Public Health England

Opportunistic Chlamydia Screening of Young Adults in England

An Evidence Summary

About Public Health England

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Purpose

To provide an overview of current, published evidence relating to chlamydia screening among young adults in England to support public health and sexual health professionals, including Directors of Public Health, elected members, commissioners and providers of sexual health and chlamydia screening services.

Background

Chlamydia is a common bacterial sexually transmitted infection which is frequently asymptomatic. The National Chlamydia Screening Programme (NCSP) recommends that all sexually active under-25 year old men and women be tested for chlamydia annually or on change of sexual partner (whichever is more frequent). Screening should be delivered opportunistically, i.e. sexually active young adults should be offered a test when they attend services such as GPs, community sexual and reproductive health services, pharmacies, and specialist genitourinary medicine services. Additionally services can be provided through outreach or via self-sampling kits ordered through the internet. Chlamydia screening has been found to be widely acceptable among young adults.

What are the consequences of having a chlamydia infection?

If left untreated, chlamydia can cause a number of complications, including: pelvic inflammatory disease (PID), ectopic pregnancy and infertility in women; epididymitis (swelling of one of the tubes in the testicles) in men and conjunctivitis and pneumonia in babies born to mothers with chlamydia. These complications result in costs to the healthcare system and reduced quality of life among those affected.

What proportion of chlamydia infections would lead to sequelae if untreated?

It is estimated that around 10%-16% of untreated chlamydia infections result in the development of clinical PID[1;2]. Due to the difficulties with studying the natural history of chlamydia infection, estimates of progression rates from chlamydia to long term health outcomes in women are subject to some uncertainty.

What is the potential impact of chlamydia screening on PID and other health outcomes?

By diagnosing and treating asymptomatic chlamydia infections, chlamydia screening can reduce the duration of an infection. This will reduce the individual's chance of developing complications, as the earlier in the course of infection that a woman with chlamydia is treated, the less risk she has of developing PID and other complications. Findings from four randomised controlled trials of chlamydia screening suggest that a single offer of a chlamydia screen can

reduce the risk of developing PID within one year by around 36% (risk ratio 0.64; 95%CI 0.45-0.90)[3]. As the uptake of screening varied in these studies, this will be an underestimate of the benefit to an individual who has an infection diagnosed and treated as a result of chlamydia screening.

Are there any harms associated with chlamydia screening?

Being diagnosed with chlamydia can lead to some anxiety among those diagnosed. This negative impact is likely to be outweighed by the benefits conferred by screening, and chlamydia screening has been found to be widely acceptable to young adults in a variety of settings. Widespread use of antibiotics prescribed as part of the screening programme may increase the risk of generating strains of chlamydia that are resistant to antimicrobial treatments, but this has not been demonstrated in practice for *Chlamydia trachomatis*.

What is the potential impact of chlamydia screening on chlamydia transmission and prevalence?

Reducing the duration of infection through screening will also reduce the time when someone is at risk of passing the infection on to others. Chlamydia screening therefore has the potential to reduce the transmission of chlamydia, and in turn reduce the prevalence of chlamydia. This has a strong theoretical basis and is supported by mathematical models and some observational studies.

Is chlamydia screening cost-effective?

Current evidence on the cost-effectiveness of chlamydia screening suggests that screening men and women under 25 years old (i.e. the NCSP screening strategy) can be cost-effective. Work is on-going to improve the assumptions used in cost-effectiveness studies, in order to provide updated economic evaluations of chlamydia screening for England.

Implications for practice

The level of benefit of chlamydia screening depends in part on how chlamydia screening is implemented. The NCSP recommends that chlamydia screening should be commissioned in conjunction with a range of sexual and reproductive health services. Chlamydia screening does not replace the need for the comprehensive service offer needed to ensure that the sexual health needs of a local population are met. Well planned and well delivered sexual health services, including genitourinary medicine, reproductive health, primary care and community based services, ensure that care is delivered efficiently and effectively to populations.

List of abbreviations

BASHH	British Association of Sexual Health and HIV
CI	Confidence interval
ECDC	European Centre for Disease Prevention and Control
GUM	Genitourinary medicine
HIV	Human Immunodeficiency Virus
IVF	In vitro fertilisation
NAATs	Nucleic acid amplification test
Natsal	National Surveys of Sexual Attitudes and Lifestyles
NICE	National Institute for Health and Care Excellence
PID	Pelvic inflammatory disease
POPI	Prevention of Pelvic Inflammation
QALY	Quality adjusted life year

Chlamydia and chlamydia screening

- This evidence summary provides an overview of current, published evidence relating to chlamydia screening among young adults in England. It sets out the available evidence on why, and in what way, the identification, diagnosis and treatment of chlamydia infections among young adults is expected to have an impact on the health of the population, and what is known about the cost-effectiveness and acceptability of chlamydia screening.

- This is intended as a resource document for use by public health and sexual health professionals, including Directors of Public Health, elected members, commissioners and providers of sexual health and chlamydia screening services.

1 What is chlamydia?

- *Chlamydia trachomatis* ('chlamydia') is a common, frequently asymptomatic bacterial infection of the genital tract that is transmitted by sexual contact, i.e. is a sexually transmitted infection (STI).

- The acute symptoms of chlamydia infection can include pain and abnormal vaginal or urethral discharge[4], but the majority of people who are infected with chlamydia will not have symptoms[5;6].
  - In a study of 16 to 24 year olds diagnosed with chlamydia following a community-based screening test, 26% of men had discharge or pain on passing urine; 32% of women reported vaginal discharge or bleeding after sex. Reported symptoms were generally mild, and were not specific to those with chlamydia[5].

- Chlamydia is easily diagnosed and treated[4], however untreated infections can persist for months or years[7], and can cause a range of complications (see section 4).

- Chlamydia is the most commonly diagnosed STI in the UK and rates of infection are highest among young adults.
  - In the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3, carried out in 2010-2012), the prevalence of chlamydia in the sexually experienced adult British general population was 1.5% (95%CI 1.1%-2.0%) among women and 1.1% (95%CI 0.7%-1.6%) among men aged 16 to 44 years old. Prevalence among 16 to 24 year olds was 3.1% (95%CI 2.2%-4.3%) among women and 2.3% (95%CI 1.5%-3.4%) in men[8]

- In 2012, routine data submitted to Public Health England show that over 1.7 million chlamydia tests were carried out in England among 15 to 24 year olds; 137,000 (~8%) of these resulted in a positive diagnosis[9].

- Highly sensitive and specific tests (nucleic acid amplification tests; NAATs) for chlamydia are widely available, and used for all chlamydia tests performed through the National Chlamydia Screening Programme. These tests can be performed on non-invasive samples (urine in men, self-taken vulvovaginal swabs or urine for women)[4]. Chlamydia tests can therefore be offered in a range of clinical and non-clinical venues. Home sampling kits can also be used, where patients can take samples at home and send by post to laboratories. In several areas these can be ordered via the internet[10]. If detected, chlamydia is easily treated with antibiotics[4].

- Unlike some other STIs, such as gonorrhoea, chlamydia is found relatively often among people with both high and low numbers of sexual partners, although those with higher numbers of sexual partners are at greater risk of infection, especially men.
  - 60% of 16-44 year old women who had a chlamydia infection in the Natsal-3 study, and 43% of the men, reported only one sexual partner in the last year[8] (Figures 1, 2).

Figure 1: Percentage of 16 to 44 year olds in the British population with a current chlamydia infection, by numbers of sexual partners in the past year (Natsal-3)[8]

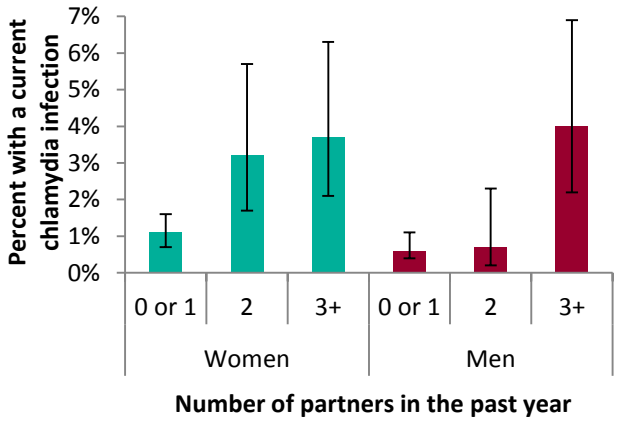
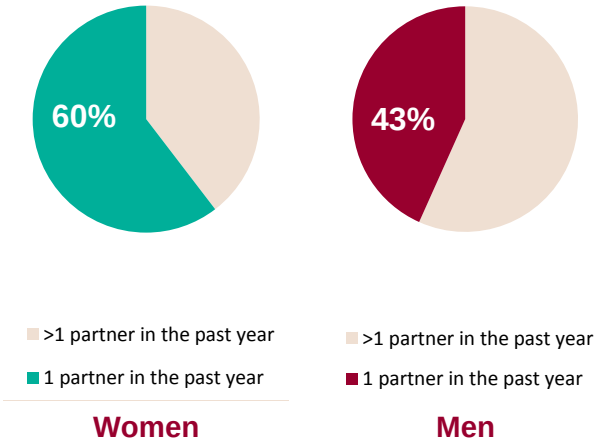


Figure 2: Percentage of women and men reporting either one, or more than one, sexual partner in the past year, among 16-44 year olds with a current chlamydia infection (Natsal-3)[8]



2 What is chlamydia screening?

- Chlamydia screening is the process whereby individuals *without symptoms* are tested for chlamydia. Those diagnosed with the infection are then offered treatment and are advised that their sexual partners should also be screened and treated.

- By diagnosing and treating asymptomatic chlamydia infections, chlamydia screening can reduce the duration of infection, which will reduce an individual's chance of developing complications (see section 4), and also reduce the time when someone is at risk of passing the infection on, which in turn will reduce the spread of chlamydia in the population.

- Chlamydia screening does not replace the need for diagnostic testing; men and women with symptoms suggestive of an STI or whose partner has been diagnosed with an STI should see a clinician[11].

3 How is chlamydia screening delivered in England?

- In England, the National Chlamydia Screening Programme (NCSP) sets standards, monitors activity and quality assures chlamydia screening. Local authorities commission comprehensive sexual health services including chlamydia screening.

- The NCSP recommends that all sexually active under 25 year old men and women be tested for chlamydia annually or on change of sexual partner (whichever is more frequent) (www.chlamydiascreening.nhs.uk).
  - The NCSP focuses on sexually active under 25 year olds, as rates of chlamydia infection are known to be highest in this group[8;12].
  - The NCSP recommends screening annually, or on change of sexual partner, because young adults are at risk of new or repeat infections[13], and therefore of developing complications[2]. Having a new sexual partner increases an individual's risk of having a new infection[12;13].

- Chlamydia screening is delivered in England on an opportunistic basis; chlamydia tests are available to under 25 year olds free of charge from a variety of venues including GPs, community sexual and reproductive health services, pharmacies, via self-sampling kits ordered through the internet or from specialist genitourinary medicine (GUM) services[14]. This differs to register-based screening programmes, where invitations are sent to the eligible population.
  - The opportunistic screening approach to chlamydia screening has achieved relatively high rates of coverage. In the Natsal-3 survey, 54% (95%CI 51%-57%) of sexually active 16 to 24 year old women, and 35% (95%CI 32%-37%) of young men, had been tested for chlamydia in the past year[8]. The survey also showed that higher levels of testing are seen among those reporting greater numbers of sexual partners, who are therefore at increased risk of infection.
  - Because a large proportion of chlamydia infections are asymptomatic[5;6], and chlamydia is not limited to 'high risk' groups[8] (see section 1), by offering screening to those without symptoms, and by providing screening in a range of community venues outside of specialist services, more infections will be diagnosed and treated than if only those with symptoms, or only those attending specialist services, were tested. In England, 59% of chlamydia diagnoses among 15 to 24 year olds were made outside specialist GUM services in 2012[15].

- Those who test positive for chlamydia should be given sexual health advice and be advised that their sexual partner(s) be tested and treated for chlamydia. The NCSP

recommends that young adults who test positive should also be offered a re-test around 3 months after treatment.

- Partner notification is recommended in order to prevent re-infection and to interrupt the transmission of infection to other sexual partners. Partner notification is an effective method of identifying individuals with infection[16]. For example in 2012, ~25,000 15 to 24 year olds were tested for chlamydia in a GUM clinic as a result of their partner having been tested; 42% of these were also diagnosed with chlamydia[17].
- The NCSP recommends re-testing at around three months after treatment for those who test positive, as young adults diagnosed with chlamydia are at higher risk of having chlamydia again*. This may be due to lack of partner management, continuing risk behaviour or, very rarely, treatment failure. Studies show that those who test positive for chlamydia are two to three times more likely to test positive at a subsequent test within one year compared to individuals with an initial negative test[13;18-24], and around 10-15% of young adults diagnosed with chlamydia test positive at their next test[13;18-26].

- As set out in the Public Health Outcomes Framework, Public Health England recommends that local authorities should be working towards achieving a diagnosis rate of at least 2,300 chlamydia diagnoses per 100,000 population aged 15-24 years.
  - Increased diagnosis of chlamydia infections will likely decrease the prevalence of chlamydia among sexually active under 25 year olds[27]. The effect of screening on prevalence is hard to monitor; mathematical models have been used to explore the likely effects under different scenarios.

4 What are the consequences of having a chlamydia infection?

- The most serious chlamydia-related complications occur in women. Chlamydia infection can ascend the female genital and reproductive tract causing a number of complications such as pelvic inflammatory disease (PID; a spectrum of clinical disorders involving inflammation of the uterus, fallopian tubes, ovaries, or adjacent peritoneum). PID can in turn cause scarring and fibrosis in the pelvic organs, which can lead to serious long-term reproductive consequences including tubal factor infertility and ectopic pregnancy[6;28-33].
  - Among 15 to 44 year olds in 2011, the estimated incidence of definite/probable cases of PID, diagnosed in GP setttings was 176 (95%CI 166-186). The incidence of ectopic pregnancies diagnosed in hospital settings was 11/1,000 conceptions. PID diagnoses have been declining, overall, since at least 2000; the rate of ectopic pregnancies has been more stable. The rates and trends in these diagnoses may be affected by diagnostic and recording practices[34].

*see NCSP position statement, Consultation Report and Evidence Summary for more information. Available at http://www.chlamydiascreening.nhs.uk/ps/resources.asp

- In men, chlamydia can cause epididymitis (swelling of one of the tubes in the testicles)[6].

- Babies born to mothers with chlamydia infection may suffer from conjunctivitis and pneumonia[6;35;36]. There is also some recent evidence to suggest that women who have previously had chlamydia may be at increased risk of adverse birth outcomes including preeclampsia, spontaneous preterm birth or stillbirth[37-39], although there is some conflict between findings from different studies. Further work would therefore be needed to establish whether chlamydia has a causal role in these outcomes[40].

- Chlamydia may also increase the risk of HIV transmission[41] and there may be an association between chlamydia and persistent high risk human papillomavirus (HPV, a sexually transmitted virus that can cause cervical cancer)[42;43].

- Chlamydia-related complications are associated with reduced quality of life[44-46] and result in considerable healthcare costs[47-50].

- These health complications can also occur for other reasons. For example, other STIs can cause PID and subsequent complications. It can be difficult to find out the underlying cause of these conditions, so there is often uncertainty in the contribution of chlamydia to these diseases.

5 What proportion of chlamydia infections would lead to sequelae if untreated?

- It is challenging to measure the effects of untreated chlamydia infection over time. It is not ethically acceptable to allow diagnosed chlamydia infections to remain untreated, chlamydia is not the only cause of PID and other outcomes, and the long follow up time required to investigate progression from chlamydia to ectopic pregnancy or tubal factor infertility prohibits detailed investigation[3].

- However some studies have calculated progression rates from untreated chlamydia to PID. This includes observational studies which have measured the rate of developing PID in the period between being tested for chlamydia and returning for treatment, studies conducted before the need to treat chlamydia was universally accepted, and from randomised controlled trials of chlamydia screening. Estimates from these different studies vary considerably[51].

- In the large and well conducted Prevention of Pelvic Inflammation (POPI) study, 9.5% (95%CI 4.7%-18.3%) of women who had chlamydia at baseline, but were randomised to the group who were not immediately treated within the study, developed PID within one year[2]. This is likely to be an underestimate of progression rates from prevalent chlamydia infection to PID, as some of these women (around one fifth) were treated outside of the trial.

- Using multi-parameter evidence synthesis, which allows estimates from several different study designs to be analysed together, Price *et al.* recently estimated that 16% (95% credible intervals 6%-25%[†]) of untreated, incident chlamydia infections result in the development of clinical PID[1].

- Due to the difficulties with studying the natural history of chlamydia infection, estimates of progression rates from chlamydia to long-term health outcomes are subject to considerable uncertainty.
  - In an economic evaluation of chlamydia screening in England[48], it was estimated that 7.6% of women with symptomatic PID would experience ectopic pregnancy and 10.8% would experience tubal factor infertility; 14.8% of babies born to mothers with chlamydia would develop neonatal conjunctivitis, 7% would develop neonatal pneumonia; and 2% of men with asymptomatic chlamydia would develop epididymitis.

The anticipated effect of chlamydia screening on population health

6 What is the potential impact of chlamydia screening on PID and other health outcomes?

- By diagnosing and treating asymptomatic chlamydia infections, chlamydia screening can reduce the duration of an infection. This will reduce the individual's chance of developing complications, as the earlier in the course of infection that a woman with chlamydia is treated, the less risk she has of developing PID and other complications.
  - Four randomised controlled trials have investigated the effectiveness of a single offer of a chlamydia screen on the risk of developing PID within one year (Table 1, Figure 1). A recent meta-analysis of these studies, carried out as part of a report by the European Centre for Disease Prevention and Control (ECDC), reported that the pooled risk ratio of all cause PID after one year of follow-up for women invited to have a chlamydia screen was 0.64 (95%CI 0.45-0.90). The reduction in the risk of PID was greater in studies with higher rates of uptake of chlamydia screening[3]. **[Evidence level Ia]**

[†] Assuming constant rate of developing PID over the course of infection.

Table 1: Randomised controlled trials investigating the impact of a single chlamydia screen on the development of PID within one year

Authors (year, country of study)	Study population	Intervention	Control	Outcome	Results
Scholes et al (1990-1992, USA)[52]	2,607 18 to 34 year old sexually active women considered at high risk of chlamydia.	Women were invited to a study clinic for a chlamydia test. Those with chlamydia were given treatment.	Women in the control group were not invited to screening; the intervention and control groups could access usual care outside the study.	PID at 12 months was measured using questionnaires and health records.	At 12 months, 0.9% of women in the intervention group and 2.1% of the control group had a confirmed case of PID (RR: 0.44; 95%CI 0.20-0.90).
Ostergaard et al (1997, Denmark)[53]	5,487 sexually active female 15 to 19‡ high school students.	Women were offered a chlamydia test by the use of a home sampling kit. Those with chlamydia were given treatment.	Women in the control group were offered a chlamydia test at their local STD clinic.	PID at 12 months was measured using questionnaires and health records.	At 12 months, 2.1% of the intervention group had been treated for PID compared to 4.2% in the control group (RR: 0.49; 95%CI 0.23-1.07[§]).
Andersen et al (1997-2006, Denmark)[54]	15,459 women and 14,980 men aged 21-23 living in one county in Denmark.	Women and men were offered a chlamydia test by the use of a home sampling kit. Those with chlamydia were given treatment.	Those in the control group did not receive an offer of a chlamydia test; the intervention and tcontrol groups could access usual care outside of the study.	PID at 12 months, as recorded in health registers or as indicated by the use of antibiotics outside of hospitals.	At ~12 months, 0.58% of women in the intervention group had a known diagnosis of PID, compared to 0.65% in the control group (RR: 0.89; 95%CI 0.56-1.42**Error! Bookmark not defined.**).
Oakeshott et al (2004-2006, London, UK)[2]	2,529 sexually active 16 to 27 year old female students.	Women were tested for chlamydia. Those with chlamydia were given treatment.	Samples provided at baseline from women in the 'deferred screening' group were stored and tested 12 months later; both intervention and control groups could access usual care outside of the study.	PID at 12 months was measured using health records.	At 12 months, 1.3% of women in the intervention group had developed PID, compared with 1.9% in the deferred screening group (RR: 0.65, 95%CI 0.34-1.22).

RR; risk ratio for intervention compared to control group, CI; confidence interval..

- These four randomised controlled trials provide valuable evidence concerning the effectiveness of chlamydia screening. However the studies are subject to some important methodological limitations, which should be considered when interpreting the results.
  - It is likely that the effect of chlamydia screening on the development of PID within one year was underestimated in the POPI study and in the trial by Andersen *et al*, as participants were tested outside of the trial. Around one fifth of women in the POPI study were tested between the time of enrolment and follow up[2], and 9% of women in the Andersen trial were tested in the first three months of the study[54].
  - Andersen *et al* used prescription information to measure cases of PID in community settings[54]. This means it is likely that a lot of cases of PID will have been missed[54;55], which adds further uncertainty to the findings from this study.
  - The Scholes[52] and Ostergaard[53] studies are both subject to bias. In the Scholes study, more effort was made to invite women in the screening group to take part, and they were followed up more rigorously than controls[56]. In the Ostergaard study, participants were randomised before they had consented to take part,

‡ A small number of participants were aged >19 years old, but the exact age range is not provided in the paper.
§ Risk ratio was not reported in the original paper. The risk ratio is reported from a meta-analysis by the ECDC[3].

almost half of the participants did not provide information at follow up, and assessment of whether someone had PID or not at follow up was not blinded[56]. This may have led to the effect of chlamydia screening being either over- or underestimated in these studies.

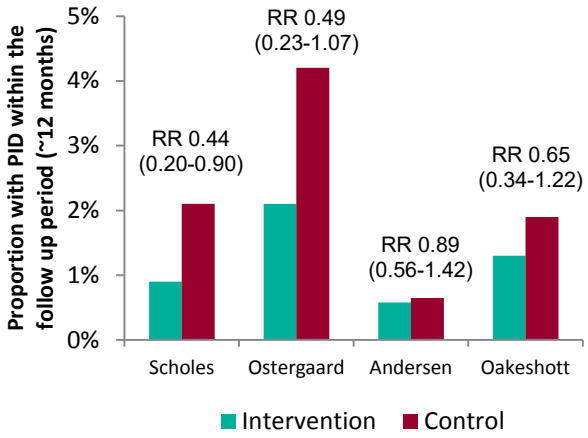
- There are also some differences between how these studies were conducted and how chlamydia screening is delivered in practice in England.
  - All of these studies considered the outcome of PID during the year following a single screen, rather than the outcome following regular screening every year and on change of sexual partner throughout the relatively highly sexually active period of life from 16 to 24 years, as recommended by the NCSP.
  - Scholes *et al*[52] investigated chlamydia screening among those considered at high risk of chlamydia, and in a slightly older age group than is targeted for chlamydia screening in England; Ostergaard[53] recruited a slightly younger age group and Oakeshott[2] *et al* recruited women from a relatively low-risk group of women in one area of England.

- The meta-analysis reported by the ECDC estimated the effect of an offer of a screen on PID arising from all causes. As the uptake of screening varied in these studies (between 29% and 100%)[3], this will be an underestimate of the benefit to an individual who has an infection diagnosed and treated as a result of chlamydia screening.
  - Findings from a multi-parameter evidence synthesis by Price *et al* suggest that diagnosing and treating incident infections identified through chlamydia screening would reduce a woman's risk of developing chlamydia-related PID by an average of 61% (95% credible intervals 55%-67%[†])[1]. This benefit would be greater if screening occurred closer to the time when someone became infected. **[Evidence level III]**

- The trial by Andersen *et al* also investigated the impact of a mailed offer of a chlamydia screen at age 21 to 23 on health outcomes other than PID among both men and women[54].
  - The study found no difference between those who had been sent an invitation and those who had not for any of the outcomes investigated (epididymitis at 12 months; ectopic pregnancy, infertility, IVF treatment or births within 9 years). **[Evidence level Ib]**
  - The finding of no difference in long-term health outcomes in women is not unexpected. It is unlikely that a single screen would have had an impact on outcomes over this period especially as screening for chlamydia was relatively common after the intervention.
  - Possible explanations for the finding of no difference in rates of epididymitis include low rates of screening uptake within the men in the intervention group

(21%), uptake of chlamydia screening outside of the trial, and/or incomplete case ascertainment.

Figure 3: Reduced risk of pelvic inflammatory disease (PID) associated with chlamydia screening among women; results of four randomised controlled trials



RR: Risk ratio for intervention compared to control group. 95% confidence intervals are shown in brackets

7 Are there any harms associated with chlamydia screening?

- Being diagnosed with chlamydia can cause anxiety and may have an adverse impact on psychosocial wellbeing[57-59].
  - Chlamydia screening has been found to be widely acceptable to young adults in a variety of settings[58;60;61].
  - Qualitative studies suggest that the potential negative impact of being diagnosed with chlamydia is likely to be outweighed by the perceived (and actual) benefits of screening[58;59].

- On very rare occasions, chlamydia tests may result in an incorrect diagnosis (either false positive or false negative). False positives may cause unnecessary anxiety; false negatives may lead to an infection remaining untreated. As the tests used for chlamydia are highly sensitive and specific, this will happen only very infrequently.

- It is possible that a negative chlamydia test result may lead to some false reassurance about an individual's risk of STI. This could feasibly lead to decreased safer sex behaviour (e.g. use of condoms). However there are no data available at present to determine whether, and the extent to which, this happens in practice in England.

- The NCSP and the British Association of Sexual Health and HIV (BASHH) recommend treatment for uncomplicated chlamydia infection with azithromycin or doxycycline[4;11]. Widespread use of antibiotics prescribed as part of the screening programme may increase the risk of generating strains of chlamydia that are

resistant to antimicrobial treatments, but this has not been demonstrated in practice for *Chlamydia trachomatis*.

- Anecdotal reports of treatment failure, and of isolates with decreased susceptibility to antimicrobial treatments, have been published. However confirmed homotypic resistance (i.e. where resistance is genetically inherited) to antimicrobials has not yet been documented in clinical chlamydia infections[62-68].
- While genetic markers of resistance are documented in *Chlamydia* species[62;67;69], the potential for these to become widespread in the *Chlamydia trachomatis* population is currently unknown.
- The Sexually Transmitted Bacteria Reference Unit at Public Health England is undertaking work to monitor chlamydia treatment failures and antimicrobial resistance in England.

8 What is the potential impact of chlamydia screening on chlamydia transmission and prevalence?

- By diagnosing and treating asymptomatic chlamydia infections, screening can reduce the duration of infection. This will reduce the time when someone is at risk of passing the infection on to others, and can therefore interrupt the transmission of infection. This, in turn, is expected to lead to a lower prevalence of infection than would occur in the absence of screening.
  - A modelling study using UK data, carried out at the start of the chlamydia screening programme, suggested that high rates of opportunistic chlamydia screening could have a substantial impact on the prevalence of infection among under 25 year olds[27]. **[Evidence level III (mathematical model)]**
  - PHE is carrying out further mathematical modelling work to investigate how chlamydia screening, as it has been delivered in practice, may affect the prevalence of infection.

- Measuring the effect of chlamydia screening on the transmission and prevalence of chlamydia in practice is very difficult. Several sources of information need to be considered to understand the impact of chlamydia screening on the transmission of infection in England. Surveys can be conducted by asking people to consent to providing a genital sample for testing, but it is difficult to recruit a large and unbiased sample of the population into such surveys. As chlamydia is largely asymptomatic, the number of infections identified depends on the behavioural and other characteristics of the people who are tested.

- Routinely collected data from young adults tested for chlamydia in England show that the proportion testing positive has reduced between 2008 and 2011, during which time chlamydia testing increased markedly. This trend is seen among both men and women, and is observed in several different testing venues. For example among 15 to 24 year old women tested in sexual and reproductive health services, the proportion testing positive fell from 10.2% to 7.4%[70]. **[Evidence level III]**

  - Interpreting trends in positivity data is challenging and should be done with caution and appropriate caveats. As chlamydia is largely asymptomatic, the number of infections identified depends on the behavioural and other characteristics of the people tested.
  - While some of the observed decline in proportion testing positive may be due to the expansion of testing into lower risk populations, some of this decline may be attributable to a reduction in the prevalence of chlamydia[71].

- A recent study suggests that the number of young women who have had an antibody-inducing infection has declined in recent years. This decline was concurrent with the substantial increases seen in chlamydia screening among young adults in England since the introduction of the NCSP. **[Evidence level III]**
  - Having antibodies to chlamydia indicates that someone has been previously infected with chlamydia: they may have been treated or the infection may have cleared on its own. Not everyone who has had an infection will have antibodies to chlamydia.
  - In a recent study, residual blood samples from young women who had had routine blood tests for any reason, were tested for antibodies to chlamydia. This group was chosen as it is considered to be broadly representative of the general population[72]. Between 2007 and 2010, when chlamydia testing increased markedly, the proportion of 17 to 24 year old women with antibodies to chlamydia in their blood fell from 20% to 15%. This suggests that the proportion of young women who had ever had an antibody-inducing chlamydia infection fell during this period.
  - The exact cause of this fall, and to what extent it reflects reduced chlamydia transmission and prevalence due to screening, is not fully understood. Further work is underway to determine the roles of infection, treatment and progression to disease in the development of antibodies, and to look at potential change in behaviour during the analysis period, in order to aid further interpretation of these data.

- A recent trial in the Netherlands found no evidence of an effect of an annual offer of a chlamydia screen on the proportion testing positive, among those who participated[73]. **[Evidence level Ib]**
  - The trial investigated the effectiveness of a register-based chlamydia screening intervention on chlamydia transmission between 2008 and 2011. Men and women aged 15 to 29 years old were identified using health registers and posted an invitation to order a free self-sampling kit from a dedicated website. Invitations were sent annually for three years, and more frequently for those who tested positive. The proportion testing positive at the third round of screening in the intervention areas was 4.1% compared to 4.3% in the first round of screening in control areas (risk ratio 0.96, 95%CI 0.84-1.09)[73].

- Participation in this trial was lower than originally expected (16% in the first year, 10% in the third year). Mathematical models suggest that high rates of testing are required to have an effect on transmission[27], so this relatively low rate of testing will have reduced the potential impact of screening in this study.
- The findings of this study are not directly generalisable to England. The approach to screening is different to that used in England, and the study achieved a much lower rate of testing coverage than is achieved in England (see section 3).

9 Is chlamydia screening cost-effective?

- Current evidence on the cost-effectiveness of chlamydia screening suggests that screening men and women under 25 years old (i.e. the NCSP screening strategy) can be cost-effective.
  - The most recent economic evaluation to explore the cost-effectiveness of chlamydia screening in terms of cost per quality adjusted life year (QALY**) using data from England was conducted at the outset of the chlamydia screening programme[48]. The authors estimated that opportunistic screening of under 25 year old men and women every year would cost £27,269 for every QALY gained, compared to no screening, and assuming a 10% rate of progression from acute chlamydia infection to PID. This is within the acceptable range used by the National Institute for Health and Care Excellence (NICE) of up to £20,000-£30,000 per QALY gained, and was thus considered cost-effective. Higher rates of testing were found to increase the cost-effectiveness of screening. Lower rates of progression from chlamydia infection to PID decreased the cost-effectiveness of screening[48].
  - A recent systematic review of the cost-effectiveness of chlamydia screening programmes compiled results from economic evaluation studies in high income countries[3]. Nine of the ten studies found at least one of the chlamydia screening strategies examined to be within national thresholds for cost-effectiveness, in terms of additional cost per QALY gained.

- The findings from all of the available economic evaluations are subject to considerable uncertainty arising from assumptions made within the models about the rate of progression from chlamydia to complications, the impact of complications on health-related quality of life, and the cost of complications. Work is needed[74], and is ongoing[1;7;33], to provide updated estimates of these parameters in order to provide an updated economic evaluation for England.

** A measure of the benefit of health interventions

Implications for practice

- In summary, chlamydia screening can reduce an individual's risk of PID following a chlamydia infection. This has a strong theoretical basis, and has been demonstrated in randomised controlled trials. Chlamydia screening also has the potential to reduce the transmission of chlamydia, and in turn reduce the prevalence of chlamydia. This has a strong theoretical basis, has been demonstrated in mathematical models, and is supported by some observational studies.

- The impact of chlamydia screening on an individual and a population level depends in part on how chlamydia screening is implemented. The NCSP recommends that chlamydia screening be used in conjunction with a range of coordinated sexual and reproductive health services. Efficient delivery of services is both better value for money and more likely to materially impact on the burden of need in the population. Chlamydia screening is only likely to address simple and uncomplicated sexual health issues and can be used to direct higher risk individuals to a more comprehensive level 3 service such as an open access genitourinary medicine clinic.

- Commissioners should ensure that they have strong links with other relevant sexual health commissioners and that strategic planning with neighbouring areas is undertaken where possible. Commissioners should be up to date with NCSP guidance relating to standards and how to improve their diagnostic rate. Local data on chlamydia screening is available at the NCSP website, the STI and HIV Portal and the Sexual Health Profiles Tool. Local commissioners should use their data to ensure that resources are deployed in services which provide a 5% to 12% positivity rate.

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Appendix: Levels and gradings of evidence

Evidence was graded according to criteria developed by the US Department of Health and Human Services' Agency for Healthcare Policy and Research for grading scientific evidence[75], now known as the Agency for Healthcare Research and Quality.

Grading was applied to concerning the effectiveness of chlamydia screening. This grading was not been applied to other sections, as this categorisation is only appropriate for efficacy or effectiveness studies.

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one type of well-designed quasi experimental study
III	Evidence obtained from well-designed, non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.