. (I recommendation)

	Screening of asymptomatic high-risk groups
ACPM (2003)	Sexually active women with risk factors should be screened annually. Risk factors include: • Age ≤25 years • A new male sex partner or two or more partners during the preceding year • Inconsistent use of barrier contraception • History of a prior STD • African-American race • Cervical ectopy
AGUM/MSSVD (2002)	No recommendations offered
CDC (2002)	In the United States, chlamydial genital infection occurs frequently among sexually active adolescents and young adults. Asymptomatic infection is common among both men and women. Sexually active adolescent women should be screened for chlamydial infection at least annually, even if symptoms are not present. Annual screening of all sexually active women aged 20--25 years is also recommended, as is screening of older women with risk factors (e.g., those who have a new sex partner and those with multiple sex partners). An appropriate sexual risk assessment should always be conducted and may indicate more frequent screening for some women.
FMSD (2004)	• It has been shown that targeted screening for chlamydial infections is effective in preventing pelvic inflammatory disease (PID) and ectopic pregnancies (Scholes et al., 1996; Egger et al., 1998; Pimenta et al., 2000). • Screening for chlamydial infection is cost-effective if the prevalence of chlamydia infection exceeds 3% in the population (Paavonen, et al., 1998). Systematic screening for chlamydial infection has been considered relevant among family planning clinic customers and in general those young women who see their physician to renew their contraceptive pill prescription, especially if there is a history of temporary sexual partners. • Tracing the contacts of the patient is the most effective way of combating the disease. Partner screening normally yields 20-30% positive cases. The practice of taking first-void urine samples from the partner at home has increased the number of detected infections by 50% compared with the usual practice of partner notification (Östergaard et al., 1998). Many young people are unaware that chlamydial infection is often asymptomatic, which reduces and delays

	testing for chlamydia.
SIGN (2000)	Testing for genital Chlamydia trachomatis infection should be performed in the following specific circumstances: • All women undergoing termination of pregnancy (A recommendation) • All patients attending genitourinary medicine clinics (B recommendation) • All patients with another sexually transmitted infection (STI), including genital warts (B recommendation) • Sexual partners of those with chlamydial infection (B recommendation) • Mothers of infants with chlamydial conjunctivitis or pneumonitis (B recommendation) • All women undergoing uterine instrumentation, including intrauterine device (IUD) insertion, who have risk factors for chlamydial infection (B recommendation) • Semen and egg donors (B recommendation) • Sexual partners of those with suspected chlamydial infection (C recommendation) Opportunistic testing could be considered in the following groups of women (B recommendation): • Women younger than 25 years and sexually active • Women aged 25 years or older with two more partners in the last year or a change of sexual partner in the last year
USPSTF (2001)	It is strongly recommended that clinicians routinely screen all sexually active women aged 25 years and younger, and other asymptomatic women at high risk for chlamydial infection. (A recommendation) Clinical considerations: • Women and adolescents through age 20 years are at highest risk for chlamydial infection, but most reported data indicate that infection is prevalent among women aged 20-25. Age is the most important risk marker. Other characteristics associated with a higher prevalence of infection include being unmarried, African-American race, having a prior history of sexually transmitted disease, having new or multiple sexual partners, having cervical ectopy, and using barrier contraceptives inconsistently. • Clinicians should consider the characteristics of the communities they serve in determining appropriate screening strategies for their patient population.

	• The optimal interval for screening is uncertain. For women with a previous negative screening test, the interval for re-screening should take into account changes in sexual partner. If there is evidence that a woman is at low risk for infection, it may not be necessary to screen frequently. Re-screening at 6-12 months may be appropriate for previously infected women because of high rates of reinfection. • Screening of high-risk men is a clinical option. • Partners of infected individuals should be tested and treated if infected or treated presumptively.
	Screening of asymptomatic pregnant women
ACPM (2003)	Pregnant women should be screened during their first trimester or at their first prenatal visit. Those with risk factors should be re-screened during their third trimester.
AGUM/MSSVD (2002)	No recommendations offered
CDC (2002)	Prenatal screening of pregnant women can prevent chlamydial infection among neonates. Pregnant women aged <25 years are at high risk for infection. Local or regional prevalence surveys of chlamydial infection can be conducted to confirm the validity of using these recommendations in particular settings.
FMSD (2004)	No recommendations offered
SIGN (2000)	No recommendations offered
USPSTF (2001)	It is recommended that clinicians routinely screen all asymptomatic pregnant women aged 25 years and younger and others at increased risk for infection of chlamydial infection. (B recommendation) No recommendation can be made for or against routine screening of asymptomatic, low-risk pregnant women aged 26 years and older for chlamydial infection. (C recommendation) Clinical considerations The optimal timing of screening in pregnancy is uncertain. Screening early in pregnancy provides greater opportunities to improve pregnancy outcomes, including low birth weight and premature delivery; however screening in the 3rd trimester may be more effective at preventing transmission of chlamydial

	infection to the infant during birth. The incremental benefit or repeated screening is unknown.
	Screening of patients with signs/symptoms of chlamydial infection
ACPM (2003)	Women with mucopurulent discharge, suggestive of cervicitis, should be tested immediately.
AGUM/MSSVD (2002)	No recommendations offered
CDC (2002)	• All male patients who have urethritis should be evaluated for the presence of gonococcal and chlamydial infection. Testing for chlamydia is strongly recommended because of the increased utility and availability of highly sensitive and specific testing methods, and because a specific diagnosis may enhance partner notification and improve compliance with treatment, especially in the exposed partner. • Female patients who have mucopurulent cervicitis (MPC) should be tested for C. trachomatis and for Neisseria gonorrhoeae with the most sensitive and specific test available. However, MPC is not a sensitive predictor of infection with these organisms; most women who have C. trachomatis or N. gonorrhoeae do not have MPC.
FMSD (2004)	Chlamydial infection can be suspected but never diagnosed on the basis of symptoms alone. A burning sensation or mucous discharge from the urethra are common symptoms in men after unprotected sexual intercourse with a temporary partner. Although Gram or methylene blue stains of plain smear specimens are usually rich in white blood cells, chlamydia is found to be the cause of the infection in only half the patients. A reliable diagnosis of chlamydial infection in both men and women can therefore be reached only by appropriate microbiological sampling.
SIGN (2000)	Testing for Chlamydia trachomatis should be performed in women and men with symptoms and signs which may be attributable to chlamydial infection (B recommendation): • Women — vaginal discharge, post coital/intermenstrual/breakthrough bleeding, inflamed/friable cervix (which may bleed on contact), urethritis, pelvic inflammatory disease, lower abdominal pain in the sexually active, or reactive arthritis in the sexually active • Men — urethral discharge, dysuria, urethritis, epididymo-orchitis in the sexually active, or reactive arthritis in the

	sexually active
USPSTF (2001)	Clinicians should remain alert for findings suggestive of chlamydial infection during pelvic examination of asymptomatic women (e.g., discharge, cervical erythema, cervical friability).
Screening Tests	
	Types of screening tests
ACPM (2003)	Any well-validated, laboratory-based amplification or antigen method may be used. (The guideline notes, however, that the decision as to which screening test to utilize must be based both on the estimated prevalence in the screened population and available funding. When economically feasible, the use of amplification tests is preferable.)
AGUM/MSSVD (2002)	• Ideal diagnostic test sensitivity is >90% with specificity >99%. The tests which most closely approach this are the NAATs. These perform better or at least as well as any of the other tests. • Only the better performing EIAs should be used, with sensitivities >80% and where sensitivity comparisons against NAAT techniques have been carried out. • With EIAs, the technique of confirmation in the negative grey zone, either by DFA or NAAT, should be introduced (Dean, Ferrero, & McCarthy, 1998; Tong, Donnelly, & Hood, 1997). This improves sensitivity by 5-30%. • Quality control to validate the sensitivity and specificity of the assay used by individual laboratories should be undertaken, in view of the reported wide range in the sensitivity of all tests. Both interlaboratory and intralaboratory control samples should be carried out, using both strong positives and negative and weakly reactive specimens.
CDC (2002)	Nucleic acid amplification tests enable detection of N. gonorrhoeae and C. trachomatis on all specimens. These tests are more sensitive than traditional culture techniques for C. trachomatis and are the preferred method for the detection of this organism.
FMSD (2004)	• Laboratory diagnostics has undergone a profound change in recent years. Conventional chlamydial culture has been relegated to a minor role, and immunological staining methods of poor sensitivity have been abandoned. New gene amplification methods have replaced previous techniques, and first-void urine samples have acquired an

	established position in chlamydial diagnostics in both men and women. • Gene amplification methods, such as PCR and LCR, are based on multiplication of chlamydial nucleic acids with specific probes. The main assets of the methods are their high sensitivity and the fact that they, unlike culture methods, yield a positive result also when there are no living chlamydia in the sample. Compared with traditional culture methods, gene amplification methods reveal 5-7% more cases of chlamydial infection, and false positives are practically nonexistent. (Pasternack, Vuorinen, & Miettinen, 1997; Puolakkainen et al., 1998). The price of these tests has come down to an acceptable level. Today chlamydia and gonorrhoea can be analysed on the same sample if required. • Chlamydial culture has been rendered secondary in importance for several reasons. It has a sensitivity of 80% but a specificity of close to 100%. (Puolakkainen et al., 1998). The sample for chlamydial culture is obtained with a special swab from the urethra or cervix. It should be transported to the laboratory without delay, and the result becomes available after two or three days. In chronic infections, the test is often negative because of low numbers of bacteria. Unlike gonorrhoea, chlamydial infections are not associated with resistance problems. • Chlamydial serology may be useful in chronic infections. High IgG antibody titres are often present in pelvic infections and also in other complications. An isolated positive test indicates that the patient has a history of chlamydial infection.
SIGN (2000)	The recommended laboratory test for Chlamydia trachomatis is a nucleic acid amplification test (e.g., LCR or PCR). (B recommendation)
USPSTF (2001)	A number of tests are available to identify chlamydial infection that use endocervical or urethral swab specimens and urine specimens. Until recently, culture has been accepted as the most specific test but it requires specialized handling and laboratory services. Antigen-detection tests (DFA assay and EIA) and non-amplified nucleic acid hybridization, as well as newer technologies based on amplified DNA assays (PCR, LCR, strand displacement assay, hybrid capture system, and transcription-mediated amplification of RNA) may provide improved sensitivity, lower expense, availability, or timeliness of results over culture. New tests that use urine specimens provide a noninvasive method of screening both men and women. Self-administered vaginal and vulvar-introital swabs using PCR and LCR, including submitting samples by mail, are being used in research settings. The sensitivities and

	specificities of nucleic acid amplification tests are all high, ranging from 82-100%. The sensitivity of antigen detection tests (EIA, DFA) is slightly lower (70-80%) but specificity remains high (96-100%).
	Specimen of choice
ACPM (2003)	The guideline notes that tests vary in the type of specimens on which they may be used, the level of skill required to collect and transport specimens, the level of skill required by the testing laboratory, and the accuracy and rapidity of results. Women • Specimens may be obtained from (1) the endocervix, using a swab; (2) urethra and vagina using a swab; and (3) first-catch urine. • Cervical or urine specimens are recommended. Men Specimens can be obtained by swabbing the anterior urethra as well as through first-catch urine.
AGUM/MSSVD (2002)	Women Antigen detection techniques - EIA and DFA: • Cervical swab is the best specimen. • 10-20% additional positives will be detected by assaying a urethral specimen as well (Hay et al., 1994; Paavonen, 1979). This can be combined with the cervical specimen for analysis. Urethral swabbing suffers from the same disadvantages as in men (see below). • Urine specimens perform significantly less well with EIA than cervical specimens and are not recommended. • EIA should not be used for detecting C. trachomatis in the rectum or pharynx. NAAT: • Cervical swabs consistently have sensitivities >80% (Black, 1997; Ridgway et al., 1996). • Urine has reported sensitivities of 44-94% (Jensen, Thorsen, & Moller, 1997; Andrews et al., 1997; Black, 1997; Ridgway et al., 1996; Horner et al., 1998; Lee et al., 1995; Rabenau et al., 1997). • Vulvo-vaginal swabs have a sensitivity ≥85%.

	Menstrual cycle and testing: • Preliminary data suggest that testing for C. trachomatis may detect more cases when undertaken in the latter part of the menstrual cycle. (Horner et al., 1998; Taylor-Robinson et al., 1998; Crowley et al., 1997). This is further supported by the findings from a community based study conducted in Denmark (Moller et al., 1999). Men Antigen detection techniques - EIA and DFA: • First voided urine sample is as good as, if not better than, a urethral swab (Caul et al., 1989; Hay et al., 1991). The former is preferred because some patients find urethral swabbing painful and tolerate it poorly and thus there is the potential for obtaining an inadequate quality specimen. Patients should hold their urine at least 1 hour before being tested and preferably longer, as otherwise sensitivity is reduced (the optimum duration is not known). • EIA should not be used for detecting C. trachomatis in the rectum or pharynx. NAAT: • First voided urine sample is the preferred specimen (Chernesky et al., 1994) (see above).
CDC (2002)	No specific recommendations are made for adult patients.
FMSD (2004)	Women • As an alternative to first-void urine, women may give urethral and cervical swab samples which are then analysed by the same gene amplification methods. Even samples from the cornea of the eye can be examined by gene amplification techniques. Men and Women • First-void urine samples are used for chlamydial diagnostics in both men and women. Samples are taken when at least five to seven days have passed since the potential time of acquirement of infection. The patient has to refrain from voiding for 2 hours before urine sampling. The sample (10 ml) is sent to a laboratory in the normal way. If needed, the sample may be kept refrigerated for

	one or two days. • First-void urine samples are well suited for home screening of risk groups or sexual partners (Östergaard et al., 1998).
SIGN (2000)	Women In women who are undergoing a vaginal examination, the specimen should be an endocervical swab. In women not undergoing a vaginal examination, a first void urine should be obtained. A self-taken vaginal swab is an alternative specimen for women who cannot void urine at the time of visit. Men In men urethral swabs and first void urine have equal sensitivity, but urethral sampling causes discomfort. Therefore, in men, a first void urine is the sample of choice. (B recommendation)
USPSTF (2001)	Women Endocervical swab specimens and first-void urine specimens had similar performance using DNA amplification tests. Urine tests allow noninvasive testing for women without the need for a pelvic examination thereby expanding opportunities for screening. Men Results of swab specimens compared to first-void urine specimens using DNA tests are similar. Although studies indicate that urine techniques are capable of improved sensitivity compared to culture, the importance of detecting and treating culture-negative infections is not yet known.
Management Recommendations	
	Antibiotic regimens in nonpregnant women and men
ACPM (2003)	No recommendations offered
AGUM/MSSVD (2002)	Ideally, treatment should be effective (microbiological cure rate >95%), easy to take (not more than twice daily), with a low side effect profile, and cause minimal interference with daily lifestyle (C recommendation). Treatment of uncomplicated infection

Recommended regimens (A recommendation):

- Doxycycline 100 mg twice a day for 7 days

  or

- Azithromycin 1 g orally in a single dose

Alternative regimens (A recommendation):

- Erythromycin 500 mg four times a day for 7 days

  or

- Erythromycin 500 mg twice a day for 14 days

  or

- Deteclo 300 mg twice a day for 7 days

  or

- Ofloxacin 200 mg twice a day or 400 mg once a day for 7 days

  or

- Tetracycline 500 mg four times a day for 7 days

Doxycycline and azithromycin (level of evidence Ia)
These have been shown to have equal efficacy in clinical studies (Weber & Johnson, 1995; Moore, McQuay & Muir Gray, 1996; Hillis et al., 1998). Azithromycin is considerably more expensive than doxycycline. Azithromycin may be particularly useful in patients with erratic healthcare seeking behaviour (Handsfield & Stamm, 1998).

Ofloxacin (level of evidence Ib)
It is unknown whether 200 mg twice a day is superior to 400 mg once a day. There is no evidence to suggest that compliance with a once a day regimen is better than twice daily regimens (Drug and Therapeutics Bulletin, 1991).

Whether missing a dose with 400 mg daily results in a less efficacious regimen than missing a dose with 200 mg twice daily is unknown. Ofloxacin has similar efficacy to doxycycline and a better side effect profile but is considerably more expensive, so is not recommended as first-line treatment.

Erythromycin (level of evidence Ib)

	Erythromycin is less efficacious than either azithromycin or doxycycline. When taken four times a day, 20-25% may experience side effects sufficient to cause the patient to discontinue treatment (Linneman, Heaton & Ritchey, 1987). There are only limited data on erythromycin 500 mg twice a day, with efficacy reported at between 73-95% (Linneman, Heaton & Ritchey, 1987; Stenberg & Mardh, 1993; Ross, Crean & McMillan, 1996). A two week course appears to be more efficacious than a one week course of 500 mg twice a day, with a cure rate $\geq$95% in a small study (Linneman, Heaton & Ritchey, 1987; Stenberg & Mardh, 1993). <u>Other tetracyclines (level of evidence Ib)</u> Deteclo is probably as efficacious as doxycycline (Munday et al., 1995). However, photosensitivity occurs more frequently and there are not as many data on efficacy if compliance is poor. Tetracycline 500 mg is effective when taken four times a day for seven days. Compliance with such a regimen is likely to be poor, particularly in less motivated patients, and whether such a regimen would then be efficacious is unknown. Oxytetracycline 250 mg four times a day has also been shown to be effective, although the published evidence is limited (Ross, Crean & McMillan, 1996).
CDC (2002)	Recommended Regimens • Azithromycin 1 g orally in a single dose OR • Doxycycline 100 mg orally twice a day for 7 days Alternative Regimens • Erythromycin base 500 mg orally four times a day for 7 days OR • Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR • Ofloxacin 300 mg orally twice a day for 7 days OR • Levofloxacin 500 mg orally for 7 days The results of clinical trials indicate that azithromycin and

	doxycycline are equally efficacious. These investigations were conducted primarily in populations in which follow-up was encouraged and adherence to a 7-day regimen was good. Azithromycin should always be available to health-care providers to treat patients for whom compliance is in question. To maximize compliance with recommended therapies, medications for chlamydial infections should be dispensed on site, and the first dose should be directly observed. To minimize further transmission of infection, patients treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen. To minimize the risk for reinfection, patients also should be instructed to abstain from sexual intercourse until all of their sex partners are treated.
FMSD (2004)	• Azithromycin 1 g as a single dose is the treatment of choice for chlamydial infection. Other alternatives are tetracycline 500 mg x3/day or doxycycline 100 mg x2/day for 7-10 days. Some 10% of patients get mild gastric side effects from azithromycin and tetracyclines. Azithromycin therapy has the benefit of 100% compliance; it is more expensive than the common tetracyclines, however. Controlled studies have shown similar therapeutic outcomes for these drugs, with 95-97% of patients being cured. • Chlamydial infections of the throat, anus or eyes are treated with azithromycin for three to five days. For mild complications, patients are given tetracycline or doxycycline for two to three weeks, for reactive arthritis triggered by chlamydial infection even longer. In pelvic infections, combinations of antibiotics are used, as other bacteria, such as anaerobes, may be involved. • The permanent sexual partner of the index patient should be tested before any treatment since the partner is not necessarily infected. The suitability of the antibiotic for the partner should also be ascertained, as well as ensuring that the female partner to be treated is not pregnant. Furthermore, the partner may have transmitted the infection to other persons, an issue that can only be clarified by having the partner visit the physician or clinic.
SIGN (2000)	Initiate treatment without waiting for laboratory confirmation of infection in patients with symptoms and signs attributable to chlamydial infection and their sexual partners. (B recommendation) Uncomplicated Infection Uncomplicated genital Chlamydia trachomatis infection may be treated with any one of the following, listed alphabetically (A

	recommendation): • Azithromycin 1g stat • Doxycycline 100mg twice daily for 7 days • Lymecycline 300mg once a day for 10 days • Minocycline 100mg once a day for 9 days • Ofloxacin 200mg twice daily for 7 days Taking into account the issue of compliance with therapy, it is recommended that uncomplicated genital Chlamydia trachomatis infection is treated with azithromycin 1g stat (B recommendation). Upper genital tract infection in women (Chlamydial salpingitis/pelvic inflammatory disease [PID]) The recommended treatment for upper genital tract infection in women is (C recommendation): • Doxycycline 100mg twice daily for a minimum of 10 days plus metronidazole 200mg three times a day or 400g twice daily for the first 7 days • Ofloxacin 400mg twice daily may be used as an alternative to doxycycline • Clindamycin 450mg four times a day may be used as an alternative to metronidazole Upper genital tract infection in men (Chlamydial epididymo-orchitis) The recommended treatment for upper genital tract chlamydial infection in men is (C recommendation): • Doxycycline 100mg twice daily for 7-14 days or • Oxytetracycline 250mg four times a day for 7-14 days
USPSTF (2001)	No recommendations offered
	Antibiotic regimens during pregnancy and breast feeding
ACPM (2003)	No recommendations offered
AGUM/MSSVD (2002)	• Doxycycline and ofloxacin are contraindicated in pregnancy • The safety of azithromycin in pregnancy and lactating mothers has not yet been fully assessed, although available data indicate that it is effective

	• Erythromycin has a significant side effect profile and is less than 95% effective. There are no trials of erythromycin 500 mg twice a day for 14 days, which would be better tolerated than four times a day • Amoxycillin had a similar cure rate to erythromycin in a meta-analysis and had a much better side effect profile (Brocklehurst & Rooney, 1998). However, amoxycillin in vitro has been shown to induce latency: there is therefore debate as to whether it is reliable Regimens (Ia, A recommendation) • Erythromycin 500 mg four times a day for 7 days or • Erythromycin 500 mg twice a day for 14 days or • Amoxycillin 500 mg three times a day for 7 days Patients should have a test of cure 3 weeks after completing therapy.
CDC (2002)	Doxycycline and ofloxacin are contraindicated in pregnant women. However, clinical experience and preliminary data suggest that azithromycin is safe and effective. Repeat testing (preferably by culture) 3 weeks after completion of therapy with the following regimens is recommended for all pregnant women, because these regimens may not be highly efficacious and the frequent side effects of erythromycin might discourage patient compliance with this regimen. Recommended Regimens • Erythromycin base 500 mg orally four times a day for 7 days OR • Amoxicillin 500 mg orally three times daily for 7 days Alternative Regimens • Erythromycin base 250 mg orally four times a day for 14 days OR

	• Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR • Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days OR • Azithromycin 1 g orally, single dose Note: Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity.
FMSD (2004)	• Patients who are pregnant should receive erythromycin 500 mg x4/day for seven days (Brocklehurst & Rooney, 2002) [B]. • Amoxicillin and erythromycin are equally effective for antenatal chlamydial cervicitis (Turrentine & Newton, 1995; DARE, 1999) [B].
SIGN (2000)	Uncomplicated genital chlamydial infection in pregnancy should be treated with (A recommendation): • Erythromycin 500mg four times a day for 7 days or • Amoxycillin 500mg three times a day for 7 days All women undergoing termination of pregnancy should receive antimicrobial therapy effective against chlamydial infection at the time of the procedure. (A recommendation)
USPSTF (2001)	No recommendations offered
	Patient education and preventive counseling
ACPM (2003)	No recommendations offered
AGUM/MSSVD (2002)	In general, compliance with therapy is improved if there is a positive therapeutic relationship between the patient and the doctor. (Sanson-Fisher, Bowman & Armstrong, 1992) This can probably be improved if the following are applied (C recommendation):

	Discuss with patient and provide clear written information on:
	
	• What chlamydia is and how it is transmitted:
	  • it is a sexually transmitted infection.
	  • if asymptomatic there is evidence that it could persist for months or even years.
	  • it can be isolated from the throat and eye without detectable infection in the lower genital tract. (Stenberg & Mardh, 1993; Postema, Remeijer & van der Meijden, 1996)
	  • It can therefore not always be assumed to be sexually acquired. (Midulla et al., 1987)
	• The diagnosis of chlamydia, particularly:
	  • it is often asymptomatic especially in women
	  • while tests are accurate, no test is absolutely so.
	• The complications of untreated Chlamydia
	• Side effects and importance of complying fully with treatment and what to do if a dose is missed
	• Interaction between antibiotics and oral contraceptive pill
	• The importance of their sexual partner(s) being evaluated and treated
	• Advice to abstain from sexual intercourse until they have completed therapy and their partner has been treated
	• Advice on safer sexual practices

CDC (2002)	• Patients should be instructed to refer their sex partners for evaluation and treatment • Patients should be instructed to avoid sexual intercourse until therapy is completed and until they and their sex partners no longer have symptoms
FMSD (2004)	No recommendations offered.
SIGN (2000)	Sexual health promotion should be an integral part of contraception provision wherever this is offered. • All patients with chlamydial infection should receive appropriate health education, including relevant reading materials (B recommendation). • Opportunities should be taken to deliver education in a wide variety of non-health care settings (e.g., youth clubs, community centres, schools). Education about chlamydia infection should be integrated with other sexual health education and condom promotion initiatives (B recommendation).

USPSTF (2001)	No recommendations offered
	Partner notification and treatment
ACPM (2003)	All partners of women with positive tests should be tested for Chlamydia trachomatis.
AGUM/MSSVD (2002)	• All patients identified with C. trachomatis infection should be referred to discuss partner notification, where possible at initial diagnosis. • The method of partner notification agreed for each partner/contact identified should be documented. • At subsequent follow up, partner notification outcomes should be ascertained and documented. <u>Look back period</u> Only limited evaluation has taken place of the incubation period following exposure to the development of symptoms. In the United Kingdom (FitzGerald et al., 1998) an arbitrary cut off of 4 weeks is used to identify those sexual partner(s) potentially at risk if the index male patient is symptomatic. As it is not known how long a patient can carry chlamydia asymptomatically, an arbitrary cut off of 6 months or until the last previous sexual partner (whichever is the longer time period), is used in women and asymptomatic men. Common sense needs to be used in assessing which sexual partner(s) may have been at risk in these situations. Those at risk should be informed and invited to attend for evaluation and epidemiological treatment even if tests are negative. This may be patient led or provider led if the patient is unwilling to undertake it.
CDC (2002)	• Patients should be instructed to refer their sex partners for evaluation, testing, and treatment. The following recommendations on exposure intervals are based on limited evaluation. Sex partners should be evaluated, tested, and treated if they had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient or diagnosis of chlamydia. The most recent sex partner should be evaluated and treated even if the time of the last sexual contact was >60 days before symptom onset or diagnosis. • Patients should be instructed to abstain from sexual intercourse until they and their sex partners have completed treatment. Abstinence should be continued until 7 days after a single-dose regimen or after completion of a 7-day regimen. Timely treatment of sex partners is essential for decreasing the risk for reinfecting the index patient.

FMSD (2004)	• Every physician treating patients with chlamydial infections is required to trace the sexual contacts of their patients (Mathews et al., 2002) [B]. The physician should enquire the index patient whether the person who is the source of the infection and any persons potentially infected have been tested for chlamydia and received treatment as needed. If desired, the attending physician may delegate the screening of sexual partners to a physician responsible for communicable diseases. • Patient assistance at facilitating patient referral and provider referral may increase partner notification for sexually transmitted diseases (Oxman et al., 1994; DARE, 1999) [C]. • Provider referral and contract referral are more effective than patient referral among patients in increasing the rate of partners presenting for medical evaluation (Mathews et al., 2002) [B]. • Tracing the contacts of the patient is the most effective way of combating the disease. Partner screening normally yields 20-30% positive cases. The practice of taking first-void urine samples from the partner at home has increased the number of detected infections by 50% compared with the usual practice of partner notification (Östergaard et al., 1998). Many young people are unaware that chlamydial infection is often asymptomatic, which reduces and delays testing for chlamydia.
SIGN (2000)	Patients should be referred to trained health advisers for support with partner notification (B recommendation). Patients should be offered the choice of patient, provider or conditional referral for partner notification (B recommendation): • Patient referral (or self referral): when index patients themselves inform their sexual contacts to seek treatment. • Provider referral: when the health care provider informs a patient's contacts anonymously that they should seek treatment. This is obviously more time consuming for the health care provider. • Conditional referral: where the health care provider notifies contacts if the patient has not done so after a given number of days. In men with symptomatic chlamydial infection, contact all partners over the four weeks prior to onset of symptoms (C recommendation). In women and asymptomatic men, contact all partners over the last six months or the most recent sexual partner (if

	outwith that time period) (C recommendation).
USPSTF (2001)	Partners of infected individuals should be tested and treated if infected or treated presumptively.
	Follow-up
ACPM (2003)	No recommendations offered.
AGUM/MSSVD (2002)	This is an important part of the management of chlamydial infection. However, some patients may not return, emphasising the importance of the initial consultation. Follow up has a number of objectives including: • Following up partner notification • Reinforcing health education • Providing reassurance • Assessment of treatment efficacy/exclusion of re-infection Patients do not need to be retested for C. trachomatis after completing treatment with doxycycline or azithromycin unless symptoms persist or re-infection is suspected, as both are highly efficacious (C recommendation). A test of cure should be considered 3 weeks after the end of treatment with erythromycin. A test of cure earlier will miss late failures and may detect non-viable organisms.
CDC (2002)	Patients do not need to be retested for chlamydia after completing treatment with doxycycline or azithromycin unless symptoms persist or reinfection is suspected. A test of cure may be considered 3 weeks after completion of treatment with erythromycin. The validity of chlamydial culture testing at <3 weeks after completion of therapy to identify patients who did not respond to therapy has not been established. False-negative results can occur resulting from infections involving small numbers of chlamydial organisms. In addition, nonculture tests conducted at <3 weeks after completion of therapy for patients who were treated successfully could yield false-positive results because of continued excretion of dead organisms. A high prevalence of C. trachomatis infection is found in women who have had chlamydial infection in the preceding several months. Most post-treatment infections result from reinfection, often occurring because patient's sex partners were not treated or because the patient resumed sex among a network of persons with a high prevalence of infection. Repeat infection confers an elevated risk of PID and other complications when compared with initial infection. Therefore,

	recently infected women are a high priority for repeat testing for C. trachomatis. For these reasons, clinicians and health-care agencies should consider advising all women with chlamydial infection to be rescreened 3--4 months after treatment. Some specialists believe rescreening is an especially high priority for adolescents. Providers are also strongly encouraged to rescreen all women treated for chlamydial infection whenever they next present for care within the following 12 months, regardless of whether the patient believes that her sex partners were treated. Rescreening is distinct from early retesting to detect therapeutic failure (test-of-cure). Except in pregnant women, test-of-cure is not recommended for persons treated with the recommended regimens, unless therapeutic compliance is in question.
FMSD (2004)	A follow-up visit should only take place after three to four weeks because the presence of gene traces may produce a false positive result in an earlier re-test.
SIGN (2000)	Patients should be interviewed at follow-up with regard to compliance with therapy and risk of re-infection (B recommendation). In those patients who have been compliant with therapy in whom there is no risk of reinfection, a test of cure need not be performed (B recommendation). Test of cure/re-infection established by molecular amplification assay should be performed a minimum of three weeks after the initiation of therapy, to avoid false positive results (B recommendation).
USPSTF (2001)	No recommendations offered.
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Evidence Rating Schemes	
ACPM (2003)	Evidence was not graded.
AGUM/MSSVD (2002)	Levels of Evidence: Ia — Evidence obtained from meta-analysis of randomised controlled trials Ib — Evidence obtained from at least one randomised controlled trial IIa — Evidence obtained from at least one well designed controlled study without randomisation IIb — Evidence obtained from at least one other type of well designed quasi-experimental study III — Evidence obtained from well-designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies IV — Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities Grading or recommendations A. (Evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation. B. (Evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation. C. (Evidence level IV): Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.
CDC (2002)	Evidence was not graded.
FMSD (2004)	Levels of Evidence A: Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results. B: Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies. C: Limited research-based evidence. At least one adequate

	scientific study. D: No scientific evidence. Expert panel evaluation of other information.
SIGN (2000)	Grades of Recommendations A. Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib) B. Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III) C. Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV) Statements of Evidence Ia — Evidence obtained from meta-analysis of randomised controlled trials. Ib — Evidence obtained from at least one randomised controlled trial. IIa — Evidence obtained from at least one well-designed controlled study without randomisation. IIb — Evidence obtained from at least one other type of well-designed quasi-experimental study. III — Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case control studies. IV — Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.
USPSTF (2001)	USPSTF grades its recommendations according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms). A. USPSTF strongly recommends that clinicians provide [the service] to eligible patients. (The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.) B. USPSTF recommends that clinicians provide [the service] to eligible patients. (USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits outweigh harms.) C. USPSTF makes no recommendation for or against routine provision of [the service]. (USPSTF found at least fair evidence

	that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.) D. USPSTF recommends against routinely providing [the service] to asymptomatic patients. (The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.) I. USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. (Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.) USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, or poor). Good — Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes. Fair — Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes. Poor — Evidence is insufficient to assess the effects on health outcomes because of limited number of power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

TABLE 3: BENEFITS AND HARMS	
BENEFITS	
ACPM (2003)	Chlamydia trachomatis urogenital infections are highly prevalent among adolescents and young adults. Sequelae of undetected, untreated infections account for substantial healthcare costs. Treatment is effective, simple, and well tolerated. The majority of infected women and many men are asymptomatic; thus, screening is necessary for detection. Recently screening for Chlamydia trachomatis was simplified through the development of noninvasive, highly sensitive, amplification screening tests. Chlamydia trachomatis screening programs can be effective, both in lowering disease prevalence

	and decreasing the incidence of sequelae.
AGUM/MSSVD (2002)	These guidelines will aid in the appropriate diagnosis, treatment and management of patients with Chlamydia trachomatis genital tract infection. This infection is common (3-5% of sexually active women attending United Kingdom general practice) and sustained by unrecognised and thus untreated symptomless infection in both men and women. Complications cost at least 50 million pounds annually in the Untied Kingdom. Approximately 40% of non-gonococcal urethritis is caused by C. trachomatis.
CDC (2002)	• Appropriate screening and management of chlamydial infection • Prevention of transmission of chlamydial infection to sex partners and infants of infected mothers
FMSD (2004)	Identification, diagnosis and effective treatment of the patient with chlamydial urethritis and cervicitis may help avoid the serious complications of prolonged or recurrent infection (e.g., pelvic inflammatory disease, infertility, ectopic pregnancy) as well as prevent the spread of infection.
SIGN (2000)	A guideline for the management of genital Chlamydia trachomatis infection has the potential to encourage the uptake of effective practice in the identification and treatment of chlamydial infection. Appropriate testing for chlamydial infections in defined clinical settings should lead to lower complication rates for individuals and in tandem with wider access to contact tracing, should lead to significant falls in re-infection rates and a reduced pool of infection within the community.
USPSTF (2001)	The strongest evidence supporting screening is a well-designed randomized trial demonstrating that screening women at risk (prevalence of infection 7%) reduced the incidence of pelvic inflammatory disease from 28 per 1000 woman-years to 13 per 1000 woman-years. The prevalence of chlamydial infection has declined in populations that have been targeted by screening programs (primarily women attending family planning and other publicly funded clinics). In addition, two ecological analyses in Europe reported reductions in ectopic pregnancy and pelvic inflammatory disease with the advent of community-based screening for chlamydial infection. There is little evidence of the effectiveness of screening asymptomatic women who are not in high-risk groups. There is fair evidence indicating that screening for chlamydial infection among asymptomatic high-risk pregnant women and

	subsequent treatment improves pregnancy outcomes. Two non-randomized trial studies demonstrated improved pregnancy outcomes following treatment of chlamydial infection: less premature rupture of membranes, less low birth weight, higher infant survival, and fewer small-for-gestational age births. There is little evidence regarding the effectiveness of screening and treatment of asymptomatic pregnant women who are not in high-risk groups. There is good evidence showing that treatment of men can eradicate chlamydial infection. Unfortunately, there are no studies describing the effectiveness of screening or early treatment of men in reducing acute infection and sequelae in men or women.
HARMS	
ACPM (2003)	• Invasiveness of some screening procedures • Potential for patient anxiety, embarrassment, and the risk of unnecessary treatment of patients with false-positive results, including potential side effects of drugs
AGUM/MSSVD (2002)	None stated
CDC (2002)	• The frequent side effects of erythromycin might discourage patient compliance with this regimen. • An association between oral erythromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks who were treated with this drug.
FMSD (2004)	• Adverse effects of medications. Some 10% of patients get mild gastric side effects from azithromycin and tetracyclines. • Harmful effects of partner notification. Partner notification evaluations may result in harmful effects, such as domestic violence.
SIGN (2000)	None stated
USPSTF (2001)	No studies were identified that directly examined adverse effects of screening. Potential harms include adverse effects of both false-positive and true-positive diagnoses of a sexually transmitted disease on patients and their partners, the inconvenience of pelvic examinations for tests employing cervical specimens, and the potential harms of adverse

	reactions from antibiotic treatment. There may be added cost for confirmation of positive results and testing of partners.

GUIDELINE CONTENT COMPARISON

The American College of Preventive Medicine (ACPM), the Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases (AGUM/MSSVD), the Centers for Disease Control and Prevention (CDC), the Finnish Medical Society Duodecim (FMSD), the Scottish Intercollegiate Guidelines Network (SIGN), and the U.S. Preventive Services Task Force (USPSTF) present recommendations for screening and management of chlamydial infection. All of the organizations except ACPM and CDC provide explicit reasoning behind their judgments by ranking the level of evidence for each major recommendation. ACPM reviews the evidence for effectiveness of screening and treatment programs, as well as their cost-effectiveness. CDC briefly discusses the evidence used as the basis for specific recommendations throughout its guideline.

Both ACPM and USPSTF focus on screening for chlamydial infection and are concerned mainly with the identification of the populations that are at highest risk for chlamydial infection and its complications. AGUM/MSSVD, CDC, FMSD, and SIGN address most aspects of chlamydial infection, including diagnosis, treatment, patient education, and follow-up. Unlike the other organizations, however, AGUM/MSSVD does not offer screening recommendations as this is the subject of ongoing research. The scope of the CDC guideline is broader than that of the others in that it includes diagnosis and management of chlamydial infections among infants and children. The CDC also addresses other sexually transmitted diseases characterized by urethritis and cervicitis, such as those caused by Neisseria gonorrhoeae and other forms of nongonococcal urethritis.

Areas of Agreement

Screening of Asymptomatic High-Risk Groups

ACPM, CDC, FMSD, SIGN and USPSTF agree that routine screening should be considered in sexually active women (ACPM, CDC, SIGN, and USPSTF specify aged 25 years or younger). In addition, these five guideline developers consider women of any age who change sexual partners at high risk for infection. They also agree that sexual partners of infected patients should be screened. Although AGUM/MSSVD does not make specific recommendations about screening, it does acknowledge risk factors for infection.

Screening of Patients with Signs/Symptoms of Chlamydial Infection

ACPM, CDC, FMSD, and SIGN recommend that men and women with signs or symptoms of C. trachomatis infection (e.g., urethritis or urethral discharge in men and cervical discharge or friability in women) be tested for chlamydial infection. USPSTF states that clinicians should be alert for signs and symptoms of infection during routine pelvic examination.

Types of Screening Tests

All six guideline groups agree that nucleic acid amplification tests (NAATs) are the most sensitive and specific diagnostic tests for chlamydial infection. NAATs include polymerase chain reaction and ligase chain reaction assays. NAATs have the additional advantage over other testing methods (cell culture, antigen detection) in that they can be performed on urine samples, thus eliminating the need for invasive testing. Although cell cultures have traditionally been held as the "gold standard," especially for medico-legal cases, NAATs have been shown to be more sensitive and easier to use than culture.

Specimen of Choice

ACPM, AGUM/MSSVD, SIGN, and USPSTF are in general agreement that endocervical swabs are the specimen of choice in adult women who are undergoing vaginal examinations for genital infection. First-void urine is recognized as an alternative for women unwilling or unable to undergo vaginal examination. FMSD recommends first-void urine for both men and women, and urethral and cervical swabs as an alternative specimen when gene amplification methods are used. All five guideline groups agree that first-void urine is the specimen of choice for men when DNA amplification tests are used as screening tests. FMSD adds that first-void urine samples are well suited for home screening. CDC does not make specific recommendations on types of screening specimens for adults.

Antibiotic Regimens in Nonpregnant Women and Men

AGUM/MSSVD, CDC, FMSD, and SIGN are in general agreement that uncomplicated genital chlamydial infection may be treated with tetracyclines (e.g., tetracycline, doxycycline, minocycline, lymecycline, Deteclo); azithromycin; or ofloxacin. Single-dose azithromycin is acknowledged by all groups as the regimen of choice in patients who may be noncompliant with multi-dose regimens. Erythromycin is indicated only when other antibiotics are contraindicated (such as during pregnancy) or not tolerated by the patient.

Antibiotic Regimens during Pregnancy and Breast Feeding

AGUM/MSSVD, CDC, FMSD, and SIGN agree that either erythromycin or amoxicillin should be used to treat chlamydial infection in pregnant women or in women who are breast feeding. In addition, both CDC and AGUM/MVSSD suggest that single-dose azithromycin may be both safe and effective during pregnancy, although data are limited in this patient group.

Partner Notification and Treatment

All six organizations recommend referral of sexual partners for screening and possible treatment. AGUM/MSSVD and SIGN agree that in men with symptomatic chlamydial infection, all sexual partners over the four weeks prior to onset of symptoms are at risk for infection and should be referred. In women and asymptomatic men, all partners over the last 6 months should be referred. CDC states that sex partners should be evaluated, tested, and treated if they had

sexual contact with an infected patient during the 60 days before onset of symptoms or diagnosis; however, they also recommend evaluation and treatment of the last sexual contact, even if that contact was more than 60 days before symptom onset. Neither APCM nor FMSD makes specific recommendations regarding time of last sexual contact for partner notification.

Follow-up

AGUM/MSSVD, CDC, FMSD, and SIGN offer recommendations on follow-up of patients after treatment. AGUM/MSSVD, CDC, and SIGN agree that retesting for C. trachomatis is not routinely necessary, after completing treatment unless noncompliance with therapy is suspected or patients are still symptomatic. AGUM/MSSVD and CDC both acknowledge, however, that retesting should be considered 3 weeks after the end of erythromycin treatment because it is less efficacious than doxycycline or azithromycin. AGUM/MVSSD, CDC, FMSD, and SIGN also emphasize that any retesting should be done a minimum of 3 weeks after initiation of therapy to avoid false-positive results.

Although CDC does not recommend retesting after treatment (i.e., test-of-cure), the guideline does recommend that physicians advise women with chlamydial infection to be rescreened three to four months after infection because of the high probability of reinfection. CDC also strongly recommends that health care providers rescreen all women treated for chlamydial infection whenever they present for care within 12 months of infection.

Patient Education and Preventive Counseling

AGUM/MSSVD and SIGN are in agreement that patients with chlamydial infections should be provided with information (including written material) on the nature of the chlamydial infection. Both guideline groups recommend counseling on safe sex practices, including condom use. CDC states that patients should receive instruction on partner referral and avoiding sexual intercourse until completion of therapy and they and their sex partners are on longer symptomatic.

ACPM, FMSD, and USPTF do not provide recommendations for patient education or preventive counseling.

Areas of Differences

There are some differences among guidelines in the asymptomatic patient groups recommended for screening tests.

Screening of Asymptomatic High-Risk Groups

SIGN is the only guideline that recommends routine screening for the following patient groups: all women undergoing termination of pregnancy, all patients with another sexually transmitted disease (STD), all women undergoing intrauterine device (IUD) insertion, all patients attending genitourinary medicine (GUM) clinics, mothers of infants with chlamydial conjunctivitis or pneumonitis, and semen and egg donors. To support its recommendation in women undergoing termination of pregnancy, SIGN cites evidence that shows that women seeking abortions are at

increased risk of chlamydial infection and that failure to treat infection carries an approximately 25% risk of postabortal salpingitis. SIGN acknowledges that no studies have specifically demonstrated the benefit of testing prior to IUD insertion, but 2 studies have shown that giving an antimicrobial agent effective against chlamydia at the time of IUD insertion reduced the rate of salpingitis. SIGN believes there is good evidence that attendees at GUM clinics and persons with other STDs have an increase likelihood of being infected with Chlamydia trachomatis, and that mothers of infants with chlamydial conjunctivitis or pneumonitis are likely to have genital chlamydial infection. Semen and egg donors should be tested for infection to reduce the risk of disease infection to the recipient.

Screening of Asymptomatic Pregnant Women

ACPM, CDC and USPSTF are the only groups that offer specific recommendations on routine screening of asymptomatic pregnant women. Specifically, ACPM recommends screening of all pregnant women during the first trimester or at their first antenatal visit, with rescreening during the third trimester for high-risk women. Their rationale is that screening and treatment for chlamydia in pregnancy is associated with a reduction in premature rupture of membranes and small-for-gestational-age infants. Furthermore, they state, the prevalence of chlamydial infection is at least as great in pregnant women as in non-pregnant women. USPSTF recommends screening in pregnant women aged 25 years and younger and those at high risk of infection. The USPSTF found fair evidence that screening and treatment of women at high risk for chlamydial infections improves pregnancy outcomes, but it also found fair evidence that the benefits of screening low-risk pregnant women are small and may not justify the possible harms. CDC maintains that prenatal screening of pregnant women, especially those under 25 years of age, can prevent chlamydial infection among neonates. Adoption of this recommendation could depend on local or regional surveys of the prevalence of infection in this population group.

This Synthesis was prepared by NGC on May 29, 2001. It was reviewed by the guideline developers on October 6, 2001. It was updated on February 20, 2002 following the withdrawal of the CTFPHC guideline from the NGC Web site. This Synthesis was to incorporate 2002 updated recommendations from AGUM/MSSVD. This Synthesis was further modified on January 16, 2004 to include new or updated recommendations from ACPM, CDC, and FMSD, and again on September 2, 2004 to reflect updated recommendations from FMSD.

Internet citation: National Guideline Clearinghouse (NGC). Guideline synthesis: Screening for and management of chlamydial infection. In: National Guideline Clearinghouse (NGC) [website]. Rockville (MD): 2001 Nov 05 (updated 2004 Sep 20). [cited YYYY Mon DD]. Available: http://www.guideline.gov.

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Date Modified: 11/8/2004