

Guideline on the Management of Chlamydia trachomatis Infections

Developed by the IUSTI-Europe Guideline Editorial Board

Subcommittee Members:

Prof. Dr. Esmee Lanjouw, Rotterdam (Netherlands) Prof. Dr. Angelika Stary, Vienna (Austria)
Prof. Dr. Sander Ouburg, Amsterdam (Netherlands) Prof. Dr. Keith Radcliffe, Birmingham (United Kingdom)
Prof. Dr. Henry de Vries, Amsterdam (Netherlands) Prof. Dr. Magnus Unemo, Örebro (Sweden)

Members of EDF Guideline Committee:

Prof. Dr. Werner Aberer, Graz (Austria) Prof. Dr. Dieter Metze, Muenster (Germany)
Prof. Dr. Martine Bagot, Paris (France) Prof. Dr. Gillian Murphy, Dublin (Ireland)
Prof. Dr. Nicole Basset-Seguin, Paris (France) PD Dr. Alexander Nast, Berlin (Germany)
Prof. Dr. Ulrike Blume-Peytavi, Berlin (Germany) Prof. Dr. Martino Neumann, Rotterdam (Netherlands)
Prof. Dr. Lasse Braathen, Bern (Switzerland) Prof. Dr. Tony Ormerod, Aberdeen (United Kingdom)
Prof. Dr. Sergio Chimenti, Rome (Italy) Prof. Dr. Mauro Picardo, Rome (Italy)
Prof. Dr. Alexander Enk, Heidelberg (Germany) Prof. Dr. Annamari Ranki, Helsinki (Finland)
Prof. Dr. Claudio Feliciani, Rome (Italy) Prof. Dr. Johannes Ring, Munich (Germany)
Prof. Dr. Claus Garbe, Tuebingen (Germany) Prof. Dr. Berthold Rzany, Berlin (Germany)
Prof. Dr. Harald Gollnick, Magdeburg (Germany) Prof. Dr. Rudolf Stadler, Minden (Germany)
Prof. Dr. Gerd Gross, Rostock (Germany) Prof. Dr. Sonja Ständer, Muenster (Germany)
Prof. Dr. Vladimir Hegyi, Bratislava (Slovakia) Prof. Dr. Wolfram Sterry, Berlin (Germany)
Prof. Dr. Michael Hertl, Marburg (Germany) Prof. Dr. Eggert Stockfleth, Bochum (Germany)
Prof. Dr. Dimitrios Ioannides, Thessaloniki (Greece) Prof. Dr. Alain Taieb, Bordeaux (France)
Prof. Dr. Gregor Jemec, Roskilde (Denmark) Prof. Dr. George-Sorin Tiplica, Bucharest (Romania)
Prof. Dr. Lajos Kemény, Szeged (Hungary) Prof. Dr. Elke Weisshaar, Heidelberg (Germany)
Dr. Gudula Kirtschig, Amsterdam (Netherlands) Prof. Dr. Sean Whittaker, London (United Kingdom)
Prof. Dr. Robert Knobler, Vienna (Austria) Prof. Dr. Fenella Wojnarowska, Oxford (United Kingdom)
Prof. Dr. Annegret Kuhn, Muenster (Germany) Prof. Dr. Christos Zouboulis, Dessau (Germany)
Prof. Dr. Marcus Maurer, Berlin (Germany) Prof. Dr. Torsten Zuberbier, Berlin (Germany)
Prof. Dr. Kai Munte, Rotterdam (Netherlands)

Chairman of EDF Guideline Committee:

PD Dr. Alexander Nast, Berlin (Germany)

Expiry date: 10/2018

GUIDELINE

2015 European guideline on the management of *Chlamydia trachomatis* infections

E Lanjouw¹, S Ouburg², HJ de Vries^{3,4,5}, A Stary⁶, K Radcliffe⁷ and M Unemo⁸

¹Department of Dermatology, Erasmus Medical Center, Rotterdam, The Netherlands;

²Laboratory of Immunogenetics, Department of Medical Microbiology and Infection Control, VU University Medical Center, Amsterdam, The Netherlands; ³Department of

Dermatology, Academic Medical Centre, University of Amsterdam, Amsterdam, The

Netherlands; ⁴STI Outpatient Clinic, Infectious Disease Cluster, Health Service

Amsterdam, Amsterdam, The Netherlands; ⁵Center for Infection and Immunology

Amsterdam (CINIMA), Academic Medical Center (AMC), University of Amsterdam,

Amsterdam, The Netherlands; ⁶Outpatients' Centre for Infectious

Venereodermatological Diseases, Vienna, Austria; ⁷University Hospital Birmingham

Foundation NHS Trust, Birmingham, United Kingdom; ⁸WHO Collaborating Center for

Gonorrhoea and other Sexually Transmitted Infections, National Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Microbiology, Faculty of

Medicine and Health, Örebro University, Örebro, Sweden

Correspondence to: M Unemo. Email: magnus.unemo@regionorebrolan.se

Lead Editor: M Unemo. Email: magnus.unemo@regionorebrolan.se

Summary: *Chlamydia trachomatis* infections, which most frequently are asymptomatic, are major public health concerns globally. Compared to the outdated 2010 European *C. trachomatis* guideline, the present 2015 European *C. trachomatis* guideline provides up-to-date guidance regarding broader indications for testing and treatment of *C. trachomatis* infections; clearer recommendation of using NAATs only for diagnosis; advice on (repeated) *C. trachomatis* testing; recommendation of increased testing to reduce the incidence of pelvic inflammatory disease and prevent exposure to infection; and recommendations to identify, verify and report *C. trachomatis* variants.

Improvement of access to testing, test performance, diagnostics, antimicrobial treatment and follow-up of *C. trachomatis* patients are crucial to control its spread. For detailed background, evidence base and discussions, see the background review for the present 2015 European guideline on the management of *Chlamydia trachomatis* infections (Lanjouw E, et al. Int J STD AIDS. 2015).

Keywords: *Chlamydia trachomatis*, chlamydial infection, European guideline, management, diagnosis, treatment, antibiotic, systematic review, meta-analysis

AETIOLOGY, TRANSMISSION AND EPIDEMIOLOGY

Chlamydia trachomatis is an obligate intracellular bacterium that infects over 100 million people each year worldwide by sexual transmission. The majority of persons with anogenital *C. trachomatis* infection are not aware of their infection because it is frequently asymptomatic. Urogenital chlamydial infection can lead to serious adverse outcomes in women, e.g., pelvic inflammatory disease (PID) that can result in tubal factor infertility, ectopic pregnancy and chronic pelvic pain.¹ Urogenital chlamydial infections do not result in any sustained immunity.

Since the 1990's, an increase of urogenital *C. trachomatis* infections has been reported from several countries, e.g., the USA, Canada, United Kingdom (UK) and the Scandinavian countries.²⁻⁴ The prevalence estimates in nationally representative samples of sexually experienced 18–26 year olds in Europe have been relatively similar in women and men (estimated ranging between 3-5.3% and 2.4-7.3%, respectively) and statistically consistent with those in other high income countries.³⁻⁶ The incidence of diagnosed *C. trachomatis* cases reported to the European Centre for Disease Prevention and Control (ECDC) from 26 European Union (EU) and European Economic Area (EEA) countries in 2013 was 182 per 100 000 population (384 555 cases). Nevertheless, there was substantial variation across the EU/EEA countries in the incidence of reported *C. trachomatis* cases, with rates ranging from below 1 to more than 600 cases per 100 000 population.⁴ Comparison between countries is considerably challenged by differences in the surveillance systems, the diagnostic methods used, the access to and amount of testing and screening (general screening programme or opportunistic testing) for

chlamydial infection, and the proportion of underreporting.³ Young age (usually below 25 years of age) and behavioural risk factors such as prior *C. trachomatis* infection, lack of consistent condom use and new or multiple partners per year are the main risk factors for acquisition of *C. trachomatis* infection.⁷

Transmission of *C. trachomatis* usually takes place by direct mucosal contact between two individuals during sexual intercourse or at birth through an infected cervical canal. It is difficult to estimate the risk of sexual transmission. One transmission dynamic mathematical modeling study provided estimates,⁸ based on data from a cross-sectional heterosexual partnership study in clinical attendees.⁹ The model estimated a median transmission probability of around 10% for a single act of vaginal coitus and around 55% over the course of a partnership in a population that has two partnerships in a six month period. Partners of people with *C. trachomatis* infection are very likely to be infected themselves,⁹ so contact notification and subsequent treatment are very important.

C. trachomatis belongs to the genus Chlamydia (phylum Chlamydiae, order Chlamydiales, family Chlamydiaceae) together with *Chlamydia muridarum* and *Chlamydia suis*. Other chlamydiae infecting humans, *Chlamydophila pneumoniae* and *Chlamydophila psittaci*, are currently classified in a separate genus.¹⁰ However, this subdivision of the family into the two genera Chlamydia and Chlamydophila has been discussed controversially during the past decade. Recently, in the light of recent genomic data and in the context of the unique biological properties of these microorganisms it was proposed to classify all the 11 currently recognized Chlamydiaceae species in a single Chlamydia genus.¹¹ Three *C. trachomatis* biovars comprising all 15 classical serovars and several additional serovars and genovars are recognized within the *C. trachomatis* species: the trachoma biovar (serovars A–C), the urogenital biovar (serovars D–K) and the LGV biovar (serovars L1–L3). This guideline only covers the urogenital and LGV biovars of *C. trachomatis*.

CLINICAL FEATURES, COMPLICATIONS AND SEQUELAE

Molano et al. described a *C. trachomatis* clearance (from the point of detection of the infection) in 54% of untreated asymptomatic women at 1 year of follow-up, 82% at 2 years, and 94% at 4 years.¹² In another study examining untreated asymptomatic women, the

clearance rate was similar (44.7%) during the first year.¹³ The long duration of undetected and untreated infection in women can result in that the bacteria cross the cervix and uterus, ascend into the upper genital tract, adhere, and ultimately result in associated complications and sequelae such as PID, ectopic pregnancy, and tubal factor infertility. Appropriate testing of symptomatic and asymptomatic sexually active individuals is necessary to identify and treat the *C. trachomatis* infections.

Urogenital infections

***Symptoms and signs in women:*¹**

- 70-95% asymptomatic
- Mucopurulent cervicitis with or without contact bleeding
- Cervical friability
- Cervical oedema
- Endocervical ulcers
- Urethritis
- Dysuria
- Vaginal discharge
- Postcoital bleeding and intermenstrual bleeding
- Poorly differentiated abdominal pain or lower abdominal pain

***Symptoms and signs suggestive of pelvic inflammatory disease (PID):*¹⁴⁻¹⁶**

- Lower abdominal tenderness and pain – usually bilateral
- Cervical motion tenderness on bimanual vaginal examination
- Adnexal tenderness on bimanual vaginal examination
- Deep dyspareunia – particularly of recent onset
- Abnormal bleeding – intermenstrual bleeding, post coital bleeding and menorrhagia can occur secondary to associated cervicitis and endometritis
- Abnormal vaginal or cervical discharge – as a result of associated cervicitis, endometritis or bacterial vaginosis
- Fever (>38°C) – in moderate to severe PID

Complications in women (see also below):

- PID (endometritis, salpingitis, parametritis, oophoritis, tuboovarian abscess and/or pelvic peritonitis)
- Chronic pelvic pain
- Tubal infertility
- Ectopic pregnancy
- Sexually acquired reactive arthritis (SARA) (<1%)
- Fitz-Hugh-Curtis syndrome (PID and perihepatitis)

Symptoms and signs in men (may be so mild that they are not noticed):^{1,17}

- Usually more than 50% (25-100%) asymptomatic
- Urethritis
- Dysuria
- Urethral discharge
- Epididymitis
- Testicular pain

Complications in men (see also below):

- SARA (<1%)
- Epididymitis, epididymo-orchitis

Rectal and pharyngeal infections

C. trachomatis infections of the rectum are typically asymptomatic, however, the infections may cause anal discharge and anorectal discomfort and also progress to proctocolitis.^{18,19} The rates of rectal chlamydial infection in men who have sex with men (MSM) have been reported to be between 3% and 10.5% in some settings.^{20,21} An 8.4% prevalence of anorectal *C. trachomatis* in women has been reported and almost all (94.5%) of these women also had urogenital *C. trachomatis*.^{22,23} Pharyngeal chlamydial infections are also usually asymptomatic, but symptoms of a mild sore throat can occur.²⁴

The rates of *C. trachomatis* detection in the pharynx in MSM can range from 0.5% to 2.3%.^{21,25,26}

Ocular infections

Ocular infections can result in conjunctivitis in neonates and adults,^{1,12,27-30} and can lead to chronic conjunctivitis and persist for several months if left untreated.

Neonatal infections

Infants born to mothers through an infected birth canal may become colonized and develop conjunctivitis and/or pneumonia.²⁹ The vertical transmission risk for a newborn is 50-75%.³⁰

Lymphogranuloma venereum (LGV)

LGV is an invasive ulcerative disease caused by the serovars L1, L2, or L3 of *C. trachomatis*.³¹ Since 2003, LGV outbreaks have been verified amongst MSM, particularly HIV positive, in several European countries.³²⁻³⁵ Most patients have presented with proctitis^{1,36} or tenesmus, anorectal discharge (often bloody) and discomfort, diarrhoea or altered bowel habits. Due to similarities between LGV and inflammatory bowel disease (IBD), LGV should be considered as a differential diagnosis in patients with proctitis or IBD-related symptoms, especially among HIV-positive men.^{37,38}

It has been shown that approximately 25% of LGV infections can be asymptomatic and form an easily missed undetected reservoir.³⁹ For additional and updated information, see the latest version of the “European Guideline on the Management of Lymphogranuloma Venereum”⁴⁰ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

Complications and sequelae

Women

In older observational treatment studies, up to 30% of women with untreated urogenital *C. trachomatis* infections developed PID.^{41,42} The reported incidence of PID has fallen in several countries over the last decades,^{2,43-46} and the risk of complications has been reported to be lower than previously estimated.⁴⁷⁻⁵¹ Regardless of symptom intensity, the

consequences of PID are severe. Of those with symptomatic PID, about 20% are subsequently infertile; 18-42% will experience debilitating, chronic pelvic pain; and 1-9% will have a life-threatening tubal pregnancy.⁵²⁻⁵⁶ For additional information regarding management of PID, see the latest version of the “European guideline for the management of pelvic inflammatory disease”⁵⁷ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

Men

Complications (e.g., epididymitis, epididymo-orchitis) affect a minority of infected men and rarely result in reproductive health sequelae.⁵⁸ There is no strong evidence base that *C. trachomatis* causes infertility in men. However, *C. trachomatis* has been indirectly associated with male sub-fertility or infertility as a result of a direct effect on sperm production, maturation, motility and viability.⁵⁹⁻⁶¹

Sexually acquired reactive arthritis (SARA)

SARA is a possible consequence of *C. trachomatis* infection (30-40/100 000 infections).^{62,63} SARA is a multisystem disease, which predominantly occurs in human leukocyte antigen B27 positive young males, and includes a combination of urethritis, conjunctivitis and arthritis. The fact that the causative agents are found in the synovial membrane or synovial fluid is indicative of infectious rather than reactive arthritis.⁶⁴ For additional and updated information regarding the management of SARA, see the latest version of the “European guideline for the management of sexually acquired reactive arthritis”⁶⁵ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

INDICATIONS FOR LABORATORY TESTING [Level of evidence IV; Grade C recommendation]

- Risk factor(s) for *C. trachomatis* infection and/or other STI (age <25 years, new sexual contact in the last year, more than one partner in the last year);
- Symptoms or signs of urethritis in men;
- Cervical or vaginal discharge with risk factor for STI;
- Acute epididymo-orchitis in a male aged <40 years or with risk factors for STI;

- Acute pelvic pain and/or symptoms or signs of PID;
- Proctitis/proctocolitis according to risk;
- Purulent conjunctivitis in a neonate or adult;
- Atypical neonatal pneumonia;
- Persons diagnosed with other STI;
- Sexual contact of persons with an STI or PID;
- Termination of pregnancy;
- Any intrauterine interventions or manipulations.

LABORATORY DIAGNOSTICS

Recommended diagnostic assays:

- Nucleic acid amplification tests (NAATs), identifying *C. trachomatis* specific nucleic acid (DNA or RNA) in clinical specimens, are recommended to be used for diagnostics, due to their superior sensitivity, specificity, and speed [I; A].⁶⁶⁻⁷⁷

Only if *C. trachomatis* NAATs are not available or affordable, isolation of *C. trachomatis* in cell culture or identification of *C. trachomatis* by direct fluorescence assays (DFA) can be used for diagnosis of acute *C. trachomatis* infection.

Evidence on the minimum period necessary before testing can be recommended is lacking, although clinical experience suggests that positive NAAT results may be observed within 1–3 days of *C. trachomatis* exposure. Patients should be tested when they first present, however, if there is concern about a sexual exposure within the last two weeks they should have a repeat NAAT test two weeks after the exposure [IV; C].

For adequate performance characteristics of all NAATs and other diagnostic methods, it is crucial to follow precisely the recommendations from the manufacturer concerning collection, transportation, and storage of samples, as well as performance of the specific assay, including internal controls (positive, negative and, if required in NAATs, inhibition controls) and participation in an appropriate national and/or international external quality assessment (EQA) scheme [I; A]. Re-evaluation of random samples by an independent laboratory with an independent test will help reduce false positive and false negative results. Furthermore, all diagnostic laboratories should have a quality assurance system

and strive towards accreditation.

Nucleic acid amplification test (NAAT)

Validated and quality assured NAATs are recommended due to their superior sensitivity, specificity, and speed of diagnosis of both symptomatic and asymptomatic chlamydial infections compared to all other diagnostic techniques [I; A].⁶⁶⁻⁷⁷ Due to the high specificity of the NAATs and risk of losing low positive results in repeated testing, confirmatory testing of positive specimens is not recommended.^{75,78}

Given the rigorous evaluation required before approval of a diagnostic test by the United States of America Food and Drug Administration (FDA), FDA-approved *C. trachomatis* NAATs are primarily recommended for diagnosis. However, internationally there are many additional commercially available or laboratory-developed *C. trachomatis* NAATs in use.⁷⁹⁻⁸¹ If non-FDA approved NAATs are used, regional (e.g. EU) and/or other national validation and regulatory processes should provide safeguards on the quality and performance of the diagnostic NAAT. If validated and approved NAATs cannot be used, it is strongly recommended that the effectiveness of the proposed NAAT for the local settings is validated and quality-assured before use against at least one internationally approved NAAT and subsequently used with appropriate positive, negative, and inhibition controls; participation in appropriate external quality assessment system is strongly recommended as well. Furthermore, laboratories should use NAATs capable of detecting all known *C. trachomatis* variants, e.g. the Swedish new variant (nvCT),⁸²⁻⁸⁴ and to further investigate any unexplained significant increases or declines in the local incidence or positivity rate [I; A].

Point of care tests (POCT)

Rapid point of care tests (POCT) provide a quick and easy test result, and diagnosis and subsequent treatment can be provided at the same visit at clinic or even in remote settings. However, compared to NAATs the sensitivity of the current, mostly immunochromatographic, tests is clearly insufficient.⁸⁵⁻⁸⁹ POCT with increased sensitivity have been developed, and newer POC NAATs are under development.^{86,89-93} Currently available rapid POCT cannot be recommended in Europe, unless other more sensitive

tests are unavailable and results are interpreted with caution.

Specimens

Urogenital specimens

- The recommended first choice specimens for diagnosis of urogenital chlamydial infections with NAATs are first-void urine for men (up to 20 ml sampled >1 h after previous micturition) and (health-care worker- or self-collected) vulvo-vaginal swabs for women [I; A].^{66,68,70,94-107}

Women can also send dry vulvo-vaginal swabs by mail to the laboratory without significant loss of sensitivity.¹⁰⁸ If clinical examination is performed, a cervical specimen can be sampled. However, according to recent data NAATs on a (self-collected) vulvo-vaginal specimen is at least as sensitive. Due to suboptimal sensitivity, first-void urine for women should only be used if other specimens are not available [II; B].^{66,74,95,96}

The use of Pap-smears is not recommended for screening, case finding or other diagnostic purposes, even though several methods to optimize detection in Pap-smears have been published.^{109,110} Penile skin swabs can not currently be recommended.¹¹¹

Pharyngeal, rectal and conjunctival specimens

No manufacturer of *C. trachomatis* NAATs has licensed extra-genital specimens for diagnosis. However, NAATs are the preferred test for all these specimens and some NAATs have been adequately validated for these specimens [IIa; B].¹¹²⁻¹¹⁷ Nevertheless, the sensitivity and specificity can be lower compared to urogenital specimens.^{114,118-121} Confirmation of the positive results with an independent assay may be appropriate [II].^{114,118,119} Collecting pharyngeal and rectal specimens should always be considered in MSM, and in heterosexuals according to risk.¹¹⁷

With the increase (or persisting presence) of rectal LGV infections, especially in MSM,^{34,122,123} it is recommended to identify LGV patients by testing all MSM who report receptive anal sex in the previous 6 months for anorectal *C. trachomatis* infection with a NAAT.¹²⁴ Furthermore, positive rectal specimens from MSM are recommended to be genotyped for LGV, irrespective of the presence of anorectal symptoms [II; B]. For

additional and updated information, see the latest versions of the “European Guideline on the Management of Lymphogranuloma Venereum”⁴⁰ and the “European Guideline on the management of proctitis, proctocolitis and enteritis caused by sexually transmissible pathogens”¹²⁴ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

Semen specimens

There is a good correlation between first-void urine positivity and semen positivity,¹²⁵⁻¹²⁷ first-void urine is easier to obtain, and it is exceedingly difficult to exclude that the *C. trachomatis* detected in semen is not only from the urethra. Accordingly, testing of semen specimens is not recommended [II; B].

Serology

Serology is not recommended for screening or diagnosis of acute uncomplicated anogenital *C. trachomatis* infections. In many patients, only invasive *C. trachomatis* infections will lead to detectable levels of antibodies and antibody levels might also remain positive for years as well as differ between persons. However, when NAATs are not available detection of specific antibodies to *C. trachomatis* may support the diagnosis of invasive disease, such as LGV involving the lymph nodes and neonatal pneumonia (*C. trachomatis* specific IgM) [I; A].^{29,128-133} Serology might also have limited value in the diagnosis of ascending infections¹³⁴⁻¹³⁶ and for infertility work-up.¹³⁷ Specificity has been greatly enhanced by using peptide-based assays, which can be useful in detecting infections in the past, for instance as testing assays in infertility work-up.

INCREASED TESTING (IN STI AND SEXUAL HEALTH CLINICS) AND REPEAT TESTING

- Annual *C. trachomatis* testing in STI or sexual health clinics is recommended for all sexually active young females and males (<25 years of age), and should be considered for MSM [2a, B].
- Repeated testing in 3-6 months should ideally be offered to young females and males (<25 years of age) who test positive for *C. trachomatis* [III; C].^{78,138-144}

Clinical guidelines in many countries recommend annual *C. trachomatis* screening for all sexually active young (<25 years of age) women^{78,138,145} and extend to young men in some countries.^{146,147} However, mathematical modeling studies have suggested that to achieve population level impact on *C. trachomatis* transmission, screening programmes need to achieve very high testing coverage and also high rates of partner notification, including treatment, and repeated testing for reinfection after treatment.¹⁴⁸⁻¹⁵¹ The main rationale for current *C. trachomatis* screening or opportunistic testing is, however, that early detection and treatment will prevent or interrupt reproductive tract morbidity, particularly in women. The reduction in the incidence of PID in randomised clinical trials (RCTs) comparing women receiving chlamydia screening interventions with control groups^{50,152-154} suggests that there must be an interval after endocervical infection during which screening can prevent or limit clinical PID.

Mathematical modelling studies in the USA have shown that repeat infection rates peak at 2-5 months after the initial infection,¹⁵⁵ supporting the US CDC recommendation that any person diagnosed as having *C. trachomatis* infection should be retested within 3-12 months of treatment [III; C].^{78,139,141,142,156} The English National Chlamydia Screening Programme (NCSP) guidelines recommend retesting annually or on change of sexual partner for all sexually active <25 years old and, in 2013, began to include recommendations of retesting around 3 months after a positive test.¹⁵⁷⁻¹⁵⁹

MANAGEMENT OF PATIENTS

Information, explanation and advice for the patient

- Patients with positive *C. trachomatis* test should be advised to abstain from sexual contact for seven days after they and their partners have completed treatment and their symptoms have resolved [IV; C];
- Patients with positive *C. trachomatis* test (and their sexual contacts) should be given information about their infection, including details about transmission, prevention and complications. It is recommended that both verbal and written information be provided [IV; C];
- Information for patients is available on the IUSTI Europe website for guidelines (<http://www.iusti.org/regions/Europe/euroguidelines.htm>);

- Patients with positive *C. trachomatis* test should be considered for and encouraged testing for other STIs, including gonorrhoea, syphilis and HIV [IV; C].

Indications for therapy [IV; C]

- Identification of *C. trachomatis* or *C. trachomatis* specific nucleic acid (DNA or RNA) in a clinical specimen;
- On epidemiological grounds, if a recent sexual contact has confirmed chlamydial infection (ideally NAAT specimen should also be sampled for testing);
- On epidemiological grounds, mother of neonate with confirmed chlamydial infection (ideally NAAT specimen should also be sampled for testing);
- On epidemiological grounds, treatment can be considered following sexual assault (ideally NAAT specimen should also be sampled for testing);
- On demonstration of a purulent urethral discharge in men or mucopurulent cervicitis in women when diagnostic tests are not available and after specimen collection for laboratory testing. In this circumstance, dependent on local gonorrhoea incidence combined treatment for chlamydial infection and gonorrhoea should be considered.

Therapy

There is still no evidence of any stable, homotypic genetic and phenotypic resistance to any therapeutic antimicrobial in clinical *C. trachomatis* strains that affects the treatment in humans.¹⁶⁰⁻¹⁶⁴ Nevertheless, in recent years concerns have been raised over clinical failures in *C. trachomatis* infected patients treated particularly with azithromycin 1 g single oral dose.¹⁶⁵⁻¹⁶⁸ Some of these treatment failures can be explained by reinfection, poor compliance or tolerance of treatment, or detection of nucleic acid from non-viable *C. trachomatis* due to test-of-cure (TOC) performed too early.^{168,169} However, the reasons for the remaining treatment failures remain unclear,¹⁷⁰ though a suboptimal duration of exposure to azithromycin after the 1 g single dose and a low-level absorption of azithromycin in some patients may be involved.¹⁶¹ Some earlier work suggested that a prolonged course of azithromycin is likely to be sufficiently bactericidal to *C. trachomatis*¹⁷¹ and in respiratory tract infections azithromycin 1.5 g administered over 3

to 5 days has been reported to achieve therapeutic levels in target tissues for up to 10 days.^{172,173} It has also been suggested that use of azithromycin 1 g stat increases the risk of inducing macrolide antimicrobial resistance in *Mycoplasma genitalium*.¹⁷⁴⁻¹⁷⁷ Accordingly, when a concomitant *M. genitalium* infection has been verified or can be suspected, treatment with azithromycin 500 mg day 1, followed by azithromycin 250 mg once a day for 4 days¹⁷⁴⁻¹⁷⁸ should be considered [III; C]. Recently, it was shown that this five days azithromycin treatment regimen can effectively eradicate also *C. trachomatis*, that is, the eradication rate for *C. trachomatis* was 98.8% (79 of 80 patients infected with both *M. genitalium* and *C. trachomatis*).¹⁷⁸ Nevertheless, appropriate RCTs using the five days azithromycin regimen to examine the eradication frequency of both *M. genitalium* and *C. trachomatis* are crucial, and when using this regimen TOC for both bacteria should be considered.

Recommended treatment for uncomplicated urogenital *C. trachomatis* infections

First-line [Ia; A]:¹⁷⁹

- Doxycycline 100 mg twice a day for 7 days (oral; contraindicated in pregnancy)
Or
- Azithromycin 1 g stat (oral)

Second-line [II; B] (TOC should be subsequently performed):¹⁸⁰⁻¹⁸⁴

- Erythromycin 500 mg twice a day for 7 days (oral)
Or
- Levofloxacin 500 mg once a day for 7 days (oral; contraindicated in pregnancy)
Or
- Ofloxacin 200 mg twice a day for 7 days (oral; contraindicated in pregnancy)

Third-line [II; B] (TOC should be subsequently performed):¹⁸⁵⁻¹⁸⁷

- Josamycin 500 mg three times or 1000 mg twice a day for 7 days (oral)

A meta-analysis of 23 RCTs comparing azithromycin 1 g stat and doxycycline 100 mg twice daily for seven days for urogenital chlamydial infections showed a statistical

superiority in favour of doxycycline.¹⁷⁹ However, the difference in efficacy was small at 1.5%-2.6% (approximately 97% versus 95% efficacy). This difference is not clinically significant and both azithromycin and doxycycline can be recommended as first-line regimens [Ia; A]. When a concomitant *M. genitalium* infection has been verified or is suspected, treatment with azithromycin 500 mg day 1, followed by azithromycin 250 mg once a day for 4 days,^{174,175,177,178} should be considered [III; C].

HIV positive patients should be treated in the same way as HIV negative ones [IV; C].

Recommended treatment for uncomplicated *C. trachomatis* non-LGV rectal and pharyngeal infections

- Doxycycline 100 mg twice a day for 7 days (oral) [I; A] (preferred if rectal infection)
Or alternatively:
- Azithromycin 1 g stat (oral) [IIa; A] (if rectal infection, a TOC should be subsequently performed)

For rectal infections, four non-randomised clinical studies have been published which showed higher efficacy rates for doxycycline (98.8-100%) than for azithromycin (74-87%) at this anatomical site.¹⁸⁸⁻¹⁹¹ Conversely, another study (also non-randomised) showed azithromycin to be 94% effective; a similar rate to that for urogenital infections.¹⁹² However, all these five studies had important limitations. Because of the low quality of the data supporting the superiority of doxycycline over azithromycin for treating rectal infections both regimens continue to be recommended as first-line. However, pending further studies and ideally double-blinded, placebo controlled RCTs, if rectal chlamydia is treated with azithromycin then a TOC should be performed [IIa, A].

Recommended treatment for uncomplicated LGV infections

For detailed and updated information regarding the management of LGV, including adjunctive therapy, see the latest versions of the “European Guideline on the Management of Lymphogranuloma Venereum”⁴⁰ and the “European Guideline on the

management of proctitis, proctocolitis and enteritis caused by sexually transmissible pathogens”¹²⁴ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

Recommended treatment for uncomplicated urogenital *C. trachomatis* infection in pregnancy and during breast feeding (TOC should be subsequently performed)

First-line [I; A].^{78,141,193-196}

- Azithromycin 1 g stat (oral)

Second line:¹⁹⁴

- Amoxicillin 500 mg 3 times a day for 7 days (oral)
- Or
- Erythromycin 500 mg 4 times a day for 7 days (oral)

Third line:¹⁸⁴

- Josamycin 500 mg three times or 1000 mg twice a day for 7 days (oral)

Azithromycin has been considered safe and effective according to clinical experience and in some studies,^{194,196} and azithromycin is also recommended by the WHO in pregnancy.

Pelvic inflammatory disease (PID)

For detailed and updated information, see the latest version of the “European guideline for the management of pelvic inflammatory disease”⁵⁷ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

***C. trachomatis* conjunctivitis**

C. trachomatis infection should be included in the differential diagnosis in sexually active individuals presenting with acute or chronic follicular conjunctivitis.^{141,197,198} *C. trachomatis* conjunctivitis should prompt for testing for genital *C. trachomatis* infection and other STIs such as HIV, gonorrhoea, and syphilis.

- Azithromycin 1 g stat (oral)¹⁹⁹ [IIa; A]

Or alternatively:

- Doxycycline 100 mg twice a day for 7 days (oral) [I; A]

CONTACT NOTIFICATION AND MANAGEMENT OF SEXUAL CONTACT(S)

- Contact notification should be performed and documented by appropriately trained professionals at the time of diagnosis to improve outcome [Ib; A];
- Sexual contacts should be contacted and offered (and encouraged) testing together with treatment and, if infected, counseling (as index patient) for chlamydial infection and other STIs [IV; C];^{78,160,200-203}
- All sexual contacts within the preceding 6 months of onset of symptoms or diagnosis should ideally be evaluated, tested and treated [IV; C];^{78,138,160,202,204}
- If sexual contact(s) does not attend for evaluation and testing, epidemiological treatment should ideally be offered [IV; C].^{78,160,202}

Where no regulatory barriers exist, expedited partner therapy or patient-delivered partner therapy can be an efficient way to treat partners and reduce the infection rates.²⁰⁴⁻²¹¹ However, patient delivered therapy should only be implemented as part of a larger system of contact notification strategies.

For further information, see the latest version of the “European guidelines for the management of partners of persons with sexually transmitted infection”²⁰² (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

FOLLOW-UP AND TEST-OF-CURE (TOC)

- A TOC is not recommended to be routinely performed in patients treated with recommended first-line regimens but should be performed in pregnancy, in complicated infections, if symptoms persist, if second-line regimens have been used, and if non-compliance to therapy or re-exposure of infection is suspected [IV; C]. It should also be considered in extra-genital infections,¹⁸⁸ particularly when azithromycin 1 g stat has been administered for treatment of rectal infections.

When indicated, TOC using NAATs should be performed 4 weeks after completion of therapy [III; B];^{78,140,160,188,213,214}

- Repeated testing, to detect reinfection, in 3-6 months should ideally be offered to young females and males (<25 years of age) who test positive for *C. trachomatis* [III; C].^{78,138-144,146,215}

Repeated testing for TOC of asymptomatic MSM with rectal chlamydia after treatment for uncomplicated chlamydial infection (azithromycin 1 g single oral dose or doxycycline 100 mg, 7 days) should be considered to ensure that any LGV infection is not missed.

For further information, see the latest version of the “European guidelines for the management of partners of persons with sexually transmitted infection”²⁰² and the “European Guideline on the Management of Lymphogranuloma Venereum”⁴⁰ (<http://www.iusti.org/regions/europe/euroguidelines.htm#Current>).

NOTIFICATION OF *C. TRACHOMATIS* CASES

C. trachomatis infections should be notified to local, regional and national authorities as mandated by statute. The ECDC is responsible for the EU/EEA-wide surveillance of communicable diseases including *C. trachomatis* infections.

ACKNOWLEDGEMENTS

The authors are grateful to Wichor Bramer, biomedical information specialist of the Medical Library of the Erasmus MC for technical assistance with the literature search. We are also grateful for valuable input on this guideline to Norbert Brockmeyer, Matilda Bylaite-Bucinskiene, Kevin Dunbar, ECDC Chlamydia Control Group (Berit Andersen, Jan van Bergen, Bethan Davies, Nicola Low, Shelagh Redmond, Anneli Uuskula, Helen Ward, Sarah Woodhall), Mikhail Gomberg, Vesta Kucinskiene, Otilia Mårdh, Thomas Meyer, Harald Moi, Mirja Puolakkainen, Jonathan Ross, Agnieszka Serwin, Elena Shipitsyna, Gianfranco Spiteri, and Andrew Winter.

Conflicts of interest

None declared.

Funding sources

None declared.

Proposed review date

June 2018

Composition of the IUSTI European STI Guidelines Editorial Board

The composition of the current IUSTI European STI Guidelines Editorial Board can be found at: http://www.iusti.org/regions/Europe/pdf/2014/Editorial_Board2014.pdf

Contributing organisations

A list of contributing organisations can be found at:
www.iusti.org/regions/Europe/euroguidelines.htm

Search strategy

This guideline represents an updated and substantially revised version of the “2010 European guideline for the management of *Chlamydia trachomatis* infections”.¹³⁹ The present guideline was produced according to the protocol for production and revision of European STI guidelines, which has been written and approved by the IUSTI European STI Guidelines Editorial Board, and an evidence-based approach.

Evidence was provided by a thorough and systemic review of the literature in the databases Embase.com, Medline (OvidSP), PubMed (articles supplied by publishers not yet indexed in Medline), Web-of-science, Scopus, Cinahl, Cochrane DARE, and Google Scholar. Searches were performed on 18th of March 2014 and on 28th of November 2014, and the following broad search terms were used: *Chlamydia trachomatis*, systematic review, meta-analysis, guideline, protocol. After deduplication, 3041 articles published from 1992 to 2014 were screened on title/abstract, which resulted in 824 references considered for inclusion when the guideline was written. Relevant STI guidelines produced by the US Centers for Disease Control and Prevention (www.cdc.gov/std/treatment/2015/) and the British Association for Sexual Health and HIV (www.bashh.org) were also reviewed.

Levels of evidence and grading of recommendations

Tables of levels of evidence and grading of recommendations that were used in the present guideline can be found at:

http://www.iusti.org/regions/Europe/pdf/2013/Levels_of_Evidence.pdf

Qualifying statement

Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual patient circumstances and available resources. All possible care has been undertaken to ensure publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

References

1. Stamm WE. *Chlamydia trachomatis* infections of the adults. In: Holmes KK, Sparling PF, et al., eds. *Sexually Transmitted Diseases*. 4th edn. New York, NY: McGraw Hill, 2008. Chapter 32
2. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2010. 2011. <http://www.cdc.gov/std/stats11/surv2011.pdf> (last checked 15 August 2015)
3. European Centre for Disease Prevention and Control. Chlamydia control in Europe: literature review. 2014. <http://www.ecdc.europa.eu/en/publications/Publications/chlamydia-control-europe.pdf> (last checked 15 August 2015)
4. European Centre for Disease Prevention and Control. Sexually transmitted infections in Europe 2013. 2015. <http://www.ecdc.europa.eu/en/publications/Publications/sexually-transmitted-infections-europe-surveillance-report-2013.pdf> (last checked 15 August 2015)
5. Dielissen PW, Teunissen DAM, Lagro-Janssen ALM. Chlamydia prevalence in the general population: Is there a sex difference? A systematic review. *BMC Infect Dis* 2013;**13**
6. Redmond SM, Alexander-Kisslig K, Woodhall SC, et al. Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis. *PLoS One* 2015;**10**(1):e0115753.

7. Mitchell PM, White LF, Rahimi LM, Jenkins D, Schechter-Perkins EM. Predictors of gonorrhea and chlamydia in emergency department patients. *Ann Emerg Med* 2012;**60**:S119
8. Althaus CL, Heijne JC, Low N. Towards more robust estimates of the transmissibility of *Chlamydia trachomatis*. *Sex Transm Dis* 2012;**39**:402-4
9. Quinn TC, Gaydos C, Shepherd M, *et al.* Epidemiologic and microbiologic correlates of *Chlamydia trachomatis* infection in sexual partnerships. *JAMA* 1996;**276**:1737-42
10. Everett KD, Bush RM, Andersen AA. Emended description of the order Chlamydiales, proposal of Parachlamydiaceae fam. nov. and Simkaniaceae fam. nov., each containing one monotypic genus, revised taxonomy of the family Chlamydiaceae, including a new genus and five new species, and standards for the identification of organisms. *Int J Syst Bacteriol* 1999;**49 Pt 2**:415-40
11. Sachse K, Bavoil PM, Kaltenboeck B, Stephens RS, Kuo CC, Rosselló-Móra R, Horn M. Emendation of the family Chlamydiaceae: proposal of a single genus, Chlamydia, to include all currently recognized species. *Syst Appl Microbiol* 2015;**38**:99-103
12. Molano M, Meijer CJ, Weiderpass E, *et al.* The natural course of *Chlamydia trachomatis* infection in asymptomatic Colombian women: a 5-year follow-up study. *J Infect Dis* 2005;**191**:907-16
13. Morre SA, van den Brule AJ, Rozendaal L, *et al.* The natural course of asymptomatic *Chlamydia trachomatis* infections: 45% clearance and no development of clinical PID after one-year follow-up. *Int J STD AIDS* 2002;**13 Suppl 2**:12-8
14. Bevan CD, Johal BJ, Mumtaz G, Ridgway GL, Siddle NC. Clinical, laparoscopic and microbiological findings in acute salpingitis: report on a United Kingdom cohort. *Br J Obstet Gynaecol* 1995;**102**:407-14
15. Morcos R, Frost N, Hnat M, Petrunak A, Caldito G. Laparoscopic versus clinical diagnosis of acute pelvic inflammatory disease. *J Reprod Med* 1993;**38**:53-6
16. *Recommendations arising from the 31st Study Group: The Prevention of Pelvic Infection*. London; RCOG Press. 1996, pp.267–70.
17. Kent CK, Chaw JK, Wong W, *et al.* Prevalence of rectal, urethral, and pharyngeal chlamydia and gonorrhea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. *Clin Infect Dis* 2005;**41**:67-74
18. Boisvert JF, Koutsky LA, Suchland RJ, Stamm WE. Clinical features of *Chlamydia trachomatis* rectal infection by serovar among homosexually active men. *Sex Transm Dis* 1999;**26**:392-8
19. Quinn TC, Goodell SE, Mkrtychian E, *et al.* *Chlamydia trachomatis* proctitis. *New Engl J Med* 1981;**305**:195-200
20. Marcus JL, Bernstein KT, Stephens SC, *et al.* Sentinel surveillance of rectal chlamydia and gonorrhea among males--San Francisco, 2005-2008. *Sex Transm Dis* 2010;**37**:59-61
21. Pinsky L, Chiarilli DB, Klausner JD, *et al.* Rates of asymptomatic nonurethral gonorrhea and chlamydia in a population of university men who have sex with men. *J Am Coll Health* 2012;**60**:481-4
22. Van Liere GAFS, Hoebe CJPA, Dukers-Muijters NHTM. Evaluation of the anatomical site distribution of chlamydia and gonorrhoea in men who have sex with men

- and in high-risk women by routine testing: Cross-sectional study revealing missed opportunities for treatment strategies. *Sex Transm Infect* 2014;**90**:58-60
23. van Liere GA, Hoebe CJ, Wolffs PF, Dukers-Muijers NH. High co-occurrence of anorectal chlamydia with urogenital chlamydia in women visiting an STI clinic revealed by routine universal testing in an observational study; a recommendation towards a better anorectal chlamydia control in women. *BMC Infect Dis* 2014;**14**:274
 24. van Rooijen MS, Schim van der Loeff MF, Morre SA, van Dam AP, Speksnijder AG, de Vries HJ. Spontaneous pharyngeal *Chlamydia trachomatis* RNA clearance. A cross-sectional study followed by a cohort study of untreated STI clinic patients in Amsterdam, The Netherlands. *Sex Transm Infect* 2014 Sep 18. pii: sextrans-2014-051633. doi: 10.1136/sextrans-2014-051633. [Epub ahead of print]
 25. Park J, Marcus JL, Pandori M, Snell A, Philip SS, Bernstein KT. Sentinel surveillance for pharyngeal chlamydia and gonorrhea among men who have sex with men--San Francisco, 2010. *Sex Transm Dis* 2012;**39**:482-4
 26. Barbee LA, Dombrowski JC, Kerani R, Golden MR. Effect of nucleic acid amplification testing on detection of extragenital gonorrhea and chlamydial infections in men who have sex with men sexually transmitted disease clinic patients. *Sex Transm Dis* 2014;**41**:168-72
 27. Jones BR, Al-Hussaini MK, Dunlop EM. Infection of the eye and the genital tract by Tric agent. *Br J Vener Dis* 1964;**40**:19-24
 28. Hu VH, Harding-Esch EM, Burton MJ, Bailey RL, Kadimpeul J, Mabey DCW. Epidemiology and control of trachoma: Systematic review. *Trop Med Int Health* 2010;**15**:673-91.
 29. Darville T. *Chlamydia trachomatis* infections in neonates and young children. *Semin Pediatr Infect Dis* 2005;**16**:235-44
 30. Hammerschlag MR. Chlamydial infections. *Journal Pediatr* 1989;**114**:727-34
 31. Martin-Iguacel R, Llibre JM, Nielsen H, et al. Lymphogranuloma venereum proctocolitis: a silent endemic disease in men who have sex with men in industrialised countries. *Eur J Clin Microbiol Infect Dis* 2010;**29**:917-25
 32. Nieuwenhuis RF, Ossewaarde JM, Götz HM, et al. Resurgence of lymphogranuloma venereum in Western Europe: an outbreak of *Chlamydia trachomatis* serovar L2 proctitis in The Netherlands among men who have with men. *Clin Infect Dis* 2004;**39**:996-1003
 33. Ahdoot A, Kotler DP, Suh JS, Kutler C, Flamholz R. Lymphogranuloma venereum in human immunodeficiency virus-infected individuals in New York City. *J Clin Gastroenterol* 2006;**40**:385-90
 34. Jebbari H, Alexander S, Ward H, et al. Update on lymphogranuloma venereum in the United Kingdom. *Sex Transm Infect* 2007;**83**:324-6
 35. van de Laar MJ. The emergence of LGV in western Europe: what do we know, what can we do? *Euro Surveill* 2006;**11**:146-8
 36. White JA. Manifestations and management of lymphogranuloma venereum. *Curr Opin Infect Dis* 2009;**22**:57-66
 37. Hoie S, Knudsen LS, Gerstoft J. Lymphogranuloma venereum proctitis: a differential diagnose to inflammatory bowel disease. *Scand J Gastroenterol* 2011;**46**:503-10

38. Lanjouw E, van Daele PL, Raes MP, van der Meijden WI. Consecutively acquired sexually transmitted infections mimicking Crohn's disease. *Am J Gastroenterol* 2009;**104**:532-3
39. de Vrieze NH, van Rooijen M, Schim van der Loeff MF, de Vries HJ. Anorectal and inguinal lymphogranuloma venereum among men who have sex with men in Amsterdam, The Netherlands: trends over time, symptomatology and concurrent infections. *Sex Transm Infect* 2013;**89**:548-52
40. de Vries HJ, Zingoni A, Kreuter A, Moi H, White JA. 2013 European guideline on the management of lymphogranuloma venereum. *J Eur Acad Dermatol Venereol* 2015;**29**:1-6
41. Stamm WE, Guinan ME, Johnson C, Starcher T, Holmes KK, McCormack WM. Effect of treatment regimens for *Neisseria gonorrhoeae* on simultaneous infection with *Chlamydia trachomatis*. *New Engl J Med* 1984;**310**:545-9
42. Rees E. The treatment of pelvic inflammatory disease. *Am J Obstet Gynecol* 1980;**138**:1042-7
43. Rekart ML, Gilbert M, Meza R, *et al*. Chlamydia public health programs and the epidemiology of pelvic inflammatory disease and ectopic pregnancy. *J Infect Dis* 2013;**207**:30-8
44. Bender N, Herrmann B, Andersen B, *et al*. Chlamydia infection, pelvic inflammatory disease, ectopic pregnancy and infertility: cross-national study. *Sex Transm Infect* 2011;**87**:601-8
45. French CE, Hughes G, Nicholson A, *et al*. Estimation of the rate of pelvic inflammatory disease diagnoses: trends in England, 2000-2008. *Sex Transm Dis* 2011;**38**:158-62
46. Bjartling C, Osseer S, Persson K. The frequency of salpingitis and ectopic pregnancy as epidemiologic markers of *Chlamydia trachomatis*. *Acta Obstet Gynecol Scand* 2000;**79**:123-8
47. Adams EJ, Turner KME, Edmunds WJ. The cost effectiveness of opportunistic chlamydia screening in England. *Sex Transm Infect* 2007;**83**:267-74;discussion 274-5
48. van Valkengoed IG, Morre SA, van den Brule AJ, Meijer CJ, Bouter LM, Boeke AJ. Overestimation of complication rates in evaluations of *Chlamydia trachomatis* screening programmes--implications for cost-effectiveness analyses. *Int J Epidemiol* 2004;**33**:416-25
49. Land JA, Van Bergen JEAM, Morre SA, Postma MJ. Epidemiology of *Chlamydia trachomatis* infection in women and the cost-effectiveness of screening. *Hum Reprod Update* 2010;**16**:189-204
50. Oakeshott P, Kerry S, Aghaizu A. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *BMJ* 2010;**340**:c1642
51. Kavanagh K, Wallace LA, Robertson C, Wilson P, Scoular A. Estimation of the risk of tubal factor infertility associated with genital chlamydial infection in women: a statistical modelling study. *Int J Epidemiol* 2013;**42**:493-503
52. Trent M, Bass D, Ness RB, Haggerty C. Recurrent PID, subsequent STI, and reproductive health outcomes: findings from the PID evaluation and clinical health (PEACH) study. *Sex Transm Dis* 2011;**38**:879-81

53. Westrom L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. *Sex Transm Dis* 1992;**19**:185-92
54. Chow JM, Yonekura ML, Richwald GA, Greenland S, Sweet RL, Schachter J. The association between *Chlamydia trachomatis* and ectopic pregnancy. A matched-pair, case-control study. *JAMA* 1990;**263**:3164-7
55. Miettinen A, Heinonen PK, Teisala K, Hakkarainen K, Punnonen R. Serologic evidence for the role of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in the etiology of tubal factor infertility and ectopic pregnancy. *Sex Transm Dis* 1990;**17**:10-4
56. Ness RB, Trautmann G, Richter HE, *et al.* Effectiveness of treatment strategies of some women with pelvic inflammatory disease: a randomized trial. *Obstet Gynecol* 2005;**106**:573-80
57. Ross J, Judlin P, Jensen J. 2012 European guideline for the management of pelvic inflammatory disease. *Int J STD AIDS* 2014;**25**:1-7
58. US Centers for Disease Control and Prevention. Male chlamydia screening consultation Atlanta, Georgia March 28 – 29, 2006. 2007. <http://www.cdc.gov/std/chlamydia/chlamydiascreening-males.pdf> (last checked 15 August 2015)
59. Bezold G, Politch JA, Kiviat NB, Kuypers JM, Wolff H, Anderson DJ. Prevalence of sexually transmissible pathogens in semen from asymptomatic male infertility patients with and without leukocytospermia. *Fertil Steril* 2007;**87**:1087-97
60. Greendale GA, Haas ST, Holbrook K, Walsh B, Schachter J, Phillips RS. The relationship of *Chlamydia trachomatis* infection and male infertility. *Am J Public Health* 1993;**83**:996-1001
61. Joki-Korpela P, Sahrakorpi N, Halttunen M, Surcel HM, Paavonen J, Tiitinen A. The role of *Chlamydia trachomatis* infection in male infertility. *Fertil Steril* 2009;**91**:1448-50
62. Carter JD, Hudson AP. The evolving story of Chlamydia-induced reactive arthritis. *Curr Opin Rheumatol* 2010;**22**:424-30
63. Taylor-Robinson D, Keat A. Observations on *Chlamydia trachomatis* and other microbes in reactive arthritis. *Int J STD AIDS*. 2015;**26**:139-44
64. Bojovic J, Strelac N, Pavlica L. Reiter's syndrome--disease of young men--analysis of 312 patients. *Med Pregl* 2014;**67**:222-30
65. Carlin EM, Ziza JM, Keat A, Janier M. 2014 European Guideline on the management of sexually acquired reactive arthritis. *Int J STD AIDS* 2014;**25**:901-12
66. Cook RL, Hutchison SL, Ostergaard L, Braithwaite RS, Ness RB. Systematic review: noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Ann Intern Med* 2005;**142**:914-25
67. Watson EJ, Templeton A, Russell I, *et al.* The accuracy and efficacy of screening tests for *Chlamydia trachomatis*: a systematic review. *J Med Microbiol* 2002;**51**:1021-31
68. Skidmore S, Horner P, Mallinson H. Testing specimens for *Chlamydia trachomatis*. *Sex Transm Infect* 2006;**82**:272-5

69. Skidmore S, Horner P, Herring A, *et al.* Vulvovaginal-swab or first-catch urine specimen to detect *Chlamydia trachomatis* in women in a community setting? *J Clin Microbiol* 2006;**44**:4389-94
70. Choe HS, Lee DS, Lee SJ, *et al.* Performance of Anyplex II multiplex real-time PCR for the diagnosis of seven sexually transmitted infections: comparison with currently available methods. *Int J Infect Dis* 2013;**17**:e1134-40
71. Gimenes F, Medina FS, Abreu AL, *et al.* Sensitive simultaneous detection of seven sexually transmitted agents in semen by multiplex-PCR and of HPV by single PCR. *PLoS One* 2014;**9**:e98862
72. Kumamoto Y, Matsumoto T, Fujisawa M, Arakawa S. Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in urogenital and oral specimens using the Cobas(R) 4800, APTIMA Combo 2(R) TMA, and ProbeTec ET SDA assays. *Eur J Microbiol Immunol (Bp)* 2012;**2**:121-7
72. Le Roy C, Le Hen I, Clerc M, *et al.* The first performance report for the Bio-Rad Dx CT/NG/MG assay for simultaneous detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* in urogenital samples. *J Microbiol Methods* 2012;**89**:193-7
74. Mushanski LM, Brandt K, Coffin N, Levett PN, Horsman GB, Rank EL. Comparison of the BD Viper System with XTR Technology to the Gen-Probe APTIMA COMBO 2 assay using the TIGRIS DTS system for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in urine specimens. *Sex Transm Dis* 2012;**39**:514-7
75. Schachter J, Chow JM, Howard H, Bolan G, Moncada J. Detection of *Chlamydia trachomatis* by nucleic acid amplification testing: our evaluation suggests that CDC-recommended approaches for confirmatory testing are ill-advised. *J Clin Microbiol* 2006;**44**:2512-7
76. van der Helm JJ, Hoebe CJ, van Rooijen MS, *et al.* High performance and acceptability of self-collected rectal swabs for diagnosis of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in men who have sex with men and women. *Sex Transm Dis* 2009;**36**:493-7
77. Cheng A, Qian QF, Kirby JE. Evaluation of the Abbott RealTime CT/NG assay in comparison to the Roche Cobas Amplicor CT/NG assay. *J Clin Microbiol* 2011;**49**:1294-300
78. Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015;**64**(RR-03):1-137
79. Unemo M, Rossouw A, James V, Jenkins C. Can the Swedish new variant of *Chlamydia trachomatis* (nvCT) be detected by UK NEQAS participants from seventeen European countries and five additional countries/regions in 2009? *Euro Surveill* 2009;**14**
80. Reischl U, Straube E, Unemo M. The Swedish new variant of *Chlamydia trachomatis* (nvCT) remains undetected by many European laboratories as revealed in the recent PCR/NAT ring trial organised by INSTAND e.V., Germany. *Euro Surveill* 2009;**14**
81. Shipitsyna E, Zolotoverkhaya E, Agne-Stadling I, *et al.* First evaluation of six nucleic acid amplification tests widely used in the diagnosis of *Chlamydia trachomatis* in Russia. *J Eur Acad Dermatol Venereol* 2009;**23**:268-76

82. Ripa T, Nilsson P. A variant of *Chlamydia trachomatis* with deletion in cryptic plasmid: implications for use of PCR diagnostic tests. *Euro Surveill* 2006;**11**:E061109 2
83. Unemo M, Seth-Smith HM, Cutcliffe LT, *et al.* The Swedish new variant of *Chlamydia trachomatis*: genome sequence, morphology, cell tropism and phenotypic characterization. *Microbiology* 2010;**156**:1394-404
84. Unemo M, Clarke IN. The Swedish new variant of *Chlamydia trachomatis*. *Curr Opin Infect Dis* 2011;**24**:62-9
85. Van Dommelen L, Van Tiel FH, Ouburg S, *et al.* Alarmingly poor performance in *Chlamydia trachomatis* point-of-care testing. *Clin Microbiol Infect* 2010;**16**:S560
86. van der Helm JJ, Sabajo LO, Grunberg AW, Morre SA, Speksnijder AG, de Vries HJ. Point-of-care test for detection of urogenital chlamydia in women shows low sensitivity. A performance evaluation study in two clinics in Suriname. *PLoS One* 2012;**7**:e32122
87. Libbus MK. Chlamydia Rapid Test was moderately accurate for diagnosing Chlamydia infection in women. *Evid Based Nurs* 2008;**11**:89
88. Hislop J, Quayyum Z, Flett G, Boachie C, Fraser C, Mowatt G. Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men Review. *Health Technol Assess* 2010;**14**:1-97,iii-iv
89. Skidmore S. Poorly performing point-of-care tests for chlamydia: What can be done? *Sex Transm Infect* 2010;**86**:330
90. Mahilum-Tapay L, Laitila V, Wawrzyniak JJ, *et al.* New point of care Chlamydia Rapid Test--bridging the gap between diagnosis and treatment: performance evaluation study. *BMJ* 2007;**335**:1190-4
91. Nadala EC, Goh BT, Magbanua JP, *et al.* Performance evaluation of a new rapid urine test for chlamydia in men: prospective cohort study. *BMJ* 2009;**339**:b2655
92. Huang W, Gaydos CA, Barnes MR, Jett-Goheen M, Blake DR. Comparative effectiveness of a rapid point-of-care test for detection of *Chlamydia trachomatis* among women in a clinical setting. *Sex Transm Infect* 2013;**89**:108-14
93. Gaydos CA, Van Der Pol B, Jett-Goheen M, *et al.* Performance of the Cepheid CT/NG Xpert Rapid PCR test for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *J Clin Microbiol* 2013;**51**:1666-72
94. Wisniewski CA, White JA, Michel CE, *et al.* Optimal method of collection of first-void urine for diagnosis of *Chlamydia trachomatis* infection in men. *J Clin Microbiol* 2008;**46**:1466-9
95. Mangin D, Murdoch D, Wells JE, *et al.* *Chlamydia trachomatis* testing sensitivity in midstream compared with first-void urine specimens. *Ann Fam Med* 2012;**10**:50-3
96. Michel CE, Sonnex C, Carne CA, *et al.* *Chlamydia trachomatis* load at matched anatomic sites: implications for screening strategies. *J Clin Microbiol* 2007;**45**:1395-402
97. Li J, Jang D, Gilchrist J, *et al.* Comparison of flocced and aptima swabs and two specimen transport media in the Aptima Combo 2 assay. *J Clin Microbiol* 2014;**52**:3808-9
98. Bialasiewicz S, Whiley DM, Buhner-Skinner M, *et al.* A novel gel-based method for self-collection and ambient temperature postal transport of urine for PCR detection of *Chlamydia trachomatis*. *Sex Transm Infect* 2009;**85**:102-5

99. Graseck AS, Shih SL, Peipert JF. Home versus clinic-based specimen collection for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Expert Rev Anti Infect Ther* 2011;**9**:183-94
100. Sexton ME, Baker JJ, Nakagawa K, *et al*. How reliable is self-testing for gonorrhea and chlamydia among men who have sex with men? *J Fam Pract* 2013;**62**:70-8
101. Sexton M, Baker J, Perkins R, *et al*. Self-administered *Neisseria gonorrhoeae* and *Chlamydia trachomatis* testing in the pharynx and rectum among men who have sex with men in Washington, DC. *Sex Transm Infect* 2011;**87**:A74-A5
102. Alexander S, Ison C, Parry J, *et al*. Self-taken pharyngeal and rectal swabs are appropriate for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in asymptomatic men who have sex with men. *Sex Transm Infect* 2008;**84**:488-92
103. Holland-Hall CM, Wiesenfeld HC, Murray PJ. Self-collected vaginal swabs for the detection of multiple sexually transmitted infections in adolescent girls. *J Pediatr Adolesc Gynecol* 2002;**15**:307-13
104. Fang J, Husman C, DeSilva L, Chang R, Peralta L. Evaluation of self-collected vaginal swab, first void urine, and endocervical swab specimens for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in adolescent females. *J Pediatr Adolesc Gynecol* 2008;**21**:355-60
105. Schachter J, Chernesky MA, Willis DE, *et al*. Vaginal swabs are the specimens of choice when screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: results from a multicenter evaluation of the APTIMA assays for both infections. *Sex Transm Dis* 2005;**32**:725-8
106. Chernesky MA, Hook EW, 3rd, Martin DH, *et al*. Women find it easy and prefer to collect their own vaginal swabs to diagnose *Chlamydia trachomatis* or *Neisseria gonorrhoeae* infections. *Sex Transm Dis* 2005;**32**:729-33
107. Hobbs MM, van der Pol B, Totten P, *et al*. From the NIH: proceedings of a workshop on the importance of self-obtained vaginal specimens for detection of sexually transmitted infections. *Sex Transm Dis* 2008;**35**:8-13
108. Gaydos CA, Farshy C, Barnes M, *et al*. Can mailed swab samples be dry-shipped for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* by nucleic acid amplification tests? *Diagn Microbiol Infect Dis* 2012;**73**:16-20
109. Fitzhugh VA, Heller DS. Significance of a diagnosis of microorganisms on pap smear. *J Low Genit Tract Dis* 2008;**12**:40-51
110. Chernesky M, Jang D, Portillo E, *et al*. Detection of *Chlamydia trachomatis* in SurePath(trademark) liquid-based Pap samples using Aptima Combo 2(registered trademark), AMPLICOR(trademark) and ProbeTec(trademark) assays. *Can J Infect Dis Med Microbiol* 2010;**21**:10A
111. Pittaras TE, Papaparaskevas J. Comparison of penile skin swab with intra-urethral swab and first void urine for polymerase chain reaction-based diagnosis of *Chlamydia trachomatis* urethritis in male patients. *Sex Transm Dis* 2008;**35**:999-1001
112. Jebakumar SP, Storey C, Lusher M, Nelson J, Goorney B, Haye KR. Value of screening for oro-pharyngeal *Chlamydia trachomatis* infection. *J Clin Path* 1995;**48**:658-61

113. Hammerschlag MR, Roblin PM, Gelling M, Tsumura N, Jule JE, Kutlin A. Use of polymerase chain reaction for the detection of *Chlamydia trachomatis* in ocular and nasopharyngeal specimens from infants with conjunctivitis. *Pediatr Infect Dis J* 1997;**16**:293-7
114. Ota KV, Tamari IE, Smieja M, et al. Detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in pharyngeal and rectal specimens using the BD Probetec ET system, the Gen-Probe Aptima Combo 2 assay and culture. *Sex Transm Infect* 2009;**85**:182-6
115. Peters RPH, Verweij SP, Nijsten N, et al. Evaluation of sexual history-based screening of anatomic sites for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection in men having sex with men in routine practice. *BMC Infect Dis* 2011;**11**
116. Tipple C, Hill SC, Smith A. Is screening for pharyngeal *Chlamydia trachomatis* warranted in high-risk groups? *Int J STD AIDS* 2010;**21**:770-1
117. Marcus JL, Bernstein KT, Kohn RP, Liska S, Philip SS. Infections missed by urethral-only screening for Chlamydia or Gonorrhea detection among men who have sex with men. *Sex Transm Dis* 2011;**38**:922-4
118. Schachter J, Moncada J, Liska S, Shayevich C, Klausner JD. Nucleic acid amplification tests in the diagnosis of chlamydial and gonococcal infections of the oropharynx and rectum in men who have sex with men. *Sex Transm Dis* 2008;**35**:637-42.
119. Alexander S, Martin I, Ison C. Confirming the *Chlamydia trachomatis* status of referred rectal specimens. *Sex Transm Infect* 2007;**83**:327-9
120. Mimiaga MJ, Mayer KH, Reisner SL, et al. Asymptomatic gonorrhea and chlamydial infections detected by nucleic acid amplification tests among Boston area men who have sex with men. *Sex Transm Dis* 2008;**35**:495-8
121. Bachmann LH, Johnson RE, Cheng H, et al. Nucleic acid amplification tests for diagnosis of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* rectal infections. *J Clin Microbiol* 2010;**48**:1827-32
122. Ward H, De Vries HJC, Van De Laar M. Re-emergence of lymphogranuloma venereum in Europe and the public health response. *Sex Transm Infect* 2011;**87**:A19-A20
123. Ward H, Martin I, Macdonald N, et al. Lymphogranuloma venereum in the United Kingdom. *Clin Infect Dis* 2007;**44**:26-32
124. de Vries HJ, Zingoni A, White JA, Ross JD, Kreuter A. 2013 European Guideline on the management of proctitis, proctocolitis and enteritis caused by sexually transmissible pathogens. *Int J STD AIDS*. 2013;**25**:465-74
125. Gdoura R, Kchaou W, Ammar-Keskes L, et al. Assessment of *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Ureaplasma parvum*, *Mycoplasma hominis*, and *Mycoplasma genitalium* in semen and first void urine specimens of asymptomatic male partners of infertile couples. *J Androl* 2008;**29**:198-206
126. Hamdad-Daoudi F, Petit J, Eb F. Assessment of *Chlamydia trachomatis* infection in asymptomatic male partners of infertile couples. *J Med Microbiol* 2004;**53**:985-90
127. Pannekoek Y, Westenberg SM, Eijk PP, et al. Assessment of *Chlamydia trachomatis* infection of semen specimens by ligase chain reaction. *J Med Microbiol* 2003;**52**:777-9

128. van der Snoek EM, Ossewaarde JM, van der Meijden WI, Mulder PG, Thio HB. The use of serological titres of IgA and IgG in (early) discrimination between rectal infection with non-lymphogranuloma venereum and lymphogranuloma venereum serovars of *Chlamydia trachomatis*. *Sex Transm Infect* 2007;**83**:330-4
129. de Vries HJ, Smelov V, Ouburg S, *et al.* Anal lymphogranuloma venereum infection screening with IgA anti-*Chlamydia trachomatis*-specific major outer membrane protein serology. *Sex Transm Dis* 2010;**37**:789-95
130. Verweij SP, Lanjouw E, Bax CJ, *et al.* Serovar D and E of serogroup B induce highest serological responses in urogenital *Chlamydia trachomatis* infections. *BMC Infect Dis* 2014;**14**:3
131. Gijssen AP, Land JA, Goossens VJ, Slobbe ME, Bruggeman CA. Chlamydia antibody testing in screening for tubal factor subfertility: the significance of IgG antibody decline over time. *Hum Reprod* 2002;**17**:699-703
132. Black CM. Current methods of laboratory diagnosis of *Chlamydia trachomatis* infections. *Clin Microbiol Rev* 1997;**10**:160-84
133. She RC, Welch R, Wilson AR, Davis D, Litwin CM. Correlation of Chlamydia and Chlamydophila spp. IgG and IgM antibodies by microimmunofluorescence with antigen detection methods. *J Clin Lab Anal* 2011;**25**:305-8
134. Clad A, Freidank HM, Kunze M, *et al.* Detection of seroconversion and persistence of *Chlamydia trachomatis* antibodies in five different serological tests. *Eur J Clin Microbiol Infect Dis* 2000;**19**:932-7
135. Mouton JW, Peeters MF, van Rijssort-Vos JH, Verkooyen RP. Tubal factor pathology caused by *Chlamydia trachomatis*: the role of serology. *Int J STD AIDS* 2002;**13 Suppl 2**:26-9
136. Verkooyen RP, Peeters MF, van Rijsoort-Vos JH, van der Meijden WI, Mouton JW. Sensitivity and specificity of three new commercially available *Chlamydia trachomatis* tests. *Int J STD AIDS* 2002;**13 Suppl 2**:23-5
137. Land JA, Evers JL. Chlamydia infection and subfertility. *Best Pract Res Clin Obstet Gynaecol* 2002;**16**:901-12
138. Lanjouw E, Ossewaarde JM, Stary A, Boag F, Van Der Meijden WI. 2010 European guideline for the management of *Chlamydia trachomatis* infections. *Int J STD AIDS* 2010;**21**:729-37
139. Ministry of Health, Wellington, New Zealand. Chlamydia Management Guidelines 2008. 2008 <https://www.health.govt.nz/system/files/documents/publications/chlamydia-management-guidelines.pdf> (last checked 15 August 2015)
140. Fung M, Scott KC, Kent CK, Klausner JD. Chlamydial and gonococcal reinfection among men: a systematic review of data to evaluate the need for retesting. *Sex Transm Infect* 2007;**83**:304-9
141. Scottish Intercollegiate Guidelines Network (SIGN). Management of genital *Chlamydia trachomatis* infection. A national clinical guideline. 2009. <http://www.sign.ac.uk/pdf/sign109.pdf> (last checked 15 August 2015)
142. Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections. <http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/index-eng.php> (last checked 15 August 2015)
143. Health Protection Agency. National Chlamydia Screening Programme (2010) National Chlamydia Screening Programme, England. 2010

144. Hosenfeld CB, Workowski KA, Berman S, *et al.* Repeat infection with chlamydia and gonorrhoea among females: A systematic review of the literature. *Sex Transm Dis* 2009;**36**:478-89
145. Royal Australian College of General Practitioners. Guidelines for Preventive Activities in General Practice, 8th edn. <http://www.racgp.org.au/download/Documents/Guidelines/Redbook8/redbook8.pdf> (last checked 15 August 2015)
146. Public Health England. National Chlamydia Screening Programme. <http://www.chlamydia-screening.nhs.uk/ps/news.asp> (last August 15 April 2015)
147. van de Laar MJ, Fontaine J. ECDC guidance on chlamydia control in Europe: next steps. *Euro Surveill* 2009;14
148. Regan DG, Wilson DP, Hocking JS. Coverage is the key for effective screening of *Chlamydia trachomatis* in Australia. *J Infect Dis* 2008;**198**:349-58
149. Glasser JW, Owusu-Edusei K, Glick SN, Aral SO, Gift TL. Controlling chlamydia: population modeling to assess promising interventions. *Sex Transm Infect* 2013;**89**(suppl 1):A57
150. Althaus CL, Heijne JC, Herzog SA, Roellin A, Low N. Individual and population level effects of partner notification for *Chlamydia trachomatis*. *PLoS ONE* 2012;**7**:e51438
151. Jamil MS, Bauer HM, Hocking JS, *et al.* Chlamydia screening strategies and outcomes in educational settings: A systematic review. *Sex Transm Dis* 2014;**41**:180-7
152. Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK, Stamm WE. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *New Engl J Med* 1996;**334**:1362-6
153. Ostergaard L, Andersen B, Moller JK, Olesen F. Home sampling versus conventional swab sampling for screening of *Chlamydia trachomatis* in women: a cluster-randomized 1-year follow-up study. *Clin Infect Dis* 2000;**31**:951-7
154. Andersen B, van Valkengoed I, Sokolowski I, Møller JK, Østergaard L, Olesen F. Impact of intensified testing for urogenital *Chlamydia trachomatis* infections: a randomised study with 9-year follow-up. *Sex Transm Infect* 2011;**87**:156-61.
155. Heijne JC, Herzog SA, Althaus CL, Tao G, Kent CK, Low N. Insights into the timing of repeated testing after treatment for *Chlamydia trachomatis*: data and modelling study. *Sex Transm Infect* 2013;**89**:57-62
156. Aghaizu A, Reid F, Kerry S, *et al.* Frequency and risk factors for incident and redetected *Chlamydia trachomatis* infection in sexually active, young, multi-ethnic women: a community based cohort study. *Sex Transm Infect* 2014;**90**:524-8
157. British Association for Sexual Health and HIV. *Chlamydia trachomatis* UK testing guidelines. 2010. <http://www.bashh.org/documents/3352.pdf> (last checked 15 August 2015)
158. Scott Lamontagne D, Baster K, Emmett L, *et al.* Incidence and reinfection rates of genital chlamydial infection among women aged 16-24 years attending general practice, family planning and genitourinary medicine clinics in England: a prospective cohort study by the Chlamydia Recall Study Advisory Group. *Sex Transm Infect* 2007;**83**:292-303
159. Public Health England. 2013. Position Statement. NCSP Recommended Case Management Change: Routine offer of re-test to young adults testing positive for

- chlamydia. http://www.chlamydia-screening.nhs.uk/ps/resources/re-testing/NCSP%20Position%20Statement_Re-testing%20of%20Positive%20Chlamydia%20Cases_August%202013_FINAL.pdf (last checked 15 August 2015)
160. British Association of Sexual Health and HIV. 2014 Draft UK national guideline for the management of genital infection with *Chlamydia trachomatis*. 2013. <http://www.bashh.org/BASHH/Guidelines/Guidelines/BASHH/Guidelines/Guidelines.aspx?hkey=072c83ed-0e9b-44b2-a989-7c84e4fbd9de> (last checked 15 August 2015)
161. Horner PJ. Azithromycin antimicrobial resistance and genital *Chlamydia trachomatis* infection: duration of therapy may be the key to improving efficacy. *Sex Transm Infect* 2012;**88**:154-6
162. Sandoz KM, Rockey DD. Antibiotic resistance in Chlamydiae. *Future Microbiol* 2010;**5**:1427-42
163. Wang SA, Papp JR, Stamm WE, Peeling RW, Martin DH, Holmes KK. Evaluation of antimicrobial resistance and treatment failures for *Chlamydia trachomatis*: a meeting report. *J Infect Dis* 2005;**191**:917-23
164. O'Neill CE, Seth-Smith HM, Van Der Pol B, et al. *Chlamydia trachomatis* clinical isolates identified as tetracycline resistant do not exhibit resistance in vitro: whole-genome sequencing reveals a mutation in *porB* but no evidence for tetracycline resistance genes. *Microbiology* 2013;**159**:748-56
165. Handsfield HH. Questioning azithromycin for chlamydial infection. *Sex Transm Dis* 2011;**38**:1028-9
166. Schwebke JR, Rompalo A, Taylor S, et al. Re-evaluating the treatment of nongonococcal urethritis: emphasizing emerging pathogens--a randomized clinical trial. *Clin Infect Dis* 2011;**52**:163-70
167. Sena AC, Lensing S, Rompalo A, et al. *Chlamydia trachomatis*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* infections in men with nongonococcal urethritis: predictors and persistence after therapy. *J Infect Dis* 2012;**206**:357-65
168. Kong FY, Hocking JS. Treatment challenges for urogenital and anorectal *Chlamydia trachomatis*. *BMC Infect Dis* 2015;**15**:293.
169. Somani J, Bhullar VB, Workowski KA, Farshy CE, Black CM. Multiple drug-resistant *Chlamydia trachomatis* associated with clinical treatment failure. *J Infect Dis* 2000;**181**:1421-7
170. Bhengraj AR, Srivastava P, Mittal A. Lack of mutation in macrolide resistance genes in *Chlamydia trachomatis* clinical isolates with decreased susceptibility to azithromycin. *Int J Antimicrob Agents* 2011;**38**:178-9
171. Mpiga P, Ravaoarino M. Effects of sustained antibiotic bactericidal treatment on *Chlamydia trachomatis*-infected epithelial-like cells (HeLa) and monocyte-like cells (THP-1 and U-937). *Int J Antimicrob Agents* 2006;**27**:316-24
172. Amsden GW. Erythromycin, clarithromycin, and azithromycin: are the differences real? *Clin Ther* 1996;**18**:56-72;discussion 55
173. Lode H, Borner K, Koeppe P, Schaberg T. Azithromycin--review of key chemical, pharmacokinetic and microbiological features. *J Antimicrob Chemother* 1996;**37 Suppl C**:1-8

174. Bjornelius E, Anagrius C, Bojs G, *et al.* Antibiotic treatment of symptomatic *Mycoplasma genitalium* infection in Scandinavia: a controlled clinical trial. *Sex Transm Infect* 2008;**84**:72-6
175. Anagrius C, Lore B, Jensen JS. Treatment of *Mycoplasma genitalium*. Observations from a Swedish STD clinic. *PloS one* 2013;**8**:e61481
176. Horner P, Blee K, Adams E. Time to manage *Mycoplasma genitalium* as an STI: but not with azithromycin 1 g! *Curr Opin Infect Dis* 2014;**27**:68-74
177. Taylor-Robinson D, Jensen JS. *Mycoplasma genitalium*: from Chrysalis to multicolored butterfly. *Clin Microbiol Rev* 2011;**24**:498-514
178. Unemo M, Endre KMA, Moi H. The five days azithromycin treatment regimen (500 mg×1, 250 mg×4) used for *Mycoplasma genitalium* infections also effectively eradicates *Chlamydia trachomatis*. *Acta Derm Venereol* 2015. In press.
179. Kong FY, Tabrizi SN, Law M, *et al.* Azithromycin versus doxycycline for the treatment of genital Chlamydia infection: A meta-analysis of randomized controlled trials. *Clin Infect Dis* 2014;**59**:193-205
180. Ibsen HH, Moller BR, Halkier-Sorensen L, From E. Treatment of nongonococcal urethritis: comparison of ofloxacin and erythromycin. *Sex Transm Dis* 1989;**16**:32-5
181. Maiti H, Chowdhury FH, Richmond SJ, *et al.* Ofloxacin in the treatment of uncomplicated gonorrhoea and chlamydial genital infection. *Clin Ther* 1991;**13**:441-7
182. Takahashi S, Ichihara K, Hashimoto J, *et al.* Clinical efficacy of levofloxacin 500 mg once daily for 7 days for patients with non-gonococcal urethritis. *J Infect Chemother* 2011;**17**:392-6
183. Cramers M, Kaspersen P, From E, Moller BR. Pivampicillin compared with erythromycin for treating women with genital *Chlamydia trachomatis* infection. *Genitourin Med* 1988;**64**:247-8
184. Worm AM, Hoff G, Kroon S, Petersen CS, Christensen JJ. Roxithromycin compared with erythromycin against genitourinary chlamydial infections. *Genitourin Med* 1989;**65**:35-8
185. Khrianin AA, Reshetnikov OV. [Is it safe to use josamycin in the obstetrics practice in Russia?]. *Antibiot Khimioter* 2007;**52**:32-6 [In Russian]
186. Primiero FM, Caruso G, Grottanelli F, *et al.* Josamycin in the treatment of *Chlamydia trachomatis* cervicitis. *J Chemother* 1989;**1**:909-10
187. Lucisano A, Vitale AM, Cinque B, *et al.* Josamycin in the treatment of chlamydial genital infections in infertile women. *J Chemother* 1989;**1**:906-8
188. Steedman NM, McMillan A. Treatment of asymptomatic rectal *Chlamydia trachomatis*: Is single-dose azithromycin effective? *Int J STD AIDS* 2009;**20**:16-8
189. Elgalib A, Alexander S, Tong CYW, White JA. Seven days of doxycycline is an effective treatment for asymptomatic rectal *Chlamydia trachomatis* infection. *Int J STD AIDS* 2011;**22**:474-7
190. Hathorn E, Opie C, Goold P. What is the appropriate treatment for the management of rectal *Chlamydia trachomatis* in men and women? *Sex Transm Infect* 2012;**88**:352-4
191. Khosropour CM, Dombrowski JC, Barbee LA, Manhart LE, Golden MR. Comparing azithromycin and doxycycline for the treatment of rectal chlamydial infection: A retrospective cohort study. *Sex Transm Dis* 2014;**41**:79-85

192. Drummond F, Ryder N, Wand H, Guy R. Is azithromycin adequate treatment for asymptomatic rectal chlamydia? *Int J STD AIDS* 2011;**22**:478-80
193. British Association for Sexual Health and HIV. UK national guideline for the management of genital tract infection with *Chlamydia trachomatis*. 2006. <http://www.bashh.org/documents/65.pdf> (last checked 15 August 2015)
194. Pitsouni E, Iavazzo C, Athanasiou S, Falagas ME. Single-dose azithromycin versus erythromycin or amoxicillin for *Chlamydia trachomatis* infection during pregnancy: a meta-analysis of randomised controlled trials. *Int J Antimicrob Agents*. 2007;**30**:213-21
195. Rahangdale L, Guerry S, Bauer HM, *et al*. An observational cohort study of *Chlamydia trachomatis* treatment in pregnancy. *Sex Transm Dis* 2006;**33**:106-10
196. Sarkar M, Woodland C, Koren G, Einarson AR. Pregnancy outcome following gestational exposure to azithromycin. *BMC Pregnancy Childbirth* 2006;**6**:18
197. Postema EJ, Remeijer L, van der Meijden WI. Epidemiology of genital chlamydial infections in patients with chlamydial conjunctivitis; a retrospective study. *Genitourin Med* 1996;**72**:203-5
198. Sulis G, Urbinati L, Franzoni A, Gargiulo F, Carvalho AC, Matteelli A. *Chlamydia trachomatis* conjunctivitis in a male teenager: a case report. *Le infezioni in medicina: rivista periodica di eziologia, epidemiologia, diagnostica, clinica e terapia delle patologie infettive* 2014;**22**:140-3
199. Members AAoO-CEDP. Preferred Practice Pattern Guidelines: Conjunctivitis - limited revision, 2011. 2014
200. Wilson TE, Hogben M, Malka ES, *et al*. A randomized controlled trial for reducing risks for sexually transmitted infections through enhanced patient-based partner notification. *Am J Public Health* 2009;**99 Suppl 1**:S104-10
201. Hogben M, Kissinger P. A review of partner notification for sex partners of men infected with chlamydia. *Sex Transm Dis* 2008;**35**:S34-9
202. Tiplica GS, Evans C, Gomberg M, Nandwani R, Rafila A, Nedelcu L, Salavastru C, Radcliffe K. 2013 European guidelines for the management of partners of persons with sexually transmitted infections. 2013. http://www.iusti.org/regions/europe/word_docs/17.1_European_guideline_on_PN.doc (last checked 15 August 2015)
203. McIlveen H. Review: partner notification interventions can reduce persistent or recurrent sexually transmitted infections. *Evidence Based Nursing* 2007;**10**:107
204. McClean H, Carne CA, Sullivan AK, Radcliffe KW, Ahmed-Jushuf I. Chlamydial partner notification in the British Association for Sexual Health and HIV (BASHH) 2011 UK national audit against the BASHH Medical Foundation for AIDS and Sexual Health Sexually Transmitted Infections Management Standards. *Int J STD AIDS* 2012;**23**:748-52
205. Geisler WM. Duration of untreated, uncomplicated *Chlamydia trachomatis* genital infection and factors associated with chlamydia resolution: a review of human studies. *J Infect Dis* 2010;**201 Suppl 2**:S104-13
206. Geisler WM. Management of uncomplicated *Chlamydia trachomatis* infections in adolescents and adults: evidence reviewed for the 2006 Centers for Disease Control and Prevention sexually transmitted diseases treatment guidelines. *Clin Infect Dis* 2007;**44 Suppl 3**:S77-83

207. Bell G, Potterat J. Partner notification for sexually transmitted infections in the modern world: A practitioner perspective on challenges and opportunities. *Sex Transm Infect* 2011;**87**:ii34-ii6
208. Ferreira A, Young T, Mathews C, Zunza M, Low N. Strategies for partner notification for sexually transmitted infections, including HIV.[Update of Cochrane Database Syst Rev. 2001;(4):CD002843; PMID: 11687164]. *Cochrane Database Syst Rev* 2013;**10**:CD002843
209. Althaus CL, Turner KME, Mercer CH, *et al.* Effectiveness and cost-effectiveness of traditional and new partner notification technologies for curable sexually transmitted infections: Observational study, systematic reviews and mathematical modelling. *Health Technol Assess* 2014;**18**:1-99
210. Pavlin NL, Parker RM, Piggin AK, *et al.* Better than nothing? Patient-delivered partner therapy and partner notification for chlamydia: The views of Australian general practitioners. *BMC Infect Dis* 2009;10
211. Hogben M, Kidd S, Burstein GR. Expedited partner therapy for sexually transmitted infections. *Curr Opin Obstet Gynecol* 2012;**24**:299-304
212. Shivasankar S, Challenor R, Ekanayaka R. Patient-delivered partner therapy in the UK: what do patients think? *Int J STD AIDS* 2008;**19**:433-6
213. Dukers-Muijers NH, Morre SA, Speksnijder A, van der Sande MA, Hoebe CJ. *Chlamydia trachomatis* test-of-cure cannot be based on a single highly sensitive laboratory test taken at least 3 weeks after treatment. *PLoS ONE* 2012;**7**:e34108
214. Renault CA, Israelski DM, Levy V, Fujikawa BK, Kellogg TA, Klausner JD. Time to clearance of *Chlamydia trachomatis* ribosomal RNA in women treated for chlamydial infection. *Sex Health* 2011;**8**:69-73
215. Judlin P, Liao Q, Liu Z, Reimnitz P, Hampel B, Arvis P. Efficacy and safety of moxifloxacin in uncomplicated pelvic inflammatory disease: the MONALISA study. *BJOG* 2010;**117**:1475-84

Conflicts of interests

The Work Under Consideration for Publication					
		Magnus Unemo	Keith Radcliffe	Esmee Lanjouw	Henry de Vries
1	Grant	No	No	No	No
2	Consulting fee or honorarium	No	No	No	No
3	Support for travel to meetings for the study or other purposes	No	No	No	No
4	Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like	No	No	No	No
5	Payment for writing or reviewing the manuscript	No	No	No	No
6	Provision of writing assistance, medicines, equipment, or administrative support	No	No	No	No
7	Other	No	No	No	No

* This means money that your institution received for your efforts on this study.

Relevant financial activities outside the submitted work					
1	Board membership	No	No	No	No
2	Consultancy	No	No	No	Willpharma, GSK
3	Employment	No	No	No	No
4	Expert testimony	No	No	No	No
5	Grants/grants pending	No	No	No	No
6	Payment for lectures including service on speakers bureaus	No	No	No	Willpharma
7	Payment for manuscript preparation	No	No	No	No
8	Patents (planned, pending or issued)	No	No	No	No
9	Royalties	No	No	No	No
10	Payment for development of educational presentations	No	No	No	No
11	Stock/stock options	No	No	No	No
12	Travel/accommodations/meeting expenses unrelated to activities listed**	No	No	No	No
13	Other (err on the side of full disclosure)	No	No	No	No

* This means money that your institution received for your efforts.

** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Other relationships					
1	Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?	No	No	No	No

Conflicts of interests

The Work Under Consideration for Publication					
		Angelika Stary	Name	Name	Name
1	Grant	No			
2	Consulting fee or honorarium	No			
3	Support for travel to meetings for the study or other purposes	No			
4	Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like	No			
5	Payment for writing or reviewing the manuscript	No			
6	Provision of writing assistance, medicines, equipment, or administrative support	No			
7	Other	No			

* This means money that your institution received for your efforts on this study.

Relevant financial activities outside the submitted work					
1	Board membership	No			
2	Consultancy	No			
3	Employment	No			
4	Expert testimony	No			
5	Grants/grants pending	No			
6	Payment for lectures including service on speakers bureaus	No			
7	Payment for manuscript preparation	No			
8	Patents (planned, pending or issued)	No			
9	Royalties	No			
10	Payment for development of educational presentations	No			
11	Stock/stock options	No			
12	Travel/accommodations/meeting expenses unrelated to activities listed**	No			
13	Other (err on the side of full disclosure)	No			

* This means money that your institution received for your efforts.

** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Other relationships					
1	Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?	No			

Conflicts of interests

The Work Under Consideration for Publication					
		Magnus Unemo	Sander Ouburg	Name	Name
1	Grant	no	No		
2	Consulting fee or honorarium	no	No		
3	Support for travel to meetings for the study or other purposes	no	No		
4	Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like	no	No		
5	Payment for writing or reviewing the manuscript	no	No		
6	Provision of writing assistance, medicines, equipment, or administrative support	no	No		
7	Other	no	No		

* This means money that your institution received for your efforts on this study.

Relevant financial activities outside the submitted work					
1	Board membership	no	No		
2	Consultancy	No	No		
3	Employment	No	No		
4	Expert testimony	No	No		
5	Grants/grants pending	No	No		
6	Payment for lectures including service on speakers bureaus	No	No		
7	Payment for manuscript preparation	No	No		
8	Patents (planned, pending or issued)	No	No		
9	Royalties	No	No		
10	Payment for development of educational presentations	No	No		
11	Stock/stock options	No	No		
12	Travel/accommodations/meeting expenses unrelated to activities listed**	No	No		
13	Other (err on the side of full)	no	No		

disclosure)				
-------------	--	--	--	--

* This means money that your institution received for your efforts.

** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Other relationships				
1	Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?	No	No	



S. Ouburg