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ECDC **GUIDANCE**

Chlamydia control in Europe

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Stockholm, June 2009

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Abbreviations

A and E	Accident and emergency medicine department
AIDS	Acquired immune deficiency syndrome
bd	Twice daily (*bis diem*)
ECDC	European Centre for Disease Prevention and Control, Stockholm
EFTA	European Free Trade Association
EIA	enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
ESSTI	European Surveillance for Sexually Transmitted Infections network
EU	European Union
HIV	Human immunodeficiency virus
IUSTI	International Union against Sexually Transmitted Infections
NAAT	Nucleic acid amplification test
OTC	Over-the-counter (i.e. tests and treatments available directly to consumers, not prescribed/administered by healthcare professionals)
PID	Pelvic inflammatory disease
SARA	Sexually acquired reactive arthritis
SCREen	Screening for Chlamydia Review in Europe project
STI	Sexually transmitted infection

Executive summary

Why chlamydia is a public health problem

Chlamydia trachomatis is one of the most common bacterial sexually transmitted infections in Europe. Rates in sexually active young people are commonly between 5 % and 10 %. The number of diagnosed cases is increasing in many European countries, in part due to increased testing and the use of more sensitive tests. People with genital chlamydia may experience symptoms of genital tract inflammation including urethritis and cervicitis, but the majority remains asymptomatic. Chlamydia is a significant public health problem because untreated chlamydia may lead to pelvic inflammatory disease, subfertility and poor reproductive outcomes in some women. Chlamydia also facilitates the transmission of HIV. The cost of treating subfertility due to chlamydia is high as it requires tubal surgery and in-vitro fertilisation. Although inexpensive and effective treatment is available, control of chlamydia is challenging since most people are asymptomatic.

Chlamydia control activities in Europe

A systematic survey of chlamydia control activities in 29 European countries [1] found wide variation in the organisation of chlamydia control. Almost half of the countries reported no organised activity, and national control programmes were only identified in two countries.

Implementing chlamydia control

The first step to a comprehensive and effective control programme is the adoption of a chlamydia control strategy based on wide consultation with key stakeholders. The strategy should take into account the specific national opportunities and limitations together with a review of the evidence for the interventions and measures comprised. The strategy can be based on the step-by-step approach outlined in this guidance.

The step-by-step approach is recommended to ensure that accurate STI prevention and patient management are in place before complex interventions such as screening are to be considered.

Four levels for chlamydia control programmes are outlined:

- Level A, primary prevention: This includes health promotion and education, school programmes and condom distribution.
- Level B, case management: This builds on Level A with the addition of routine case surveillance, accurate chlamydia diagnostic services, clinical services, and patient and partner management services. Each of these requires clear evidence-based guidance and regular audit.
- Level C, opportunistic testing: This builds on Level B with the addition of testing which is routinely offered to one or more specified group of people attending other clinical services, with the aim of case finding, e.g. identifying asymptomatic cases.
- Level D, screening programme: This builds on Level C with the addition of the organised provision of regular chlamydia testing to cover a substantial proportion of a defined population, with the aim of reducing chlamydia prevalence in the population.

The evidence for the impact of level C and D programmes is limited and therefore where implemented they need to be carefully evaluated to guide future policies. In particular, the impact of such programmes on the control of chlamydia in the population needs to be monitored and evaluated. Introducing a screening programme for chlamydia should be considered with the same care as any other screening programme, with an assessment of all the potential benefits, harms and costs.

Effective resourcing and implementation of national chlamydia control strategies requires leadership and commitment from healthcare policy makers. The most appropriate national strategies are likely to vary across countries, and national strategies should be developed in consultation with professional medical organisations, funders and providers of healthcare and diagnostic services.

Evaluation of chlamydia control programmes

Control programmes aim to reduce the prevalence of chlamydia, but this is difficult to monitor as it requires periodic population surveys. However, there are many other indicators of the effectiveness which should be built into any programme from the outset.

At the national level, programmes should monitor indicators relating to the policies and guidelines of the programme, the implementation and processes, and the outcome of the programme. These must be based on the specific objectives appropriate to the level of implementation.

If countries move from one level of control to the next, they will need to make decisions based on a rigorous appraisal of the evidence for effectiveness, cost-effectiveness and harms. This will be assisted if countries ensure that all activities are fully evaluated and results shared with others in Europe. This way investments in programmes made now will strengthen the evidence base for chlamydia control and facilitate future decision-making and improve population health.

At the European level, the target should be to reduce the proportion of countries reporting no organised activity.

Purpose of this document

This document provides guidance to health policy makers in the European Union about national strategies for chlamydia control. It does not provide specific clinical or diagnostic guidelines but rather a framework for developing, implementing or improving national strategies to prevent and control chlamydia. Recent systematic reviews should be consulted as the basis for such detailed guidelines.

Health policies, like clinical guidelines, should be based on the best available evidence. However, there is generally less evidence on which to base these policy decisions. In this guidance document we aim to facilitate the development of local, evidence-based guidelines within the context of sound national chlamydia strategies. Such strategies need to take account not only of clinical and epidemiological factors (such as the prevalence of chlamydia in the population) but also of local systems of healthcare delivery, infrastructure and resourcing.

The guidance has been developed by a technical expert group using the evidence gathered in the ECDC report 'Review of chlamydia control activities in EU countries' [1], a survey of chlamydia control activities which was considered alongside recent systematic reviews of chlamydia screening and control [2,3].

This guidance covers the common sexually transmitted form of *Chlamydia trachomatis* (serovars D to K) and does not cover *Lymphogranuloma venereum* or trachoma.

1 Why is chlamydia a public health problem?

1.1 Background

Genital infection with *Chlamydia trachomatis* (commonly known as 'chlamydia') is the most common bacterial sexually transmitted infection in many European countries [4]. However, as chlamydia is usually asymptomatic in both women and men it continues to be spread unknowingly despite the availability of cheap and effective treatment.

Chlamydia is a serious public health concern because, although the infection often causes no symptoms, it can have severe long-term consequences in a proportion of cases [5]. In women, chlamydia can lead to pelvic inflammatory disease (PID), tubal infertility and ectopic pregnancy. In the UK it has been estimated that 64 000 cases of PID and 3 000 ectopic pregnancies each year are attributable to chlamydial infection, although the evidence for these statements is weak. These complications cause considerable distress to the individuals and, in the case of infertility, have major cost implications for health services [6]. Infection during pregnancy is associated with premature rupture of the membranes, low birth weight and miscarriage [7]. Chlamydia can also be transmitted from mother to baby during labour, causing eye and respiratory infections [8]. In men, chlamydia can lead to acute genital inflammation (epididymitis, epididymo-orchitis) and occasionally to sexually-acquired reactive arthritis (SARA). In men and women chlamydia may produce proctitis. Individuals with chlamydia are at increased risk of acquiring or transmitting HIV [9].

The number of cases of chlamydia being diagnosed in a number of EU countries continues to rise [1]. This increase is in part due to more widespread testing and greater sensitivity of the tests used, both of which make it difficult to interpret time trends. Variations in screening and reporting also result in a wide range of reported rates of chlamydia across different countries (Figure 1). Despite increases in testing, most cases remain undetected and therefore untreated.

The highest rates of chlamydia occur in young people aged < 25 years, and risk increases with the number of sexual partners [10, 11] but there are no other clear risk factors.

How common is chlamydia?

- Surveys in seven countries estimated a population prevalence of 1.4 to 3.0 % in people aged 18 to 44 years [1].
- In England the National Chlamydia Screening Programme offers screening to young men and women (aged under 25); around 10 % of tests have been positive [12], with estimates of up to 450 000 young people infected.
- In the USA, there are probably around 2.8 million new cases of chlamydia each year [13].

What is the cost of chlamydia?

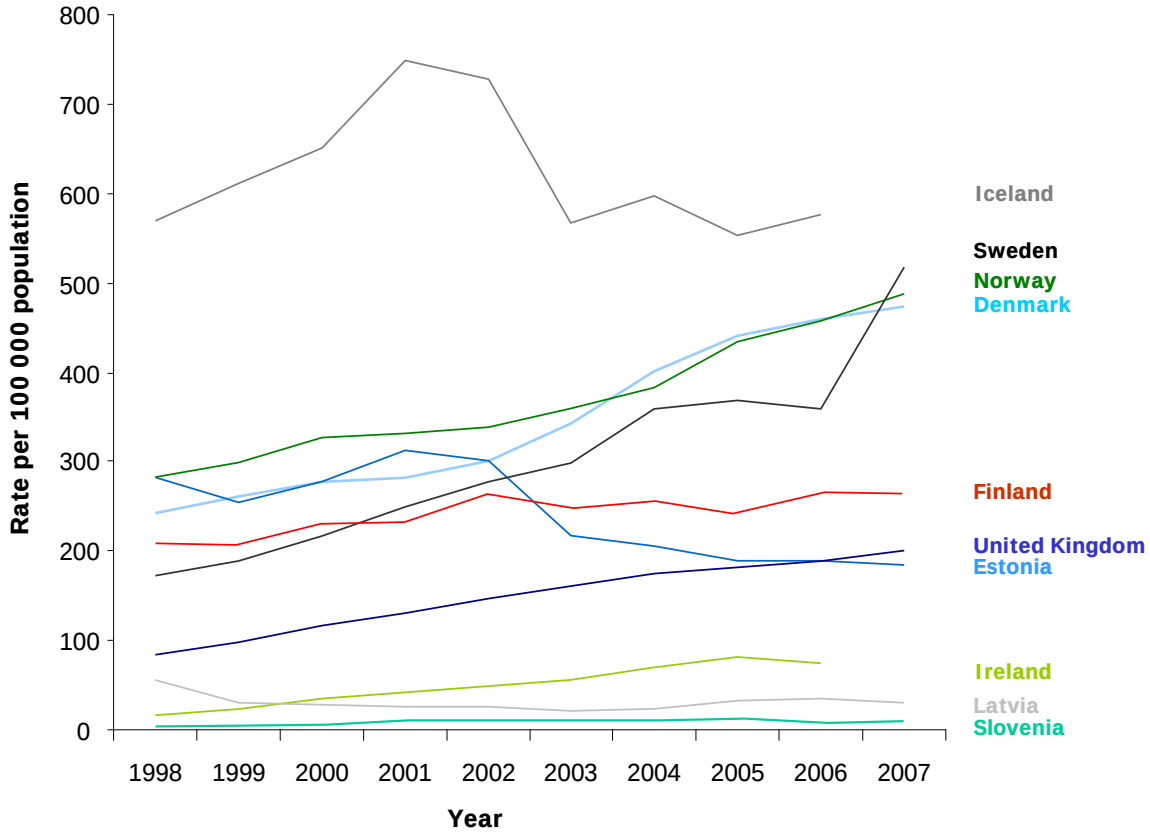
The cost of treating the complications of chlamydia is unknown due to uncertainty in both the prevalence of chlamydia and the incidence of complications.

- The UK has estimated the cost of complications at a minimum of €110 million annually [14].
- In the USA the direct costs of chlamydia and its complications have been estimated at between one and three billion euros annually [24, 25]

Table 1: Complications of chlamydia

In women		In men
Infection at any time	**Infection during pregnancy**	
Pelvic inflammatory disease	Miscarriage	Epididymitis
Tubal infertility	Premature rupture of membranes	Epididymo-orchitis
Ectopic pregnancy	Low birth weight	Sexually-acquired reactive arthritis
Sexually-acquired reactive arthritis	Transmission from mother to baby leading to ophthalmia neonatorum and atypical neonatal pneumonitis	

Figure 1: Rate of reported chlamydia cases per 100 000 population: 1998–2007



Source: ESSTI. Sexually Transmitted Infections in Europe. Health Protection Agency, 2008. No. 3 [32]

1.2 Challenges for chlamydia control

The spread of an STI in the population is mainly dependent on three parameters:

- probability of transmission: how easily the pathogen can be passed from an infected to a susceptible individual;
- contact rate: the rate of contact between infected and susceptible individuals; and
- duration of infection: how long the infection persists.

Controlling chlamydia requires interventions to reduce each of these parameters. For example, the probability of transmission can be reduced by the use of condoms, and the contact rate can be reduced by having fewer sexual partners and concurrent partnerships. The particular challenge for chlamydia control is reducing the duration of infection through diagnosis and treatment. Since most cases are asymptomatic, infected individuals may have no reason to present to clinical services. Unless the person presents for a check up, is notified by a partner who has developed symptoms, or is actively screened, the infected person will remain infectious for a long period until the infection spontaneously resolves.

Chlamydia control therefore requires a range of activities including:

- primary prevention particularly involving young adults, including sexual health and relationship education;
- the promotion of safer sex and condom use;
- effective diagnosis and treatment of those with infection;
- identifying and treating partners of infected individuals; and
- active case-finding, e.g. screening, to identify and treat asymptomatic cases.

2 Review of chlamydia control activities in Europe

The ECDC report 'Review of chlamydia control activities in EU countries' [1] presents a systematic survey of chlamydia control activities in 29 countries, including 24 EU Member States. It appears that the organisation of chlamydia control varies widely, with many countries having no organised activity according to the suggested classification (see Table 2).

Table 2: Current chlamydia control in Europe, based on classification as presented in [1]

Category		Criteria	Countries at this level (%)	
			All n=29	EU Member States n=24
1	No organised activity	No national guidelines for chlamydia diagnosis and management	13 (45 %)	10 (42 %)
2	Case management	Guidelines on chlamydia diagnosis and treatment for at least one group of healthcare professionals	5 (17 %)	5 (21 %)
3	Case finding	Case management guidelines plus partner notification	3 (10 %)	3 (13 %)
4	Opportunistic testing	Case finding plus chlamydia testing is offered to at least one specified group of asymptomatic people	6 (21 %)	4 (17 %)
5	Screening programme	Organised chlamydia screening is available to a substantial part of the population within the public health system	2 (7 %)	2 (8 %)

The 'Review of chlamydia control activities in EU countries' [1] revealed that while there are many chlamydia-related activities in different countries, including chlamydia testing and management in different clinical settings, only a few countries have a systematic approach with standard guidance about clinical care or screening recommendations. To develop a consistent control programme it would require the development of clearly defined aims and appropriate management to draw together and guide initiatives. A programme also needs to ensure that activities are supported by the necessary infrastructure. For example, it was noted that, although some countries have good policies on chlamydia testing, these are not always implemented because reliable testing itself is not widely available. Although effective chlamydia control may eventually reduce spending on the long-term consequences of infection, developing control programmes is likely to require additional resources and capacity for testing and screening. Healthcare funders are therefore key stakeholders and should be involved in discussions about chlamydia control programmes. Funding for and delivery of screening, diagnosis and treatment need to be coordinated, especially in countries that do not have a national healthcare system. Any new initiatives will also require training for the healthcare professionals involved. The use and effects of guidelines should be audited periodically.

2.1 Summary of main outcomes

In 2007, a review has been conducted for chlamydia control programmes in 29 European countries. This includes information from Austria, Belgium, Bulgaria, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, The Netherlands, Norway, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

The survey documented a wide variation in approaches to and capacity for control of chlamydia which are briefly summarised here. For further details, please see the full report [1].

Chlamydia guidelines

Among the 29 countries, 17 already had at least one set of national guidelines on chlamydia management, and three had guidelines in development. In some countries, separate guidelines exist for different healthcare settings (e.g. primary care or specialist STI clinics) but these are not always consistent. Similarly, there is variation in the recommendations between different guidelines, for example in the need for repeat testing.

Availability of chlamydia testing

In most countries, chlamydia testing is available at gynaecology and STI clinics; it may also be provided by urology, primary care and family planning clinics. However, many countries do not have guidelines applicable to each setting. For example, half the participating countries with dedicated STI clinics did not have national chlamydia guidelines for practitioners in these clinics. Over-the-counter kits for self-testing are sold in five countries.

Laboratory diagnosis of chlamydia

Nucleic acid amplification tests (NAATs) are available in all but one country surveyed, but are not always used routinely. In nine countries, NAAT is used for under 50 % of tests.

Chlamydia surveillance

Most countries have a system for surveillance of chlamydia infections. The most common system was a statutory requirement for all laboratory-diagnosed chlamydia cases to be reported at the national level (in 16 countries). However, in some countries only cases diagnosed in selected settings (e.g. STI clinics) are reported. Four countries had no reporting system for chlamydia, and about a third of EU Member States do not report chlamydia surveillance data.

Screening

Eighteen EU Member States indicated that no chlamydia screening programme was in place. In six countries, asymptomatic individuals may be tested for chlamydia when they attend other health services. The groups targeted for such opportunistic screening vary between and within countries. For example, in Iceland chlamydia testing is offered to women who have an abortion; in Estonia it is offered to pregnant women and those who frequently change sexual partners; in Norway it is offered to women attending for an abortion or antenatal care, young people under 25 years with recent partner change and partners of patients with an STI; in Denmark, two communities receive annual postal invitations for chlamydia testing.

Chlamydia screening programmes were introduced throughout England in 2007 for sexually active men and women aged under 25 attending various clinical and non-clinical settings (e.g. universities and sporting events). In the Netherlands, a pilot programme of annual postal invitation in three regions for 16- to 29-year-olds was introduced in early 2008. A register-based screening programme using mailed home-collected specimens is planned in Norway. A further nine countries plan to introduce opportunistic chlamydia screening programmes in the future.

Although screening is widespread in Sweden, chlamydia control activities are funded and implemented by each county and are not coordinated nationally. High per capita rates of screening are also achieved in Norway despite the lack of a national programme. Pilot programmes using register-based postal invitations are underway or planned in the Netherlands, Norway and Denmark.

Table 3: Chlamydia testing for asymptomatic individuals: summary of national guidelines

Denmark	Testing in primary care for asymptomatic people with frequent sex partner change, women under 26 before intrauterine device insertion or hysterosalpingogram
Estonia	Testing in all settings for pregnant women and asymptomatic people with frequent sex partner change, clients of commercial sex workers, and following sexual assault
Iceland	Testing for women presenting for termination of pregnancy, egg and sperm donors
Latvia	Testing recommended for pregnant women and for STI patients and their partners
Norway	Testing for women presenting for termination of pregnancy or antenatal care, under-25s with recent partner change, and partners of people with STI
Sweden	Multiple guidelines including testing for asymptomatic people but target groups differ between counties

Table 4: Opportunistic testing for selected asymptomatic individuals

Denmark	Guideline includes opportunistic chlamydia testing in primary care (where most tests are done) for asymptomatic people with frequent sex partner change, women under 26 before intrauterine device insertion or hysterosalpingogram. Also annual postal invitation for screening in two communities.
Estonia	Guideline for all practitioners includes opportunistic testing for pregnant women and asymptomatic people with frequent sex partner change, clients of commercial sex workers, following sexual assault.
Iceland	Guideline for all practitioners includes opportunistic testing for women presenting for termination of pregnancy, egg and sperm donors.
Latvia	Opportunistic testing recommended for pregnant women.
Norway	Guideline for all practitioners includes opportunistic testing for women presenting for termination of pregnancy or antenatal care, under-25s with recent partner change, and partners of people with STI. Plans for proactive chlamydia screening by postal invitation following randomised controlled trial in one region.
Sweden	Multiple guidelines for different practitioners. Include opportunistic testing for asymptomatic people with target groups differing between counties.

2.2 Epidemiology

Chlamydia continues to be the most frequently reported STI and reportable disease in Europe, accounting for the majority of all STI reports. In 2007, 253 386 confirmed cases of chlamydia infection were reported by 22 EU and EEA/EFTA Member States, with an overall rate of 122.6 per 100 000 population. The true incidence of chlamydia infections is most likely higher than these reported rates. Chlamydia mainly affects young persons between 15 and 24 years of age, with a notification rate of 367.5 per 100 000 population; young women are diagnosed more often than young men, but notification rates are more likely to reflect screening practices and testing volume rather than true incidence.

Lack of consistency in chlamydia surveillance and variations in testing policies and practices (e.g. diagnostic methods used) make it difficult to estimate the incidence and prevalence of chlamydia in Europe or to make cross-country comparisons. However, in Sweden and Finland, where testing has been widespread for many years, the incidence of chlamydia fell in the early 1990s but has been increasing since 1995. The decrease in the first half of the 1990s mirrors that of other STIs which declined across many parts of Europe probably as a result of safe sex campaigns and the fear of AIDS [20-22].

Prevalence studies based on samples of the general population were available from seven European countries. These provide fairly consistent results, with chlamydia prevalence of between 1.4 and 3.0 % in age groups 18 to 44 years. Studies reporting higher rates tend to have lower response rates, suggesting selection bias in the surveys. Prevalence rates are similar in men and women.

Prevalence or positivity data reported from surveillance programmes tend to report higher infection rates. In those European countries which collect denominator data, positivity rates ranged from 3.2 to 10.4 %.

In England, the national screening programme reported a rate of 10.1 % in sexually active under-25-year-olds in 2005/06 (from almost 97 000 tests) [12].

3 Developing a chlamydia control strategy

3.1 A step-by-step strategy for chlamydia control

In this guidance, a step-by-step approach is suggested to ensure that accurate STI patient management infrastructures (as a basic infrastructure) and quality controls are in place before other community-based interventions such as screening are introduced.

A very important step to develop and ensure the sustainability of a comprehensive and effective control programme is the adoption of a *national chlamydia control strategy*. National authorities should convene a group of key stakeholders including policy makers, clinicians, microbiologists, surveillance experts, public health specialists, healthcare economists, and healthcare funders to develop and adopt a broad consensus on a strategy for chlamydia control, taking into account the specific national opportunities and limitations and addressing available and future services and resources.

Effective resourcing and implementation of national chlamydia control strategies requires *leadership and commitment* from healthcare policy makers. The most appropriate national strategies are likely to vary between countries depending on the prevalence of chlamydia, the organisation of healthcare systems and sexual behaviours (such as the use of condoms). Therefore national strategies should be developed in consultation with professional medical organisations, funders and providers of healthcare and diagnostic services.

The next stages include national primary prevention programmes and *STI patient management guidelines.* Effective case management needs to be established (Level B), which requires systems for diagnosis, facilities for testing and treatment, a method of surveillance, and guidelines to ensure that each of these are evidence-based and meet the same standards across health services. Partner notification should be part of case management, as part of active or passive case finding; it is shown that this not routinely provided in many countries.

With these diagnostic, clinical and surveillance activities in place, it should be considered to develop policies aimed at individuals who are infected but not presenting for care, e.g. opportunistic testing (Level C). Opportunistic testing could be targeted at particular populations at increased risk, such as women attending for termination of pregnancy. However, as noted before, it is difficult to define risk factors for chlamydia other than young age and numbers of sexual partners, and therefore a more systematic approach could be advocated, i.e. a screening programme (Level D).

At present, the evidence for the impact of Level C and D programmes is limited, and therefore where implemented they need to be evaluated to guide future policies. In particular, the impact of such programmes on the control of chlamydia in the general population needs to be monitored carefully.

The next sections provide more detailed guidance on Levels A to D. Guidance on primary prevention will be very limited in this context as it is beyond the scope of this guidance but countries should develop their own evidence-based guidelines for use in education, social and healthcare organisations.

Table 5: Suggested step-by-step approach to developing national chlamydia control programmes

Level		Essential activities	Essential policies	Evaluation
A	Primary prevention	Sexual health and relationship education, awareness campaigns, promotion of condoms	Health promotion policies	Periodic surveys including knowledge and behaviour
B	Case management	As above plus:		
		• routine surveillance of cases; • chlamydia diagnostic services; • clinical services; • partner notification services.	• chlamydia case reporting policy; • guidelines for chlamydia diagnosis; • guidelines for chlamydia case management; • guidelines for partner notification.	• trends in case reports; • quality control of diagnosis; • periodic clinical audit; • periodic audit.
C	Opportunistic testing*	As above plus:		
		• chlamydia testing routinely offered to one or more specified group of asymptomatic people*.	• policy on who should be offered chlamydia testing and in which settings.	• coverage of target group(s).
D	Screening programme*	As above plus:		
		• organised provision of regular chlamydia testing to cover a substantial proportion of a defined population.	• policy on chlamydia screening.	Monitoring of: • coverage; • positivity/prevalence; • quality (including proportion treated, partners screened/treated). Evaluation: • trends in complications (PID, ectopic pregnancy, neonatal infections); • periodic survey of prevalence.

** Impact of opportunistic testing and of screening programmes needs thorough evaluation, including trials, as evidence (of individual and population impact and cost effectiveness) is currently weak.*

3.2 Primary prevention (Level A)

Good primary preventive interventions are the very base for STI control in general. Chlamydia is a risk for all young people who are sexually active and therefore population-wide information and education is appropriate. Young people should have sexual health and relationship education at school, including information about contraception and STI, ways of reducing the risk including the use of condoms, and they should be told about symptoms of infections, the existing of asymptomatic conditions, and the long-term complications of untreated infections. They should also know where they can find more information and how to access youth-friendly sexual health services. Sexual health education in schools should go together with information in different media and approaches adapted to the target group. Communication and information should be coordinated and planned by actors responsible for prevention and health promotion.

3.3 Case management and surveillance (Level B)

Effective case management requires systems for diagnosis, facilities for testing, treatment, partner notification, a method of surveillance, and guidelines to ensure that each of these are evidence-based and meet the same standards across health services.

Patient management guidelines should be used and concern all health practitioners involved in chlamydia diagnosis, treatment and counselling. Guidelines should reflect local conditions and resources and should be developed in conjunction with the appropriate professional organisations. Adherence to guidelines should be monitored and guidelines should be reviewed periodically to ensure they are up-to-date and reflect the latest evidence. Promotion of STI patient management guidelines should encourage best practice and reduce inconsistencies in the standard of care across different healthcare settings. Campaigns to disseminate new or revised guidelines will also provide opportunities for training healthcare professionals and increasing their awareness about chlamydia.

Chlamydia diagnosis

The first requirement for effective case management is access to reliable diagnostic methods. Programmes should ensure that clear guidelines are in place and applicable to all laboratories and clinical settings where testing may be done. Systems must be in place for regular quality control. Several diagnostic methods are available, and their relative advantages and disadvantages are shown in Table 6. This is a rapidly changing field and guidelines must be regularly reviewed and updated.

Decisions about which test to use in which setting will need to be based on a range of criteria, including the setting of the testing, whether patient recall is reliable (e.g. primary care and STI clinics), where recall may be difficult (e.g. drop-in centres), and whether patients would prefer minimally invasive sample collection.

Chlamydia diagnostic testing and treatment should be widely available, ideally in primary care, contraceptive services, sexual health and STI clinics, gynaecology services, urology departments, termination of pregnancy clinics, antenatal clinics, emergency departments and general medical outpatients.

Quality control programmes should ensure that there are systems for quality control in place to make sure that clinicians have access to valid tests and that organisations providing chlamydia diagnostic services are subject to external quality control. This is best achieved by having nationally agreed testing guidelines. In addition, monitoring of the test quality and effectiveness is required through a reference laboratory. A number of new variants of *Chlamydia trachomatis* have recently been described that were not detected by some standard testing platforms [15, 16]. This can be monitored through repeated sentinel testing of specimens using a range of platforms.

Table 6: Methods for diagnosing chlamydia

Method	Advantages	Disadvantages
Diagnostic method		
Nucleic acid amplification tests (NAATs) • polymerase chain reaction [PCR] • strand displacement amplification [SDA] • transcription-mediated amplification [TDA]	• High sensitivity (90–95 %) • Can be used on urine samples and vulvo-vaginal swabs (including self-administered tests) • Validated for extragenital sites, including rectum	• Expensive • False positive results may be a problem in some settings • Not licensed for extragenital sites
EIA (enzyme-linked immunosorbent assay)	• can be adapted for point-of-care tests • cheap	• low sensitivity (40–70 %) • not appropriate for urine and self-collected swabs
Cell culture	• can be used on all specimen types • high specificity	• low sensitivity (60–80 %) • expensive – requires technical expertise and is labour intensive • not suitable for large through-put
Direct fluorescent antibody (DFA) tests	• can be used on all specimen types • rapid turnaround time	• low sensitivity for urine • labour intensive • requires expertise
Specimen collection		
Clinician-obtained	Ability to obtain good quality sample, e.g. endocervical swab which may increase sensitivity	• less acceptable to some patients • more expensive in staff time
Self-collected	• More acceptable to some patients • Less clinical facilities required	May be less sensitive
Delivery		
Point-of-care tests (administered by healthcare professionals)	Treatment can be offered at same time as diagnosis, so no need for patient recall	Currently all EIA-based, therefore less sensitive than NAATs
Over-the-counter, self-administered tests	May be more acceptable and accessible for some groups	• Reliability of method needs to be assured — currently few quality controls • Need to be linked to access to effective treatment
Postal tests	• Patients can take samples in their homes • Tests are carried out by laboratory	• Good regulation and quality control required • Need to be linked to access to treatment

Clinical services

Guidelines for chlamydia case management should be available for healthcare practitioners in all settings where chlamydia may be diagnosed. Such guidelines should be consistent across different settings (e.g. primary care and STI clinics) and should be developed through consultation with and endorsed by appropriate professional organisations. Guidelines should be effectively disseminated; training should be provided as required. Adherence to the guidelines should be monitored by means of audits.

National guidelines should cover:

- clinical indications for chlamydia testing;
- optimal diagnostic technique(s) (see section on diagnosis);
- treatment of positive cases;
- partner notification (contact tracing);

- follow-up and advice to patients; and
- recommendations on re-testing.

Clinical indications for chlamydia testing

1. In specialist STI services: chlamydia testing should be offered routinely to patients who present to specialist STI services, whether or not they have symptoms of an STI.

2. In other healthcare settings: chlamydia testing should be offered to all patients where clinically indicated, as shown in Table 7. The following clinical indications should be considered. The index of suspicion should be greatest for young, sexually active individuals.

Table 7: Clinical indications for chlamydia testing (in sexually active individuals)

Women with:	Men with:	Men and women with:
• post-coital/intermenstrual bleeding • deep dyspareunia • pelvic pain • frequency/dysuria syndrome with negative mid-stream urine culture • mucopurulent cervical discharge • vaginal discharge • inflamed/friable cervix	• dysuria • urethral discharge • urethritis • epididymitis, epididymo-orchitis	• reactive arthritis conjunctivitis • proctitis • inguinal syndrome • genital ulceration

Chlamydia testing should also be considered prior to any procedure involving instrumentation of the cervix, such as termination of pregnancy or insertion of an intrauterine device.

Case management guidelines are needed for all settings in which chlamydia is diagnosed. The settings will vary depending on where testing is offered and how healthcare delivery is organised within a country. However, it is important that if treatment occurs in different settings, there is a consistent standard of care. At present, many countries have case management guidelines only for some settings and, where multiple guidelines exist, they are not always consistent.

Guidelines for treating chlamydia should be evidence-based and should recommend an effective treatment which is acceptable to the target population. Treatment should be prompt (i.e. without delay following diagnosis) and choice of treatment should consider not only efficacy under ideal conditions but also options likely to be acceptable to patients and therefore most likely to be adhered to (e.g. single-dose treatments). Guidelines should include recommendations for treatment during pregnancy and be updated regularly to take account of the latest evidence.

Current basic treatment options include doxycycline and azithromycin. Erythromycin and ofloxacin are the current basic treatment options when doxycycline is contraindicated. Examples for international guidelines describing further and more specific treatment options are the guidelines issued by the Centers for Disease Control and Prevention (CDC Atlanta) or the International Union against Sexually Transmitted Infections (IUSTI). (http://www.iusti.org/regions/Europe/euroguidelines.htm).

Guidelines should include advice to be given to patients (e.g. about sexual activity during treatment) and recommended systems for partner notification.

Advice to patients/partner notification might include the following:

- advice to refrain from sex for one week during treatment and, ideally, until current partner(s) has/have been tested and treated (as necessary);
- counselling to reduce future risk of reinfection or new infection with chlamydia and other STIs (e.g. condom use, safer sex); and
- notification of current and former sexual partners to offer testing and treatment.

Guidelines should include recommendations on the need for follow-up and repeat testing. Early follow-up, by telephone or in person, is important to establish compliance with treatment and partner notification. Routine test of cure is no longer widely recommended because treatment failure is rare with current treatments and repeat early testing can be unreliable with false positives. However, given the risk of reinfection (from an untreated partner) or newly acquired infection (from a new partner), many care guidelines include suggestions for repeat testing after three to six months. The indications for this will vary between populations and therefore country programmes should carry out their own evaluations to inform local guidelines.

Partner management

The notification and management of sexual partners is an essential component of chlamydia case management. Contacting sexual partners of people with STIs has been shown to reduce rates of reinfection and provides a mechanism for targeting those who are already infected or may be at high risk of becoming infected [26]. This is particularly important for chlamydia, when infected partners are unlikely to seek treatment and are therefore unlikely to receive a diagnosis or treatment in the absence of other screening programmes.

There is a number of approaches to partner management, and guidelines should be developed for local practice and the appropriate procedures put in place to ensure that it is carried out effectively. Partner notification (or contact tracing) involves a range of activities to identify the sexual partners of people with chlamydia in order to inform them that they are at high risk of having, or acquiring, chlamydia and to offer diagnosis and treatment. Partner notification therefore provides a mechanism of targeted case finding. Various methods of contact tracing are used in different countries, and the method adopted needs to take account of legal and regulatory frameworks.

Approaches to partner management

Partner notification [26, 27] (or contact tracing) which can be through:

- patient referral, where the index case is asked to inform their partners and ask them to attend for testing and treatment;
- provider referral, when the index case provides information about partners to allow the healthcare professional to inform the partner(s) directly; and
- contract referral, where the index case agrees to inform partners, but if they have not attended within a defined period of time the healthcare professional informs them directly.

Programmes should also consider:

- provision of specific information to partners together with home sampling kits;
- patient-delivered partner therapy (PDPT) where the index patient is provided with antibiotics for their partner(s).

Healthcare practitioners should be appropriately trained to initiate and follow up partner notification by patient referral, or should follow a documented care pathway for provider referral, e.g. to a specialist contact tracer.

Surveillance

Monitoring chlamydia and measuring the effectiveness of control measures requires effective national surveillance systems to be in place. At present, there is considerable variation in chlamydia surveillance policies between EU Member States, making inter-country comparisons difficult. In some countries, all diagnosed cases of chlamydia are reported, while in others, only cases from certain settings are reported (e.g. in the UK, there are different systems for recording chlamydia diagnoses in specialist STI clinics, the chlamydia screening programme and primary care).

Ideally there should be a single system for surveillance to include:

- the number of cases of chlamydia diagnosed, including age, sex, sexual orientation and geographic area;
- the number of diagnostic tests done (to provide a denominator for calculating positivity rates); and
- the way cases were identified (e.g. from screening, symptomatic individuals or partner notification).

Taken together, these should help to quantify the problem of chlamydia and, with consistent methods over time, can provide information on trends and potentially comparison within and between countries. Information about risk factors (such as sexual behaviour) can also be useful to identify individuals at risk and to estimate the spread in the untreated population.

3.4 Opportunistic testing (Level C)

Opportunistic testing is where chlamydia testing is routinely offered to one or more specified sub-populations. The offer of the test occurs when a person presents to health services for some other reason, and does not require the facilities and costs of a full screening programme. The goal of opportunistic testing is to identify asymptomatic cases with the aim of reducing complications in those individuals; it may also reduce onward transmission of infection. Opportunistic testing is usually offered to people who are at increased risk. As we noted earlier, the only consistent risk factors for chlamydia are young age and numbers of sexual partners and therefore these are the most common indications.

Opportunistic testing occurs in some countries as shown in Table 4, and is recommended for many different groups. It is generally recommended in primary care and reproductive health services, and offered to individuals with frequent or recent sexual partner change, women under the age of 25, pregnant women, sex workers and their clients, and people who have been assaulted. The wide range of indications reflects the limited evidence of effectiveness for this strategy [28] although it has been shown to reduce PID at four weeks in women undergoing termination of pregnancy [29].

While the theoretical benefits of opportunistic testing are attractive, few programmes have been rigorously evaluated to provide firm evidence of the long-term benefits. The most appropriate programmes will depend on how healthcare services are delivered within a country. The cost-effectiveness of such testing will also depend on the prevalence of chlamydia within the community, patterns of sexual behaviour, and the frequency of attending healthcare facilities which provide the point of contact for offering testing.

The organisation of healthcare delivery systems will affect the ease and costs of implementing opportunistic testing. For example, in Sweden, testing is offered to all attendees at youth clinics, resulting in a widespread testing in young adults despite the absence of a national screening programme. The provision of, and attitudes towards, contraception may also affect the feasibility of opportunistic screening. While a full sexual history and questions about number of sexual contacts is routine in specialist STI clinics, general practitioners are less likely to discuss such matters; this may prevent guidelines that people with frequent sexual partner change should be tested from being implemented.

National policies on opportunistic testing should be based on reliable information about chlamydia prevalence and the characteristics of those at risk.

Where programmes are introduced, they should be rigorously evaluated in terms of coverage and, where possible, measuring the impact through an experimental trial or careful observational study. This will then help inform future policies.

3.5 Screening programme (Level D)

A screening programme is the organised provision of regular chlamydia testing with the aim of covering a substantial proportion of the defined population. The aim is to identify people who do not know they are infected so that they and their sexual partners can be offered treatment. Theoretically, it should not only benefit infected individuals and their partners but can also have public health benefits. The latter will occur if it succeeds in reducing the prevalence of infection which could in turn reduce incidence, meaning there should be fewer infections that progress to cause complications. To achieve these aims, screening and treatment must cover enough of the target population regularly enough to detect and treat reinfections and to prevent transmission from carriers to new partners.

A screening programme has a number of potential advantages over opportunistic testing:

- It has a clear target population which will enable coverage to be monitored.
- It defines and monitors frequency of testing. Opportunistic testing usually occurs only once or at irregular intervals. There is evidence from opportunistic cervical smear screening programmes that those at high risk are tested infrequently or not at all, while regular users of health services who are at lower risk tend to be tested repeatedly but unnecessarily [17].
- Quality assurance can be built into the screening programme. With opportunistic testing in a wide range of settings it can be difficult to coordinate quality assurance, monitoring and evaluation of the outcomes [18].

Evidence

Although the theoretical benefits of screening are apparent, there is limited evidence from well-controlled studies that chlamydia screening can reduce long-term complications and transmission [3]. Studies have shown that systematic screening for chlamydia in targeted populations can halve the incidence of PID one year later [3]. However, there are no trials to show whether this benefit is sustained, nor are there any trials showing a similar effect from opportunistic screening. There is no firm empirical evidence that chlamydia screening reduces transmission in the population. Mathematical models predict that screening should reduce transmission [30] but it is not clear how many people would need to be tested, nor how often, to reduce chlamydia effectively.

The lack of experience with large-scale organised screening programmes in Europe, and the limited evidence from smaller-scale studies, make it difficult to formulate evidence-based recommendations on the relative merits and cost-effectiveness of different types of screening. Even when target populations and ideal testing frequency can be defined, there is little evidence about the acceptability (and therefore uptake) of different screening methods (e.g. postal invitations to attend for screening in different settings, use of the internet, use of home testing kits, etc.) and these may vary in different communities.

Examples of national screening programmes

- In England, since 2007, testing has been offered to sexually active men and women under 25, with repeat tests annually if the first test is negative, or after a change of sexual partner.
- In the Netherlands, a pilot implementation project has been introduced in three regions in 2008. The intervention uses a register-based population approach to invite the target population aged 16 to 29 years to be screened regularly for chlamydia.

Costs and benefits of screening

The benefits of any screening programme (i.e. increased rates of diagnosis and therefore treatment, leading to reduced complications) must always be weighed against the costs not only to healthcare providers but also to individuals. Screening, and in particular false positive results, may cause anxiety, repeat visits may be inconvenient and costly in terms of travel or time off work, false negative results could lead to unintended onward transmission, and screening may lead to a false sense of security.

In countries with insurance-based healthcare systems, health funders must be involved in discussions about screening programmes since these will only be effective if diagnosis is coordinated with treatment. Available treatments for chlamydia are inexpensive and simple to administer, so the cost implications of diagnosing more cases are not likely to be great, and the long-term benefits and savings in terms of reducing complications such as PID, tubal infertility and ectopic pregnancies are potentially large.

The costs and potential benefits of chlamydia screening will depend on:

- the prevalence of chlamydia in a population or country;
- the ability to identify and reach high risk populations;
- sexual behaviour (which will affect rates of transmission and reinfection);
- the sensitivity and specificity of testing methods used;
- uptake of screening in target populations; and
- uptake of/compliance with treatment in infected individuals.

Establishing a screening programme

Introducing a screening programme for chlamydia should be considered with the same care as any other screening programme, with an assessment of all the potential benefits, harms and costs (see box on national screening programmes).

Screening programmes may be based on a systematic or an opportunistic approach. In the former, a register is created of people in the target population. People on the register are invited to for testing, reminded if they fail to attend, and invited again after the appropriate interval. Although, in theory, such a systematic approach can reach the widest population groups, the uptake of screening by invitation alone, particularly for stigmatised conditions like STIs, has been lower than needed to interrupt transmission.

An opportunistic programme promotes chlamydia screening when people attend primary care or other healthcare providers for unrelated reasons. This is similar to opportunistic testing, but aims to achieve wider coverage and includes organised monitoring of process and outcome. As noted above, there is as yet very limited evidence for the effectiveness of opportunistic chlamydia screening.

National screening programmes

National screening programmes [19] should:

- cover a defined population;
- have a simple set of objectives;
- develop valid and reliable criteria to measure performance and produce an annual report;
- relate performance to explicit quality standards;
- organise quality assurance systems to help professionals and organisations prevent errors and improve performance;
- communicate clearly and efficiently with all interested individuals and organisations; and
- coordinate the management of these activities, clarifying the responsibilities of all individuals and organisations involved.

4 Evaluation of chlamydia control programmes

Control programmes aim to reduce the prevalence of chlamydia and the burden of disease caused by chlamydia. It is difficult to monitor the prevalence rates as it requires repeated population surveys. However, there are other indicators of the effectiveness which should be built into any control programme from the outset.

4.1 Policies and guidelines

Is there a national programme with clear aims, policies and organisation, including chlamydia guidelines and policies for:

- primary prevention;
- diagnostic methods;
- case management;
- partner management;
- surveillance;
- indications for opportunistic testing (if adopted);
- a screening programme (if adopted)?

A periodic programme review should be performed, which should also ensure that the guidelines are regularly reviewed and updated.

4.2 Implementation and process

What proportion of the population has access to diagnostic testing and treatment services? This can be measured through periodic mapping of diagnostic and care services.

What proportion of patients receive care (diagnosis, treatment, partner notification, follow-up) of the standard specified in the guidelines? This can be measured through regular audit and quality control.

Are regular surveillance reports produced and disseminated to key groups?

If opportunistic testing is implemented, what proportion of the target groups are covered by the testing? What is the positivity in the target group?

If a screening programme is implemented, a wide range of indicators will be required relating to implementation, quality control, uptake, coverage (including repeat testing).

4.3 Outcome

Indicators to measure the outcome of the programme must be based on the specific objectives appropriate to the level of implementation (see Table 5).

- Primary prevention: appropriate outcome measures include the proportion of the population that have relevant knowledge and behaviours (from population surveys).
- Case management: outcomes should include a reduction in chlamydia complications (PID, ectopic pregnancy, tubal infertility, epididymitis and epididymo-orchitis, ophthalmia neonatorum, atypical pneumonitis). These should be monitored, but interpreted with care due to difficulties in consistent diagnosis (particularly for PID), inconsistent reporting systems, and uncertainty about the fraction attributable to chlamydia.
- Partner management should lead to a reduction in reinfection rates.

Opportunistic testing and screening programmes should have an impact on complications and reinfection rates, but also on the prevalence and incidence of chlamydia. Although difficult, it is essential to define impact measurements. Trends in chlamydia case-reports are *not* a useful indicator of outcome from a control programme, since a good programme will lead to a considerable increase in diagnosed cases. Periodic prevalence surveys are the best indicator, but are expensive; positivity in the screened population can be a useful indicator, but only if the coverage is high and there is no change in participation bias.

4.4 Measuring cost-effectiveness

As with any public health intervention, the cost-effectiveness of chlamydia control programmes should be evaluated. Dynamic mathematical models may be helpful to predict the transmission of chlamydia and therefore the effects of reducing the incidence and prevalence of chlamydia. Cost-effectiveness models should not be based solely on the direct costs of treating chlamydia, since the benefits of chlamydia control lie in preventing long-term consequences such as tubal infertility and pelvic inflammatory disease.

In the short-term, screening and treatment may increase costs, because previously unrecognised cases will be identified. However, the long-term benefits of reducing the incidence of chlamydia throughout the population (and therefore reducing rates of reinfection and avoiding long-term consequences) need to be taken into account.

4.5 Monitoring at international level

At the European level, the target should be to reduce the proportion of countries reporting no organised activity (see Table 2, currently 45 % of countries) as measured by a repeat of the ECDC survey on chlamydia control activities.

A second target should be an increase in the evidence on which to base recommendations for screening.

Surveillance at European level should be enhanced in order to contribute to the evaluation of the outcome and impact of control programmes, especially in young people.

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