SCIENTIFIC ADVICE

Guidance on chlamydia control in Europe

2015

www.ecdc.europa.eu

SCIENTIFIC ADVICE

Guidance on chlamydia control in Europe

2015

This guidance document was commissioned by the European Centre for Disease Prevention and Control (ECDC) and coordinated by Otilia Mårdh and Andrew J. Amato-Gauci. Technical input was received from Gianfranco Spiteri and Helena de Carvalho Gomes.

This guidance document was written by Bethan Davies and Prof Helen Ward from Imperial College London, United Kingdom, and reviewed by ECDC.

This guidance is informed by the literature reviews and the Member States survey delivered through the *Chlamydia control in Europe* framework service contract commissioned by ECDC. The *Chlamydia control in Europe* programme of work was completed by an international team led by Nicola Low at the University of Bern, Switzerland: Shelagh Redmond (University of Bern); Karin Alexander (Institute of Social and Preventive Medicine, University of Bern); Jan van Bergen (National Institute of Public Health (RIVM) and STI/AIDS Foundation and University of Amsterdam, Netherlands); Anneli Uusküla (University of Tartu, Estonia); Berit Andersen (Randers Regional Hospital, Denmark); Hannelore Götz (Municipal Health Service, Rotterdam, Netherlands); Björn Herrmann (University of Uppsala, Sweden); Ingrid van den Broek (National Institute of Public Health (RIVM)); Helen Ward (Imperial College London, UK) and Sarah Woodhall (Public Health England, London, UK). All experts were invited to review a draft of this guidance document.

Invaluable input was received from the ECDC chlamydia guidance evaluation expert panel which met on 20 and 21 March 2014): Eszter Balla, Hungary; Viviane Bremer, Germany; Maria Jose Borrego, Portugal; Anna Chuchu-Schindele, Sweden; Viara Georgieve, Bulgaria; Hilde Kløvstad, Norway; Vasileia Konte, Greece; Dijana Mayer, Croatia; Anneli Uusküla, Estonia; Inga Veliko, Sweden; Ruth Verbrugge, Belgium.

ECDC would also like to thank the STI contact points in the Member States for their participation in the 2012 survey *Chlamydia control in Europe*.

Prof Clionda McNulty (Public Health England, UK), Kevin Dunbar (Public Health England, UK), Sarah Woodhall (Public Health Englan, UK), Prof Jan van Bergen (National Institute of Public Health (RIVM) and STI/AIDS Foundation and University of Amsterdam, Netherlands), Maarit Kokki, Ben Duncan, Lara Tavoschi, Caroline Daamen and Goritsa Zlatanova (all ECDC) are gratefully acknowledged for helpful comments on the draft guidance.

Suggested citation: European Centre for Disease Prevention and Control. Guidance on chlamydia control in Europe – 2015. Stockholm: ECDC; 2016.

Stockholm, March 2016

ISBN 978-92-9193-737-0

doi 10.2900/667703

Catalogue number TQ-01-16-029-EN-N

Contents

Figures

Tables

Abbreviations

CI	Confidence interval
CM	Case management
DALY	Disability-adjusted life year
EP	Ectopic pregnancy
EU/EEA	European Union and European Economic Area
NAAT	Nucleic acid amplification test
OR	Odds ratio
PID	Pelvic inflammatory disease
PN	Partner notification
RCT	Randomised controlled trial
STI	Sexually transmitted infections
TFI	Tubal factor infertility
WHO	World Health Organization

Glossary

Asymptomatic testing	Tests performed in people with no symptoms of chlamydia. Used as a method of case finding; can also be used for opportunistic testing or in a screening programme.
Case management	The care of people diagnosed with chlamydia that is supported by clinical guidelines. Clinical guidelines should be evidence-based and cover history-taking and clinical examination, diagnostic tests, treatment, partner notifications, health promotion advice, follow-ups and surveillance [1,2].
Case finding	Actively seeking people who are thought to have been exposed to chlamydia infection [1,3] (e.g. sexual partners of people diagnosed with chlamydia). The people identified through case finding may be symptomatic or asymptomatic but have not sought healthcare independently. This differs from opportunistic testing because it requires the healthcare practitioner to make contact with the person they want to offer a test to.
Clinical audit	An ongoing process used to monitor and improve the quality of a service compared to pre-defined objective criteria.
Clinically-indicated testing	Chlamydia testing that is offered during a healthcare consultation where symptoms of chlamydia infection or risk factors for the acquisition of an STI are present. This includes people who have been exposed to, or diagnosed with, other STIs.
Evaluation	An ongoing activity that compares the performance and impact (including unintended events) of an intervention to its anticipated benefit. Evaluation is an essential component of quality management in healthcare and should be planned before an intervention is implemented. The findings of an evaluation may be used to determine future healthcare provision.
Opportunistic testing	Chlamydia testing that is offered to one or more specified groups of asymptomatic people in a healthcare or outreach setting [1]. The person who is offered the test is not required to undertake any specific activity related to seeking a test.
Partner notification	The practice of notifying the sexual partners of people who were diagnosed with chlamydia about their potential exposure to infection. Ideally, the management of partners is supported by evidence-based clinical guidelines and is likely to include testing and treatment. It is a method of case finding [1].
Primary prevention	Activities that aim to prevent new cases of chlamydia, e.g. the promotion of sexual health (health education, sex and relationship education in schools, condom promotion and distribution).

Screening programme	A continuous organised service where chlamydia tests are regularly offered to a defined population at a high enough coverage to benefit the population while minimising harms [1,4]. Screening programmes can be register-based, i.e. people are invited from a maintained register (e.g. population register or healthcare register) to take a test, or opportunistic, i.e. professionals offer a test to eligible people in a predetermined setting. Nationally managed screening programmes have shared organisational characteristics.
Secondary prevention	Activity that aims to reduce the risk of complications following infection and the risk of transmission to sexual partners. It involves the detection and treatment of chlamydia in infected individuals. Individuals with chlamydia can be detected through symptomatic presentation, partner notification (or other case finding) and other asymptomatic testing (e.g. opportunistic testing or screening programme).
Surveillance	The systematic and continuous collection, analysis and dissemination of information about chlamydia testing, diagnosed cases of chlamydia, or the complications of infection. It is used to monitor the epidemiology of infection and evaluate the impact of control interventions.

Executive summary

This evidence-based guidance updates the 2009 ECDC *Chlamydia control in Europe* guidance [5]. It was developed by a technical expert group using evidence gathered by the *Chlamydia control in Europe* programme of work, which ECDC commissioned in 2011 and presented in three accompanying technical reports in 2014 and 2015. The work included a critical review and update of the scientific evidence on the epidemiology and natural history of chlamydia and the clinical and cost-effectiveness of screening programmes, an update of information about chlamydia prevention and control activities in EU/EEA Member States, and a review of the impact of the 2009 ECDC chlamydia control guidance. In 2014, an expert consultation provided in-depth information about the use of the 2009 guidance within countries and made suggestions for the revision of the guidance.

The aim of this guidance is to support Member States to develop, implement or improve national or local strategies for chlamydia control. This guidance sets out the current evidence base behind the proposed options, highlights key gaps in knowledge, and suggests effective options for national chlamydia control strategies. It is directed primarily at policy advisors but should be useful for programme managers and experts in sexual health, especially those at the European or national levels.

The evidence-based options presented here should be interpreted and applied according to clinical, epidemiological, healthcare and resource environments: there is marked variation in current chlamydia control strategies across EU/EEA Member States which reflects differences in available resources, health priorities and uncertainties in the evidence-base for chlamydia control interventions. The evidence base for primary prevention activities is still deficient but expert opinion is that it is prudent to offer these interventions to all at-risk individuals. Diagnosing and treating cases of chlamydia can improve the health of the affected individual, and there is good evidence that offering young women (under 25 years of age) a chlamydia test can reduce the risk of developing pelvic inflammatory disease. Partner notification is an effective way of identifying infected individuals. At present, there is no strong evidence that widespread testing reduces the prevalence of infection or the incidence of long-term reproductive complications. There are also no randomised controlled trials of the impact of a screening programme in an antenatal setting to prevent adverse pregnancy outcomes.

ECDC recommends that EU/EEA Member States have a national strategy or plan for the control of STIs (including chlamydia), especially in the light of the forthcoming WHO Global Strategy on STIs, due to be adopted in May 2016. The strategy should include the provision of primary prevention interventions to at-risk individuals and groups, evidence-based case management guidelines (that include partner notification) for each setting in which chlamydia may be diagnosed, improved systems for the surveillance of diagnosed infections, and an evaluation plan for the strategy. At present, widespread opportunistic testing or a screening programme is only recommended if resources are available and suitable monitoring and evaluation is in place. A screening programme offered in pregnancy (with the aim of preventing adverse pregnancy outcomes) can only be recommended in the context of research. There are marked gaps in the evidence base underpinning population-level chlamydia control activity. The focus of future research should include strengthening knowledge of the natural history of infection and the impact of interventions at the population level. Any future randomised controlled trials of screening programmes should explore the potential adverse consequences of the intervention.

This guidance is limited to the common sexually transmitted form of *Chlamydia trachomatis* (serovars D to K) and does not cover *Lymphogranuloma venereum*. Clinical or diagnostic guidance is also outside the scope of this document.

1 Introduction

The aim of this guidance is to provide support to European Union and European Economic Area (EU/EEA) Member States to develop, implement or improve evidence-based national or local strategies for chlamydia control. It is written primarily for policy advisors but it may also be useful for programme managers and experts in sexual health at the European or national levels.

This guidance updates the ECDC chlamydia control guidance published in 2009 and reflects advances in knowledge described by ECDCs recent *Chlamydia control in Europe* programme of work [1,4-6] which had three overarching aims: to critically review and update the scientific evidence on the epidemiology and natural history of chlamydia and the clinical and cost-effectiveness of screening programmes; to update information about chlamydia prevention and control activities in EU/EEA Member States; and to review the impact of the 2009 ECDC chlamydia control guidance on policy. The findings from this work stream are reported in a series of technical reports [1,4,6].

This guidance outlines the case for chlamydia control in Europe in Chapter 2. A description of the development of this guidance is presented in Chapter 3, and the proposals to Member States are described in Chapter 4. Chapter 5 considers the issues around the implementation and evaluation of a chlamydia control strategy, while Chapter 6 looks at the current gaps in the evidence base for chlamydia control.

This document updates the 2009 guidance in one significant area: it reinforces ECDC's proposal that chlamydia control activity in Member States should focus on effective primary prevention, case management that includes partner notification, and robust surveillance of diagnosed cases. Published research to date (after 2009) has not definitely demonstrated an impact of population-based approaches (e.g. opportunistic testing programmes or screening programmes) on the prevalence of infection. Therefore ECDC's previous proposal remains unchanged: widespread opportunistic testing or screening programmes should be considered on the basis of individual benefit in those tested, but only if sufficient resources are available and suitable monitoring and evaluation is in place [1].

2 Background: The case for chlamydia control in Europe

Overview of chlamydia and chlamydia control

Genital infection with *Chlamydia trachomatis* (chlamydia) is the most commonly reported sexually transmitted infection (STI) in Europe. Chlamydia is often asymptomatic in both women and men. It is straightforward to diagnose and there are cheap and effective antibiotic treatments. However, chlamydia is a public health concern because it can progress to damage the upper reproductive tract and cause serious reproductive tract complications (including pelvic inflammatory disease, ectopic pregnancy and tubal factor infertility) in some people. Chlamydia can also be transmitted from mother to baby during labour leading to disease in the neonate.

Early clinical studies demonstrated that treating chlamydia reduced women's risk of pelvic inflammatory disease [7-9]. Ecological studies from the 1990s reported a decline in the hospitalisation rates for pelvic inflammatory disease (PID) and ectopic pregnancy following the introduction of chlamydia control [10-12]. This led many settings to introduce widespread chlamydia testing for asymptomatic people [4]. The rationale for this was that identification and treatment of asymptomatic infections would reduce transmission and reduce the probability of infection progressing to upper reproductive tract damage [1,13].

The number of diagnosed cases of chlamydia in settings with widespread asymptomatic testing continues to rise [14]. This is partly explained by the increased sensitivity of diagnostic tests and the increase in the numbers of test performed. However, there is no good-quality evidence to suggest that widespread testing strategies have had an impact on the transmission of chlamydia in the population [1]. Randomised controlled trials have demonstrated that offering women chlamydia tests and treatment can reduce the risk of pelvic inflammatory disease at 12 months after testing by 35% [1]. The increase in diagnosed cases of chlamydia that has been seen over recent decades in many high-income countries has been accompanied by a decline in the incidence of PID. However, interpretation of trends in PID case reports is complicated by multiple aetiologies and variations in diagnostic and coding practices across settings and over time. A cross-national comparison has found that at the level of the population there is no consistent association between the rate of diagnosed chlamydia cases and the incidence of diagnosed female reproductive tract chlamydia complications [1,15]. The important gaps in the evidence base for chlamydia control policy include information about how easily the infection spreads, how long it can remain in the body, the risk of progressing to complications, and the benefits of widespread testing at the level of the population [6].

There is considerable variation in chlamydia control policy across EU/EEA Member States [4]. This is probably a reflection of the differences in available resources, health priorities, and uncertainty in the evidence base for chlamydia control interventions [6].

Epidemiology of chlamydia in Europe

A detailed description of the epidemiology of chlamydia in Europe is presented in the ECDC surveillance report *STI in Europe – 2013* [16]. A brief overview is presented here; please refer to the full report for further details.

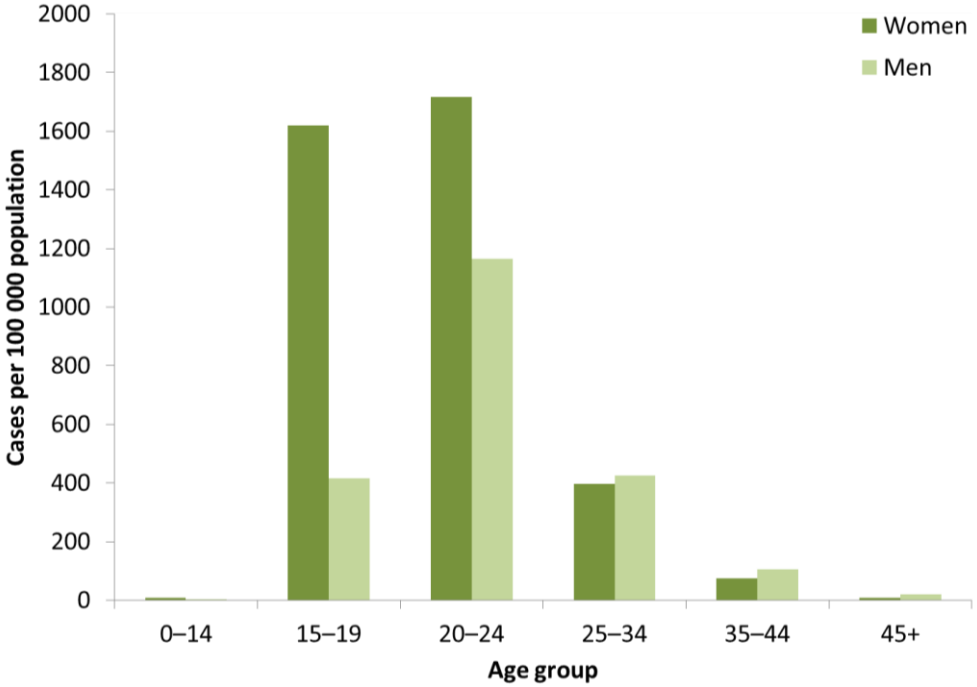
The number of reported cases of chlamydia in Europe has gradually increased since 2004. Chlamydia is the most commonly reported STI in Europe despite many countries not having nationally comprehensive reporting systems. The continual increase in the number of diagnosed cases of chlamydia in Europe is in part due to the policy shift towards more widespread testing of asymptomatic people and the introduction of diagnostic tests with greater sensitivity (change from culture-based methods to nucleic acid amplification tests (NAATs)). These progressive changes in chlamydia testing activity make it difficult to interpret trends over time.

In 2013, there were 384 555 reported cases of chlamydia from 26 EU/EEA Member States, with a total of 182 notified cases per 100 000 population [16]. However, as the majority of infections are asymptomatic, the true incidence of infection is likely to be significantly higher. Two thirds (67%) of all reported cases in Europe in 2013 were in young adults aged 15–24 years; the highest rate of reported infection was in women aged 20–24 years (1 717 cases per 100 000) (Figure 1). These patterns are likely to reflect current testing practices in asymptomatic people as well as the true underlying disease incidence and prevalence.

There are differences in chlamydia testing and reporting practices between the EU/EEA Member States. For a full description of surveillance systems please refer to the ECDC STI surveillance report [16]. Chlamydia control activities are described in an ECDC report entitled *Chlamydia control in Europe* – a survey of Member States [4] (summarised in Table 1).

In 2013, most countries (27/30) had a surveillance system in place. This system was considered comprehensive in twenty countries. The reported rates of chlamydia infection tended to reflect the level of chlamydia control activity (see Figure 2) [4]. This geographical variation in chlamydia testing activity (policy and practice) makes it difficult to make cross-country comparisons.

Figure 1. Age- and gender-specific rates of reported chlamydia infections per 100 000 population (n=383 793 cases), 2013, EU/EEA



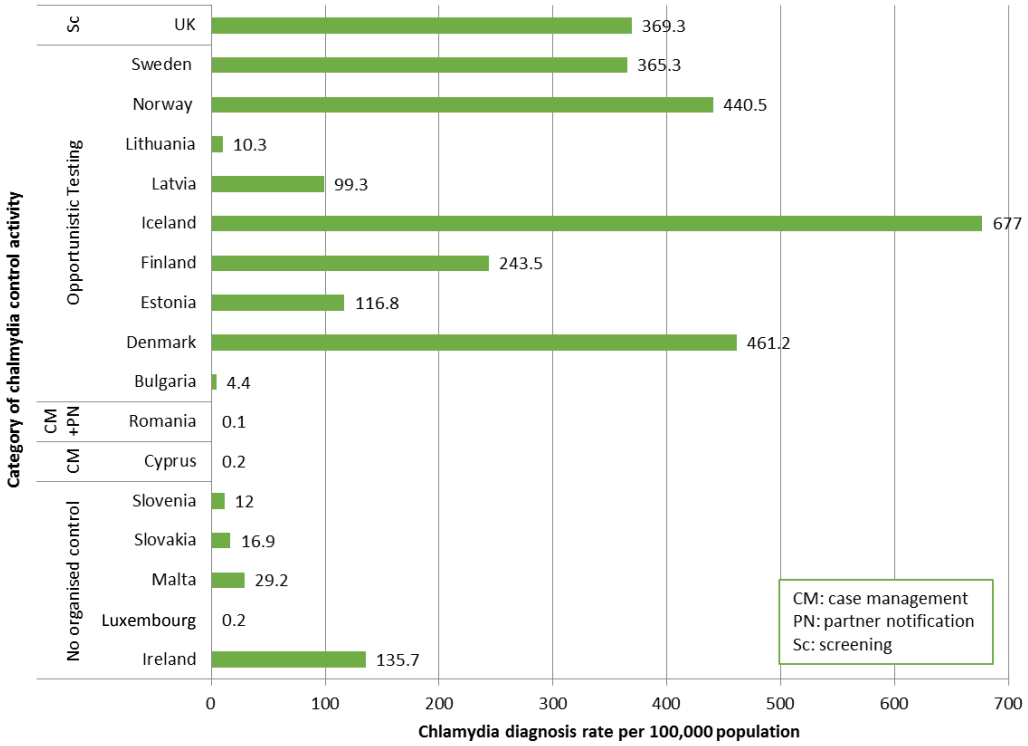
Source: Reproduced from ECDC Surveillance Report – Sexually transmitted infections in Europe*, 2013 [16]*

Note: Includes data from Bulgaria, Cyprus, Denmark, Estonia, Finland, Greece, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Norway, Romania, Slovakia, Slovenia, Sweden and the United Kingdom.

The estimated pooled average prevalence of chlamydia in sexually experienced young adults (aged 18–26 years) is 3.6% (95% confidence interval (CI) 2.4%–4.8%) in women and 3.5% (95% CI 1.9%–5.2%) in men [1]. These figures, however, are based on a small number (n=5) of nationally representative cross-sectional surveys from EU/EEA Member States or the USA [17].

In studies of the general population (i.e. without restrictions on age or sexual experience), the estimated prevalence of chlamydia in women ranged from 1.1% in Norway to 6.9% in Estonia. In men, it ranged from 0.4% in Germany to 6.2% in Norway [1]. These studies suggest that the prevalence of chlamydia varies by age, geographic coverage and sexual experience. [1]. As outlined in the accompanying technical report, these estimates are also subjected to selection bias from the population surveyed, which makes it more likely to overestimate the prevalence of infection in studies with low response rate [1].

Figure 2. Rate of chlamydia diagnosis per 100 000 population, by level of chlamydia control activity, EU/EEA Member States in 2013



Source: Adapted from Chlamydia control in Europe: a survey of Member States *[4] (Table 21) and updated with 2013 surveillance data.*

Note: A country's level of chlamydia control was defined based on a set of key indicators as presented in Appendix 1. Countries not included: Poland, did not participate in the survey; Czech Republic, Germany, Liechtenstein and Portugal: no surveillance data available; Austria, Belgium, France, Greece, Hungary, Italy, Netherlands and Spain: surveillance systems are not comprehensive

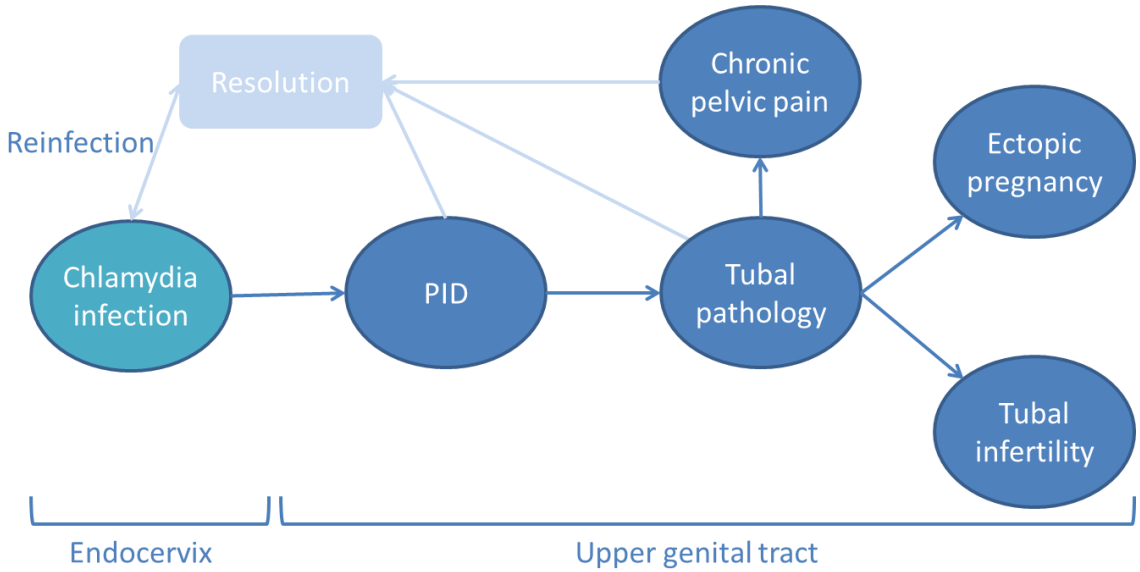
Complications of chlamydia

Figure 3 describes the progression from chlamydia to reproductive tract complications in non-pregnant women. There is a lack of high-quality studies that report the risk of reproductive tract complications in women who have had chlamydia. It was therefore not possible to present consensus estimates of the risk of progression along each arrow in Figure 3 because marked uncertainties in the parameters remain [1]. For example, the duration from infection to progression to the upper genital tract is not known, and the role of subclinical pelvic inflammatory disease (i.e. pelvic inflammation in the absence of symptoms) in the progression from chlamydia to tubal pathology is uncertain. For a full description of these risks and the gaps in the evidence, please refer to the ECDC technical report [1].

PID, ectopic pregnancy and tubal factor infertility all have multiple aetiologies, including chlamydia and gonorrhoea. The proportion of cases of PID, ectopic pregnancy and tubal factor infertility that are caused by chlamydia has not been adequately described, which further complicates the estimation of the risk of progression.

Chlamydia is strongly associated with an increased risk of pelvic inflammatory disease; the risk, however, appears to be lower in studies of women from the general population compared to studies of women presenting for healthcare [1]. The most recent and robust estimate of the risk of pelvic inflammatory disease in untreated asymptomatic women infected with chlamydia is 9% (95% CI 4–19%) at 12 months [1,18]. There are still no direct estimates of the risk of ectopic pregnancy or tubal factor infertility following untreated chlamydia. This is because it is not practical to follow a woman's clinical progression for the potentially long time interval between chlamydia infection and the diagnosis of these complications.

Figure 3. Natural history and sequelae of chlamydia infection in non-pregnant women



Length of arrows is not proportional to time. Pale blue arrows point from conditions that can resolve spontaneously or with treatment. The double-headed pale arrow from Resolution *to* Chlamydia Infection *indicates that reinfection can occur after spontaneous clearance or treatment.*

Source: Reproduced from Chlamydia control in Europe – literature review *[1]*

Mathematical modelling studies have been used to estimate the risks of progression because of the challenges of studying this *in vivo*. These have estimated risks of PID (10–15% after one year) and TFI (1% in lifetime) that are lower than estimates used in some studies of the clinical and cost-effectiveness of chlamydia control interventions [1].

There is growing evidence that repeated chlamydia infections increase the risk of reproductive tract complications in women. It is not yet known if this is due to an increase in the cumulative time individuals with repeated infection have been exposed to chlamydia or whether each subsequent infection carries a higher probability of progression to complications [19]. The timing of tubal damage following chlamydia infection has not been determined therefore it is not possible to estimate the most effective interval for repeat chlamydia testing [1].

Since the late 1990s there have been stable or declining rates of pelvic inflammatory disease, ectopic pregnancy and infertility in high income countries [1]. It is difficult to determine the contribution of population-based chlamydia control interventions to these trends because there have been several other major changes over the same period including changes in lifestyle through the provision of widespread health promotion advice and especially improved reproductive health services [1,20].

Impact on population health and financial cost of chlamydia and its complications

The WHO Global Burden of Disease estimated 9 000 deaths from chlamydia in 2004 globally. All were in women and all occurred outside of the WHO European Region (89% in the South-East Asia Region and 11% in the Eastern Mediterranean Region) [21]. Also for 2004, chlamydia was estimated to have been responsible for 0.2% of the global burden of disability-adjusted life years (DALYs), equal to 3.7 million DALYs lost (91% in women); 6.3% of which were estimated to have occurred in Europe, corresponding to 0.2 million DALYs lost (both sexes) [21]. In the WHO European Region, chlamydia ranked slightly below tuberculosis, with 1.7 million DALYs lost, and HIV/AIDS, with 1.2 million DALYs lost. However, chlamydia had a higher disease burden than other sexually transmitted infections like gonorrhoea and syphilis, with 0.1 and 0.02 million DALYs lost, respectively.

Accurate estimation of the cost-effectiveness of chlamydia control interventions requires the combination of detailed information about the epidemiology and natural history of chlamydia and its complications (including the contribution of chlamydia to complications and the risk of a progressing infection), the clinical effectiveness of interventions (to prevent both complications and transmission), the financial costs of interventions, and the impact of chlamydia and its complications on quality of life. Due to uncertainties in all of these parameters, it is difficult to produce a robust economic evaluation of chlamydia control interventions [22].

Interventions for the control of chlamydia

Overview

The term 'chlamydia control' describes a broad range of deliberate, sustained activities that aim to reduce (or prevent increases in) the incidence and prevalence of chlamydia and the incidence of reproductive tract complications [1]. The spread of chlamydia in the population is determined by how easily the organism can spread from an infected person to a person who is at risk of the infection (probability of transmission), the rate at which this spread can occur (sexual contact rate), and how long a chlamydia-infected person can transmit the infection (duration of infectiousness). Interventions designed to control the spread of chlamydia in the population must target at least one of these three parameters.

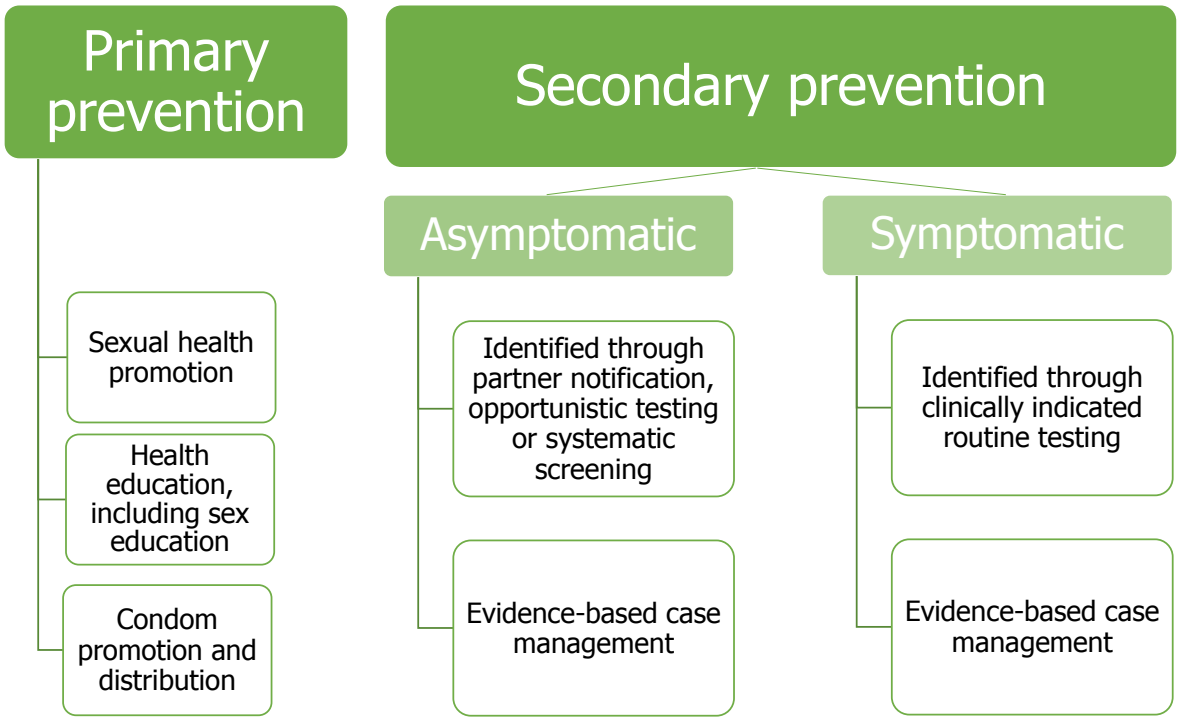
In general terms, interventions designed to control chlamydia can be grouped into **primary and secondary prevention** (Figure 4). Primary prevention aims to prevent new cases of infection, and the mainstay of this are **sexual health promotion activities** (including health education, sex and relationship education in schools, and condom promotion and distribution). Secondary prevention involves the detection and treatment of chlamydia in people who are already infected. People who are infected with chlamydia can be identified when they attend a healthcare provider with symptoms or another relevant clinical presentation (**clinically-indicated testing**) or through **asymptomatic testing**. Asymptomatic testing is the offer of a chlamydia test to a person who does not have symptoms suggestive of chlamydia infection. There are three main methods of asymptomatic testing: **partner notification** (where it is used for case finding, actively seeking people who are thought to have been exposed to chlamydia infection) [1,3]; **opportunistic testing**; and **screening programmes**. The subsequent care of all people diagnosed with chlamydia is called **case management**. The quality of chlamydia control interventions should be the subject of **clinical audits**, and the impact of control interventions should be **monitored and evaluated**.

Primary prevention

Primary prevention activities are those that aim to prevent the occurrence of new cases of chlamydia. Good primary prevention is at the centre of STI control. The overarching aim of primary prevention is to encourage behaviour change that leads to a reduction in the risk of becoming infected with chlamydia. Primary prevention activities seek to improve knowledge and awareness of chlamydia (including the methods that can be used to prevent infection) and encourage relevant behaviour change [4]. Primary prevention activities include sexual health promotion (e.g. health education, media campaigns, sex and relationship education in schools, condom promotion and distribution). They can be aimed at the population (for example public education and awareness campaigns or sex and reproductive health education in schools) or at the individual (for example brief advice in a healthcare setting). A mapping of primary prevention activities in the EU/EEA as of 2012 can be found in the ECDC chlamydia control in Europe survey report [4].

There is no available evidence clearly demonstrating the effectiveness of primary prevention. However, expert opinion strongly favours that prevention should still be offered to all at-risk individuals [6]. Further information about primary prevention for STI/HIV can be found in an ECDC technical report (*Comprehensive approach to HIV/STI prevention in the context of sexual health in the EU/EAA*) [23]. A programme-based response and the promotion of sexual health through information campaigns are described in the WHO guidance *Developing sexual health programmes: a framework for action'* [24].

Figure 4. Interventions for the control of chlamydia in the population



Detection of cases

Figure 5 illustrates the available case detection methods and their relationship to symptomatic or asymptomatic infections.

Clinically indicated testing

Clinically indicated (rather than opportunistic) chlamydia testing occurs during a healthcare consultation where the presenting complaint is related to risk factors for the acquisition of chlamydia or the symptoms of an STI. This includes the testing of patients who have been exposed to other STIs and partner notification.

Partner notification

Partner notification is the practice of notifying, testing and treating the known sexual partners of people diagnosed with chlamydia [25,26]. The UK's National Institute of Health Research has recently published a health technology assessment on the clinical and cost-effectiveness of partner notification technologies for curable STIs including chlamydia [27]. This report also describes the available methods for providing partner notification (Box 1).

Table 1. Methods of partner notification [27]

Methods of partner notification		
Simple	Patient referral	Sexual partners are referred to a healthcare service by their partner and attend.
	Provider referral	Sexual partners are referred to a healthcare service by a member of the healthcare team treating their partner and attend.
Enhanced	Expedited partner therapy	Index case given prescription/antibiotics for their partner. No healthcare consultation required.
	Accelerated partner therapy	Telephone consultation or pharmacist consultation before medications dispensed.

Asymptomatic testing

The term 'asymptomatic testing' refers to chlamydia tests offered to people who do not have symptoms. This can include partner notification, opportunistic testing and screening programmes.

Opportunistic testing

Opportunistic chlamydia testing refers to chlamydia tests which are offered to people in predefined risk groups (e.g. based on age and sex) in healthcare settings, through outreach programmes, or via internet-based services. A test is considered to be opportunistic if the original reason for the interaction is not related to the microorganism for which it has been used (*Chlamydia trachomatis*), its symptoms or risk factors. In addition, the person who is

being offered the test is not required to actively seek a test [1]. Nonetheless, opportunistic testing can occur both with and without a structured programme targeting a certain population.

Screening programme

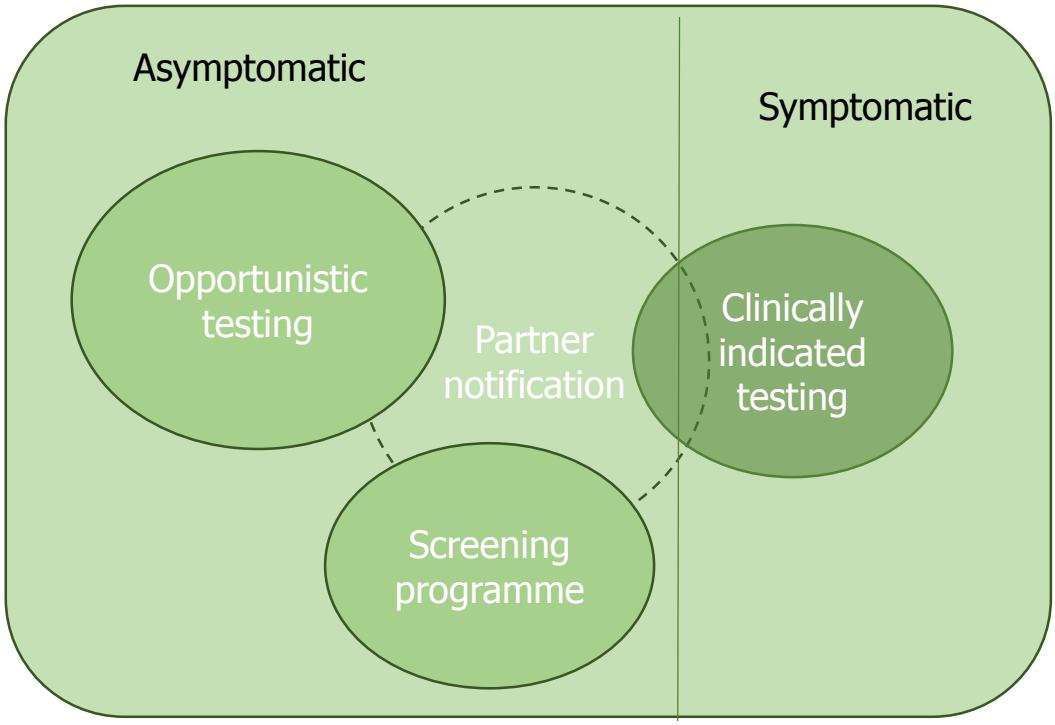
Screening refers to offering chlamydia tests to asymptomatic people in a defined population who are considered to be at increased risk of infection compared with the general population and are also more likely to be helped rather than harmed by the test [1,28]. A screening programme is targeted at a particular population, and it is a continuous process during which chlamydia tests are offered regularly to a defined subpopulation [5]. Screening programmes can be register-based (people are proactively invited from a maintained register to take a test (e.g. population register or healthcare register) or opportunistic (professionals offer a test to eligible people in predetermined settings).

It is possible that settings with well-implemented opportunistic testing programmes have higher rates of testing and case detection than settings with a formal screening programme. Therefore the difference between both approaches is not related to the proportion of the population who are tested, but to the target population, the way how people are identified and offered a test, and to the measures used for evaluation. Opportunistic testing programmes target the users of healthcare services or other places where the target population can access testing, whereas screening programmes target the population. A screening programme requires an element of 'advertising' the service to the target population, either through a specific personal invitation or by generally raising awareness of the screening programme, in order to generate demand.

Screening programmes require costly resources, including infrastructure, monitoring and evaluation [1]. When assessing the cost implications of a screening programme, determining the costs of these resources is essential, in addition to the actual costs of opportunistic testing (e.g. practitioner, test and treatment costs).

The evidence-review commissioned by ECDC reported that there was evidence from randomised controlled trials (RCTs) that a single offer of chlamydia screening may reduce the incidence of pelvic inflammatory disease at one year by 36% (RR 0.64 (95% CI 0.45–0.90))[1] [1]. The same review did not find any RCTs that reported on the impact of screening programmes on chlamydia prevalence at the population level or the level of annual screening required to reduce chlamydia prevalence. There is also no evidence from RCTs on the effectiveness of antenatal chlamydia screening in reducing adverse pregnancy outcomes.

Figure 5. Case detection methods



[1] GRADE assessment of the quality of this evidence is 'moderate'. For further details please refer to [1].

Case management

There is evidence that treating chlamydia can reduce the risk of reproductive tract complications [7,29,30]. The management of all detected cases of chlamydia should be based on evidence-based clinical guidelines that include guidance on partner notification. These guidelines should be systematically applied to all people with chlamydia, irrespective of detection method (e.g. symptomatic presentation, opportunistic testing, partner notification or screening programme) or the diagnostic setting (e.g. primary care, hospital or outreach activity).

Surveillance

Surveillance is the continuous and systematic collection and analysis of information, in this case, about chlamydia testing and diagnoses. Surveillance of most communicable diseases is usually conducted at the national level, and the collected data are used to monitor the epidemiology of the disease and the implementation of control interventions. Surveillance can be comprehensive (entire population coverage) or sentinel (coverage limited to an informative group, e.g. population subgroup, region, healthcare services, selected STI clinics, etc.). The monitoring of chlamydia control interventions can be achieved through the implementation and maintenance of high-quality surveillance systems (sentinel or comprehensive) that systematically monitor the incidence of diagnosed infections, the number of selected complications, and the number of performed chlamydia tests. Monitoring of chlamydia tests is essential to be able to adequately interpret chlamydia infection surveillance data [31].

Chlamydia control strategy

The first step towards the implementation of a comprehensive and effective chlamydia control programme is the universal, systematic adoption of a chlamydia control strategy. Commitment and leadership from healthcare policymakers is required to ensure the effective resourcing and implementation of the strategy. The strategy should take into account the national context (including opportunities and limitations) and the contemporary evidence base.

It is essential that national strategies are tailored to the national situation and developed in consultation with key local stakeholders which – depending on the context – may include policymakers, healthcare funders, healthcare commissioners, healthcare providers (including diagnostic services), public health authorities, national professional healthcare organisations, health economists, clinicians, microbiologists, related services (e.g. schools and youth centres), surveillance experts, and sexual health charities.

Chlamydia control in Europe

ECDC performed a systematic survey of chlamydia control activities in Member States in 2012 [4]. The survey covered thirteen key indicators across seven domains (Appendix 1). The survey report compares responses from the 28 participating EU/EEA Member States with reported local activity in 2007 [4,32]. The findings of this report are summarised below; please refer to the technical report for a full description of the methods and results.

Overall, there has been considerable progress in the development and implementation of chlamydia control policies in Europe since 2007. There has been an increase in the proportion of countries with organised chlamydia control activities. Other increases are in the proportion of countries that include partner notifications in their case management guidelines and countries that offer opportunistic testing to at least one population group (Table 1). However, the strengthening of control activities is not consistent across all countries, and there is still a marked variation in the reported chlamydia control activity across EU/EEA Member States.

Table 2. Comparison of chlamydia control activities in Europe in 2007 and 2012 based on the hierarchical classification used for/in ECDC survey [5]

Chlamydia control category	Countries at this level in 2007 (n=27)	Countries at this level in 2012 (n=28)
No organised chlamydia control activity	11 (41%)	6 (21%)
Case management guidelines	5 (19%)	3 (11%)
Case management guidelines that include partner notification	3 (11%)	5 (18%)
Opportunistic testing	6 (22%)	13 (46%)
Screening programme	2 (7%)	1 (4%)

Source: ECDC [4]

The 2012 survey explored additional aspects that were not addressed in the 2009 guidance, like policy indicators, existence of formal plans and primary prevention activities. Less than half (39%, 11/28) of the EU/EEA Member States that participated in the 2012 survey reported having a coordinated national strategy or plan for the control of STIs, and chlamydia was named in only six of these plans. Organised primary prevention activities were reported

by 22/27 (81%) countries (including general media campaigns (n=6) and education in schools (n=11)). The majority of countries (93%, 26/28) reported having a system to report and monitor diagnosed chlamydia cases. Reporting was comprehensive (i.e. it involved all settings) in 18 countries. In 89% of countries (25/28), healthcare for people with STIs is provided within the general healthcare system (including specialised services). The cost of healthcare (diagnosis and treatment) is at least partially covered by national health insurance systems in 93% (26/28) of countries.

The majority of countries (79%, 22/28) reported having at least one national case management guideline. In 68% (19/28) of countries this guidance included partner notification, and in 32% (9/28) it included health promotion advice about preventing reinfection. Mandatory partner notification was reported to be applied in 8 (29%) countries. All the countries that responded to the survey reported that nucleic acid amplification tests (NAATs) are available; in 82% of these countries (23/28), NAATs were the main method of diagnosis (defined as >90% of cases). The majority of countries (79%, 22/28) reported that diagnostic services participated in internal quality assessment programmes. Almost all countries (93%, 26/28) maintain a system for reporting and monitoring the incidence of diagnosed infections.

Opportunistic testing for at least one asymptomatic population group was recommended by clinical guidelines in 18 (64%) countries. Targeted groups include young people (n=10); pregnant women (n=10); those at high risk of infection, e.g. sex workers (n=3); men who have sex with men (n=6); and migrants (n=1). However, only five countries reported that opportunistic testing was actually implemented, and only three of these countries had a specific guideline for this.

The survey did not collect information about the coverage of opportunistic testing programmes. In 2012, England was the only EU/EEA Member State with an organised opportunistic national chlamydia screening programme [33]. The Netherlands trialled a registry-based screening programme that was halted following RCT evidence indicating that it was not cost-effective [34]. There were three countries who reported plans to introduce a chlamydia screening programme.

Seven of the 12 countries who reported a change in their level of chlamydia control between 2007 and 2012 reported that they used the 2009 version of the ECDC guidance document on chlamydia. This version of the guidance was also used by 6 of the 13 countries that did not report a change in their level of chlamydia control [6].

Evaluation of the 2009 ECDC Chlamydia control guidance

ECDC commissioned an evaluation of the impact of the 2009 Chlamydia control guidance, which was published in 2015 [6]. The majority (92%, 24/26) of country representatives who responded to the 2012 survey reported that they were aware of the 2009 guidance document. The conclusion of the evaluation was that the structure and content of the 2009 guidance document should be revised in light of the advances to the evidence base and that the document should be more accessible to its target audience.

Challenges of chlamydia control

Challenges in the prevention and control of chlamydia originate from the complicated natural history of the infection, the stigma associated with STIs, and the gaps in the evidence base (Table 2). The asymptomatic nature of infection and the lack of immunity contribute to the ongoing transmission of infection in the population [4]. Societal influences have a noticeable impact on participation numbers in chlamydia control interventions, and gaps in the evidence hamper the design of an evidence-based control strategy.

Table 3. Major challenges to chlamydia control

Challenge	Implication/effect
Natural history of infection	
The majority of chlamydia infections are asymptomatic	If the uptake of partner notification or other asymptomatic testing is low, infected people without symptoms can remain infectious to others until their infection resolves spontaneously. Mathematical modelling has estimated that an untreated infection can persist for 1.36 years (95% CI 1.1 to 1.6 years) [35] and that progression from chlamydia to pelvic inflammatory disease can happen at any point during this period [36].
No lasting immunity to infection	After the completion of successful treatment, individuals remain susceptible to reinfection. If health promotion and safe sex advice is not provided, individuals may be reinfected by their current/next partner.
No vaccine	At present there is no vaccine available to protect against chlamydia infection or subsequent complications.
Societal influences	
Stigma	Provision of successful interventions (including partner notification) to control chlamydia is hampered by the stigma associated with STIs.

Challenge	Implication/effect
Resource limitations	The costs of the components of a chlamydia control strategy are variable between settings. High costs may lead to patchy or reduced implementation.
Gaps in the evidence	
Burden of disease in the population is not known	The population prevalence and incidence of infection is challenging to measure accurately, which compromises the ability to evaluate the performance of control interventions against an accurate benchmark.
Timing of tubal damage	The timing is not known therefore there is insufficient evidence to comment on the most effective timing of asymptomatic testing in order to prevent tubal damage in women [13].
Contribution of chlamydia to complications	Pelvic inflammatory disease, ectopic pregnancy and tubal factor infertility have multiple aetiologies. The proportion attributable to chlamydia has not been described in a contemporary setting and it is likely to vary geographically and temporally.
Role of repeat infection in tubal damage (i.e. pathogenesis)	The immunological processes that lead to tubal damage are not known. Therefore it is not possible to determine whether the primary focus of control efforts should be the prevention/early detection/treatment of primary infection, repeat infection, or both [13].

3 Guidance development

Evidence review

The *Chlamydia control in Europe* programme of work was commissioned by ECDC in 2011 and undertaken by a consortium of researchers led by Professor Nicola Low at the University of Bern (see acknowledgements). ECDC has published three technical reports that detail the methods and findings of this project:

- *Chlamydia control in Europe*: Literature review [1]
- *Chlamydia control in Europe*: Survey of Member States [4]
- *Chlamydia control in Europe*: Evaluation of the 2009 guidance [6]

Developing the chlamydia guidance 2015

This guidance updates the ECDC Chlamydia control guidance published in 2009 [5]. The evidence presented in the three technical reports of the *Chlamydia control in Europe* programme of work (2011–2015) was used as the basis for revisions to the 2009 version of the guidance [1,4,6]. The authors took into account the policy implications of this evidence and updated the 2009 guidance accordingly.

A draft version of this guidance was discussed at an expert meeting hosted by ECDC in March 2015. The participants at the expert meeting reviewed the summary of the key advances in knowledge, the content, and the format of the guidance. Subsequently, the authors made content changes and updated the format of the document based on the ECDC guidance template. A revised draft was then reviewed by members of the *Chlamydia control in Europe* project team in June 2015. Consensus was obtained on the conclusions presented in this guidance.

4 Conclusions

Overview

This guidance is aimed at the control of the common sexually transmitted form of *Chlamydia trachomatis* (serovars D to K). Because health promotion efforts relating to sexual health, risk factors and complications are similar for most STIs, countries that want to implement a chlamydia control strategy should consider chlamydia control activities within the wider framework of a generic sexual health programme/strategy, rather than a separate, stand-alone activity.

The standard minimum level of chlamydia prevention and control in EU/EEA Member States should include (Figure 6):

- a national strategy or plan for STI control;
- primary prevention activities for STIs;
- evidence-based chlamydia case management guidelines that address criteria for testing, diagnostic method, treatment, partner notification, and reporting of cases;
- surveillance of diagnosed chlamydia cases;
- monitoring and evaluation of activities.

It is not yet known whether the effective implementation of a robust chlamydia control strategy will reduce the overall costs of chlamydia infections and its reproductive tract consequences in the long term. Developing and implementing control programmes, however, will require additional resources and capacities in order to handle the increased volume of testing. It is therefore recommended that the key components of a chlamydia control strategy are already in place before further expanding control interventions.

Figure 6. Key components of a chlamydia control strategy

The evidence base for chlamydia control has improved since 2009 when the first version of this guidance was published: there is a growing body of evidence and the overall quality of publications has improved. The following section presents ECDCs recommendations for a chlamydia control strategy informed by the advances in the evidence. Recommendations build on the information presented above in Chapter 2 and the ECDC literature review *Chlamydia control in Europe* [1]. Additional sources of information are cited where relevant.

Primary prevention

Primary prevention of STIs may be covered by existing national public health guidance, for example a sexual and reproductive health strategy.

Young people who are sexually active are at risk from chlamydia. Educational efforts relating to sexual health and primary prevention should therefore be directed at schools, youth venues, and healthcare settings. Healthcare consultations involving sexual health or contraception should also cover chlamydia, as should sexual health and relationship education at schools. Other topics to be addressed are the symptoms and complications of STIs, protection against infection (e.g. condoms, advice on sexual behaviour), and how to access sexual healthcare

services. The effectiveness or acceptability of primary prevention interventions aimed at young people may be improved if the target group is involved in their development and implementation.

There are no systematic reviews of the clinical or cost-effectiveness of primary prevention activities for the control of chlamydia [23]. However, there is a body of expert opinion that these intervention should still be offered because they can produce broader benefits to sexual health and carry a limited risk of harm [6].

Case management

This guidance does not cover the development of evidence-based clinical case management guidelines. There are useful case management guidelines published by professional medical bodies (e.g. International Union against STI (IUSTI): *2015 European guideline on the management of* Chlamydia trachomatis *infections* [37]; CDC: *2015 sexually transmitted diseases treatment guidelines* [44]) or existing comprehensive guidelines from other countries that may be consulted.

The key components of case management include:

- target population and indications for testing (i.e. who to test);
- history taking and clinical examination;
- which diagnostic test to use;
- which treatment to use;
- method of partner notification and management;
- information about follow up (including when to re-test);
- the prevention of reinfection (i.e. advice on sexual behaviour and condom use);
- how to report cases for surveillance [2].

Detection of cases

Clinically-indicated testing

Clinical case management guidelines should contain a description of the clinical indications for a chlamydia test.

Partner notification: Partner notification is an essential component of case management. The UK NIHR report on partner notification suggest that enhanced patient referral should be provided in primary care and specialist sexual health services [27]. For full details please refer to this report.

Opportunistic testing and/or screening programme: individual level

There is growing evidence of the benefits of opportunistic testing in women. The combined findings from four RCTs indicate that opportunistic chlamydia testing in asymptomatic young women can reduce the risk of developing pelvic inflammatory disease. Overall, the risk of pelvic inflammatory disease at 12 months was 35% lower in women who were offered a chlamydia test compared with the control groups [1,30].

Screening programmes have not been shown to reduce the risk of ectopic pregnancy, female infertility or epididymitis in men, but there is very limited evidence available, which may in part be due to long timelines involved in this sort of evaluation [1,38].

None of the RCTs of screening programmes reported on the potential adverse effects of the intervention (e.g. relationship breakdown or psychological distress) [1], and there are no RCTs of the effectiveness of chlamydia screening programmes in pregnancy (to prevent adverse pregnancy outcomes, neonatal morbidity (e.g. pneumonia or conjunctivitis), or neonatal mortality) [1].

Offering a chlamydia test opportunistically during a healthcare consultation or outreach activity, or systematically inviting people to be tested, increases the testing rates in young heterosexual men and women [4,28].

Opportunistic testing and/or screening programme: population level

There is very little high-quality evidence of the population-level impact of widespread testing or screening programmes, which may be in part due to the difficulty in measuring this impact. Mathematical models suggest that population-based screening could reduce the prevalence of chlamydia in the population [1,39-41]. However there is an absence of evidence from RCTs to demonstrate that chlamydia screening programmes are able to do this in practice [1,42].

Most studies suggest that chlamydia screening programmes are cost-effective under certain assumptions, but the underlying assumptions are based on weak evidence [1]. The gaps in the evidence-base for chlamydia make it difficult to disperse the uncertainty over the actual cost-effectiveness of screening programmes.

For these reasons, widespread opportunistic testing or screening programmes for sexually active men and women under 25 years of age is only recommended if sufficient resources are available and suitable monitoring and evaluation is in place [4].

If delivered, opportunistic testing or screening programme guidelines need to define who should be offered a test and how and how often a person should be tested or offered a test.

Surveillance

National surveillance systems should use consistent epidemiological methods (e.g. for defining target populations, clear sampling frames, etc.) and clearly documented case definitions and diagnostic methods. This is necessary to ensure that collected data can be used to describe trends in chlamydia epidemiology or to perform a pre-post comparison of changes in strategy or practice. Information from surveillance systems can prove to be very useful in the evaluation of the performance of healthcare interventions. The scope of a surveillance system should be clearly defined (e.g. population group, location, clinical data) and information has to be collected systematically. The collated information should include the following:

- Number of diagnosed chlamydia cases (ideally stratified by age, sex, place of residence, sexual orientation)
- Number of diagnostic tests performed (used as denominator to calculate positivity)
- Indication for test (e.g. symptomatic, clinically indicated, partner notification, opportunistic testing)
- Type of test
- Type of sample (e.g. urine, rectal)
- Location of test (e.g. primary care)

Surveillance could also be extended to monitor the incidence and trends for selected complications. Detailed information about the specification for a surveillance system is outside the scope of this guidance.

5 Next steps

Public health and healthcare interventions recommended as part of a local or national chlamydia control strategy should be supported by evidence of their clinical and cost-effectiveness, or by expert opinion if this evidence is absent. All aspects of the implementation should be carefully planned. Activities following the start-up phase should be supported by locally gathered evidence in order to ensure that the intended outcomes are actually achieved.

In many EU/EEA Member States the responsibility for commissioning and providing the range of interventions that contribute to chlamydia control is likely to lie with many different organisations. A coordinated approach to implementation, monitoring and evaluation is required at all levels in order to inform a comprehensive evaluation of the performance of an applied control strategy. Clinical audit is a key tool to measure and monitor compliance against standards for service delivery.

Implementation

All chlamydia control activity should be underpinned by appropriate resources, guidelines and training. In 2011, Turner et al. published a tool, based on data from England's National Chlamydia Screening Programme, which can assist in estimating the potential cost of population-based chlamydia testing at the local, national and international levels [43]. To improve accuracy, the tool can be adapted to accommodate local data.

The successful implementation of a strategy requires cooperation between stakeholders and organisations to achieve a coordinated approach. An implementation plan can be developed in consultation with stakeholders to facilitate this process and align expectations. An implementation plan should detail the activities, resources, responsible individuals, timescale, and monitoring and evaluation.

Evaluation

Evaluation is a fundamental component of any public health intervention strategy and should therefore be part of any chlamydia control strategy. Evaluation considers the broader perspective of whether the control intervention, or programme of interventions, should be continued, amended or discontinued. An evaluation and its findings are specific to an individual service. Broadly, the evaluation of a chlamydia control strategy can be divided into the following components: 1) dissemination and implementation/uptake of the strategy; 2) performance of the interventions (including health promotion, clinical services and surveillance); and 3) impact of the strategy at the population level.

A robust plan to evaluate the impact of a chlamydia control strategy or an amended control strategy should be in place before a new approach is implemented. Evaluation at the local level should be designed to measure the impact of the strategy together with its unintended outcomes. Information from a comprehensive evaluation can be used by policymakers, local programme coordinators, commissioners, or providers to monitor the performance of the interventions and make changes if necessary. Improvements in chlamydia control do not necessarily require a change in the type of control interventions but can often be achieved by strengthening existing interventions [6].

Ideally, evaluation should focus on the results delivered by a chlamydia control strategy. Because of the considerable length of time between chlamydia infection and certain disease outcomes (e.g. infertility), it is also necessary to monitor process measures. Defining appropriate process and outcome measures for the components of a chlamydia control strategy can be challenging because of the uncertainties in the evidence base. For example, a process target that looks at a proportion of the tested target group can provide information about the uptake of an intervention, but it may not be linked to population prevalence.

6 Possible implications for public health practice and research

Overview

The publication of this updated guidance is in response to the ECDC *Chlamydia control in Europe* framework contract, initiated in 2011. Readers of this guidance are advised to review local chlamydia control strategies against the suggested components of a strategy presented in Figure 6 and the 13 key indicators for chlamydia control activity presented in the Appendix.

Gaps in the evidence

Despite more than thirty years of research into the epidemiology and control of chlamydia there are still fundamental gaps in the evidence base that impede the development of evidence-based recommendations for chlamydia control [6]. The *Chlamydia control in Europe* programme of work identified the following major gaps:

- Evidence base for primary prevention (for chlamydia and other STIs)
- Evidence base for case management
- Evidence base for screening programmes in pregnancy to prevent adverse pregnancy outcomes
- Natural history of chlamydia including the duration of untreated infection, the risk of transmission, and the proportion of infections that are asymptomatic
- Quantitative estimates of the true risk of complications following treated and untreated infections (in men and women)
- Estimates of the impact of chlamydia on quality of life
- Effectiveness of control interventions at the population level (including the impact on prevalence)
- Potential negative consequences of widespread testing interventions for asymptomatic populations

References

1. European Centre for Disease Prevention and Control. Chlamydia control in Europe: literature review. Stockholm: ECDC; 2014.
2. World Health Organization. Guidelines for the management of sexually transmitted infections; revised version. Geneva: WHO; 2006.
3. Last JM. A dictionary of epidemiology. Oxford: Oxford University Press; 2001.
4. European Centre for Disease Prevention and Control. Chlamydia control in Europe: a survey of Member States. Stockholm: ECDC; 2014.
5. European Centre for Disease Prevention and Control. Chlamydia control in Europe. Stockholm: ECDC; 2009.
6. European Centre for Disease Prevention and Control. Chlamydia control in Europe – Qualitative evaluation of the impact of the 2009 ECDC guidance document *Chlamydia control in Europe*. Stockholm: ECDC; 2015.
7. Rahm VA, Belsheim J, Gleerup A, Gnarpe H, Rosen G. Asymptomatic carriage of *Chlamydia trachomatis* – a study of 109 teenage girls. Eur J Sex Transm Dis. 1986;3:4.
8. Schachter J, Causse G, Tarizzo ML. Chlamydiae as agents of sexually transmitted diseases. Bull World Health Organ. 1976;54(3):245-54.
9. Stamm WE, Guinan ME, Johnson C, Starcher T, Holmes KK, McCormack WM. Effect of treatment regimens for *Neisseria gonorrhea* on simultaneous infection with *Chlamydia trachomatis*. N Engl J Med. 1984;310(9):545-9.
10. Egger M, Low N, Smith GD, Lindblom B, Herrmann B. Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. BMJ. 1998;316(7147):1776-80.
11. Hillis SD, Nakashima A, Amsterdam L, Pfister J, Vaughn M, Addiss D, et al. The impact of a comprehensive chlamydia prevention program in Wisconsin. Fam Plann Perspect. 1995;27(3):108-11.
12. Kamwendo F, Forslin L, Bodin L, Danielsson D. Decreasing incidences of gonorrhea- and chlamydia-associated acute pelvic inflammatory disease. A 25-year study from an urban area of central Sweden. Sex Transm Dis. 1996;23(5):384-91.
13. Gottlieb SL, Martin DH, Xu F, Byrne GI, Brunham RC. Summary: The natural history and immunobiology of *Chlamydia trachomatis* genital infection and implications for Chlamydia control. J Infect Dis. 2010;201 Suppl 2:S190-204.
14. European Centre for Disease Prevention and Control. Annual epidemiological report 2014 – Sexually transmitted infections, including HIV and blood-borne viruses. Stockholm: ECDC; 2015.
15. Bender N, Herrmann B, Andersen B, Hocking JS, van Bergen J, Morgan J, et al. Chlamydia infection, pelvic inflammatory disease, ectopic pregnancy and infertility: cross-national study. Sex Transm Infect. 2011;87(7):601-8.
16. European Centre for Disease Prevention and Control. Sexually transmitted infections in Europe 2013. Stockholm: ECDC; 2015.
17. Redmond SM, Alexander-Kisslig K, Woodhall SC, van den Broek IV, van Bergen J, Ward H, et al. Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis. PloS one. 2015;10(1):e0115753.
18. Oakeshott P, Kerry S, Aghaizu A, Atherton H, Hay S, Taylor-Robinson D, et al. Randomised controlled trial of screening for *Chlamydia trachomatis* to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. BMJ.2010;340.
19. Haggerty CL, Gottlieb SL, Taylor BD, Low N, Xu F, Ness RB. Risk of sequelae after *Chlamydia trachomatis* genital infection in women. J Infect Dis. 2010;201 Suppl 2:S134-55.
20. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013;11:66.
21. World Health Organisation. The global burden of disease: 2004 update. Geneva, Switzerland: WHO; 2008.
22. Jackson LJ, Auguste P, Low N, Roberts TE. Valuing the health states associated with *Chlamydia trachomatis* infections and their sequelae: a systematic review of economic evaluations and primary studies. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2014;17(1):116-30.
23. European Centre for Disease Prevention and Control. A comprehensive approach to HIV/STI prevention in the context of sexual health in the EU/EEA. Stockholm: ECDC: 2013.
24. Aggleton P, Wood K, Thomas F. Developing sexual health programmes. A framework for action. World Health Organization. Geneva, Switzerland; 2010.
25. Ward H, Bell G. Partner notification. Medicine (Abingdon). 2014;42(6):314-7.

26. European Centre for Disease Prevention and Control. Public health benefits of partner notification for sexually transmitted infections and HIV. Stockholm: ECDC; 2013.

27. Althaus CL, Turner KM, Mercer CH, Auguste P, Roberts TE, Bell G, 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 technology assessment (Winchester, England). 2014;18(2):1-100, vii-viii.

28. Low N. Screening programmes for chlamydial infection: when will we ever learn? BMJ. 2007;334(7596):725-8.

29. 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*. N Engl J Med. 1984;310(9):545-9.

30. Gottlieb SL, Xu F, Brunham RC. Screening and treating *Chlamydia trachomatis* genital infection to prevent pelvic inflammatory disease: interpretation of findings from randomized controlled trials. Sex Transm Dis. 2013;40(2):97-102.

31. Kløvstad H, Aavitsland P. Denominators count: supplementing surveillance data for genital *Chlamydia trachomatis* infection with testing data, Norway, 2007 to 2013. Euro Surveill 2015;20(36):pii=30012

32. European Centre for Disease Prevention and Control. Review of chlamydia control activities in EU countries. 2007. Stockholm: ECDC; 2007.

33. Public Health England. National chlamydia screening programme. Available from: http://www.chlamydiascreening.nhs.uk/ [accessed 20 Jan 2016].

34. de Wit GA, Over EA, Schmid BV, van Bergen JE, van den Broek IV, van der Sande MA, et al. Chlamydia screening is not cost-effective at low participation rates: evidence from a repeated register-based implementation study in the Netherlands. Sex Transm Infect. 2015;91(6):423-9.

35. Price MJ, Ades AE, Angelis DD, Welton NJ, Macleod J, Soldan K, et al. Mixture-of-exponentials models to explain heterogeneity in studies of the duration of *Chlamydia trachomatis* infection. Stat Med. 2013;32(9):1547-60.

36. Herzog SA, Althaus CL, Heijne JC, Oakeshott P, Kerry S, Hay P, et al. Timing of progression from *Chlamydia trachomatis* infection to pelvic inflammatory disease: a mathematical modelling study. BMC Infect Dis. 2012;12:187.

37. Lanjouw E, Ouburg S, de Vries HJ, Stary A, Radcliffe K, Unemo M. 2015 European guideline on the management of *Chlamydia trachomatis* infections. Int J STD AIDS. 2015.

38. Andersen B, van Valkengoed I, Sokolowski I, Moller JK, Ostergaard 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(2):156-61.

39. Kretzschmar M, Turner KME, Barton PM, Edmunds WJ, Low N. Predicting the population impact of chlamydia screening programmes: comparative mathematical modelling study. Sex Transm Infect. 2009;85(5):359-66.

40. Kretzschmar M SC, Leichliter J, Berman S. Effects of screening and partner notification on Chlamydia positivity in the United States: a modeling study. Sex Transm Dis. 2012;39(5):6.

41. Schmid BV OE, van den Broek IV, Op de Coul EL, van Bergen JE, Fennema JS, et al. Effects of population-based screening for *Chlamydia* infections in the Netherlands limited by declining participation rates. PloS one. 2013;8(3).

42. van den Broek IV vBJ, Brouwers EE, Fennema JS, Götz HM, Hoebe CJ, et al. Effectiveness of yearly, register based screening for chlamydia in the Netherlands: controlled trial with randomised stepped wedge implementation. BMJ: British Medical Journal. 2012;345:e4316.

43. Turner K, Adams E, Grant A, Macleod J, Bell G, Clarke J, et al. Costs and cost effectiveness of different strategies for chlamydia screening and partner notification: an economic and mathematical modelling study. BMJ. 2011;342.

44. Workowski KA, Bolan GA; CDC. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(3).

Appendix

Topic headings and key indicators used for the assessment of chlamydia control activities in EU/EEA Member States in the 2012 survey.

Topic headings		Activity level in ECDC guidance
Indicator no.*	Description	
Chlamydia strategies and plans		
1	The Member State has published specific strategy or plan for the control of STIs, either as a standalone document or as part of an HIV/AIDS/STI control strategy or plan.	A
Primary prevention		
2	A strategy or plan addresses sexual health promotion, including the primary prevention of chlamydia.	A
3	The Member State has organised activities to improve knowledge, behaviour and awareness of chlamydia prevention, diagnosis and treatment in a) the whole population or b) specific population groups.	A
Case management guidelines		
4	The Member State or professional organisation in the Member State endorses a clinical guideline for chlamydia case management for one or more medical professional groups (including diagnosis and treatment).	A/B
5	Case management guidelines explicitly address: a) case finding through partner notification; b) advice or counselling on prevention of future infection.	B
Opportunistic testing and screening programmes		
6	Asymptomatic people from a) specific high-risk groups or b) larger groups in the population are offered chlamydia testing opportunistically.	C
7	A national or regional programme that offers screening to a substantial part of the population at risk is in place.	D
Activities not explicitly stated in levels A to D of the 2009 guidance (but included in the survey):		
Organisation of STI services		
8	Healthcare services that diagnose and treat people with STI symptoms are accessible within the general health system or in specialised STI clinics.	
Laboratory diagnosis		
9	Laboratories use reliable diagnostic tests for chlamydia.	
10	Laboratories take part in a recognised quality control programme.	
Surveillance		
11	Surveillance of chlamydia cases, trends in specific groups are analysed.	
12	Surveillance of chlamydia testing, high and lower risk groups are covered.	
13	Data about occurrence of potential complications from chlamydia, such as PID, ectopic pregnancy and infertility are monitored.	

PID, pelvic inflammatory disease; STI, sexually transmitted infection

** The survey covered 13 indicators across seven domains. Survey questions relating to each key indicator are shown in [5], Appendix, Table 2.*

Source: ECDC [4]

European Centre for Disease Prevention and Control (ECDC)

Postal address:
Granits väg 8, SE-171 65 Solna, Sweden

Visiting address:
Tomtebodavägen 11A, SE-171 65 Solna, Sweden

Tel. +46 858601000
Fax +46 858601001
www.ecdc.europa.eu

An agency of the European Union
www.europa.eu

Subscribe to our monthly email
www.ecdc.europa.eu/en/publications

Contact us
publications@ecdc.europa.eu

Follow us on Twitter
@ECDC_EU

Like our Facebook page
www.facebook.com/ECDC.EU

ECDC is committed to ensuring the transparency and independence of its work

In accordance with the Staff Regulations for Officials and Conditions of Employment of Other Servants of the European Union and the ECDC Independence Policy, ECDC staff members shall not, in the performance of their duties, deal with a matter in which, directly or indirectly, they have any personal interest such as to impair their independence. Declarations of interest must be received from any prospective contractor(s) before any contract can be awarded.
www.ecdc.europa.eu/en/aboutus/transparency

HOW TO OBTAIN EU PUBLICATIONS

Free publications:

- one copy:
  via EU Bookshop (http://bookshop.europa.eu);
- more than one copy or posters/maps:
  from the European Union's representations (http://ec.europa.eu/represent_en.htm);
  from the delegations in non-EU countries (http://eeas.europa.eu/delegations/index_en.htm);
  by contacting the Europe Direct service (http://europa.eu/europedirect/index_en.htm) or
  calling 00 800 6 7 8 9 10 11 (freephone number from anywhere in the EU) (*).

  (*) The information given is free, as are most calls (though some operators, phone boxes or hotels may charge you).

Priced publications:

- via EU Bookshop (http://bookshop.europa.eu).

Publications Office