Has opportunistic screening among young adults in England led to a reduction in *Chlamydia trachomatis* infection? Identifying and appraising outcome measures for the evaluation of chlamydia control programmes.

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Thesis submitted for the degree of Doctor of Philosophy

Sarah Charlotte Woodhall

UCL

Statement of Authorship

I, Sarah Woodhall, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed: _____ Date: _____

The systematic review of chlamydia prevalence studies presented in Chapter 3 was carried out as part of a collaborative project on chlamydia control in Europe.[2,3] I contributed to the design and interpretation of the review and extracted data with two other reviewers. The other literature reviews presented in Chapter 3 were conducted independently. I planned, conducted, and interpreted all analyses in Chapters 4 to 8. I designed and implemented the pilot study in Chapter 4 including focus groups to develop the study materials, which were conducted with one other facilitator. Other investigators collected the data in three of the datasets used in this thesis. The National Surveys of Sexual Attitudes and Lifestyles (Natsal) used in Chapters 6 and 7 were collected by NatCen Social Research in collaboration with University College London, the London School of Hygiene and Tropical Medicine and the Health Protection Agency (now part of Public Health England).[4,5] Surveillance data used in Chapter 4 on tests carried out as part of the National Chlamydia Screening Programme (NCSP) (www.chlamydiascreening.nhs.uk) and in genitourinary medicine clinics, reported via the genitourinary medicine clinic activity dataset (GUMCAD)[6] were collected by the HIV & STI department of the Health

Protection Agency. Questionnaire data and serum samples in the Health Survey for England (HSE) used in Chapter 8 were collected by NatCen Social Research in collaboration with University College London[7]. Serum samples were tested for anti-chlamydia antibodies by Imperial College London. I carried out the data linkage between the questionnaire data and antibody test results.

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Abstract

Genital infection with *Chlamydia trachomatis* (‘chlamydia’) is the most commonly diagnosed sexually transmitted infection in England. Chlamydia is often asymptomatic and can lead to serious complications, especially in women. Chlamydia screening offers one approach to controlling chlamydia and its consequences. In England, chlamydia screening is offered opportunistically to sexually-active under-25 year-olds through the National Chlamydia Screening Programme, which was introduced in 2003 and nationally implemented by 2008.

Evaluating the real-world impact of chlamydia screening against its aims of interrupting transmission and reducing the prevalence of infection presents a considerable challenge, in part due to the absence of a robust outcome measure.

The research presented in this thesis sought to address this challenge. Four approaches to outcome measurement were investigated:

- Analysis of trends in percentage testing positive for chlamydia among 15-24 year-olds accessing chlamydia testing using surveillance data;
- Pilot of a postal survey of 17-18 year-old women to measure population prevalence;
- Analysis of chlamydia prevalence among 16-24 year-old participants in the second and third National Surveys of Sexual Attitudes and Lifestyles (Natsal-2: 1999-2000; Natsal-3: 2010-12);
- Application of a novel antibody assay to stored sera from 16-44 year-old participants in the Health Survey for England (HSE) between 1994 and 2012 to measure prevalence of antibodies in serum as a marker of previous *C. trachomatis* infection.

In summary, no definitive evidence was found in these or other published analyses to suggest that chlamydia screening, as delivered in practice, has led to a reduction in the incidence or prevalence of chlamydia infection among young adults in England up to 2012. Possible reasons for the absence of such evidence are discussed in light of findings presented in the thesis.

The strengths and limitations of these approaches to outcome measurement are discussed, and recommendations regarding the future evaluation and delivery of chlamydia control programmes are presented.

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Glossary of terms

***Chlamydia trachomatis; C. trachomatis;* chlamydia**	This thesis follows the convention for microbial nomenclature set out by Low *et al*.[8] *Chlamydia trachomatis* (abbreviated to *C. trachomatis*) is used to describe the organism. 'Chlamydia' is the name of the condition, and is used to describe genital infection with *C. trachomatis*.
Percentage testing positive	The percentage of tests for current infection with *C. trachomatis* that return a positive result. Percentage testing positive is distinct from chlamydia prevalence, as the tests are not necessarily drawn from a representative sample of the general population.
Prevalence	The percentage of a defined population who have chlamydia at a given point in time.
***C. trachomatis* antibody/ Pgp3 seropositive**	The percentage of sera tested where *C. trachomatis* or Pgp3 antibodies are detected.
***C. trachomatis* antibody/ Pgp3 seroprevalence**	The percentage of a defined population who test positive for *C. trachomatis* or Pgp3 antibodies in serum.
Incidence	The rate at which chlamydia infections occur in a defined population during a specified period.
Cumulative incidence	The probability of having been infected with chlamydia by a given point (i.e. by a given age or number of years after first sex).
Diagnosis rate	The number of diagnoses per 100,000 population (generally applied to 15 to 24 year-olds)
Coverage	The number of chlamydia tests divided by the population (expressed as a percentage of a given age group)
Opportunistic screening	Screening offered to people at the time of attending healthcare or other specified venues. Not register-based.
Register-based screening	Screening offered systematically via active invitation of the eligible population in a given age/demographic group.
Sexually-experienced	Reports at least one sexual partner by the time of measurement/interview.
Lifetime sexual partners	Number of sexual partners by the time of measurement/interview.

Table of abbreviations

AC2	Aptima-Combo 2 assay (Hologic Gen-Probe)
AOR	Adjusted odds ratio
CDC	Centers for Disease Prevention and Control
CI	Confidence interval
ClaSS	Chlamydia Screening Studies
CMO	Chief Medical Officer
CSI	Chlamydia Screening Implementation project
CSO	Chlamydia screening office
DFA	Direct fluorescent antibody assay
ECDC	European Centre for Disease Prevention and Control
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
EU/EEA	European Union/European Economic Area
GP	General practice
GUM	Genitourinary medicine
GUMAMM	Genitourinary medicine access monthly monitoring
GUMCAD	Genitourinary medicine clinic activity dataset
HIV	Human immunodeficiency virus
HSE	Health Survey for England
HPA	Health Protection Agency
HPV	Human papillomavirus
IgG	Immunoglubulin G
IMD	Index of Multiple Deprivation
IPP	Infertility Prevention Program
LCx	Ligase chain reaction assay (Abbott Diagnostics)
LGV	Lymphogranuloma venereum
LSOA	Lower super output area
MSM	Men who have sex with men
MSW	Men who have sex with women
NAAT	Nucleic acid amplification test
NAO	National Audit Office
Natsal-2	2nd National Survey of Sexual Attitudes and Lifestyles
Natsal-3	3rd National Survey of Sexual Attitudes and Lifestyles
NCSP	National Chlamydia Screening Programme
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
PCT	Primary care trust
PHE	Public Health England
PID	Pelvic inflammatory disease
R_0	Basic reproductive number
RCT	Randomised controlled trials
SRH	Sexual and reproductive health
STI	Sexually transmitted infection
UK	United Kingdom
US	United States
USPSTF	United States Preventive Services Task Force
VVS	Vulvovaginal swab

1 Introduction

Genital infection with *Chlamydia trachomatis* ('chlamydia') is the most commonly diagnosed bacterial sexually transmitted infection (STI) in England.[9] Most chlamydia infections are asymptomatic[10,11] and infection can lead to serious reproductive sequelae in women.[12-15] In England, the National Chlamydia Screening Programme (NCSP) recommends that sexually active under-25 year-olds are screened for chlamydia annually and on change of sexual partner with the aim of reducing transmission and preventing future complications. The programme was introduced in England in 2003 and nationally implemented by 2008.

As set out in the following chapter, chlamydia screening is expected to lead to a reduction in the incidence and prevalence of infection. However, the effectiveness of screening in practice has not yet been shown and evidence from previous research is inconclusive. When the NCSP was established no strategy was put in place to monitor the impact of screening on health-related outcomes. The impact of chlamydia screening to date on either the incidence or prevalence of chlamydia is unknown.

One of the major challenges in evaluating the impact of chlamydia screening is the availability of a robust and valid outcome measure. As the majority of infections with *C. trachomatis* are asymptomatic, true incidence of chlamydia (i.e. the rate at which chlamydia infections occur in a defined population during a specified period) cannot be directly measured without incredibly intensive studies of large samples with frequent and repeated chlamydia testing. Such an approach is not feasible for evaluating the impact of chlamydia screening at a

national level over a long time period. Instead, the research presented in this thesis focusses on three outcome measures: the prevalence of chlamydia among the general population (hereafter termed 'prevalence'); the percentage testing positive for chlamydia among people accessing testing; and the prevalence of *C. trachomatis* antibodies detected in serum (hereafter termed '*C. trachomatis* antibody seroprevalence') as a measure of the percentage of the population who have had at least one *C. trachomatis* infection by a given age (hereafter termed 'age-specific cumulative incidence').

1.1 Aims

The aims of this PhD are:

1. to identify and appraise outcome measures, and methods of their measurement, for the purpose of evaluating the impact of opportunistic chlamydia screening on the incidence and prevalence of infection (or related measures); and

2. using the outcome measures and methods identified in (1), to examine whether widespread opportunistic chlamydia screening, as it has been delivered in practice, has led to a reduction in the incidence or prevalence of chlamydia among young adults in England up to 2012 that would otherwise have been seen in the absence of opportunistic chlamydia screening.

The findings from this research can contribute to public health policy by producing recommendations on methods to evaluate the impact of chlamydia screening and on the future development of chlamydia control policies in England.

1.2 Structure of the thesis

This thesis is based on original analyses of nationally-collected surveillance data, a pilot of a chlamydia prevalence survey involving primary data collection, original analyses of data from the second and third National Surveys of Sexual Attitudes and Lifestyles (Natsal), and the application of a novel *C. trachomatis* antibody test to stored sera from the Health Survey for England (HSE).

Chapter 2 sets out the background and rationale for the research. It includes an overview of chlamydia and chlamydia screening, describes limitations of the evidence base for the effectiveness of chlamydia screening and sets out the challenges of evaluating the impact of chlamydia screening on the incidence and prevalence of infection. Key features of how chlamydia screening has been implemented in practice in England are presented.

Chapter 3 presents a review of the literature around methods of measuring a) the prevalence of chlamydia in the general population, b) changes over time in the percentage testing positive for chlamydia among people accessing testing and c) *C. trachomatis* antibody seroprevalence as a marker of age-specific cumulative incidence. The key methodological issues around selection bias and confounding are highlighted and discussed.

Chapter 4 uses nationally-collated surveillance data from women and men tested for chlamydia to explore the use of trends in percentage testing positive for chlamydia as a proxy for changes in chlamydia prevalence in the general population over time.

Chapter 5 describes the design and implementation of a pilot survey to measure prevalence of chlamydia among 17 to 18 year-old women.

Chapter 6 presents analyses of data from the second and third National Surveys of Sexual Attitudes and Lifestyles, conducted in 1999-2000 (Natsal-2) and 2010-12 (Natsal-3). Age-specific prevalence of *C. trachomatis* detected in urine is compared between Natsal-2 and Natsal-3. Differences between the design of the surveys and context in which they were carried out are examined to assess changes in chlamydia prevalence in the decade between the surveys.

Chapter 7 uses data from Natsal-3 and presents a detailed analysis of the epidemiology of prevalent *C. trachomatis* infection in relation to reported testing to explore the extent to which opportunistic chlamydia screening up to 2012 was reaching groups at risk of chlamydia.

Chapter 8 presents a *C. trachomatis* antibody seroprevalence survey using a novel assay to investigate change in age-specific cumulative incidence over time during a period of increasing chlamydia screening.

Chapter 9 brings together the findings from the previous chapters to summarise the strengths and weaknesses of each method and to examine whether there is any evidence for there having been a decrease in chlamydia prevalence or age-specific cumulative incidence since the implementation of the NCSP, up to 2012. This chapter summarises the contribution made by this research by discussing the implications for future monitoring and evaluation, for chlamydia control strategies and for future research.

2 Background

In this chapter I present an overview of the epidemiology and clinical impacts of genital infection with C. trachomatis and the putative role of chlamydia screening in its control. I discuss the limitations in available evidence for the effectiveness of chlamydia screening with particular reference to its impact on the incidence and prevalence of infection, thereby setting out the rationale for the thesis. I also provide a summary of how chlamydia screening has been implemented in practice in England over the last decade.

2.1 What is chlamydia?

C. trachomatis is a bacterium, belonging to the genus *Chlamydia*. Serotypes A-C cause ocular infections; L1, L2, L3 and L2b are responsible for lymphogranuloma venereum (LGV) and serotypes D to K cause urogenital tract infections,[16] which are the focus of this thesis. Genital infection with *C. trachomatis (*hereafter termed 'chlamydia') is the most commonly diagnosed STI in the UK and elsewhere.[9,17] Untreated chlamydia can persist for several months or years[18], and can cause a range of complications (see section 2.1.1). The acute symptoms of chlamydia infection include pain and abnormal discharge,[19] but a large proportion of people who are infected with *C. trachomatis* remain asymptomatic.[10,11,20]

Highly sensitive and specific nucleic acid amplification tests (NAATs) that detect the presence of *C. trachomatis* are available in most diagnostic laboratories in England, and can be performed on non-invasive samples (urine in men, self-taken vulvovaginal swabs or urine for women).[19] Chlamydia testing can therefore be offered in a range of clinical and non-clinical settings. Once

detected, chlamydia is easily treated with antibiotics.[19] Systemic and local antibodies to *C. trachomatis* can be detected in those with a current or previous chlamydia infection.[21,22]

The prevalence of chlamydia is highest among young adults. In the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3, carried out in 2010-12), the prevalence of *C. trachomatis* (detected in urine) in the sexually-active adult British general population was 1.5% (95% confidence interval [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%) in women and 2.3% (95%CI 1.5%-3.4%) in men.[23]

2.1.1 Sequelae and natural history of infection

Although largely asymptomatic, chlamydia presents a serious public health problem, as genital infection with *C. trachomatis* can cause several severe complications which are associated with losses of quality of life[24-26] and incur substantial healthcare costs.[27-30] In women, infection with *C. trachomatis* can ascend the genital and reproductive tract and lead to pelvic inflammatory disease (PID), a spectrum of clinical disorders involving inflammation of the uterus, fallopian tubes, ovaries, or adjacent peritoneum. PID can resolve without any damage caused to the reproductive tract. However, PID can lead to scarring and fibrosis in the pelvic organs, which in turn can lead to serious long-term reproductive consequences including tubal factor infertility and ectopic pregnancy.[11,15,31-34] The scarring and fibrosis of pelvic organs occur as a result of the immunological processes involved in response to chlamydia infection, although the exact biological mechanism(s) by which genital chlamydia infections cause tissue damage are not fully understood.[35] In men, chlamydia

can cause epididymitis (swelling of one of the tubes in the testicles).[11] Babies born to mothers with chlamydia infection are at risk of neonatal conjunctivitis and pneumonia.[11,36,37]

There are considerable uncertainties concerning the natural history of chlamydia.[38] However available data suggest that in the region of 10% to 15% of untreated genital infections with *C. trachomatis* result in diagnosed clinical PID;[14,38,39] 10% to 15% of these cases may then lead to tubal factor infertility.[38] Progression rates from chlamydia to other outcomes are less well understood.[38] In an economic evaluation of chlamydia screening in England, it was estimated that 7.6% of women with symptomatic PID would progress to ectopic pregnancy; 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.[28]

More recently, chlamydia has been suggested as a possible cause of adverse birth outcomes including pre-eclampsia, spontaneous preterm birth or stillbirth,[40-42] although study findings vary and further work is needed to fully understand this relationship.[43] Chlamydia may also increase the risk of disease arising from other sexually transmitted pathogens, through facilitation of human immunodeficiency virus (HIV) transmission[44] and increasing the persistence of high-risk human papillomavirus (HPV).[45,46]

Genital infection with *C. trachomatis* confers, at best, only partial immunity to subsequent infection.[47] Therefore re-infections are possible either from untreated or new sexual partners. Re-infection with chlamydia is common and those who test positive for chlamydia are at greater risk of testing positive at

subsequent tests than those who test negative. Studies have found that around 10% to 15% of young adults diagnosed with chlamydia also test positive at their next test[48-57] and that the percentage testing positive at a repeat test is around two to three times higher in those with an initial positive than in those with an initial negative test.[48-55] Repeat diagnoses may be due to re-infection due to incomplete treatment of sexual partner(s), re-infection due to continuing risk behaviour (i.e. unprotected sex with new or existing partners) or detection of a persistent infection due to incomplete or ineffective treatment. The extent to which treatment affects the development of protective immunity is unclear.[47,58,59]

2.2 What is chlamydia screening?

One way of trying to control chlamydia and reduce the adverse consequences associated with infection is to screen people for current chlamydia infection. Screening is a process of identifying apparently healthy people who may be at increased risk of a disease or condition. They can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition.[60] In the case of chlamydia screening, people diagnosed with chlamydia following asymptomatic testing can be offered treatment and advised that their sexual partners should also be screened and treated (hereafter termed 'partner notification').

Criteria for determining whether a disease or condition is a suitable target for screening were originally set out by Wilson and Junger in 1968.[61] These criteria remain the basis of definitions of screening, although they have been adapted and developed to be more applicable to modern public health practice, emerging technologies and to emphasise the need for evidence of

effectiveness, evaluation and quality assurance in any screening programme.[60,62-64] In summary, in order for a disease or condition to be considered a suitable target for screening, it should present an important public health problem, have a recognisable latent or early symptomatic stage and its natural history including development from early/latent period to active disease should be understood. There should be a precise and acceptable test and an accepted and effective treatment. The cost of screening should be economically-balanced in relation to medical expenditure as a whole and the benefits of screening should outweigh the harms.[60-64]

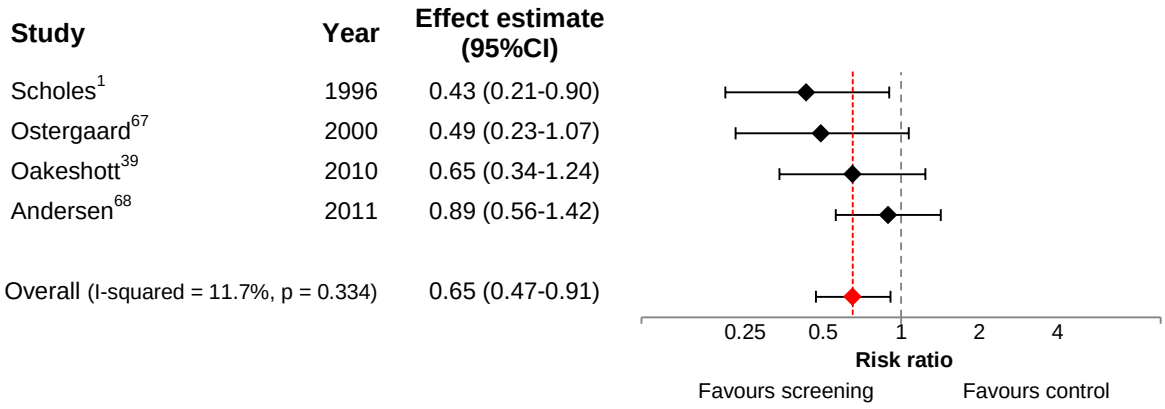
Chlamydia presents a potential target for screening as a significant public health problem, especially among young people, as it is the most commonly diagnosed STI in the UK and as untreated chlamydia infections can have serious long term consequences. Accurate and acceptable[65] tests are available and safe and effective antibiotics to treat chlamydia infection are available and included in clinical guidelines.[19] As the majority of chlamydia infections are asymptomatic, chlamydia screening should result in the diagnosis and treatment of infections that would otherwise go undiagnosed, or be detected later in the course of infection, thereby reducing the average duration of infection.

By reducing the duration of infection, chlamydia screening is expected to reduce an individual's risk of developing complications such as PID, ectopic pregnancy or tubal factor infertility.[39,66] The potential for chlamydia screening to interrupt the development of tubal pathology has been shown in four randomised controlled trials (RCT) that have investigated the effectiveness of a single offer of a chlamydia screen on the risk of developing PID within one year (Figure 2-1). A recent meta-analysis of these studies reported the pooled risk ratio of

all-cause PID after one year of follow-up for women invited to have a chlamydia screen to be 0.64 (95%CI 0.45-0.90). Uptake of screening in the intervention arm varied between 29% and 100% and the reduction in the risk of PID was greater in studies with higher rates of uptake of chlamydia screening.[2]

Figure 2-1: Reduced risk of pelvic inflammatory disease (PID) within one year associated with a single offer of a chlamydia screen among women: results of four randomised controlled trials

Adapted from European Centre for Disease Control and Prevention Report[2]



In contrast to other screening programmes such as screening for breast cancer or for cervical cancer, screening for chlamydia, as an infectious disease, includes a strong element of infection control through treatment of the infected individual and their sexual partner(s). Chlamydia screening is therefore expected to confer benefits at a population level by interrupting transmission, thereby reducing the incidence of infection. The logical basis for this can be seen using the epidemiological concept of the 'basic reproductive number', denoted as R_0. R_0 is defined as the average number of secondary infections caused by an infected person in a totally susceptible population. For STI, R_0 is dependent on three parameters, such that $R_0=\beta cD$, where β denotes the average probability that an infected individual will infect a susceptible partner over the duration of their relationship; c denotes the average number of new

partners acquired per unit of time; and D the average duration of infection.[69] When R_0 is greater than one, infection will spread through a population and the larger the value of R_0, the more quickly the infection will spread. Chlamydia screening, which is expected to reduce the average duration of infection (D), should therefore reduce R_0 and hence the incidence of infection.[70] Chlamydia screening is also expected to lead to a fall in the prevalence of chlamydia, given the relationship prevalence=incidence x duration.[71]

2.2.1 The National Chlamydia Screening Programme (NCSP) in England

Although the validity of some of the earlier RCTs of chlamydia screening and PID was later questioned (see section 2.3), the landmark trial by Scholes *et al* in 1996 and subsequent trial by Ostergaard *et al* in 2000 provided strong evidence in the late 1990s and early 2000s in support of chlamydia screening, having reported a significant reduction of ~50% in PID among those invited to screen compared to the control arm.[1,67] Observational data from Sweden and the USA were also considered to support the argument for chlamydia screening.[72] Increases in testing in women in Sweden had been found to correlate with a fall in the number of diagnoses made[73] and in the US, a before and after study found the percentage testing positive among women attending family planning clinics in Wisconsin to be lower after the implementation of a selective screening policy.[74]

In 1998, the Chief Medical Officer (CMO) in England commissioned an Expert Advisory Group to review the case for chlamydia screening, the report of which concluded that:

> *"Action is required to reduce the prevalence and morbidity associated with chlamydial infection. The sequelae of chlamydial infection are*

severe and can have lifelong implications. There is evidence that the effective management of chlamydial infection will result in considerable health benefit."[75]

And that,

"The evidence supports opportunistic screening of sexually active women aged under 25."[75]

Following this report and two pilots of chlamydia screening in 1999,[75-77] the Department of Health in England announced the planned roll-out of a national screening programme for chlamydia in targeted groups (women attending genitourinary medicine (GUM) clinics, seeking termination of pregnancy or having their first cervical smear) from 2002, with a broader national programme to follow.[76] The National Chlamydia Screening Programme (NCSP) was implemented on a phased roll-out basis in 2003, with national implementation by March 2008. The NCSP remains in place to this date and recommends that sexually active women and men aged under 25 are tested annually and on change of sexual partner, with the aim of reducing the incidence and prevalence of chlamydia and its consequences.[78] Although the original recommendation from the CMO's Expert Advisory Group referred to asymptomatic screening in women, the NCSP included recommendations for opportunistic screening in men from the start of the programme. Men were included to highlight the role of both sexes in controlling onward transmission and in preventing reproductive complications in women and to increase both sexes' ability to take responsibility for their sexual health.[79]

The delivery of chlamydia screening in England is described in detail in section 2.5. Briefly, chlamydia screening is offered to under-25 year-olds when they attend a range of clinical and non-clinical venues. This approach differs to

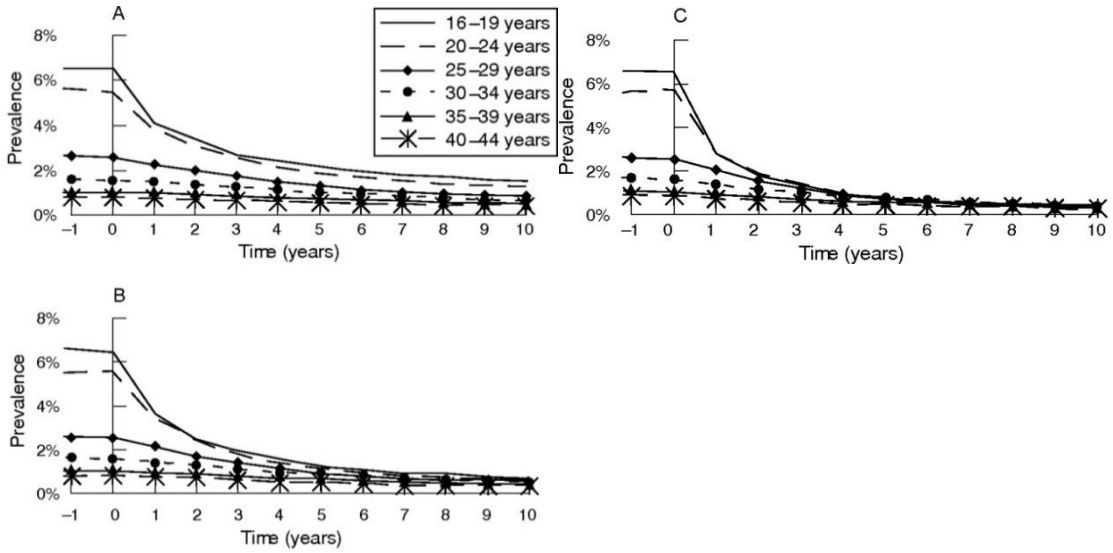
register-based screening programmes, where the eligible population are actively invited and recalled on a regular basis. The NCSP is therefore defined as an opportunistic screening programme and is referred to as such throughout this thesis to distinguish this approach from register-based screening.

The expected impact of opportunistic chlamydia screening on the prevalence of chlamydia was explored using a mathematical model developed by the then Health Protection Agency (HPA)[i] in 2006.[80,81] Turner *et al* modelled scenarios based on offering chlamydia screening to women only or women and men, attending general practice (GP) settings. The model explored the impact of different assumptions including: the age group screened; the proportion of people who accepted screening; different rates of partner notification; the proportion of the eligible population who attended GP settings and the interval between offers of screening. The results from three of the modelled screening strategies, using the base case assumptions of the model are shown in Figure 2-2. The model results suggested that opportunistic chlamydia screening of women or women and men aged <25 years could at least halve the prevalence of chlamydia within ten years, providing that the healthcare settings offered screening to the entire eligible population when they attend, that 50% of those offered screening accept the invitation and that 20% of partners were treated.[81] As seen in Figure 2-2, decreases in chlamydia prevalence in women aged 16 to 19 and 20 to 24 were predicted within the first few years of implementation of chlamydia screening, with more gradual declines seen in later years. These findings again supported the expectation that chlamydia screening could have a beneficial impact on population health.

[i] The HPA was incorporated into Public Health England (PHE) in April 2013.

Figure 2-2: Age specific impact of three screening strategies in those aged under 25 on chlamydia prevalence in women using the base case parameter set.

Reproduced with kind permission from Sexually Transmitted Infections from Turner et al 2006.[81] *Age-specific impact of screening strategies in those aged less than 25 years on chlamydia prevalence in women using the base case parameter set. The different figures show different screening strategies: A (offer annual screen to women); B (offer annual screen to women and if changed their partner in the past 6 months) and C (offer annual screen to women and men). Time (years) shows years from implementation of hypothetical screening scenarios.*



Several countries in Europe, North America and Australasia recommend asymptomatic testing for chlamydia among groups considered to have a higher risk of chlamydia. This includes young people (e.g. aged <25), men who have sex with men (MSM), pregnant women, and women undergoing abortion.[82] Scotland and Wales do not have an organised screening programme, but guidelines recommend opportunistic testing for chlamydia among young adults[82], with a focus on those at high risk of infection, including individuals attending GUM clinics, those who have been previously diagnosed with chlamydia, or those who have a partner who has been diagnosed with chlamydia, and those with two or more sexual partners in the last year.[83] In the US, the United States Preventive Services Task Force (USPSTF) and the Centers for Disease Prevention and Control (CDC) recommend testing in

asymptomatic young women and older women at increased risk.[84] However England is the only country with an organised – albeit opportunistic - chlamydia screening programme.[82] [ii]

2.3 Questioning the evidence base for the effectiveness of chlamydia screening

As set out above, there is a strong logical basis for chlamydia screening and evidence from RCTs and mathematical modelling support the notion that chlamydia screening can benefit population health. However, the evidence base relating to the effectiveness of chlamydia screening is subject to some important limitations and has come under scrutiny in recent years.

While evidence from the available RCTs and observational data was used to support chlamydia screening in the early 2000s, from around 2006, the validity of evidence on the effectiveness of chlamydia screening began to be questioned in the public health literature.[77,85,86] It is now thought that HIV prevention messages in the late 1980s and early 1990s led to a reduction in sexual risk behaviour, which in turn reduced STI transmission during this period. It is therefore likely that the role of chlamydia screening in observational studies had been over-emphasised.[86] Re-appraisal of the early RCTs by Scholes *et al* and Ostergaard *et al* highlighted some important methodological issues.[85] In the Scholes study, more effort was made to invite women in the screening group to

[ii] As defined by criteria set out by the European Centre for Disease Prevention and Control (ECDC), who define an organised screening programme as one *"that offers regular chlamydia screening to asymptomatic individuals in a well-defined target population. People found to be infected are managed according to guidelines for treatment and partner notification services. [The country also has] primary prevention activities"*[82]

take part, and they were followed up more rigorously than controls.[1,85] In the Ostergaard study, participants were randomised before they had consented to take part, 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.[67,85] Thus the effect of chlamydia screening may have been over- or underestimated in these studies.

Furthermore, more recent studies found smaller and non statistically-significant effect sizes. Oakeshott *et al* reported a 35% reduction in risk of PID at one year (risk ratio [RR] 0.65, 95%CI 0.34-1.24)[39] and Andersen *et al* reported an 11% reduction (RR 0.89, 95%CI 0.56-1.42). The meaning of these smaller effect sizes is subject to some uncertainty. In the well-conducted study by Oakeshott *et al*, around one fifth of women in both the intervention and control arms were tested outside of the study between the time of enrolment and follow up[39] and 9% of women in the Andersen *et al* study were tested in the first three months of the study.[68] This would have biased both studies towards a smaller effect size. Andersen *et al* used prescription information to measure cases of PID in community settings.[68] This means it is likely that a lot of cases of PID will have been missed,[68,87] which adds further uncertainty to the findings from this study. However, the magnitude of the effect seen in these two studies was substantially smaller than that reported in the two earlier RCTs by Scholes and Ostergaard that found ~50% reduction in risk of PID within one year of screening.

The effectiveness of chlamydia screening was further called into question with the publication of a cluster RCT of register-based chlamydia screening in the Netherlands in 2010. In the Chlamydia Screening Implementation (CSI)

project,[88] 16 to 29 year-old women and men living in three areas of the Netherlands were offered chlamydia screening annually for three years. Postal invitations were used to offer screening. Those who accepted used an internet site to request a home sampling kit, which was then posted to a laboratory for testing. The study was conducted with stepped-wedge implementation, with those in the first phase being sent three yearly invitations, and the final group participating only in the final round of screening. The study found no statistically significant reduction in the percentage testing positive for chlamydia among those tested or in estimated prevalence and no difference between areas that had participated in all three rounds of screening versus those in the comparison group who had been offered screening only once. This study had lower uptake than expected (16% in round one, decreasing to 10% in round three), which may have limited the impact of screening on transmission. However, the potential for chlamydia screening to reduce the incidence or prevalence of infection had yet to be demonstrated in practice.

The implications of the findings from these RCTs for the expected impact of chlamydia screening on population health in England are unclear. There are some important differences between the study interventions or populations which limit the generalisability of findings from the RCTs. None of the RCTs of chlamydia screening and PID investigated the impact of repeated offers of chlamydia screening and there are differences in the age groups, genders, and risk groups targeted. While the RCT in the Netherlands did investigate the impact of three rounds of annual offers of screening, the intervention was delivered using a registry to send invitations, which differs to the opportunistic approach in England and uptake of screening in the Netherlands was not comparable to that in England.[88]

At the outset of the NCSP, surveillance systems were established to collect data on numbers of tests and diagnoses among the target population tested through the NCSP (see Chapter 4). However, no system was established to monitor the health outcomes of the programme in terms of the incidence or prevalence of chlamydia or the incidence of chlamydia-related sequelae. No baseline survey of chlamydia prevalence was carried out at the start of the NCSP and there was no clear strategy as to how the programme would be shown to have delivered (or not) against its expected objectives.[89]

Thus ten years after widespread opportunistic chlamydia screening among young adults had been recommended in England,[75] there remained uncertainty about the expected or actual impact of the NCSP on population health. This uncertainty in the evidence base for chlamydia screening as it had been delivered in practice in England was epitomised in a National Audit Office (NAO) review of chlamydia screening among young people,[89] which was carried out in 2009, six years after the introduction of the NCSP. The NAO concluded that:

> *"A good understanding of two key aspects of chlamydia – the prevalence of the infection in the general population of young adults, and the probability of chlamydia leading to severe health complications – are crucial to any assessment of the Programme's impact and its cost-effectiveness. The scientific evidence in both these areas is limited and the interpretation of the existing data is subject to debate. Some of the studies which have been carried out since the Programme's launch have not strengthened the case for testing."* [89]

The research presented in this thesis was undertaken in response to this evidence gap.

2.4 How should chlamydia screening be evaluated?

There is a large body of literature on methods of evaluating public health and other policy interventions.[90-97] One of the key pieces of work in this area in the UK in recent years has been the publication and development of the Medical Research Council Framework on the Development and Evaluation of Complex Public Health Interventions.[94] The research presented in this thesis was not carried out within a specific theoretical evaluation framework. However, there are several key features of the literature on evaluation that are of particular relevance. Specifically: the choice of outcome measures, the role of non-experimental evaluation and the importance of process evaluation, each of which is dealt with in more detail below.

2.4.1 Choice of outcome measure

Choosing a suitable outcome measure is crucial to impact evaluation of public health interventions. The choice of outcome measure should be guided by a theoretical understanding of the expected impact of an intervention. All public health programmes will (either implicitly or explicitly) be underpinned by a theory of change, which can direct the evaluator to the target outcomes of interest.[90,98]

As set out above, chlamydia screening is expected to have an impact on a number of health outcomes, specifically on the incidence and prevalence of chlamydia infection and the incidence of chlamydia-related complications such as PID and ectopic pregnancy. However achieving robust measures of these outcomes is a major challenge.

As chlamydia is largely asymptomatic, case reports per year do not equate to the annual incidence of infection. Nonetheless, measurement of the incidence of chlamydia infection has been attempted. For example, Lamontagne *et al* in their 2007 study of women attending GP, GUM and family planning clinics attempted to measure incidence of infection by inviting women to be tested for chlamydia and then re-tested either six (for those who originally tested negative) or three (for those who originally tested positive) months later. While the authors reported incidence rates per person year calculated on the basis of infections measured at follow-up, they could not take account of infections that had been acquired and cleared in between measurements.[51] Direct measurement of the true incidence of chlamydia is not possible without incredibly intensive studies of large samples with frequent and repeated chlamydia testing. Such an approach is not feasible for impact evaluation of chlamydia screening at a national level over a long time period, and is not, therefore, explored any further in this thesis.

The prevalence of infection presents another obvious target outcome measure. As described above, chlamydia screening is expected to reduce the prevalence of infection both by reducing the average duration of infection and by interrupting transmission. However, as described further in the next chapter, measures of chlamydia prevalence in the general population are hard to achieve. The percentage testing positive for chlamydia among people accessing testing or screening will not equate directly to population prevalence if the population accessing testing is not representative of the general population. Measures of population prevalence from surveys require robust sampling frames and ways of protecting against or dealing with non-response. This thesis explores the use of percentage testing positive (Chapter 4) and

population prevalence measured in cross-sectional surveys (Chapters 5 to 7) as outcome measures for the evaluation of screening.

Measuring *C. trachomatis* antibodies in serum has been proposed as an alternative approach for evaluating the impact of chlamydia screening.[99] The presence of antibodies to *C. trachomatis* in serum indicate that someone has been previously infected, even if they have been treated, or the infection has cleared on its own. The use of antibody seroprevalence as an outcome measure for evaluating chlamydia control programmes is promising for a number of reasons. Firstly, using stored or retrospectively collected blood samples that have been collected for a purpose other than chlamydia testing may avoid the bias associated with data from populations who are seeking or accepting chlamydia testing. Secondly, chlamydia antibodies persist and thus provide a longer-term marker of age-specific cumulative incidence.[100] Thirdly, as age-specific cumulative incidence will by definition be higher than the prevalence, smaller sample sizes should be needed to monitor change over time. The use of *C. trachomatis* antibody seroprevalence as a marker of age-specific cumulative incidence is the subject of Chapter 8.

Chlamydia-related outcomes such as rates of PID, ectopic pregnancy and tubal factor infertility are all also potential outcome measures for evaluation. As with infection-related measures, the use of these conditions as outcome measures is problematic as they are difficult to measure consistently across sites and over time,[101,102] they all have causes other than chlamydia[38] and infection doesn't necessarily lead result in these adverse outcomes. Ethical considerations of allowing a diagnosed infection to remain untreated also make it challenging to establish the incidence of complications following untreated compared to

treated infections.[2] Ectopic pregnancy and tubal factor infertility are rare outcomes that may be diagnosed a considerable time after infection, thus studies aimed at measuring these complications would require large sample sizes and long follow up times. Investigation of the impact of screening on sequelae, while warranted, is therefore beyond the remit of this thesis. Similarly, the thesis does not include an economic evaluation, since an understanding of the costs, benefits and harms of screening warrant detailed investigation in their own right and is beyond the scope of this thesis.

2.4.2 The role of non-experimental approaches to evaluation

Another important consideration in evaluation is how to establish causal associations between any change in an outcome measure of interest and the intervention under evaluation. RCTs are considered the gold standard of evidence for investigating causal associations on specified outcomes among a defined population.[103] However the role of RCTs in the evaluation of public health interventions has received considerable attention in recent years,[96,104,105] and they are not feasible or desirable in all circumstances. As set out by Bonell and colleagues in their summary of a multi-disciplinary symposium held in 2006, interventions that have already been delivered across an entire area are not conducive to RCT methodology as it is not possible to establish a control group.[103,106] This is the case with chlamydia screening in England, as the NCSP has been operational across all areas of England since 2008. Thus estimating the effect of chlamydia screening in England via a RCT would not now be feasible without withdrawing existing service provision in order to establish a true control group.

Parts of the chlamydia screening pathway would be amenable to RCT methodology, for example comparing screening intervals, and the effectiveness of interventions to increase or target uptake in certain groups.[107] However the overall question of whether the NCSP has had a beneficial effect on population health, can no longer be answered through an RCT in England. Alternative, non-experimental approaches are therefore required. In this thesis I use several novel approaches to outcome measurement and identify the strengths and weaknesses of each. I then draw together the findings from these different approaches to evaluate what they, together, can tell us about whether chlamydia screening has reduced either the incidence or prevalence of chlamydia among young adults up to 2012.

There are other approaches to evaluating the impact of chlamydia screening on incidence and prevalence that could have been explored. Mathematical models of *C. trachomatis* transmission can help understand the potential impact of chlamydia screening.[108] The ability of such models to recreate actual transmission events over time is limited by the available data on chlamydia prevalence at baseline, tests, diagnoses, sexual behaviours and transmission dynamics over the last decade which are required for parameterisation and fitting, all of which are subject to considerable gaps[109] or uncertainty.[108] Mathematical modelling may be complementary to evaluation based on empirical outcome measurement by exploring the potential impact of screening frequency or target populations. However, this approach was beyond the remit of this thesis.

2.4.3 The importance of process evaluation

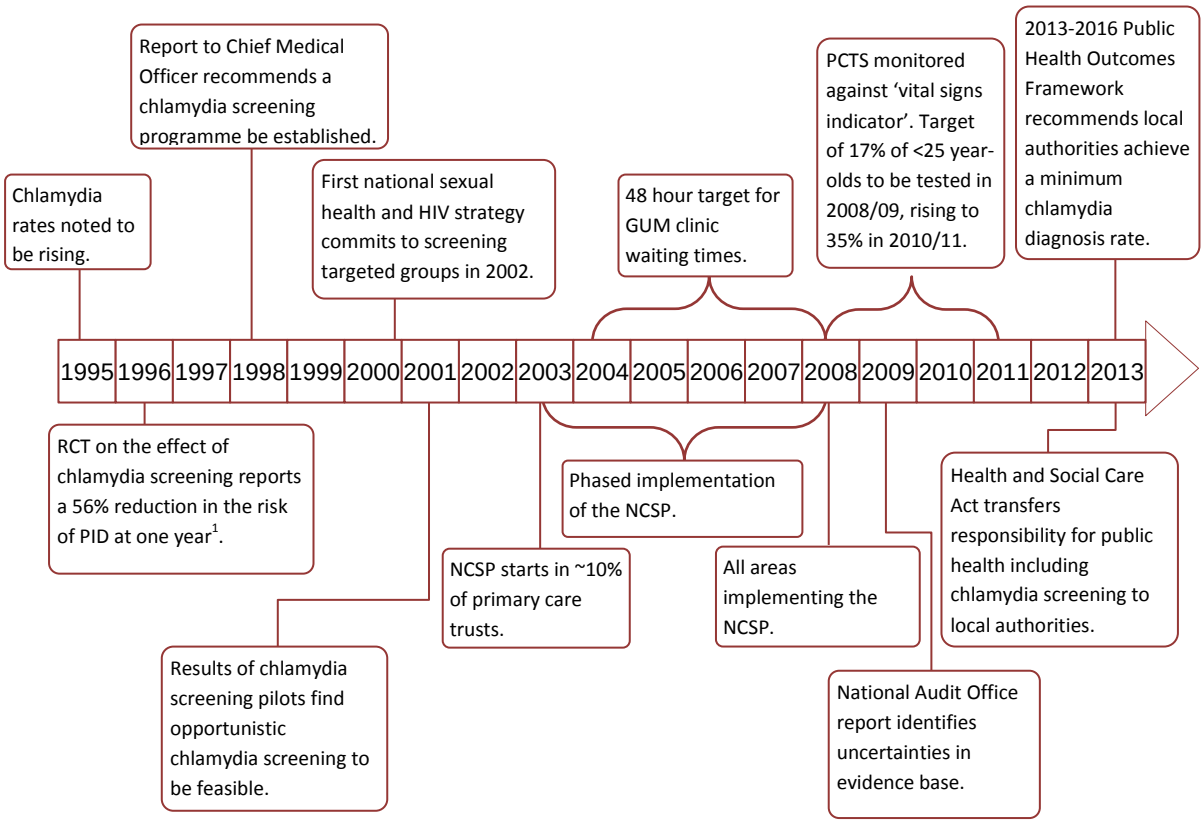
The importance of process evaluation has received more attention in the public health literature in recent years, in recognition of the multifactorial aetiology of many public health problems and of the multiple components of interventions.[110] Post-implementation process evaluation of an intervention includes a description of what was actually delivered, the interaction between the intervention and the people targeted and an appreciation of the context in which an intervention was implemented, in order to understand whether what was done would be expected to have had an impact given the theoretical understanding of mechanisms of action.[90,111]

The potential impact of chlamydia screening on incidence and prevalence will vary according to uptake of testing in different populations, the rates of treatment and testing and the index case and their sexual partner(s). In order to move beyond the generic question of 'does chlamydia screening work', we therefore need to understand what is meant by 'chlamydia screening' in the specific evaluation context. Section 2.5 below therefore describes how chlamydia screening has been delivered in practice in England via the NCSP since its implementation, thus providing the context in which the impact of chlamydia screening will be evaluated. Additionally, the analysis presented in Chapter 7 examines whether chlamydia testing and screening reported in 2010-12 was reaching 16 to 24 year-olds at risk of prevalent infection, thus exploring whether chlamydia screening has been implemented in such a way that we would expect there to have been an impact on transmission.

2.5 How has chlamydia screening been implemented in practice in England?

Figure 2-3 shows some of the key milestones and developments in the implementation of chlamydia screening in England. The way in which the NCSP has been implemented and delivered has changed substantially since the start of the programme in 2003. This variation has been driven by several factors, including local approaches to commissioning and service provision;[112] technological developments;[113] the development and constant review of national guidance on screening;[114] changes in the political and economic context in which screening is delivered and the re-organisation of health and public health services.[115] Some of the main features of chlamydia screening as delivered in practice, and changes in the implementation of chlamydia screening over time are described below.

Figure 2-3: Timeline showing implementation of chlamydia screening



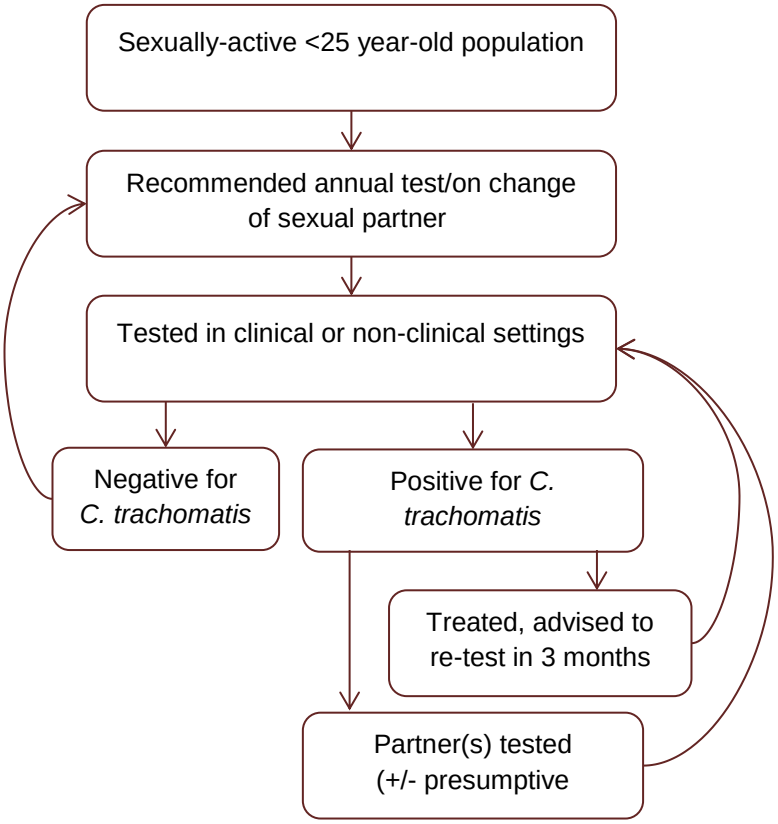
**Adapted from National Audit Office Report*[89]

The NCSP recommends that sexually-active under 25 year-old women and men are tested for chlamydia annually and on change of sexual partner (Figure 2-4). Chlamydia screening in England is offered opportunistically to under-25 year-old women and men when they attend a range of settings. These include specialist sexual health services (GUM clinics, sexual and reproductive health services, and abortion services) where young adults may be attending for sexual health-related reasons. Screening is also offered in non-specialist, clinical settings such as GPs and pharmacies. The availability of testing in non-clinical settings varies by area, but includes testing offered in schools, colleges and universities, and in bars, pubs and clubs. In several areas it is also possible to order home sampling kits online, where samples are taken at home and then returned back to a laboratory for testing.[113] The relative contribution to tests and diagnoses made by each of these settings, and the percentage testing positive in each, varies. This is explored in more detail in Chapter 4.

Young adults who test positive for chlamydia should be provided with timely antibiotic treatment. Azithromycin (1g) and doxycycline (100mg twice a day for 7 days) are both recommended as first-line treatments.[19] In the first full year of the NCSP (2008-09), 88% of people who tested positive through the programme[iii] were recorded as having received treatment.[89] The proportion of cases that has been treated with azithromycin versus doxycycline or whether this has changed over time is unknown, although anecdotal evidence suggests 1g azithromycin is more widely used for asymptomatic genital infections with *C. trachomatis* as compliance with treatment is considered more likely (personal communication, Paula Baraitser).

[iii] *Not including GUM clinics*

Figure 2-4: Schematic showing the chlamydia screening pathway according to National Chlamydia Screening Programme recommendations



Partner notification is the process of informing and treating sexual partners of individuals who have been diagnosed with STIs. Partner notification is an essential element of chlamydia control and confers benefit by reducing risk of re-infection and its adverse consequences in the original patient, preventing onward transmission of infection by infected sexual partner(s), and reducing risk of complications in infected sexual partner(s).[116,117] For asymptomatic chlamydia infection, an arbitrary period of six months (or to date of most recent sexual partner, whichever is longest) is used as a cut-off to determine which sexual partners should be followed up as contacts. Achieving high partner notification rates is notoriously challenging, and rates vary substantially by

clinic.[118] Up to 2012,[iv] the NCSP monitored partner notification performance against a standard of 0.4 partners treated per index case in a large city and 0.6 elsewhere[89]. In 2008-09 almost three-quarters of areas delivering chlamydia screening did not meet these standards.[89] Although rates of treatment and of partner notification are both subject to underreporting, the available data described above suggest that the screening pathway has not always been delivered in an optimal fashion, leaving infected individuals at risk of persistent or repeat infections.

The frequency of screening and timing of testing in relation to time since infection are also likely to affect the impact of chlamydia screening. The NCSP recommends that young adults are tested annually and on change of sexual partner, as young adults continue to be at risk of new and repeat infections after having been tested.[51] The proportion of young adults who get tested every year or upon change of sexual partner is unknown, as routinely collected data do not include a unique personal identifier, and to date this has not been investigated in national surveys. Given the frequency of chlamydia re-infections (section 2.1.1), following an evidence review and consultation with professionals and young people, the NCSP amended their case management guidelines in 2013 to recommend that those who test positive for chlamydia should be advised to re-test around 3 months after completing treatment.[119] An analysis of surveillance data from 2010 by Woodhall *et al* found the incidence rate of re-testing to be 18.4 and 26.1 per 100 person years in 15 to 24 year-olds testing

[iv] *National monitoring of treatment and partner notification for tests carried out as part of the NCSP was discontinued in 2012, as central data collection was deemed to place an unnecessary burden on local areas at a time when chlamydia screening offices were being integrated into sexual health services. Local areas are advised to monitor treatment and partner notification rates locally.*

via the NCSP and in GUM clinics respectively.[120] Rates of re-testing before this period are not known.

2.5.1 Changes in performance management, public health indicators and standards

From the time when the NCSP had been nationally implemented in 2008, local areas were monitored against national targets for chlamydia screening coverage, defined as the proportion of the population tested each year. These 'vital signs' indicators were set by the Department of Health for 2008-09 to 2010-11 (Figure 2-3). The target for local areas increased from 17% of all 15 to 24 year-olds tested per year in 2008/09 to 35% in 2010/11 (tests performed in GUM clinics did not initially contribute towards this target, although were latterly included).[89] The introduction and implementation of these targets led to a step change in the number of tests and diagnoses reported in each year (Figure 2-5 ; Figure 2-6). In Natsal-3 (carried out in 2010-12) 57.1% of 16 to 24 year-old women and 37.3% of men living in England who reported at least one sexual partner over their lifetime reported having been tested for chlamydia in the last year.[23]

After 2011, following a change of government, the national target for screening coverage was removed. Chlamydia control remained a public health priority, and an indicator relating to chlamydia screening was included in the 2013 to 2016 Public Health Outcomes Framework for England.[121] Since 2013, the Department of Health has recommended that local areas aim to achieve a

diagnosis rate[v] (defined as the number of chlamydia diagnoses per head of the 15 to 24 year-old population) of 2,300 per 100,000 or higher. The change in focus from coverage to a diagnosis rate indicator for programme monitoring was partly because the coverage target had driven high volumes of testing in relatively low risk populations resulting. The diagnosis rate indicator was considered a more appropriate measure of programme performance as treating infections is thought to reduce subsequent ill health and as a higher diagnostic rate would be expected to lead to greater reductions in chlamydia prevalence.[121] As with the use of a coverage target there are some potential limitations of using a diagnosis rate to monitor programme performance. Diagnosis rate will depend on volumes of testing, who is being tested as well as the underlying prevalence in each area. It is therefore feasible that areas with high underlying prevalence in the population may be able to achieve the specified diagnosis rate of 2,300/100,000 more easily than those who have a low underlying prevalence of infection. In areas of particularly high or low prevalence this may create a perverse incentive where screening activity required to reach a specified diagnosis rate would be inverse to sexual health need. There is no evidence at present to support local geographical variation of population prevalence, so the extent to which diagnosis rate may operate as a perverse incentive is unclear. However local authorities are encouraged to consider local needs across sexual health when commissioning services to rather than consider this as a fixed target.[121]

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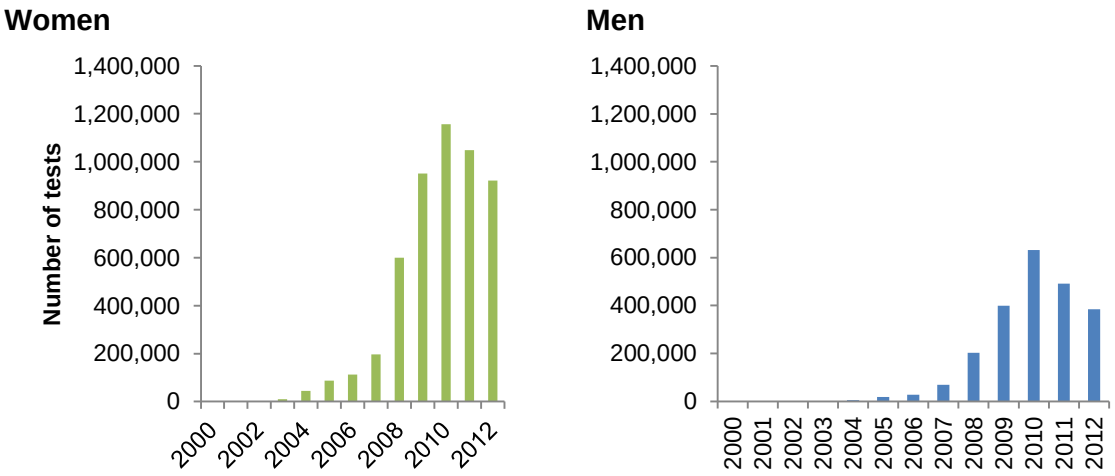
[v] *The name of this indicator changed in 2014, and is now referred to as the 'detection rate'. For the purposes of consistency, 'diagnosis rate' is used throughout this thesis.*

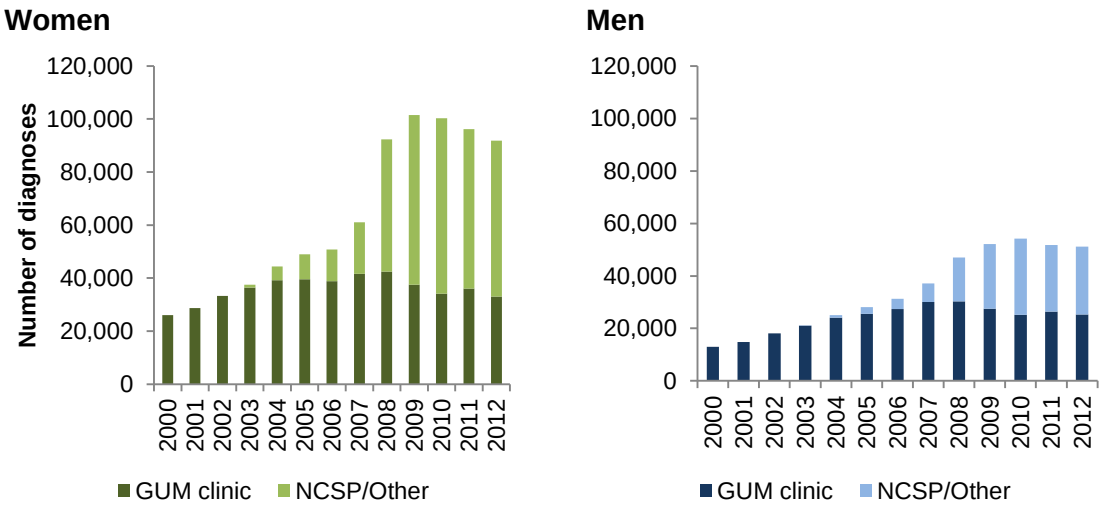
Since 2010, the NCSP has also encouraged the integration of chlamydia screening services into sexual health services for young adults.[122] In addition to continued provision in specialist GUM clinics, local areas are advised to focus on provision in general practice, community sexual and reproductive health services, pharmacies, termination of pregnancy clinics. Individuals tested in these services tend to have a moderate to high risk of chlamydia.[20,123,124] These settings present sustainable options for screening in services that can address other aspects of sexual health including contraception and other STI testing and interventions.[124]

Figure 2-5: Number of test reported among 15-24 year-olds in NCSP and other non-GUM settings, 2000 to 2012



GUM: genitourinary medicine. NCSP: National Chlamydia Screening Programme.
**Tests reported from non-NCSP, non-GUM clinics were reported from April 2008 onwards only. Tests were not reported by age group in GUM clinics until 2009 so are not included. Tests reported of unknown age have been re-allocated according to year- and gender-specific distributions.*

Figure 2-6: Number of diagnoses reported among 15-24 year-olds in all settings (GUM clinics, NCSP and other) 2000 to 2012[a]



GUM: genitourinary medicine. NCSP: National Chlamydia Screening Programme.
[a]Diagnoses reported from non-NCSP, non-GUM clinics were collected from 2008 onwards. Diagnoses reported of unknown age have been re-allocated according to year- and gender-specific distributions.

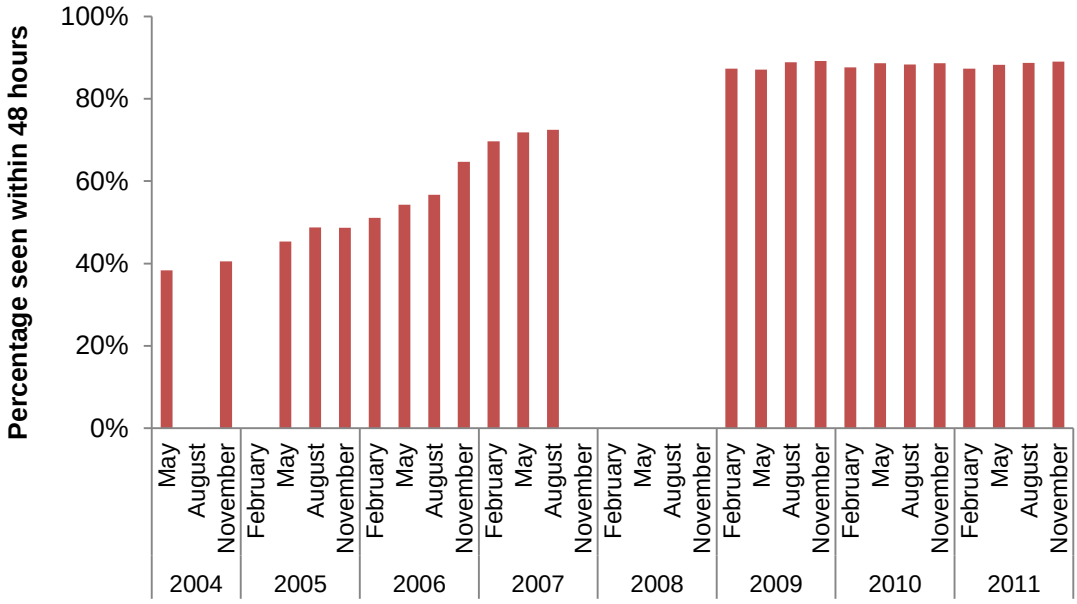
2.5.2 Changes in the context of chlamydia screening delivery

As shown in Figure 2-5 and Figure 2-6 chlamydia testing of young adults has increased substantially in England over the last decade. In evaluating the role of chlamydia screening on changes in prevalence over this period, the role of other interventions should also be considered. Along with increases driven by the national scale-up of the NCSP increases in testing occurred in GUM clinics as a result of improved access to sexual health services[125-127] and increased availability of diagnostic testing using non-invasive samples (urine or vulvovaginal swabs).[128]

Following the introduction of waiting time targets for patients attending a GUM clinic in 2004,[76,129,130] the proportion of GUM attenders who were seen within 48 hours increased from 38% in May 2004 to 87% in February 2009 (Figure 2-7). Reduced waiting times were achieved, to some extent, through increased capacity and the expansion of the role of primary care in sexual health service provision.[130] Numbers of chlamydia tests and diagnoses reported in GUM clinics increased from at least 2004 onwards (when data on tests in GUM clinics are first available), which likely indicates increased attendance as well as increased testing among attenders over this period. Findings from Natsal-2 and Natsal-3 demonstrate an increase in attendances at GUM clinics over this period: the percentage of 16 to 44 year-old women with at least one lifetime sexual partner who reported attendance at a GUM clinic in the past 5 years increased from 7% (95%CI 6%-8%) in Natsal-2 (carried out in 2000) to 21% in Natsal-3 (95%CI 20%-23%); and among men reported attendance increased from 8% (95%CI 7%-9%) to 20% (95%CI 18%-21%)[23]. This increase was seen across all age groups, but most notably among 16 to 24 year-olds.

Figure 2-7: Proportion of genitourinary medicine (GUM) clinic attendees seen within 48 hours

Between May 2004 and August 2007, data were collected as part of the HPA GUM Waiting times audit, which was performed quarterly and based on questionnaire provided to attendees in a 1 week period[125]. From 2009 onwards, data are derived from the 48 Hour Genitourinary Medicine Access Monthly Monitoring (GUMAMM) dataset[131]. Data were reported on a monthly basis, but the corresponding months are presented here for comparison purposes. Data were not collected between November 2007 and December 2009. Data collection was discontinued after 2011.



2.6 Summary

In summary, chlamydia presents an important public health problem in England. The implementation of the NCSP and increased access to sexual health services led to substantial increases in chlamydia testing in the decade up to 2012, with sustained rates of diagnoses among 15 to 24 year-olds since 2008. The way in which screening has been delivered has changed considerably during the course of the programe. Despite this moving target, there is a need to evaluate the impact of chlamydia screening - as it has been delivered in practice - against its objectives of reducing the incidence and prevalence of infection. However at the outset of the NCSP there was no system established

to do this and obtaining robust measures of incidence, prevalence or related measures is challenging.

In the next chapter the challenge of outcome measurement is addressed in more detail through a review of the relevant literature.

3 Review of the literature

In the previous chapter I summarised the evidence and theoretical basis for a chlamydia screening programme. I set out the need and rationale for evaluating the impact of the NCSP on outcomes relating to the incidence and prevalence of infection. In this chapter I provide a summary of studies that have estimated chlamydia prevalence among general population samples or that have estimated changes over time in either chlamydia prevalence, percentage testing positive or antibody seroprevalence as a marker of age-specific cumulative incidence. Methodological considerations arising from these studies are discussed, which provide the basis by which the methods of outcome measurement presented in chapters 4 to 8 are appraised.

3.1 Methods

3.1.1 Chlamydia prevalence studies using population-based sampling methods

Studies of chlamydia prevalence measured among general population samples were identified as part of a systematic review of chlamydia prevalence studies, which was carried out as part of a collaborative project on chlamydia control in Europe[2], the full methodology and results of which have been reported (Appendix 4).[3]

Cross-sectional surveys that used population-based sampling and tested genital specimens from adult participants for *C. trachomatis* were eligible for inclusion. Population-based sampling was defined as studies that used a sampling frame and method that are potentially representative of the resident population of a

particular area. This includes surveys based on household sampling and/or population registers and GP registers (although the limitations of GP registers are discussed in section 3.2.2.2 below). Studies of populations attending clinical settings who were tested for chlamydia as part of routine clinical care were identified but not included.

The review focussed on studies of adults living in European Union (EU)/European Economic Area (EEA) Member States. Studies from other high-income countries (as defined by the Organisation for Economic Cooperation and Development) were also eligible for inclusion. Electronic databases (Ovid Medline, EMBASE, Popline and The Cochrane Library) were searched from January 1990 to 17 October 2011. Search strategies included terms for 'chlamydia infection' and 'prevalence' and names of the eligible countries. The titles and abstracts were screened by two reviewers (Redmond, Alexander-Kissling) and assessed against the predefined inclusion criteria. Two reviewers (Redmond and Woodhall or Redmond and Alexander-Kissling) extracted data independently in duplicate onto standardised data collection forms, compared the extracted data for each paper and resolved differences where necessary. Discrepancies were adjudicated by a third reviewer (Low). Study characteristics, numbers eligible, numbers tested and with *C. trachomatis* detected and estimated prevalence and 95% confidence intervals were extracted from each paper. Chlamydia prevalence estimates were compiled by sex, age group, country (EU/EEA or non EU-EEA), whether the study was conducted at a national or sub-national level and whether prevalence was estimated among the total population or limited to those who reported at least one sexual partner by the time of the survey (hereafter termed 'sexually-experienced'). Chlamydia prevalence and 95% confidence intervals were estimated using the number of

positive tests divided by the number of people tested unless stratified sampling methods were used in which case the estimates presented in the papers were used.[3]

The results of Natsal-3 were published after completion of the systematic review and therefore fell outside of the review's eligibility criteria. Results from Natsal-3 are included in the text and table below, but not in the meta-analyses. The systematic review also incorporated a meta-analysis to pool chlamydia prevalence estimates where appropriate and a meta-regression to examine the association between estimated chlamydia prevalence in ≤25 year-old women and men and the calculated response rate.[3] These aspects of the review were carried out by other investigators, but results of these analyses are presented below for completeness.

3.1.2 Reviews of trends in outcome measures of interest

The reviews of literature presented in this chapter relating to: a) repeated, cross-sectional estimates of chlamydia prevalence using population-based sampling, b) trends in percentage testing positive using clinical/routinely-collected data and c) trends in *C. trachomatis* antibody seroprevalence, were not carried out as systematic reviews. For these reviews, electronic databases (including Ovid Medline, EMBASE) were searched using terms for chlamydia infection, prevalence, percentage testing positive and seroprevalence for papers up to November 2012. For the review of studies reporting trends in *C. trachomatis* antibody seroprevalence studies published up to the end of February 2014 were also included due to important contributions to the literature being published after the initial review had been carried out.[132] Studies of *C. trachomatis* antibody seroprevalence were included if they aimed to

investigate the burden of genital infection with *C. trachomatis*; studies aimed at monitoring *C. trachomatis* associated with ocular infections are not reported.

3.2 Systematic review of chlamydia prevalence studies using population-based sampling methods: Results

The search strategy identified a total of 1,003 reports. A total of 91 publications, describing 39 studies of chlamydia prevalence in the general population (25 EU/EEA, 14 non-EU/EEA) were included.[3] Table 3-1 presents a summary of included studies. Point estimates of chlamydia prevalence in these studies ranged from 0.2% to 8.0% in women and 0.4% to 6.9% in men. Five studies (not including Natsal-3) reported chlamydia prevalence in nationally-representative samples of sexually-experienced adults aged ≤26 years (Figure 3-1). The pooled estimate of chlamydia prevalence in these studies was 4.3% (95%CI 3.6%-5.0%) among women and 3.6% (95%CI 2.8%-4.4%) in men. Point estimates of prevalence ranged from 3.0%[133] to 5.3%[134] in women and 2.4%[135] to 7.3%[134] in men. Further details of the studies carried out in the UK are provided below.

Table 3-1a: Summary of characteristics of studies included in systematic review of chlamydia prevalence, studies with national coverage

Adapted from Redmond SM, Kissling KA, Woodhall SC et al.[3] The red shaded area indicates Natsal-3 survey, findings of which were not included in the original systematic review.

Country, year	Sex, age (years)	Prevalence estimated in whole study Sample, sexually experienced only or both	Number invited for testing (response rate overall, %)	Study name (acronym), if known; purpose of study, setting and sampling strategy
EU/EEA Countries				
Croatia 2011[134]	W&M, 18–25	S-E	1005 participants. 861 sexually experienced. 280 provided urine sample (women 37.5%, men 27.9%)	Cross-sectional survey of sexual behaviour and STI prevalence. Nationally representative sample from all 21 counties in Croatia, with multi-stage probability sampling.
France 2010[135]	W&M, 18–44	S-E	4957 eligible by age and sexual experience (women 54.4%, men 49.3%)	Sexual behaviour survey (subsample of Contexte de la Sexualité en France study, NatChla). Random subsample of sexually experienced people from a national population-based survey on sexual behaviour with two-phase stratified sampling. Urine testing kit only sent to women if no swab returned after 1 month.
Germany 2012[136]	W&M, 12–17	Both	5755 in this age group (women and men 14–17 years 63%)	General health survey (Kinder und Jugendgesundheitsstudie, KiGGS). Two-stage stratified cluster sampling, nationally representative sample of 0–17 year-olds. Only tested samples from participants in this age group.
Netherlands 2005[137]	W&M, 15–29	Both	20791 (women 47.0%, men 33.0%)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility (CT PILOT). Stratified probability sample of randomly selected men and women in 4 regions of the Netherlands according to population density. Regions not sampled at random.
Slovenia 2004[138]	W&M, 18–49	Both	2616 invited (women 60.0%, men 50.9%)	Sexual behaviour study. Stratified two stage probability sample of the general population of Slovenia in this age group. All participants invited to provide specimen for chlamydia testing.
Britain 2001[133]	W&M, 18–44	S-E	5026 invited to give urine sample (women 71.1%, men 68.7%)[a]	Sexual behaviour study (National Survey of Sexual Attitudes and Lifestyles, Natsal-2), conducted 1999-2001. Random sample of sexually experienced people taking part in a stratified probability sample of people aged 16–44 years resident in Britain (total 11 161 interviewed).
Britain 2012	W&M, 16-44	S-E[b]	8047 eligible participants invited to provide a urine sample, 4828 (W 59.7%, M 60.4%)[c]	Sexual behaviour study (National Survey of Sexual Attitudes and Lifestyles, Natsal-3), conducted 2010-12. Random sample of sexually experienced people taking part in a stratified probability sample of people aged 16–74 years resident in Britain (total 15 162 interviewed).
Non-EU/EEA countries, including high-income OECD countries				
USA 2002a[139]	M, 18–19, 22–26	WSS	1995 survey: data from 470 aged 18–19, and 995 aged 22–26 who were aged 15–19 in 1988 survey (insufficient data to calculate)	National Surveys of Adolescent Males (NSAM). Sexual health survey. Nationally representative sample of never-married, noninstitutionalised men aged 15–19 (1995 survey), and aged 22–26 (aged 15–19 in 1988 survey but re-interviewed in 1995). Oversampling of black and Hispanic youths.
USA 2004[140]	W&M, 18–26	Both	Wave III: 14322 (women and men 84%)	Cohort study (US National Longitudinal Study of Adolescent Health, Add Health). Nationally representative sample of young people in the USA. Total in first survey, Wave I: 18924.
USA 2012[141]	W&M, 14–39	WSS	20836 selected 17190 interviewed (women 80.4%, 2007–2008, men 74.5%, 2007–2008) [d]	General health survey (US National Health and Nutrition Examination Surveys, NHANES). Stratified multistage probability cluster sampling. Data from five 2-year survey cycles.

Table 3-1b: Summary of characteristics of studies included in systematic review of chlamydia prevalence, sub-national studies

Adapted from Redmond SM, Kissling KA, Woodhall SC et al.[3]

Country, year	Sex, age in years	Prevalence estimated in whole study Sample (WSS), sexually experienced only (S-E)	Number invited for testing (response rate overall, %)	Study name (acronym), if known; purpose of study, setting and sampling strategy
EU/EEA Countries				
Denmark 1998[142]	W&M, mean 18.0 women, 18.2 men	S-E	2603 women 928 eligible (women 33.3%) 1733 men 442 eligible (men 24.8%)	RCT of home sampling versus usual care. Random sample (half) of all high schools in Aarhus County. All students invited. Eligible if sexually experienced. (Only data from home sampling group included).
Denmark 1999[143]	W, 20–29	WSS	16345 eligible 11088 in cohort (women 67.8%)	Cohort study about risk factors for cervical cancer. Random sample of women born in Denmark, in catchment area of Righospitalet, Copenhagen taking part in a cohort study, who had cervical swab sample taken by gynaecologist.
Denmark 2001[144]	M, 17–32	Both	2500 (men 53.8%)	Cross-sectional survey to estimate chlamydia prevalence. All men in Northern Jutland, Aarhus or Copenhagen counties liable for military service and seen by a medical board.
Denmark 2002[145]	W&M, 21–23	S-E	4000 women (women 32.5% group 1, Response rates from online results for 26.3% group 2) 5000 men (men 25.9% group 1, 15.4% group 2)	RCT on effectiveness of outreach screening strategies. Simple random sample from all residents of Aarhus County in this age group. Group 1 received sampling kit, group 2 had to request kit by post.
Estonia 2008[146]	W&M, 18–35	WSS	1398 reachable (women 48%, men 32%)	Cross-sectional survey to estimate chlamydia prevalence. Stratified random sample of residents of Tartu county.
Netherlands 2000[147]	W&M, 15–40	WSS	5714 women (women 50.8%) 5791 men (men 33.0%)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility. Simple random sample of patients on the lists of 16 general practices in Amsterdam.
Netherlands 2010[137]	W&M, 16–29	S-E	140058 Amsterdam (women 22.4%, men 10.8%) 107806 Rotterdam (women 19.6%, men 10.5%)	Cluster controlled trial of chlamydia screening effectiveness (Chlamydia Screening Implementation, CSI). All 16–29 year-old residents of Amsterdam, Rotterdam, parts of South Limburg. Sexually active people invited to request test kit. South Limburg excluded because eligibility depended on response to questionnaire assessing risk of chlamydia.
Norway 2005[148]	W&M, 18–29	WSS	646 reached (women 43.8%, men 25%)	Cross-sectional survey to estimate chlamydia prevalence. All patients on the list of a group practice in Oslo.
Norway 2012[149]	W&M, 18–25	S-E	10000 invited 1670 returned sample (women 18.9%, men 11.9%)	Cross-sectional survey to estimate chlamydia prevalence. Simple random sample of 10,000 people in this age group living in Rogaland county using unique personal identification number.
Spain 2007[150]	W, 15–44	S-E	1821 invited 916 reached or accepted (women 66.1%)	Cross-sectional multinational HPV prevalence survey. Random age stratified sample of the adult female general population from census list of 4 urban communities in metropolitan Barcelona.
Sweden 1992[151]	W, 15–34	S-E	543 reached and were sexually experienced women (68.9%)	Cross-sectional survey to estimate chlamydia prevalence. All women in this age group in a primary health care area in Nättraby invited, only sexually experienced screened.
Sweden 1995[152]	W, 19, 21, 23, 25	WSS	816 reached 611 participated (68.3% women)	Cross-sectional survey to estimate chlamydia prevalence. All women of this age living in primary health care area of Ålidhem community centre in Umeå.
Sweden 2003[153]	M, 22	WSS	1074 (men 35.6%)	Cross-sectional survey to investigate feasibility of chlamydia screening. All males of this age living in Umeå.
Sweden 2004[154]	W&M, 20–24	WSS	200 (women 65%, men 45%)	Cross-sectional survey to estimate chlamydia prevalence and cost-effectiveness of home sampling. Simple random sample of 100 men and 100 women in this age group living in Umeå.
Sweden 2007[155]	M, 19–24	WSS	1936 reached (men 14.5%)	Cross-sectional survey to estimate chlamydia prevalence. Sampling method unclear, 1000 men living in Uppsala county (from population register), and 1000 Uppsala university students (from student register database).
United Kingdom 2000a[156]	M, 18–35	WSS	919 invited by post and reachable (men 45.3%)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility. Postal recruitment of all men aged 18–24 and a random sample of men aged 25–35 in 4 general practices in North West London.

United Kingdom 2000b[157]	W&M, 18–35	S-E	166 women reached (women 39%) 175 men reached (men 46%)	Pilot study of acceptability of home sampling. Simple random sample of patients on the lists of 3 general practices in North West London and Avon. Urine samples from random 50% of women, vulval swabs from other 50%.
United Kingdom 2007[10]	W&M, 16–39	WSS	14382 reached (women 37.6%, men 27.9%)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility (Chlamydia Screening Studies project, ClaSS). Random sample of general population in Birmingham and Bristol areas, selected from 27 general practice lists.
United Kingdom 2012[158]	W&M, 18–24	WSS	29917 invited (women 13.2%, men 9.8%)	Cross-sectional survey investigating feasibility of postal screening invitations. All people in this age group registered with any GP in North East Essex Primary Care Trust.
Non-EU/EEA countries, including high-income OECD countries				
Australia 2003[159]	W&M, 15–40+	WSS	6431 eligible 2862 participated (women and men 43.8%)	General health survey. All people living in 26 rural indigenous Australian and Torres Strait Islander communities in northern Queensland taking part in Well Person's Health Check.
Australia 2004[160]	W&M, 15–35	WSS	2703 eligible listed 1219 screened (women 50.7%, men 39.3%)	Cross-sectional survey to estimate chlamydia and gonorrhoea prevalence. Indigenous Australian people aged 15–35 living in Alice Springs area
Australia 2006[161]	W, 18–35	Both	1532 eligible households 979 women interviewed 657 gave urine sample (women 42.9%)	Cross-sectional survey to estimate chlamydia prevalence. Simple random sample from Melbourne residential telephone directory.
Australia 2008[162]	W&M, 14–40	WSS	ca. 1300 in 1996 (insufficient data to calculate)	Cross-sectional survey in STI control programme screening for chlamydia, gonorrhoea and syphilis. All resident indigenous Australians living in the Anangu Pitjantjatjara Yankunytjatjara Lands.
Canada 2002[163]	W&M, 15–39	WSS	1075 women (women 29.3%) 1130 men (men 16.2%)	Chlamydia mass screening study. All adults from remote Inuit communities in Nunavik region. All sexually experienced or in this age group especially encouraged to take part.
Canada 2009[164]	W&M, 15–65	WSS	224 estimated eligible (insufficient data to calculate) 181 screened (80.8% for women and men)	Chlamydia and gonorrhoea mass screening study. All men and women in this age group living in a rural Inuit community from Baffin Region, Nunavut.
New Zealand 2002[165]	W&M, 16+	S-E	1582 invited 1136 consented 582 sexually active (insufficient data to calculate)	Cross-sectional survey to estimate chlamydia prevalence. Random sample of 50% of classes in all private and public high schools, Christchurch. Only sexually active had their samples tested.
Switzerland 2008[166]	M, 18–26	Both	521 eligible and gave written consent (insufficient data to calculate)	Cross-sectional survey to estimate chlamydia prevalence. All young Swiss men attending obligatory medical board before army recruitment (French speaking region only).
USA 2001[167]	W, 18–29	S-E	2148 eligible 1439 enrolled 1370 tested 1314 sexually active (women 61.2%)	Household survey of risk behaviour and chlamydia prevalence. All English- or Spanish speaking women in this age group in a random sample of low income housing blocks from the 1990 census (<10th percentile) in 3 counties in California.
USA 2002[c] [168]	W&M, 18–35	WSS	1224 adults aged 18–45 reached 728 age-eligible for screening (women and men 79.5%)	Cross-sectional survey to estimate chlamydia and gonorrhoea prevalence. Stratified probability sampling of households in Baltimore; urine samples requested from those in study age group.
USA 2011[169]	W&M, 15–35	Both	4998 eligible (women and men 42.7%)	Cross-sectional survey to estimate STI prevalence (Monitoring STI Survey Program). Probability sample of Baltimore residents.

EU/EEA, European Union or European Economic Area Member States; M, men; OECD, Organization for Economic Cooperation and Development; S-E: Sexually-experienced; STI, sexually transmitted infections; W: women; WSS: Whole study sample. [a]Numbers from technical report Erens et al. 2001[4]. [b]Specimens were collected from all 16 to 17 year-olds regardless of reported sexual activity; prevalence of chlamydia infection was estimated among sexually-experienced only [c]Numbers from technical report Erens et al.[5] [d]Response rates from online results for 2007–2008 www.cdc.gov/nchs/nhanes/response_rates_CPS.htm

Figure 3-1a: Forest plot, estimates of chlamydia prevalence in women ≤ 26 years in EU/EEA and other high-income countries

Reproduced from Redmond SM, Kissling KA, Woodhall SC et al.[3] For references, see Table 3-1 above.

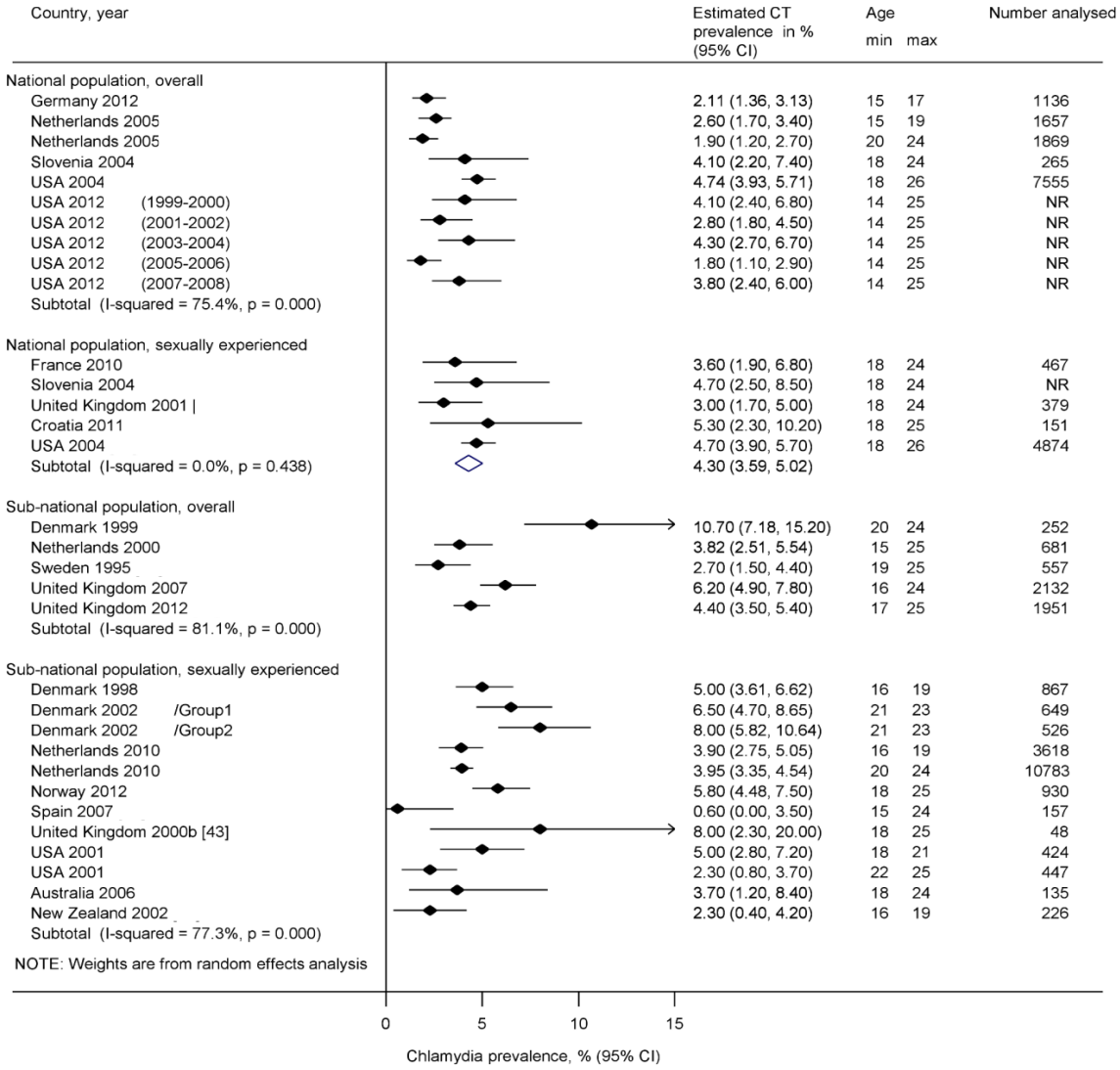
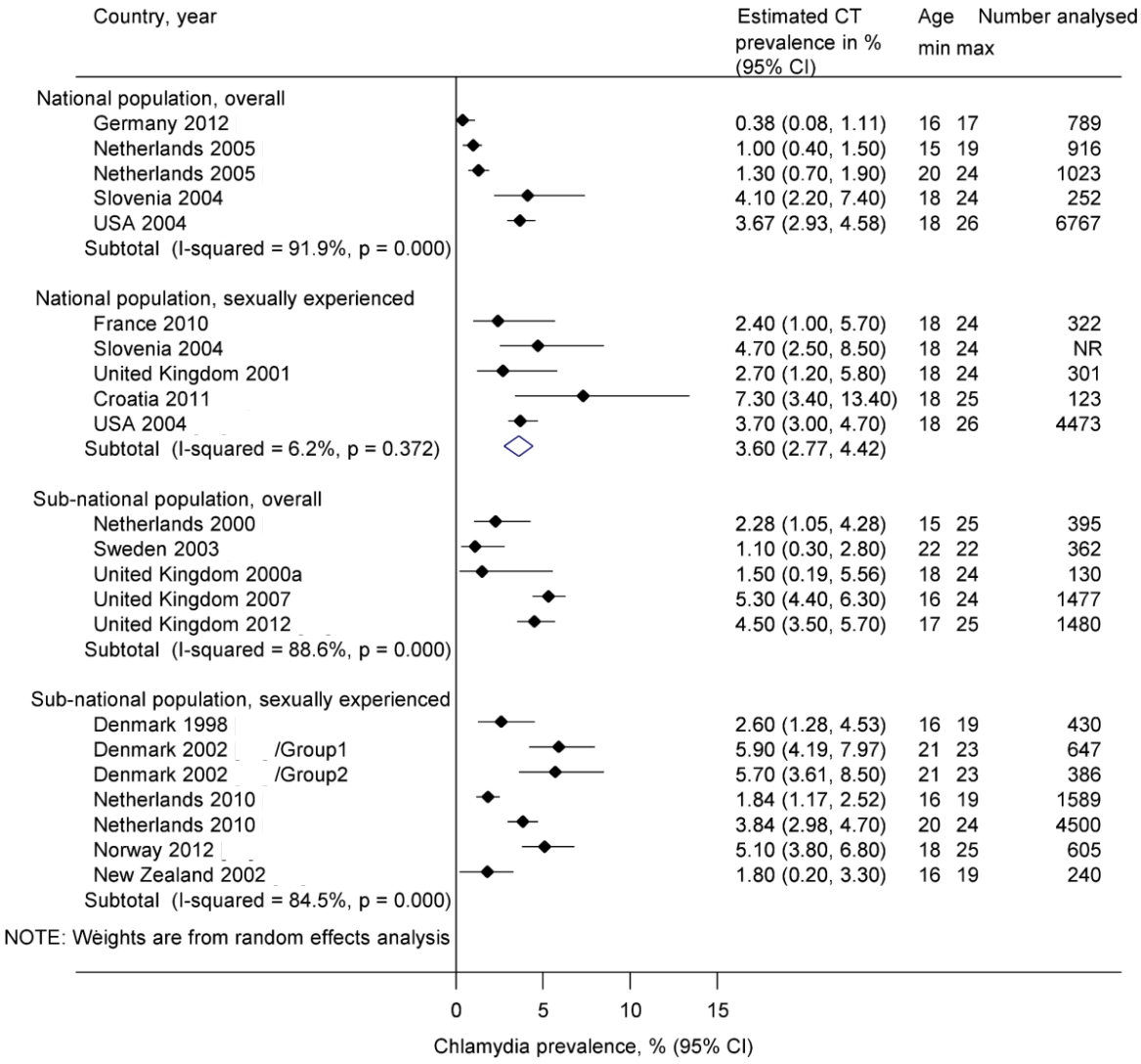


Figure 3-1b: Forest plot, estimates of chlamydia prevalence in men ≤ 26 years in EU/EEA and other high-income countries.

Reproduced from Redmond SM, Kissling KA, Woodhall SC et al.[3] For references, see Table 3-1 above.



3.2.1 UK-based studies of chlamydia prevalence

The National Surveys of Sexual Attitudes and Lifestyles (Natsal) are three, stratified probability sample surveys of the British general population (covering England, Scotland and Wales; Northern Ireland is not included). The first survey (Natsal-1) was conducted in 1990-1991[170], Natsal-2 in 1999-2001[171] and Natsal-3 in 2010-12[172]. In both Natsal-2 and Natsal-3, chlamydia prevalence was estimated among a subset of participants[23]. Natsal-2 and Natsal-3 are the only studies to have estimated population prevalence at a national level within the UK[f]. In both surveys a sample of households was identified using a national postcode list, and interviewers visited the selected homes to identify eligible participants and carry out face to face interviews. The response rate to the overall survey was 65% in Natsal-2 and 58% in Natsal-3.[g] Natsal-2 recruited 11,161 men and women aged 16 to 44; Natsal-3 recruited 15,162 16 to 74 year-olds. In Natsal-2, a sub-sample of sexually-experienced 18 to 44 year-olds in Natsal was also invited to provide a urine sample for chlamydia testing, 71% of whom (n=3,569) agreed. The prevalence of chlamydia among sexually-experienced 18 to 44 year-olds was estimated to be 2.2% (95%CI 1.5% to 3.2%) among men and 1.5% (95%CI 1.1% to 2.1%) among women. Among 18 to 24 year-olds, chlamydia prevalence was 3.0% (95%CI 1.7%–5.0%) among women and 2.7% (95%CI 1.2%-5.8%) among men.[133] In Natsal-3, as well as all sexually-experienced 18 to 24 year-olds and a subset of 18 to 44 year-olds, all

[f] The Natsal surveys were conducted in Britain (England, Scotland, Wales, not Northern Ireland). Studies in this review are labelled with the country of origin. UK is used to denote studies that were conducted in any of the countries of the UK.

[g] As eligibility within households was not known for those households not contacted, these calculated response rates use an estimated denominator of eligibles using data from households that could be contacted.[4,5]

16 and 17 year-olds - regardless of reported sexual activity - were invited to provide a urine specimen for anonymous testing for *C. trachomatis* infection. The estimated chlamydia prevalence among sexually-experienced 16 to 24 year-olds was 3.2% (95%CI 2.2%-4.6%) in women and 2.6% (95%CI 1.7%-4.0%) in men.[23]

The other UK-based study to have estimated chlamydia prevalence using population-based methods was conducted on a sub-national basis. Chlamydia prevalence was estimated for two areas of England (West Midlands and Avon) as part of the Chlamydia Screening Studies (ClaSS) project in 2001/02. Lists of 16 to 39 year-old men and women registered with GPs were used to identify the eligible target population. Individuals were then randomly selected from these lists and sent a postal invitation to participate in chlamydia screening by providing a urine sample for chlamydia testing. A total of 35% of those who were successfully contacted agreed to a test. The estimated population prevalence was 3.6% in women (95%CI 3.1%-4.9%) and 2.8% among men (95%CI 2.2%-3.4%) aged 16 to 39. Prevalence was higher among 16 to 24 year-olds (women 6.2%; 95%CI 5.2%-7.8%; men 5.1% 95%CI 4.0%-6.3%).[10]

A small number of studies of population prevalence of chlamydia conducted at the national level have been conducted outside of the UK (Table 3-1; Figure 3-1). The most established of these is the National Health and Nutrition Examination survey (NHANES) in the US. NHANES is a series of cross-sectional surveys using a stratified, multistage probability cluster design to select a representative sample of the US civilian, non-institutionalised population. Interviews are conducted in the household, and biological samples

are collected at mobile examination units. Recruitment is continuous, and data are presented in two-yearly cycles.[141]

3.2.2 Methodological issues in general population studies

Selection bias is error that arises from procedures used to select subjects or from factors that influence study participation[173]. Bias occurs when members of the study population differ in an important way from those who are not included in the study, with respect to the outcome or outcomes of interest. Some types of selection bias are particularly relevant for studies of chlamydia prevalence and are explored in more detail below.

3.2.2.1 Non-response bias

In the absence of 100% response rates, non-response bias occurs when members of the study population differ in an important way from non-participants. In the case of chlamydia prevalence surveys, non-response bias occurs when the prevalence of chlamydia is different among participants and non-participants[174,175].

The response rates in the prevalence surveys reported in section 3.2 ranged from 9.8%[158] to 84%[140]. The standard view in survey research has been that high response rates (ranging from more than 50% to more than 85% participation) are required in order to reduce the risk of non-response bias. However the relationship between response rate and non-response bias is not straightforward, and several studies have shown that non-response bias is not directly correlated with the survey response rate. Thus Groves argues that "there is no minimum response rate below which survey estimates are *necessarily* subject to bias"[174]. The extent to which an estimate among

participants will be a biased estimator of the target population depends on whether the factors affecting the likelihood that an individual will participate in a survey are related to the outcome of interest. If the factors relating to participation are entirely unrelated to the outcome, then estimates will be unbiased[174]. While this is theoretically possible, this is unlikely to happen in practice. An individual's propensity to participate is often related to their interest in the topic, or in this case risk of infection, and thus is likely to lead to a difference in the outcome measure between participants and non-participants[176].

The studies among general population samples described in section 3.2 provide some important evidence to suggest that participation in surveys of chlamydia prevalence is indeed likely to depend on factors relating to risk of infection, including sociodemographic characteristics and sexual behaviours. In Natsal-2 and Natsal-3, chlamydia testing was performed among a subsample of respondents to the main survey. In both surveys the probability of providing a urine sample was associated with demographic factors including gender, ethnicity, and social class, as well as sexual risk factors, including history of condomless intercourse, having had a same-sex partner or reporting anal sex. Some of this differential participation would have led to participants being more at risk of having a prevalent infection than non-participants (e.g. those reporting more sexual partners without a condom and reporting a previous STI diagnosis were more likely to participate) whereas other factors may have tended towards a bias in the opposite direction (e.g. respondents of non-white ethnicity were more likely to participate in the urine study than those of other ethnicities).[177,178]

As part of the CSI project in the Netherlands, findings from a survey of non-respondents versus respondents found some evidence that demographic factors associated with increased risk of infection (young age, ethnic minority groups, living in areas with high community risk), were associated with a *decreased* likelihood of participation. Conversely, individual sexual behavioural risk factors for chlamydia (casual or multiple sexual partners or a recent STI diagnosis), were associated with an *increased* likelihood of participation in screening, thus demonstrating the complexity of the factors affecting participation.[179,180] Uusküla *et al* used linked data from a healthcare utilisation database in Estonia to compare the characteristics of respondents and non-respondents in their population-based survey of chlamydia prevalence. Individuals who had a STI or related diagnosis within the past 12 months were more likely to participate in the survey, suggesting those with an interest in the topic had a higher propensity to participate.[181] The higher rates of infections seen in populations attending clinical settings for testing are consistent with this evidence, suggesting that individuals who seek or accept testing are likely to be, on average, at higher risk of infection.[123,182] Further evidence of this is found in the meta-regression presented by Redmond *et al* in their systematic review of chlamydia prevalence studies, which found that surveys with lower response rates had higher estimates of chlamydia prevalence.[3] However, as the surveys were carried out in different countries and at different times, the extent to which this association is due solely to different participation rates is unclear.

Given the relationship between propensity to participate and risk of infection demonstrated above, the extent to which estimates are subject to non-response bias is likely to differ by study design. For example studies with a broad health focus (e.g. NHANEs), or those using stored samples collected for another

purpose, may be subject to different biases than those with a specific focus on sexual health (e.g. Natsal), as the decision to participate in the survey or provide a biological sample would be informed by considerations other than those that relate specifically to sexual risk behaviour. Similarly, those designed specifically as chlamydia screening interventions (e.g. CSI and ClaSS), are likely to be subject to selection biases, and may be more similar to study populations of individuals accepting testing in other clinical settings. Assessing the scale of bias in each case is, however, extremely difficult and the different methods (if any) used for assessing non-response bias make it infeasible to quantitatively compare bias between studies.

Where the variables that predict participation are perfectly measured in both the target population and the survey population, non-response bias can theoretically be eliminated.[174,183] However in practice, this is limited by the data available, and only minimal information is usually available from non-participants. Where the studies reported above have tried to address non-response, this has usually been limited to applying post-stratification weightings, to weight the sample population to a known distribution in the target population, for example age, gender and ethnicity. While this approach can go some way to correcting for non-response bias, this assumes that the prevalence of chlamydia among participants and nonparticipants is the same within specified demographic subgroups. Weights that only allow for basic demographic characteristics are likely to be inadequate, as the studies where non-response has been investigated show that these factors do not fully capture the risk difference between participants and non-participants. A few studies have applied more detailed weights. In Natsal-2 and Natsal-3, as well as weighting

for age, sex and geographical distribution of the target population, additional weights were applied to allow for the differential response patterns to the request to provide a sample for chlamydia testing.[5,133,177] However, even this approach is imperfect, as it does not allow for any self-selection in participating in the main Natsal-2 survey beyond age, sex and region.[177] In order to estimate prevalence, rather than percentage testing positive using data from participants in the CSI project in the Netherlands, weights were applied to match the age, gender, ethnicity and a community-level risk score of the population of the regions where the study took place. Further weights were applied to allow for an estimated proportion of the population who were sexually experienced, and to adjust for the use of a risk score to determine eligibility in one of the three participating regions (South Limburg, where population prevalence was thought to be lower than in the other two, largely urban regions). No weights were applied to account for any other sexual behaviour differences.[88]

3.2.2.2 Coverage bias

Coverage bias is a form of selection bias that occurs when the sample from which a study population is selected is not representative of the target population, for which conclusions from the study are to be drawn.[184] The availability of adequate sampling frames varies by country, and identifying a representative population can be difficult and can have a large impact on the cost of the study.

The studies presented in section 3.2 above used a range of different sampling frames. Some studies were able to use a population registry, for example in Estonia, Uusküla *et al* selected a random sample of 18 to 35 year-olds living in Tartu from the national population registry in 2005/06. Forty percent of those

who were contacted participated, 86% of whom returned both a questionnaire and a sample for testing.[146] In the Netherlands, the CSI project[137] and the prevalence survey carried out before the implementation of the trial[185] used municipal population registers to access addresses of the eligible population.

However not all countries have reliable population registers available and alternative approaches have been used. For example, telephone directory listings have been used as a sampling frame in studies conducted in Australia[161] and France.[141] In Britain, in the absence of a readily-available population registry, Natsal-2 and Natsal-3 used the national Postcode Address File as the initial sampling frame, from which postcodes and subsequently addresses were selected. Interviewers at the household then assessed eligibility upon contact with the household.[133] Where the eligibility criteria are relatively broad (e.g. adults), this approach will potentially be more efficient than where more restrictive criteria are applied (e.g. 15 to 24 year-old women), as fewer households would have to be contacted in order to identify one eligible person.

One alternative sampling frame to population or household lists in England is to use GP registers, as used by the CLaSS survey.[10] Almost all residents of England are registered with a GP. In 2011, an estimated 98% of 15 to 24 year-old females were registered.[h] However GP lists have substantial limitations. The names and addresses held on GP registers may be inaccurate due to

[h] Calculated using ONS mid-2011 population estimates, plus data from the NHS Information Centre Attribution Dataset of GP registered populations scaled to ONS population estimates, 2011, assuming that 1 registration = 1 person. http://www.ic.nhs.uk/statistics-and-data-collections/population-and-geography/gp-registered-populations/attribution-dataset-gp-registered-populations-scaled-to-ons-population-estimates-2011

registrations that relate to deceased patients, duplicate records or patients who have either moved out of the area or moved within the area but not updated their contact details (so-called 'ghost patients'). As part of the ClaSS study, intensive efforts were used to identify whether people actually received the postal invitation to screen. Individuals were classified as 'ghosts' if they were either confirmed as not resident at the address held by the practice or not contactable by any method. 26% of the invited 16 to 24 year-olds women were classed as 'ghosts'[10]. While there has been a move in recent years to improve the accuracy of these lists,[186] GP lists are still likely to be subject to inaccuracies.

In summary, few nationally-representative studies in EU/EEA or other high income countries have estimated chlamydia prevalence, although prevalence has been estimated in Natsal-2 and Natsal-3 in Britain. Surveys are subject to non-response bias and coverage bias. Although weighting has been used to correct for this in some surveys, this potential for bias remains a challenge for achieving robust estimates of prevalence in the general population. These biases are relevant for single estimates of chlamydia prevalence but are also important to consider when using repeated measures, which is the subject of the next section.

3.3 Repeated, cross sectional estimates of chlamydia prevalence in the general population

One option for monitoring changes in chlamydia prevalence would be to have regular, repeated measurements of a random sample of the population. Only two published studies using repeated sampling among a general population

sample to measure chlamydia prevalence over time had been published at the time of carrying out this review.

In the US, NHANES has measured chlamydia prevalence since 1999. The estimated prevalence among 14 to 39 year-olds declined from 2.6% to 1.6% between 1999/2000 and 2007/2008. However there was no statistically significant fall measured among 14 to 25 year-old women, the population targeted for annual screening in the US.[141]

In the Netherlands, chlamydia prevalence was repeatedly estimated as part of the CSI project. As described in section 3.2.2.1, prevalence was derived from percentage testing positive using post-stratification weightings. No significant change was seen in either the overall percentage testing positive or estimated prevalence. A small decline was observed in one of the three regions (South Limburg), where the percentage testing positive declined from 5.1% to 3.1% and the estimated population prevalence declined from 3.2% to 1.8%.[88]

While these two studies used general population sampling frames, they have some limitations.

The sampling strategy of the NHANES survey means that different areas are sampled in each two year survey cycle. While this is based on probability sampling, and thus will be generally representative of the US population, prevalence estimates for diseases that are highly geographically clustered may be very sensitive to the chance selection of areas. For this reason, NHANES is no longer used for estimating the population prevalence of gonorrhoea, as selecting areas where a cluster of infections exists may lead to erroneous conclusions about the prevalence of infection in the general population.[187]

Chlamydia is more evenly distributed through the population,[188] but it is feasible that the clustering of infection within sexual networks may make such estimates more prone to measurement error.

In the CSI project in the Netherlands, participants had higher levels of sexual risk behaviour than the general population, and the proportion reporting sexual risk behaviours increased in each year (among those with available data on sexual behaviour).[88] Therefore not only are prevalence estimates within each year likely to be overestimated, but the change between years is subject to confounding by the change in the participating population in each year. Specifically, the change over time is likely to be underestimated, as the sample includes an increasingly higher-risk population over time.

The publication of findings from Natsal-3 in 2013, provided a third study which used repeated cross-sectional estimates of population prevalence. Comparisons between these two surveys are investigated in detail in Chapter 6.

3.4 Trends in percentage testing positive for chlamydia using clinical and routinely-collected data

Given that few studies have used repeated population-based measurement of prevalence, one potential alternative is to use data from populations accessing chlamydia testing to look at changes over time.

Two systematic reviews have demonstrated the existence of numerous studies of populations attending clinical settings who were tested for chlamydia as part of routine clinical care.[2,123] The percentage testing positive in these studies does not equate to the prevalence of chlamydia among the general population

as individuals seeking or accepting a chlamydia test will not be representative of the general population. This is clearly demonstrated in the systematic review by Adams et al, who found that estimates of percentage testing positive conducted in healthcare settings were higher than prevalence estimates conducted in population-based studies.[123] This distinction can also be seen in a comparison of NCSP data from 2008 and findings from Natsal-2 by Riha *et al*, which found that the percentage testing positive among women and men aged 18 to 24 years who were tested as part of the NCSP was higher than estimated population prevalence in Natsal-2 (8.5% versus 3.1% in women and 9.4% versus 2.9% in men).[182]

While studies using data from populations accessing testing cannot provide estimates of population prevalence of chlamydia, they may have some utility as outcome measures of changes in the burden of chlamydia infections over time, albeit in subgroups of the population.

Reports of trends in percentage testing positive for chlamydia using data from sexual health or family planning clinics have been published or included in routine surveillance reports for several countries, including the UK,[189] the US,[190-192] Australia,[193-195] New Zealand,[196] Finland,[197] the Netherlands,[198] Sweden[73] and Norway.[199] In the US, trends have also been reported among men and women tested through the National Job Training Program (NJTP), representing a high-risk subgroup of socioeconomically-disadvantaged 16 to 24 year-old men and women.[200] In contrast to trends seen in England (section 4.4.1), increasing trends in percentage testing positive for chlamydia have been seen since around 2000 in Denmark, Sweden and New Zealand.[101] In Australia, increases in percentage testing positive have been observed in several

populations,[193] although stable trends or decreases have been seen among men who have sex with men (MSM).[194] In the US, test positivity in family planning clinics and among young people entering the NJTP has been increasing in the last decade.[200] After adjusting for test technology and known changes in the test population however, either stable or declining trends were seen. Analyses at a sub-national level have shown increases in percentage testing positive during this period, even after adjustment.[192]

3.4.1 Methodological issues in studies of trends in chlamydia prevalence or percentage testing positive

3.4.1.1 Measured and unmeasured confounding

Confounding occurs when the estimated effect of an exposure of interest is distorted, as it is mistaken for the effect of another exposure (or exposures). In order for this to happen, the confounder must be correlated with both the outcome and the exposure of interest, and must not be part of the causal pathway from the exposure of interest to the outcome of interest.[173] Whether using repeated prevalence measures from population-based samples, or trends in percentage testing positive in populations accessing testing, estimates will be subject to confounding if there are any changes in the characteristics of the population tested or the way that infection status is measured that are also associated with risk of infection.[201] Where all confounders are perfectly measured, the main effect of time on chlamydia result can be measured by including confounders as covariates in multivariable models, or by carrying out stratified analyses. In practice, it is unlikely that all potential confounders can be measured, but it may be possible to reduce the impact of confounding on estimates of trends in infection over time.

3.4.2 Changes in demographics or sexual behaviour of those tested

The potential for confounding was seen in the CSI project in the Netherlands.[88] Among those who completed the questions on sexual behavioural at the time of screening, reported levels of sexual risk behaviours were higher than the general population and increased with each round of screening invitation, while the overall uptake of screening in the study decreased with each round from 16% in round one to 10% in round three.[88] Even though the project used population-based sampling (i.e. invited the total eligible population) it is reasonable to expect that the true prevalence of infections would be lower than that estimated in the CSI project's main findings and that the decline in prevalence would be steeper than was observed.[88]

Depending on the specific context, it is easy to see how trends in the percentage testing positive among tested populations may be even more subject to changes in who is tested than in population-based studies.[201] Changes in national or local screening policies or rates of partner notification may lead to different populations being tested. Media campaigns may increase awareness of chlamydia, and lead to people either requesting a test or accepting the offer of a test that may not have done before. While several reports have been published that examine the trends in percentage testing positive, relatively few have made any attempts to control for potential confounding introduced by the observational nature of the data.

In the US, Satterwhite *et al* examined trends in percentage testing positive in women tested in Infertility Prevention Program (IPP) family planning clinics[191] and antenatal settings.[202] In both settings, trends in percentage testing positive were adjusted for test technology, age, ethnicity and region. No sexual

behaviour data were available. The analysis was performed using the clinic as the unit of analysis. The unadjusted trend in percentage testing positive in the IPP clinics showed 2% annual increase in percentage testing positive (odds ratio (OR) 1.02, 95%CI: 1.01 to 1.03). After adjustment, the authors found that there was no change in percentage testing positive in women attending IPP FP clinics between 2004 and 2008 (adjusted odds ratio (AOR) 1.00, 95%CI: 0.99 to 1.00) and a decline in percentage testing positive among women attending IPP prenatal clinics between 2004 and 2009 (AOR 0.93, 95%CI 0.92-0.95). While this method was able to control for unmeasured confounding arising from a changing distribution of clinics, it assumes that the populations attending each clinic are largely stable over time, within the demographic stratum.

Fine *et al* explored trends in percentage testing positive among women attending IPP FP clinics in the Pacific Northwest region of the US between 1997 and 2004. Enhanced demographic and sexual behaviour data are collected at a regional level, and thus they were able to examine the trend in percentage testing positive adjusting for age, state, race/ethnicity, city size, test technology and several sexual behaviour variables. Adjusting for all these factors together had little effect on the measured trend in percentage testing positive, with both unadjusted and adjusted analyses showing a 5% increase per year in the odds of testing positive (AOR 1.05, 95%CI 1.03 to 1.05).[192]

Two papers have examined adjusted trends in percentage testing positive in Australian settings. O'Rourke *et al* reported trends in percentage testing positive among women attending the Melbourne Sexual Health Centre, and Vodstrcil *et al* reported trends among men from the same setting. Among women, the self-reported characteristics of attendees were found to be relatively stable over the

analysis period, with only minor changes observed, such as an increase in the proportion reporting 2 or more sexual partners in the previous 3 months from 25% in 2003 to 30% in 2007.[193] More substantial changes were observed among men who have sex with women (MSW), among whom the proportion reporting 2 or more sexual partners increased from 42% in 2002 to 53% in 2009. Among men who have sex with men (MSM), the only notable change was the proportion reporting symptoms or contact with infection, which decreased from 39% in 2002 to 35% in 2009. Although these changes in the population tested were noted, adjusting for these characteristics made negligible difference to the measured trend in percentage testing positive, suggesting that the changes in the population were not sufficient to explain any of the trend in percentage testing positive over time. After adjusting for available risk factors, percentage testing positive was found to increase among women and MSW (women: AOR 1.12; 95%CI: 1.05-1.20; MSW: AOR 1.04, 95%CI: 1.01-1.07), but no change was found among MSM (AOR = 0.99, 95%CI: 0.93-1.06).[194]

3.4.3 Changes in test technologies

While relatively few studies have attempted to deal with potential changes in the demographic or behavioural characteristics of those tested, more have tried to address the impact of changes in test technologies. A change to a more sensitive test could result in an increase in percentage testing positive for chlamydia without a change in the prevalence of infection among the tested population, whereas a change to a more specific test could result in a decrease in the percentage testing positive, due to fewer false positive results. Changes in the test technology may also result in changes in the population tested. Less invasive sampling for both men and women may increase the likelihood of

someone either seeking a test, being offered a test, or accepting the offer of testing.

Three studies aimed specifically at determining the change in percentage testing positive that can be attributed to the change in test were identified in this literature review. Burckhardt *et al* used data from a GUM clinic in Scotland between 1992 and 2003, where the test used switched from culture to ligase chain reaction (LCR) in September 1998;[203] Dicker *et al* examined data from two regions of the Infertility Prevention Program (IPP), and compared percentage testing positive in the calendar quarters immediately before and after changes from a DNA probe to LCR in one region (1996-1997) and from direct fluorescent antibody (DFA) to enzyme immunoassay (EIA) with confirmatory DFA in another (1993-1994);[204] Gotz *et al* compared changes in percentage testing positive in laboratories that did and did not change their testing procedures in Sweden between 1996 and 1998, and 1998 and 1999.[205] In all cases, some, but not all of the increase in percentage testing positive was attributable to changes in the test used.

Consistent with the expected increase in percentage testing positive with increasingly sensitive test technology, Satterwhite *et al* found that adjusting for test technology had a substantial impact on the observed trend in percentage testing positive among men and women tested in the National Job Training Program (NJTP) in the US. Comparison of unadjusted data showed an increase in percentage testing positive between 2003 and 2007 (OR 1.11, 95%CI: 1.10 – 1.14), however after adjusting for test technology and other variables, the adjusted trend showed an average 5% decline in percentage testing positive per year (AOR 0.95, 95%CI: 0.93-0.97).[200]

In summary, in considering trends in prevalence or percentage testing positive for chlamydia, if the population tested or test used varies over time then changes in the measured outcome may be wrongly attributed to a change in the amount of infection in the population over time. This has been demonstrated in studies in the US and Australia, but the impact of differences in the population accessing testing has not been explored in England. This is the subject of Chapter 4.

3.5 Trends in *C. trachomatis* antibody seroprevalence as a marker of age-specific cumulative incidence

Seroepidemiology has been widely used for the monitoring of vaccine-preventable diseases where there is a clear correlation between previous vaccination and/or wild-type infection and detectable antibodies and to identify susceptible sections of the population.[206,207] As the presence of *C. trachomatis* antibodies in serum provides a marker of previous infection, serological analyses have been used to establish the association between previous chlamydia infection and reproductive complications including PID, ectopic pregnancies and tubal factor infertility.[208] However seroepidemiology has rarely been used to investigate trends in genital infection over time, or as a marker of control of genital chlamydia infections.[99]

This is, in part due to the lack of a suitable assay. Until recently, serological testing for *C. trachomatis*-specific antibodies was problematic as several assays were subject to cross-reactivity with other chlamydiae species[21,208] and sensitivity and specificity of commercially available assays was relatively poor.[99] In recent years, tests with higher specificity and which are not subject to cross-

reaction have become available[209] and present new opportunities for chlamydia seroepidemiology.

At the outset of this PhD, three studies had reported on trends in antibodies to chlamydia using samples collected from pregnant women. In Japan, the percentages testing positive for *C. trachomatis* antibodies (hereafter '*C. trachomatis* antibody seropositive') were compared between pregnant women in 1987, 1992 and 1996/97 (n=275, 297 and 9,652 respectively). Women in the later sample were routinely screened at the time, whereas the earlier results were obtained by testing stored serum samples. The percentage *C. trachomatis* antibody seropositive was found to decline[i] in all age groups, for example from 35% to 31% among women aged 20 to 24 years old.[210] Two studies in Finland have reported trends in *C. trachomatis* antibody seroprevalence among pregnant women up to the age of 28, using stored serum from the Finnish Maternity Cohort serum bank.[211,212] Both studies report a fall in antibody seroprevalence from around 1990 to the early 2000s. For example, seroprevalence among 23 to 28 year-olds decreased from 22% (95%CI 19%-25%) in 1989-1991 to 12% (95%CI 10%-15%) in 1998 to 2000.[212]

More recently, in the Netherlands, van Aar *et al* have reported results from a study using stored sera from participants in two nationally-representative surveys of the general population in 1995-1996 and 2006-2007. Sera were tested using the Medac quantitative CT IgG ELISA. There was no statistically significant evidence of a difference in seroprevalence between birth cohorts.[132]

[i] Statistical significance of the decline was not reported.

In England, two studies to date have investigated trends in percentage *C. trachomatis* antibody seropositive. Horner *et al* used residual sera submitted to laboratories in England for routine microbiological or biochemical investigations.[213] A second study by the same group used residual sera from individuals tested for syphilis at two GUM clinics in England.[214] In both studies, sera were tested using an "in-house" indirect immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) based on the Pgp3 antigen (hereafter 'indirect Pgp3 ELISA', see section 8.3.2.1 for more details), which have demonstrates superior sensitivity to commercially-available assays such as that used in the studies in Japan, Finland and the Netherlands above.[209] Reductions in percentage with Pgp3 antibodies detected in serum ('Pgp3 seropositive') among young women were observed in both studies, consistent with a decline in exposure to antibody inducing infection in the mid- to late-2000s, at a time when there was increasing uptake of chlamydia testing and treatment. In the first study using sera collected for routine testing in non-GUM settings, the age-standardised seroprevalence among 17 to 24 year-old women decreased from 20% (95% CI 17%–23%) to 15% (95%CI 12%–17%) in 2010 (p=0.0001).[213] In the second study that used sera from women attending GUM services, the percentage Pgp3 seropositive among women <20 years old decreased from 42% in 1998 to 30% in 2009.[214]

Antibody seroprevalence surveys are potentially less subject to selection bias as they can use stored or retrospectively collected blood samples that have been collected for a purpose other than chlamydia testing. However the studies above remain subject to bias and confounding. Pregnant women may have a different risk of infection to the general population and seroprevalence trends may be subject to confounding from changes in age-specific characteristics of

women who become pregnant. The studies from the UK were based on clinic-attending populations rather than nationally-representative samples and in both studies it is also possible that the population who contributed serum samples changed over time. Sera in the study by Horner *et al* were excluded if they were listed as coming from GUM clinics. However it is feasible that the accuracy of coding improved over time meaning that the proportion of sera from high-risk populations may have changed (personal communication, Kate Soldan). Patterns in access to clinics may have affected the population being tested for syphilis testing in the UK study from GUM clinics.[214]

Along with general considerations of bias and confounding, seroprevalence studies are also subject to some specific limitations. The interpretation of age-specific trends in seroprevalence is complicated by the fact that serum antibody levels are likely to depend on several factors including the time since infection, the duration and seriousness of infection as well as number of infections. Thus trends in seroprevalence can only provide an indicator of trends in exposure to antibody-inducing infection, and all tests will underestimate the number of people who have ever been infected. These limitations are discussed further in Chapter 8).

3.6 Summary

Studies in Europe and the US that have used population-based methods to estimate chlamydia prevalence at a national level among sexually-experienced under 26 year-olds report prevalence estimates of 3.0% to 5.3% in women and 2.4% to 7.3% in men. Achieving robust measures of chlamydia prevalence is challenging due to the need for appropriate sampling frames with sufficient

information to adjust for non-response bias and changes in sampling or response over time.

The percentage testing positive among samples from clinical populations or those accessing testing is typically higher than prevalence estimated in population-based studies as those who access testing will be at higher risk than the general population.

In the absence of RCTs, interpreting trends over time in chlamydia-related outcome measures (chlamydia prevalence, the percentage testing positive, or antibody seroprevalence) is problematic due to changes in the population tested, changes in sexual behaviour and changes in tests. It is possible to control for confounding where all confounders are perfectly measured, but this is unlikely in practice. The confounding effect of changing test technology on trends in chlamydia infection has received some attention in the literature, but there have been relatively few studies that have attempted to control for potential confounding due to behavioural factors.

In the next chapter, I describe an analysis of nationally-collated surveillance data, which was carried out to address the issue of confounding and investigate the potential use of these data for monitoring changes in chlamydia infection over time.

4 Trends in percentage testing positive for chlamydia using routinely-collected surveillance data

As set out in the previous chapter, changes in the percentage testing positive for chlamydia among populations accessing testing may be due to changes in the population tested rather than a change in the underlying amount of infection in the population. Changes in percentages testing positive may also be due to changes in sexual behaviour rather than due to the effect of a chlamydia control intervention such as chlamydia screening. In this chapter, I investigate the use of surveillance data for the purposes of evaluating the impact of chlamydia screening. I explore the extent to which trends in percentage testing positive for chlamydia in England are affected by changes in the characteristics of the population tested and in turn whether these data provide any evidence of there having been a decline in chlamydia infections in the context of widespread chlamydia screening among under-25 year-olds.

4.1 Background

Public health surveillance involves the ongoing and systematic collection, analysis and interpretation of health-related data for the purposes of informing public health action, including planning and implementation of services or interventions and evaluation of public health practice.[215,216] Infectious disease surveillance encompasses a spectrum of activities from collation of case reports to active, population-based surveillance that aims to capture the total picture of infection or disease within a population.[216] These different approaches have different strengths and limitations. Systems based on case reports, even if augmented with additional demographic or clinical data, will often rely on routinely-collected information, the quality and completeness of which may vary depending on the setting and purpose for which it is collected. Data collected

from people who have accessed health services for testing or diagnosis of an infection will also be biased towards the health-seeking population. For asymptomatic infections such as chlamydia, this is particularly problematic. Systems based on more complete pictures of a population of interest that employ a sampling strategy to achieve a representative population of interest may avoid some of these problems but will often be much more resource-intensive and may still be subject to bias depending on who participates or from whom data are available.

During the course of the 2000s, a number of developments were made in STI surveillance in England. The KC60 data return, which reported aggregate data on STI diagnoses in GUM clinics with limited demographic data, was replaced in 2009 by the genitourinary medicine clinic activity dataset (GUMCAD). GUMCAD is a patient-level data return including all STI diagnoses made (including chlamydia) and services provided (including chlamydia tests) in STI clinics in England along with patient demographic information.[6]

Alongside the implementation of the NCSP from 2003 onwards, data reporting systems were set up to collect information on chlamydia tests carried out through the programme. From 2003 to 2011, all chlamydia tests performed outside of GUM clinics as part of the NCSP were reported by service providers to the Health Protection Agency (HPA)[j] (hereafter termed 'NCSP dataset').[217] The NCSP dataset includes tests performed in a range of settings including GP, community sexual and reproductive health services, community pharmacies,

[j] The Health Protection Agency (HPA) was incorporated into Public Health England (PHE) from April 2013.

education and youth venues and tests accessed via the internet. From 2008 to 2011, the HPA also collected aggregate data on tests among 15 to 24 year-olds performed outside of GUM settings, but not reported to the NCSP, via a quarterly return from testing laboratories (the Non-NCSP, Non-GUM dataset, representing 14% to 17% of tests among 15 to 24 year-olds each year from 2008 to 2011).

Taken together, these datasets provide a complete picture of NHS-commissioned chlamydia tests among 15 to 24 year-olds in England up to 2011. Since the start of the programme, these data have been used to monitor the performance of local areas and drive service improvement in terms of chlamydia testing coverage and, in more recent years, diagnosis rates.[114,218] While this is a key function of surveillance data, the extent to which this routinely-collected information from individuals accessing chlamydia testing can be used to monitor burden of infection within the population is unclear given both the bias associated with healthcare-attending populations and the considerable changes in the way that screening has been implemented in England over the past decade (section 2.5). As set out in the previous chapter it is feasible that trends in the number of case reports and percentage testing positive for chlamydia may be confounded by a change in the population tested, which in turn may limit the utility of routine data for monitoring the burden of infection.

4.2 Aims & objectives

The aim of this analysis was to determine whether trends in the percentage testing positive for chlamydia provide any evidence to suggest a decrease in

chlamydia prevalence since the national implementation of chlamydia screening in 2008. This aim was addressed through the following objectives:

- To describe trends in percentage testing positive for chlamydia among 15 to 24 year-olds tested for chlamydia as part of the National Chlamydia Screening Programme (between 2008 and 2011), or tested in GUM clinics (between 2009 and 2011).
- To investigate the extent to which time trends in percentage testing positive for chlamydia are subject to confounding due to changes over time in the characteristics of the population tested by adjusting trends for a range of sociodemographic and behavioural variables.

4.3 Methods

4.3.1 Data sources

Data on chlamydia tests among 15 to 24 year-old women and men in England reported through the NCSP dataset or GUMCAD were included[k]. The analysis period varied slightly between datasets: 2008 was included as the earliest year for analysis of the NCSP dataset as this was the first full year of the NCSP; the earliest year for analysis of GUMCAD was 2009 as this was the first year the system was nationally-implemented. From 2012 onwards, the NCSP dataset and the Non-NCSP Non-GUM dataset were replaced by a laboratory-based reporting system (the Chlamydia Testing Activity Dataset, CTAD). This dataset does not incorporate the same demographic and sexual behaviour variables as

[k] Data are subject to minor revision due to retrospective submission of data, thus exact numbers may vary from published figures. These analyses are based on extracts dated February 2012 (NCSP dataset) and 17 August 2012 (GUMCAD).

the NCSP dataset, thus analyses were limited to tests performed up to the end of 2011.

Within the NCSP dataset, test records with a matching postcode of residence, date of birth and gender were considered to refer to the same person and were used for de-duplication.[l] In GUMCAD, individuals with more than one clinic visit were linked using their clinic number (this is unique within a clinic)[m]. All analyses were conducted on the basis of 'testing episodes' Test (and diagnosis) records within 6 weeks of a previous test were considered to be the same testing episode and were excluded. Individuals were allowed to contribute more than one testing episode during the analysis period. Analyses were carried out separately in the NCSP and GUMCAD datasets, as although individuals can attend more than one service they cannot be linked between the datasets.

Demographic, test and behavioural information are collected in the NCSP dataset and GUMCAD, although different items are collected in each (Table 4-1). An area-level indicator of socioeconomic deprivation (the Index of Multiple Deprivation, IMD[220]) was assigned to all test records by mapping postcodes of residence to lower super output areas (LSOA, an area of average population of 1,500 individuals[221]) of residence. Ranks of IMD scores were grouped into quintiles. Having a previous chlamydia diagnosis is a known risk factor for

[l] Where a test record in the NCSP dataset had a postcode of residence equal to the postcode of testing venue, the postcode of residence was set to 'missing', as this was considered a likely data entry error.

[m] Chlamydia tests and diagnoses are recorded separately in GUMCAD, and may be recorded on different dates. All recorded sexual health screens were considered to include a chlamydia test (as specified in coding guidelines[219]). A test was considered positive if there was a chlamydia diagnosis recorded on the same day or within the following 6 weeks. A chlamydia diagnosis reported without an accompanying sexual health screen was included as a positive test.

subsequent infection.[48,51,56] Testing episodes were therefore categorised as having a recorded chlamydia diagnosis in the past 12 months by linking tests records for individuals within each dataset. The sexual behaviour variables were combined into a single 'risk group' variable, in order to avoid collinearity in multivariable models (high risk: answered 'yes' to both sexual behaviour variables; medium risk: answered 'yes' to one sexual behaviour variable; low risk: answered 'no' to both sexual behaviour variables).

Table 4-1: Comparison of data items included in the NCSP dataset and the genitourinary medicine clinic activity dataset (GUMCAD) used in the analysis

	NCSP Dataset	GUMCAD
Date of test	✓	✓
Year of age	✓	✓
Ethnic group	✓	✓
Region (Strategic Health Authority)	✓	✓
LSOA of residence*	✓	✓
Testing venue type	✓	Not applicable
Specimen type (urine/vulvovaginal swab/cervical swab)	✓	✖
Reports having a new sexual partner in the previous three months (yes/no)^	✓	✖
Reports and more than one sexual partners in the previous 12 months (yes/no)^	✓	✖
Sexual orientation$	✖	✓

**LSOA: Lower super output area*
^These sexual behaviour variables were included in the 'core dataset', which all local areas were required to submit as part of the NCSP dataset return. Other optional items were available as part of the NCSP dataset (including condom use), but were not included in this analysis as not all areas returned these items.
$Sexual orientation is collected in GUMCAD at each clinic visit. Men who reported having sex with a man at any clinic visits were categorised as men who have sex with men (MSM).

4.3.2 Statistical analyses

Test, demographic and sexual behavioural characteristics were compiled for NCSP and GUMCAD testing episodes. The total number of testing episodes,

percentage testing positive and reported test, demographic and behavioural characteristics, are presented by year, calendar quarter and dataset.

The relative annual change in the percentage testing positive was estimated using univariable logistic regression, with test result included as the outcome variable, and year as a continuous predictor variable. Odds ratios were interpreted as a reasonable proxy for relative risk, due to the generally low prevalence of chlamydia in these analyses.[222] Annual trends were calculated by gender and other factors including age, venue of test, sexual risk group (NCSP dataset) and sexual orientation (GUMCAD).

It is reasonable to assume that the likelihood of attending a GUM clinic with a symptomatic STI may be less subject to changes in sexual health policies and service provision than the likelihood of an asymptomatic attendance, meaning individuals attending with symptoms may provide a more stable population in which to monitor chlamydia infection. The proportion of attendances in 2009 to 2011 where a chlamydia testing episode was recorded was higher for those where a diagnosis of genital warts, candidosis, genital herpes or - for women - bacterial vaginosis was made (Table 4-2). Trends in percentage testing positive for chlamydia were therefore also explored in a subgroup analysis limited to GUM clinic attendances where a diagnosis of these selected symptomatic conditions was made.

Table 4-2: Proportion of GUM attendances with a chlamydia testing episode recorded, by gender (15 to 24 year-old women and men, GUMCAD, 2009-2011)

	Women		Men	
	N	% tested	N	% tested
All GUM attendances	1,628,320	59%	996,862	63%
Attendances with diagnosis of selected symptomatic condition:				
Genital warts	68,148	83%	57,025	85%
Candidosis	121,518	88%	12,968	87%
Genital herpes	26,307	66%	10,782	85%
Bacterial vaginosis	137,552	92%		

4.3.3 Factors associated with testing positive

The association between demographic and sexual behaviour variables and testing positive for chlamydia were explored using univariable and multivariable logistic regression. All variables significant in univariable analyses ($p<0.05$) were entered into a multivariable model.

4.3.4 Assessment of confounding of time trends in percentage testing positive introduced by changes in risk factors over time

In order to investigate potential confounding of trends in percentage testing positive for chlamydia arising from changes in the population tested, a series of 'bivariable' logistic regression models were constructed, which included test result as the outcome variable, and year (entered as a continuous variable) and one other variable as predictors (e.g. year and age, year and ethnicity, year and region). The estimated annual change in percentage testing positive was compared between the models when each variable was included or excluded to explore whether allowing for changes in each variable would change the estimated trend in percentage testing positive. Variables that were significantly

associated ($p<0.05$) with testing positive in each of the bivariable models were included in a multivariable model, along with year.

NCSP testing episodes had considerable levels of item non-response for variables of interest (Table 4-3). The percentage of testing episodes with missing data increased between 2008 and 2011, from 42% to 58% among women and 58% to 69% among men, and varied by venue of testing service. The lowest levels of missing data were seen for testing episodes returned through remote testing (29% missing data among women, 32% among men). The percentage testing positive was higher among testing episodes with complete data compared to those with missing data for both women (6.9% versus 6.0%) and men (6.4% versus 4.5%). As the purpose of the analysis was to compare the impact on the annual change in percentage testing positive when adjusting for different variables, this analysis was limited to testing episodes with complete data on all of the variables of interest. A sensitivity analysis was carried out to determine whether the same patterns were observed when using data that were complete on each individual item of interest. Sensitivity analyses were not carried out in the GUMCAD analysis as the percentage of GUMCAD tests with missing data was lower (13.9%).

All tabulations and models were constructed separately by gender and by dataset. All statistical analyses were performed using Stata version 12.0 (StataCorp, College Station, Texas, USA). Statistical significance is considered as $p<0.05$ for all analyses.

Table 4-3: Percentage of tests with missing data on one or more variable (NCSP dataset, 15-24 year-old women and men, 2008-2011)

	Women		Men	
	N (Total=2,564,925)	**% missing**	**N** (Total=1,537,178)	**% missing**
By variable of interest				
>1 sexual partner in previous year		43%		56%
At least 1 new sexual partner in previous 3 months		40%		53%
Ethnicity		25%		34%
IMD of LSOA of residence		10%		17%
Known chlamydia diagnosis in previous year		10%		17%
Specimen type		2%		n/a
One or more of the above		52%		66%
By venue type of testing				
Hospital	90,751	51%	15,281	54%
Outreach	305,175	74%	441,452	78%
Occupational Health	717	54%	1,298	73%
Pharmacy	71,300	41%	27,192	47%
Sexual and Reproductive Health Services	767,747	48%	207,617	54%
General Practice	475,269	47%	157,400	48%
Remote testing	257,782	29%	151,556	32%
Military[$]	5,590	87%	55,242	93%
Prisons & Youth Offender Institutions[$]	4,758	89%	55,396	96%
Chlamydia Screening Offices	114,054	50%	87,836	60%
Abortion services	89,639	57%	884	56%
Education	297,569	69%	278,137	75%
Youth	84,574	53%	57,887	61%
By year of test				
2008	385,483	42%	181,539	58%
2009	645,276	48%	357,241	61%
2010	830,172	56%	569,272	68%
2011	703,994	58%	429,126	69%

*IMD: Index of multiple deprivation, quintile based on lower super output area (LSOA) of residence; *All tests had age, gender and venue of test; [$]Missing data in these venues is largely accounted for by missing postcode of residence, as the validation algorithm for postcodes did not allow postcode of residence was not allowed to equal the postcode of testing venue.*

4.4 Results

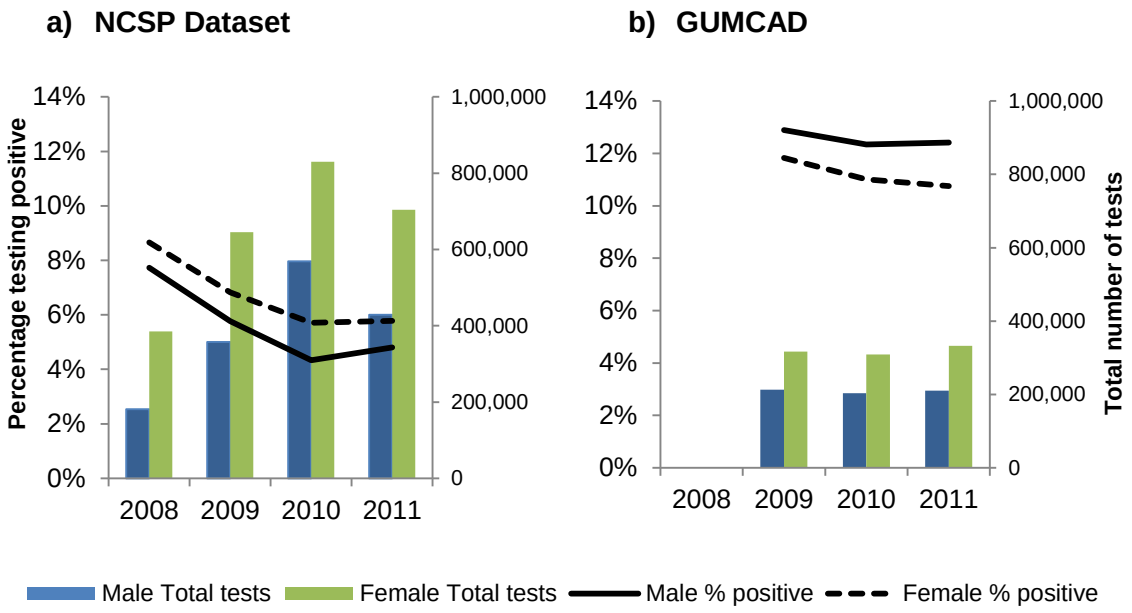
4.4.1 Number of tests and percentage testing positive in the NCSP dataset and GUMCAD

Between 2008 and 2011, 4,102,103 chlamydia testing episodes among 15 to 24 year-olds (62.5%, [2,564,925] in women) were reported in the NCSP dataset, of which 6.5% among women and 5.2% among men resulted in a positive diagnosis. Between 2009 and 2011 there were 1,585,395 testing episodes (60.5% [958,864] in women) reported in GUMCAD; 11.2% in women and 12.6% among men were positive.

Between 2008 and 2011, the number of NCSP chlamydia testing episodes almost doubled, from 567,022 to 1,133,120 (Figure 4-1a, Table 4-4). The percentage testing positive during this period decreased among both women (from 8.7% to 5.8%, OR per additional year 0.86, 95% confidence interval[CI] 0.86 to 0.87) and men (from 7.7% to 4.8%, OR 0.84, 95%CI 0.83-0.84).

The number of GUMCAD chlamydia testing episodes remained relatively stable during the analysis period (Figure 4-1b, Table 4-5). The percentage testing positive declined from 11.8% in 2009 to 10.8% 2011 among women (OR 0.95, 95%CI 0.94 to 0.95) and 12.9% to 12.4% among men (OR 0.98, 95%CI 0.97 to 0.99).

Figure 4-1: Numbers of testing episodes and percentage testing positive by gender, NCSP dataset and GUMCAD



4.4.2 Factors associated with testing positive

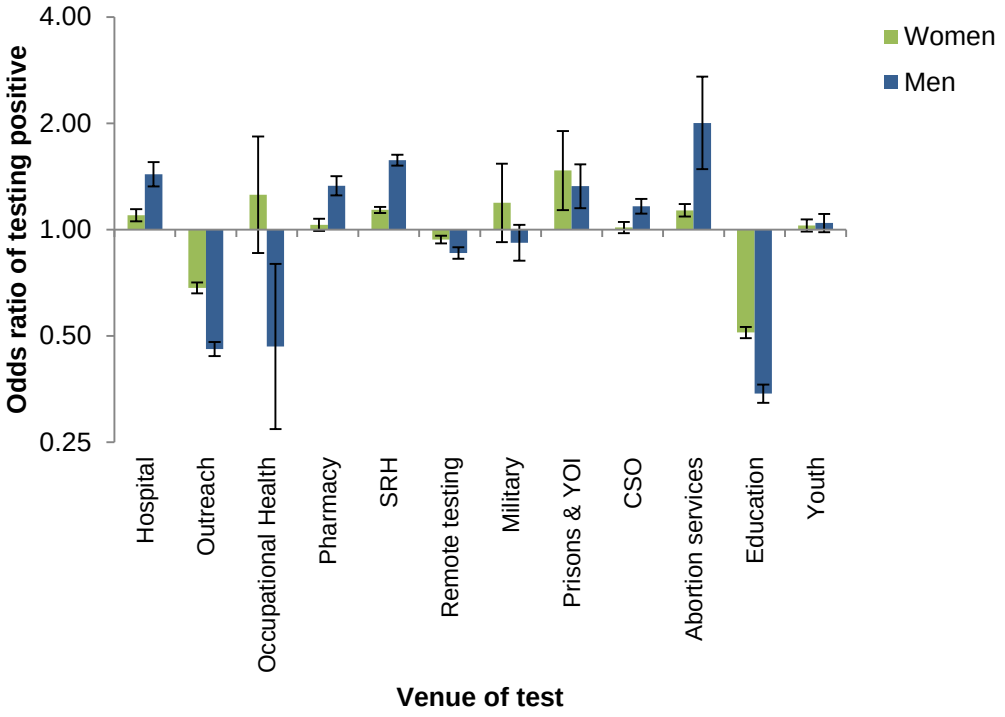
All variables were statistically significantly associated with testing positive in univariable and multivariable analyses for NCSP (Table 4-4) and GUMCAD testing episodes (Table 4-5). Among NCSP testing episodes, there was substantial variation in the percentage testing positive by the type of testing venue, which remained after adjusting for the other variables in the multivariable analysis (Figure 4-2; Table 4-4). Testing episodes in educational venues and outreach settings were less likely to result in a positive diagnosis than those in general practice, whereas tests in sexual and reproductive health services, abortion services, prisons and hospital settings were more likely to be positive.

In NCSP testing episodes, reporting both a new sexual partner in the past three months and more than one sexual partner in the previous year was associated with at least a two-fold increase in the odds of testing positive compared with those reporting no more than one sexual partner in the last year and no new

sexual partner in the last three months (women: AOR 2.24, 95%CI 2.20-2.28; men: AOR 2.09, 95%CI 2.03-2.16). In both the NCSP dataset and GUMCAD, the odds of testing positive were higher in those with a known chlamydia diagnosis than those without in both women (AOR NCSP: 1.13, 95%CI 1.09-1.18; AOR GUMCAD: 1.04, 95%CI 1.01-1.07) and men (NCSP AOR: 1.27, 1.17-1.37; GUMCAD AOR: 1.15, 1.10-1.20).

Being of black or mixed ethnicity and living in more deprived LSOA was significantly associated with having higher odds of testing positive after controlling for other variables, with the exception of in GUMCAD testing episodes among women, where those of black ethnicity had a lower odds pf testing positive than those of white ethnicity. MSM had a lower risk of testing positive compared to non-MSM in both univariable and multivariable analyses (AOR, 0.64 95%CI 0.62-0.67) of GUMCAD testing episodes.

Figure 4-2: Adjusted* odds ratio (and 95% confidence intervals) of testing positive by venue of test and gender, compared to General Practice (NCSP testing episodes, 15-24 year-old women and men)



**Adjusted for age, ethnicity, risk group, IMD quintile of LSOA of residence, known chlamydia diagnosis in the previous 12 months and year of test.*
SRH: Sexual and reproductive health services; CSO: chlamydia screening office; YOI: Youth offending institution. Outreach: tests performed in non-clinical settings including entertainment and leisure venues; Remote testing: tests performed without face to face contact with a health professional at the time of test, includes tests performed through the internet.

Table 4-4 (a): Number of tests, percentage testing positive, unadjusted and adjusted odds ratios for testing positive by sociodemographic, sexual behavioural, and test characteristics (NCSP dataset, 15-24 year-old women, 2008-2011)

	Number of tests	% positive	Univariable analysis OR	95%CI	p	Multivariable analysis AOR	95%CI	p
Overall	2,564,925	6.5%						
Sociodemographic characteristics								
Age (years)								
15	146,897	5.2%	Ref		<0.001	Ref		0.000
16	298,915	5.8%	1.11	1.08 - 1.14		1.22	1.17 - 1.27	
17	343,314	6.8%	1.32	1.29 - 1.36		1.44	1.39 - 1.50	
18	341,651	7.5%	1.47	1.43 - 1.51		1.58	1.52 - 1.64	
19	311,826	7.6%	1.50	1.46 1.54		1.60	1.54 - 1.66	
20	278,653	7.2%	1.41	1.38 - 1.45		1.51	1.45 - 1.57	
21	243,679	6.7%	1.30	1.26 - 1.34		1.38	1.33 - 1.44	
22	216,592	5.9%	1.13	1.10 - 1.16		1.21	1.16 - 1.26	
23	199,985	5.0%	0.96	0.93 - 0.99		1.03	0.98 - 1.07	
24	183,413	4.6%	0.87	0.84 - 0.89		0.95	0.91 - 1.00	
Ethnic group								
White	1,638,982	6.8%	Ref		<0.001	Ref		0.000
Black	107,978	8.1%	1.22	1.19 - 1.25		1.32	1.28 - 1.36	
Asian	77,163	3.3%	0.47	0.45 - 0.49		0.57	0.54 - 0.60	
Chinese	9,401	4.7%	0.68	0.62 - 0.75		0.92	0.82 - 1.03	
Other	12,486	5.5%	0.80	0.74 - 0.86		0.95	0.86 - 1.06	
Mixed	70,359	8.6%	1.29	1.26 - 1.33		1.28	1.24 - 1.32	
Unknown	648,556	5.5%						
Region								
London	385,755	5.7%	Ref		0.000	Ref		0.000
North East	113,668	6.5%	1.15	1.12 - 1.18		1.47	1.41 - 1.53	
North West	379,340	7.9%	1.40	1.38 - 1.43		1.35	1.32 - 1.39	
Yorkshire & Humber	232,092	7.3%	1.29	1.27 - 1.32		1.36	1.32 - 1.40	
East Midlands	203,013	6.2%	1.08	1.06 - 1.11		1.25	1.21 - 1.29	
West Midlands	246,320	6.5%	1.14	1.12 - 1.17		1.28	1.24 - 1.32	
East of England	229,985	5.6%	0.96	0.94 - 0.99		1.09	1.06 - 1.12	
South East Coast	152,567	5.6%	0.97	0.95 - 1.00		1.02	0.98 - 1.06	
South Central	169,175	5.7%	1.00	0.97 - 1.02		1.08	1.04 - 1.12	
South West	202,890	6.9%	1.21	1.18 - 1.23		1.20	1.16 - 1.24	
Other / Unknown	250,120	6.2%						
IMD quintile of LSOA of residence[y]								
Least deprived	317,630	5.1%	Ref		<0.001	Ref		<0.001
2	356,775	5.7%	1.13	1.11 - 1.15		1.09	1.06 - 1.12	
3	428,577	6.0%	1.19	1.17 - 1.22		1.17	1.14 - 1.20	
4	541,366	6.7%	1.33	1.30 - 1.35		1.28	1.25 - 1.31	
Most deprived	670,007	7.7%	1.54	1.51 - 1.57		1.42	1.39 - 1.46	
Unknown	250,570	6.2%						

Table 4-4(a) continued.

	Number of tests	% positive	Univariable analysis OR	95%CI	p	Multivariable analysis AOR	95%CI	p
Sexual behaviour characteristics								
>1 sexual partner in last year								
No	797,995	5.0%	Ref		<0.001			
Yes	670,897	9.4%	1.97	1.95 - 2.00				
Unknown	1,096,033	5.7%						
≥1 new sexual partner in last 3 months								
No	828,197	5.3%	Ref		<0.001			
Yes	721,027	8.9%	1.73	1.71 - 1.75				
Unknown	1,015,701	5.6%						
Sexual risk group[x]								
Low	607,446	4.6%	Ref		<0.001	Ref		<0.001
Medium	405,590	7.4%	1.66	1.63 - 1.69		1.65	1.62 - 1.68	
High	493,167	9.8%	2.28	2.24 - 2.31		2.24	2.20 - 2.28	
Unknown	1,058,722	5.6%						
Test and clinical characteristics								
Venue of test[z]								
GP	475,269	6.1%	Ref		<0.001	Ref		<0.001
Hospital	90,751	6.6%	1.10	1.07 - 1.14		1.10	1.06 - 1.14	
Outreach	305,175	4.2%	0.69	0.67 - 0.70		0.68	0.66 - 0.71	
Occupational Health	717	7.8%	1.31	1.00 - 1.73		1.26	0.86 - 1.83	
Pharmacy	71,300	7.0%	1.18	1.14 - 1.21		1.03	0.99 - 1.07	
Sexual and Reproductive Health Services	767,747	8.4%	1.43	1.41 - 1.45		1.14	1.11 - 1.16	
Remote testing	257,782	6.4%	1.06	1.04 - 1.08		0.94	0.91 - 0.96	
Military	5,590	6.5%	1.08	0.97 - 1.20		1.19	0.92 - 1.54	
Prisons & Youth Offending Institutions	4,758	9.4%	1.60	1.45 - 1.77		1.47	1.14 - 1.90	
Chlamydia Screening Offices	114,054	6.8%	1.13	1.10 - 1.16		1.01	0.98 - 1.05	
Abortion services	89,639	7.1%	1.18	1.15 - 1.22		1.13	1.09 - 1.18	
Education	297,569	3.3%	0.53	0.52 - 0.55		0.51	0.49 - 0.53	
Youth services	84,574	7.9%	1.32	1.29 - 1.36		1.03	0.99 - 1.07	
Specimen type								
Urine	1,376,209	6.2%	Ref		<0.001			<0.001
Cervical swab	98,527	7.0%	1.13	1.10 - 1.16		1.04	1.00 - 1.08	
Vulvovaginal swab	1,020,224	6.7%	1.08	1.07 - 1.10		1.07	1.05 - 1.09	
Other	30,878	7.3%	1.19	1.14 - 1.24		1.27	1.19 - 1.35	
Unknown	39,087	5.0%						
Known chlamydia diagnosis in last year								
No	2,261,502	6.4%	Ref		<0.001	Ref		<0.001
Yes	53,921	9.1%	1.47	1.43 - 1.51		1.13	1.09 - 1.18	
Unknown	249,502	6.2%						
Year of test								
2008	385,483	8.7%	Ref		<0.001	Ref		<0.001
2009	645,276	6.8%	0.77	0.76 - 0.78		0.81	0.80 - 0.83	
2010	830,172	5.7%	0.64	0.63 - 0.65		0.72	0.71 - 0.74	
2011	703,994	5.8%	0.65	0.64 - 0.66		0.72	0.71 - 0.74	

Table 4-4 (b): Number of chlamydia tests, percentage testing positive, unadjusted and adjusted odds ratios for testing positive by sociodemographic, sexual behavioural, and test characteristics (NCSP dataset, 15-24 year-old men, 2008-2011)

	Number of tests	% positive	Univariable analysis OR	95%CI	p	Multivariable analysis OR	95%CI	p
Overall	1,537,178	5.2%						
Sociodemographic characteristics								
Age (years)								
15	64,416	1.6%	Ref		<0.001	Ref		<0.001
16	180,426	1.9%	1.23	1.14-1.32		1.36	1.22-1.52	
17	211,271	3.4%	2.19	2.05-2.34		2.30	2.08-2.55	
18	225,775	4.8%	3.18	2.98-3.40		3.34	3.02-3.70	
19	206,138	6.2%	4.10	3.84-4.37		4.19	3.78-4.63	
20	179,374	6.7%	4.52	4.24-4.82		4.53	4.09-5.01	
21	145,461	7.1%	4.77	4.47-5.09		4.62	4.17-5.11	
22	121,871	7.2%	4.85	4.54-5.18		4.62	4.17-5.11	
23	107,345	6.7%	4.45	4.16-4.76		4.16	3.75-4.61	
24	95,101	6.6%	4.40	4.12-4.71		4.13	3.72-4.58	
Ethnic group								
White	834,785	5.7%	Ref		<0.001	Ref		<0.001
Black	66,682	8.8%	1.58	1.54-1.63		1.69	1.61-1.76	
Asian	71,650	2.0%	0.33	0.31-0.35		0.46	0.42-0.49	
Chinese	3,882	3.0%	0.51	0.42-0.61		0.65	0.52-0.81	
Other	8,533	4.1%	0.70	0.63-0.78		0.74	0.62-0.88	
Mixed	34,200	7.6%	1.36	1.30-1.42		1.33	1.26-1.41	
Unknown	517,446	4.2%						
Region								
London	246,329	4.1%	Ref		<0.001			<0.001
North East	97,200	4.7%	1.13	1.09-1.18		1.93	1.83-2.05	
North West	160,533	7.2%	1.81	1.76-1.86		1.68	1.61-1.75	
Yorkshire & Humber	131,424	6.8%	1.70	1.65-1.75		1.88	1.79-1.97	
East Midlands	125,824	4.5%	1.09	1.05-1.12		1.48	1.40-1.56	
West Midlands	161,981	4.5%	1.11	1.07-1.14		1.49	1.42-1.56	
East of England	120,757	4.6%	1.13	1.09-1.17		1.32	1.26-1.39	
South East Coast	63,808	4.7%	1.14	1.09-1.19		1.33	1.25-1.41	
South Central	77,906	4.9%	1.18	1.14-1.23		1.32	1.25-1.40	
South West	85,516	6.7%	1.66	1.60-1.72		1.58	1.51-1.66	
Other / Unknown	265,900	5.1%						
IMD quintile of LSOA of residence[y]								
Least deprived	182,535	4.1%	Ref		<0.001	Ref		<0.001
2	195,929	4.7%	1.13	1.10-1.17		1.10	1.05-1.14	
3	234,047	4.8%	1.17	1.14-1.21		1.14	1.09-1.18	
4	293,142	5.3%	1.30	1.27-1.34		1.21	1.16-1.26	
Most deprived	365,386	6.2%	1.52	1.48-1.56		1.31	1.26-1.36	
Unknown	266,139	5.1%						

Table 4-4(b) continued.

	Number of tests	% positive	Univariable analysis OR	95%CI	p	Multivariable analysis OR	95%CI	p
Sexual behaviour characteristics								
>1 sexual partner in last year								
No	283,042	3.9%	Ref		<0.001			
Yes	397,964	8.3%	2.24	2.19-2.29				
Unknown	856,172	4.2%						
≥1 new sexual partner in last 3 months								
No	307,386	4.7%	Ref		<0.001			
Yes	411,533	7.7%	1.71	1.68-1.75				
Unknown	818,259	4.1%						
Sexual risk group[x]								
Low	205,729	3.6%	Ref		<0.001	Ref		<0.001
Medium	186,169	6.3%	1.79	1.74-1.84		1.71	1.65-1.77	
High	311,664	8.5%	2.48	2.41-2.54		2.09	2.03-2.16	
Unknown	833,616	4.1%						
Test and clinical characteristics								
Venue of test[z]								
GP	157,400	6.2%	Ref		<0.001	Ref		<0.001
Hospital	15,281	9.1%	1.51	1.42-1.60		1.44	1.33-1.55	
Outreach	441,452	2.7%	0.42	0.41-0.43		0.46	0.44-0.48	
Occupational Health	1,298	4.2%	0.65	0.50-0.86		0.47	0.27-0.80	
Pharmacy	27,192	8.1%	1.33	1.27-1.40		1.33	1.25-1.42	
Sexual and Reproductive Health Services	207,617	11.1%	1.88	1.83-1.92		1.57	1.52-1.63	
Remote testing	151,556	6.5%	1.05	1.02-1.08		0.86	0.83-0.89	
Military	55,242	5.3%	0.84	0.81-0.88		0.92	0.82-1.03	
Prisons & Youth Offending Institutions	55,396	7.8%	1.27	1.22-1.32		1.33	1.15-1.53	
Chlamydia Screening Offices	87,836	7.2%	1.17	1.13-1.21		1.16	1.11-1.22	
Abortion services	884	10.3%	1.73	1.39-2.15		2.01	1.48-2.71	
Education	278,137	1.7%	0.26	0.25-0.27		0.34	0.32-0.36	
Youth services	57,887	5.8%	0.92	0.89-0.96		1.04	0.98-1.11	
Known chlamydia diagnosis in last year								
No	1,259,011	5.2%	Ref		<0.001	Ref		<0.001
Yes	12,601	11.2%	2.33	2.202.46		1.27	1.17-1.37	
Unknown	265,566	5.1%						
Year of test								
2008	181,539	7.7%	Ref		<0.001	Ref		<0.001
2009	357,241	5.8%	0.73	0.71-0.75		0.76	0.74-0.79	
2010	569,272	4.3%	0.54	0.53-0.55		0.68	0.65-0.70	
2011	429,126	4.8%	0.60	0.59-0.62		0.72	0.69-0.74	

OR: Odds ratio; AOR: Adjusted odds ratio; [x]Sexual risk group: High: more than 1 sexual partner in the last year and at least one new sexual partner in the last 3 months; Medium: either more than 1 sexual partner in the last year or at least one new sexual partner in the last 3 months; Low: neither more than 1 sexual partner in the last year nor at least one new sexual partner in the last 3 months; [y] IMD: Index of multiple deprivation, quintile based on lower super output area (LSOA) of residence; Outreach: tests performed in non-clinical settings including entertainment and leisure venues. Remote testing: tests performed without face to face contact with a health professional at the time of test, includes tests performed through the internet.

Table 4-5 (a): Number of tests, percentage testing positive, univariable and multivariable logistic regression results by reported characteristics (GUMCAD, <u>women</u> aged 15-24, 2008 to 2011)

			Univariable analysis			Multivariable analysis		
	Total (n)	% positive	OR	95%CI	p	OR	95%CI	p
Overall	958,864	11.2%						
Age (years)								
15	17,866	13.4%	Ref		<0.001	Ref		<0.001
16	40,984	15.2%	1.15	1.10-1.21		1.17	1.11-1.24	
17	70,783	14.6%	1.10	1.05-1.15		1.13	1.07-1.19	
18	100,665	14.5%	1.09	1.04-1.15		1.14	1.08-1.19	
19	124,957	13.2%	0.98	0.93-1.02		1.02	0.97-1.07	
20	133,549	11.5%	0.84	0.80-0.88		0.87	0.83-0.91	
21	131,255	10.4%	0.75	0.72-0.79		0.78	0.74-0.82	
22	122,945	9.2%	0.65	0.62-0.68		0.69	0.66-0.73	
23	113,470	8.2%	0.58	0.55-0.61		0.62	0.58-0.65	
24	102,390	7.4%	0.52	0.49-0.54		0.55	0.52-0.58	
Ethnicity								
White	725,062	11.6%	Ref		<0.001	Ref		<0.001
Mixed	41,600	11.8%	1.02	0.99-1.06		1.03	1.00-1.06	
Asian	21,256	7.5%	0.62	0.59-0.66		0.70	0.66-0.73	
Black	85,950	10.1%	0.86	0.84-0.88		0.92	0.90-0.95	
Other	16,636	9.4%	0.80	0.76-0.84		0.91	0.86-0.96	
Unknown	68,360	9.8%						
Region					<0.001			<0.001
London	217,730	9.2%	1.58	1.54-1.63		1.47	1.42-1.52	
North East	51,094	13.7%	1.57	1.53-1.60		1.50	1.46-1.54	
North West	109,266	13.6%	1.53	1.49-1.57		1.43	1.39-1.47	
Yorkshire & Humber	85,812	13.3%	1.59	1.55-1.63		1.56	1.51-1.61	
East Midlands	61,558	13.8%	1.34	1.31-1.37		1.31	1.28-1.35	
West Midlands	91,282	11.9%	1.20	1.17-1.23		1.28	1.24-1.32	
East of England	81,575	10.8%	1.05	1.02-1.08		1.10	1.07-1.13	
South East Coast	74,954	9.6%	1.00	0.97-1.03		1.05	1.02-1.08	
South Central	79,494	9.1%	1.16	1.13-1.19		1.20	1.16-1.24	
South West	81,707	10.4%	1.58	1.54-1.63		1.47	1.42-1.52	
Unknown	24,392	11.7%						
IMD quintile of LSOA of residence[x]								
Least deprived	130,793	9.6%	Ref		<0.001	Ref		<0.001
2	142,850	10.2%	1.07	1.04-1.10		1.05	1.03-1.08	
3	172,915	10.6%	1.12	1.09-1.15		1.15	1.12-1.18	
4	211,293	11.4%	1.22	1.19-1.25		1.26	1.23-1.30	
Most deprived	235,443	12.8%	1.39	1.36-1.42		1.42	1.38-1.45	
Unknown	65,570	11.6%						
Known chlamydia diagnosis in last year								
No	921,201	11.2%	Ref		<0.001	Ref		<0.001
Yes	37,663	12.2%	1.11	1.07-1.14		1.04	1.01-1.07	
Year								
2009	317,081	11.8%	Ref		<0.001	Ref		<0.001
2010	309,295	11.0%	0.92	0.91-0.94		0.93	0.91-0.95	
2011	332,488	10.8%	0.90	0.88-0.91		0.91	0.89-0.92	

Table 4-5(b): Number of tests, percentage testing positive, univariable and multivariable logistic regression results by reported test characteristics (GUMCAD, men aged 15-24, 2008 to 2011)

			Univariable analysis			Multivariable analysis		
	Total (n)	% positive	OR	95%CI	p	OR	95%CI	p
Overall	626,531	11.2%						
Age (years)								
15	3,777	8.0%	Ref		<0.001	Ref		<0.001
16	11,819	10.9%	1.40	1.22-1.59		1.48	1.28-1.70	
17	26,134	12.7%	1.67	1.47-1.89		1.73	1.52-1.98	
18	48,424	13.9%	1.85	1.64-2.09		1.91	1.68-2.18	
19	72,174	13.8%	1.83	1.63-2.07		1.93	1.69-2.20	
20	88,315	13.6%	1.80	1.60-2.03		1.89	1.66-2.15	
21	95,575	13.3%	1.75	1.56-1.98		1.83	1.61-2.08	
22	96,274	12.4%	1.63	1.45-1.84		1.74	1.53-1.98	
23	93,941	11.4%	1.48	1.31-1.66		1.58	1.39-1.80	
24	90,098	10.7%	1.38	1.22-1.55		1.48	1.30-1.69	
Ethnicity								
White	466,201	12.4%	Ref		<0.001	Ref		<0.001
Mixed	24,701	14.5%	1.20	1.16-1.25		1.24	1.19-1.29	
Asian	20,587	6.9%	0.53	0.50-0.56		0.55	0.52-0.58	
Black	57,530	16.3%	1.38	1.34-1.41		1.46	1.42-1.50	
Other	10,080	10.2%	0.81	0.76-0.86		0.88	0.82-0.95	
Unknown	47,432	11.8%						
Region								
London	128,002	10.9%	Ref			Ref		<0.001
North East	35,713	15.1%	1.46	1.41-1.51		1.59	1.54-1.66	
North West	78,871	13.9%	1.33	1.29-1.36		1.45	1.41-1.50	
Yorkshire & Humber	60,094	14.0%	1.34	1.30-1.38		1.47	1.42-1.52	
East Midlands	43,295	14.5%	1.40	1.35-1.44		1.57	1.51-1.62	
West Midlands	59,142	13.2%	1.25	1.21-1.28		1.38	1.33-1.43	
East of England	53,295	12.0%	1.12	1.09-1.16		1.33	1.28-1.38	
South East Coast	46,545	11.2%	1.03	1.00-1.07		1.29	1.24-1.34	
South Central	49,477	10.7%	0.99	0.95-1.02		1.17	1.13-1.21	
South West	51,526	12.2%	1.15	1.11-1.18		1.33	1.28-1.38	
Unknown	20,571	12.9%						
IMD quintile of LSOA of residence[x]								
5 (Least deprived)	87,870	10.6%	Ref		<0.001	Ref		<0.001
4	94,222	11.6%	1.10	1.07-1.14		1.10	1.06-1.13	
3	110,858	12.1%	1.16	1.13-1.20		1.17	1.14-1.21	
2	131,768	13.1%	1.27	1.24-1.30		1.30	1.26-1.33	
1 (Most deprived)	154,169	14.2%	1.40	1.36-1.43		1.38	1.34-1.42	
Unknown	47,644	12.4%						
Ever MSM[y]								
No	577,650	12.9%	Ref		<0.001	Ref		<0.001
Yes	48,881	8.4%	0.62	0.60-0.64		0.64	0.62-0.67	
Known chlamydia diagnosis in last year								
No	606,099	12.5%	Ref		<0.001	Ref		<0.001
Yes	20,432	15.1%	1.25	1.20-1.30		1.15	1.10-1.20	
Year								
2009	213,012	12.9%	Ref		<0.001	Ref		<0.001
2010	203,076	12.3%	0.95	0.93-0.97		0.96	0.94-0.98	
2011	210,443	12.4%	0.96	0.94-0.98		0.97	0.95-0.99	

[x]IMD: Index of multiple deprivation, quintile based on lower super output area (LSOA) of residence; [y]Ever MSM: Any record in GUMCAD where reports having sex with a man. OR: Odds ratio; AOR: Adjusted odds ratio.

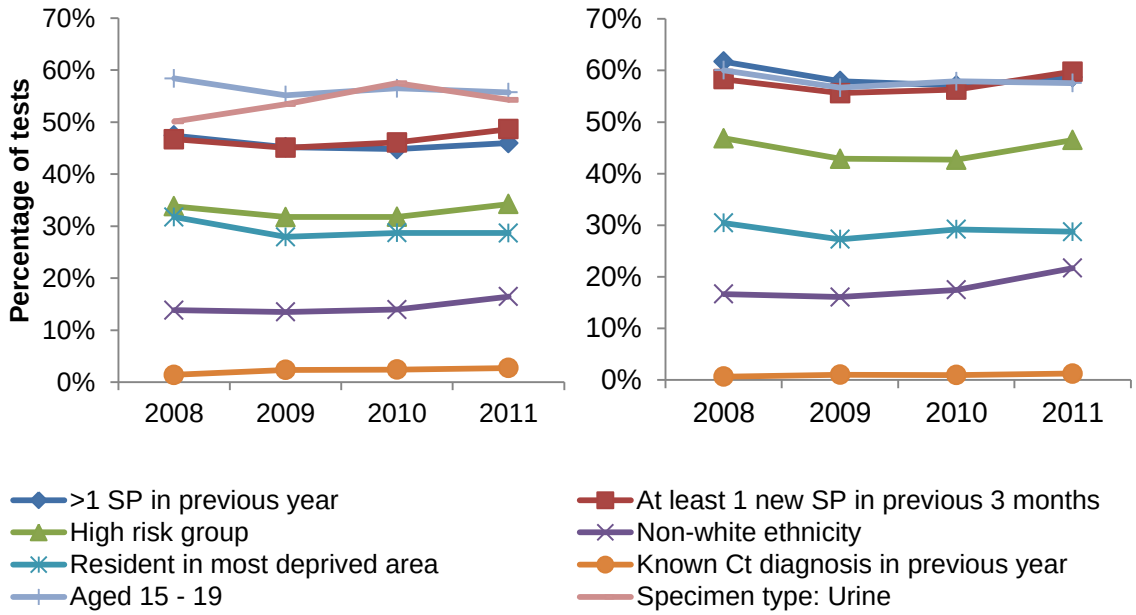
4.4.3 Trends in test, demographic and sexual behaviour characteristics

Among NCSP testing episodes, demographic and sexual behaviour variables remained relatively stable during the analysis period, although between 2010 and 2011 there was a small increase seen in the proportion where the individual tested reported having at least one new sexual partner in the last year and in the proportion of tests among those of non-white ethnicity (Figure 4-3). In both women and men there was a small increase between 2010 and 2011 in the percentage with a known previous diagnosis in the last year, increasing from 2.4% to 2.7% in women and from 0.9% to 1.2% in men.

The distribution of testing venue types within the NCSP dataset changed considerably over the analysis period (Figure 4-4). Among women, the percentage of tests which were from sexual and reproductive health services declined from 41% in 2008 to 29% in 2011, while the percentage from GP settings increased from 16% in 2008 to 20% in 2011. Among men, the percentage of tests reported through outreach settings (including testing in non-clinical venues such as bars and pubs, music festivals and other one off events), increased substantially between 2008 and 2010, from 18% to 35%, and then fell to 29% in 2011. The percentage of tests that were from sexual and reproductive health services decreased from 20% in 2008 to 14% in 2011.

Figure 4-3: Trends in reported characteristics (NCSP dataset, 15-24 year-old women and men, 2008-2011)

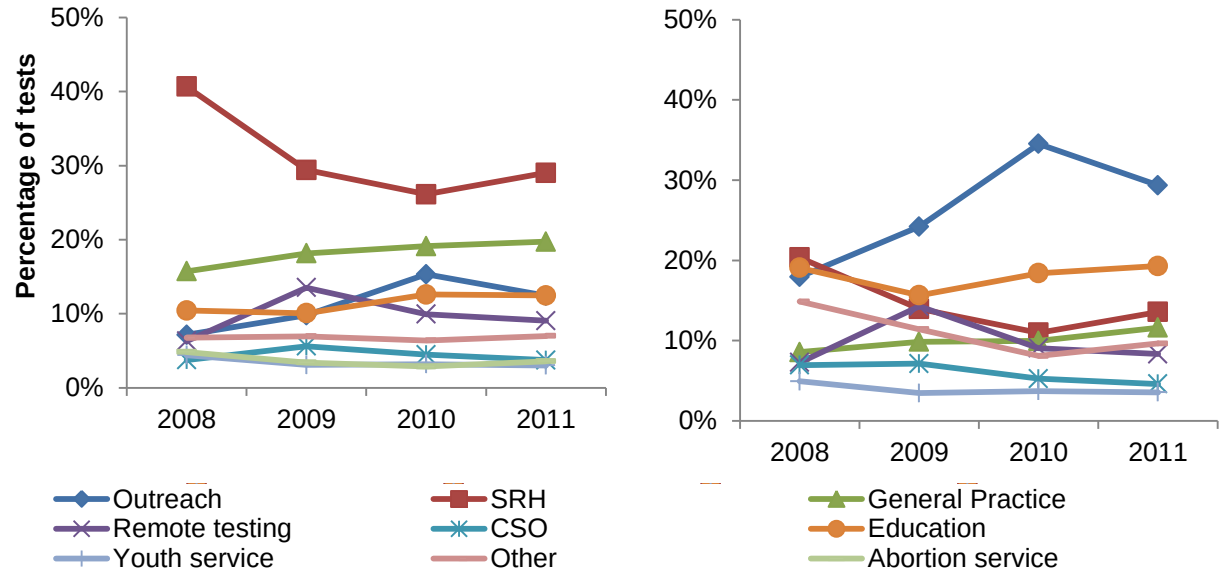
a) Women **b) Men**



**Proportions reported among tests with complete data on each variable; High risk group: reported more than 1 sexual partner in the previous year and at least one new sexual partner in the previous 3 months; SP: sexual partner; Resident in most deprived area: resident in one of the 20% most deprived LSOAs in England, as defined by the Index of Multiple Deprivation (IMD); Ct: Chlamydia.*

Figure 4-4: Percentage of NCSP tests carried out in different testing venue types (15 to 24 year-old women and men, 2008 to 2011)

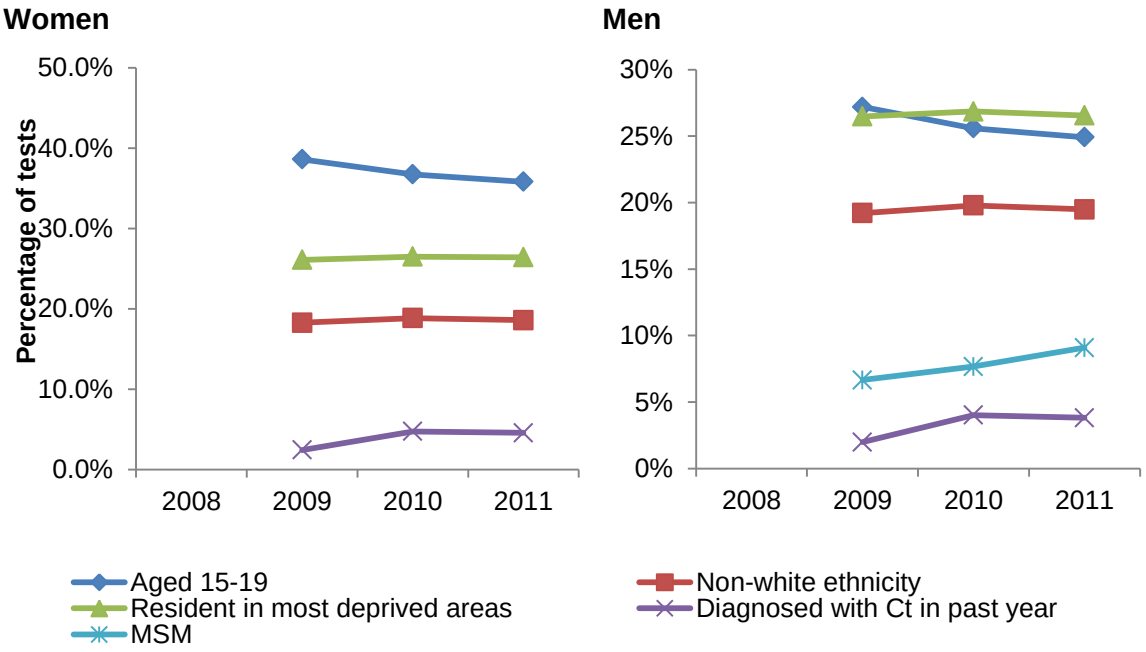
a) Women **b) Men**



**Other: Hospital, occupational health, pharmacy, military, prisons & youth offenders institutions and abortion services (abortion services included in 'other' category in men only); CSO: Chlamydia Screening Office; SRH: Sexual and Reproductive Health services*

There was no change during the analysis period in the proportion of GUMCAD testing episodes that were in people of non-white ethnicity, nor in that among those living in the most deprived areas (Figure 4-5). A slight decline in the percentage of testing episodes from 15 to 19 year-olds was observed among both women and men (39% to 36% among women; 27% to 25% among men). The percentage of testing episodes among men that were in MSM increased from 7% to 9%. In both women and men there was a small decrease between 2010 and 2011 in the percentage with a known previous diagnosis in the last year, decreasing from 4.8% to 4.6% in women and from 4.0% to 3.8% in men.

Figure 4-5: Trends in reported characteristics, GUMCAD (15 to 24 year-old women and men, 2009 to 2011)



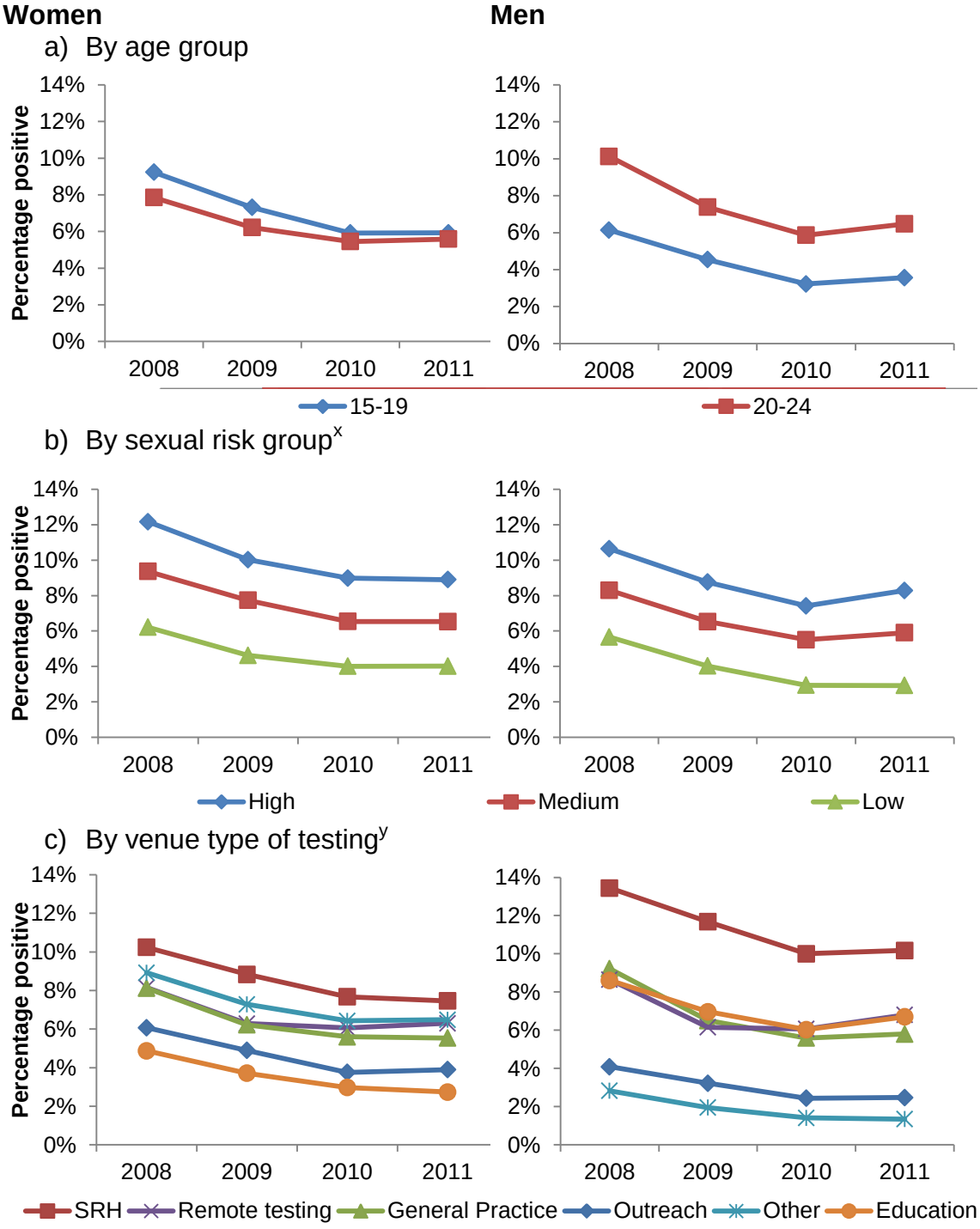
**Proportions reported among tests with complete data on each variable; Resident in most deprived area: resident in one of the 20% most deprived LSOAs in England, as defined by the Index of Multiple Deprivation (IMD); Ct: Chlamydia; MSM: Men who have sex with men.*

4.4.4 Trends in percentage testing positive by subgroup

Among NCSP testing episodes, the percentage testing positive declined during the analysis period across all subgroups defined by age group, sexual risk group and venue of testing (Figure 4-6). In several subgroups among men, increases in the percentage testing positive were observed between 2010 and 2011.

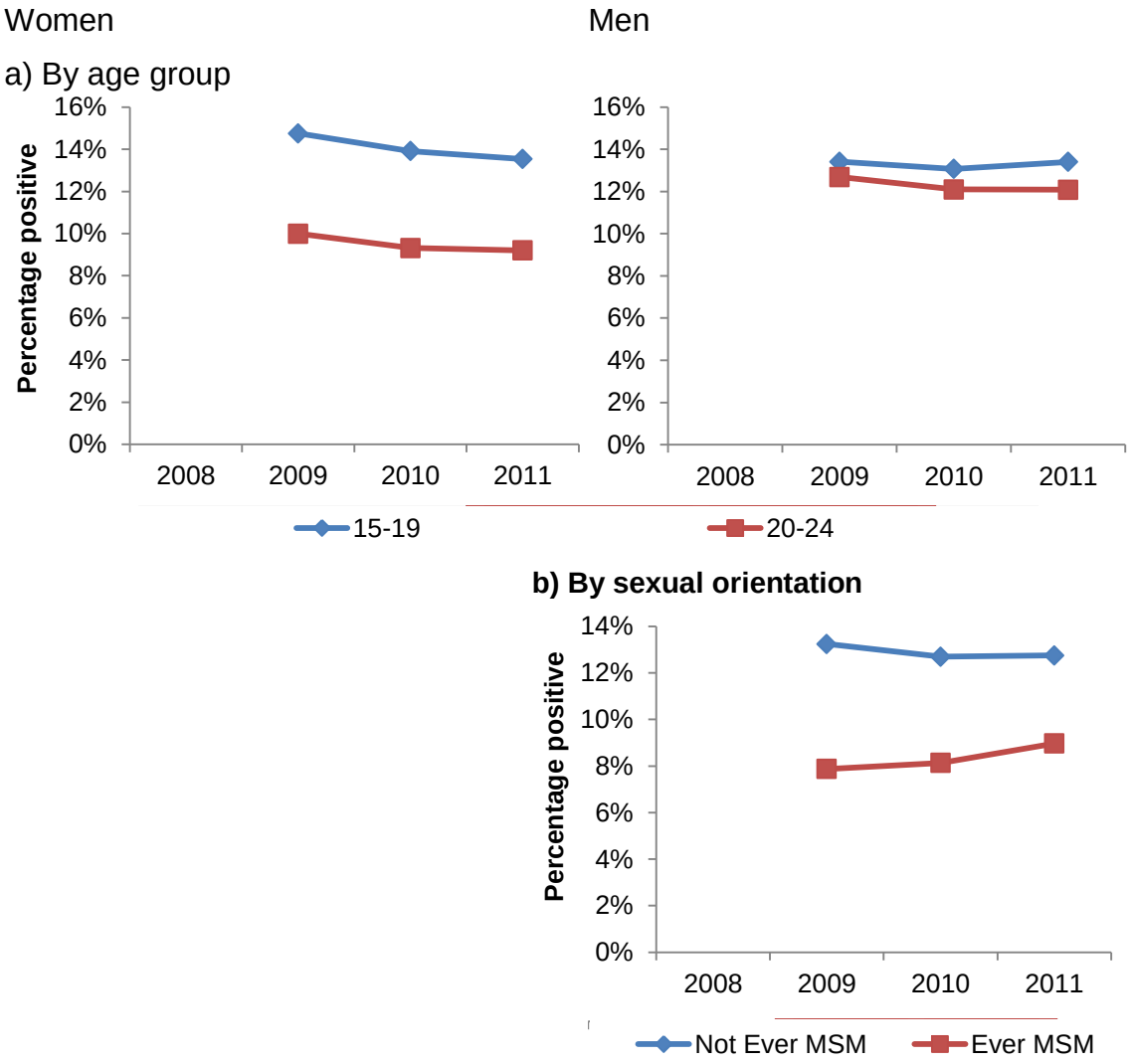
Among GUMCAD testing episodes, between 2009 and 2011 the percentage testing positive declined among both 15 to 19 year-old and 20 to 24 year-old women (Figure 4-7). Among men, the percentage testing positive declined among 20 to 24 year-olds, but there was no change among 15 to 19 year-olds. In contrast to other subgroups, the percentage testing positive among MSM in GUMCAD increased from 7.9% in 2009 to 9.0% in 2011 (OR 1.08 95%CI 1.03 to 1.12). A declining trend in percentage testing positive was observed in all the symptomatic condition subgroups (i.e. in attendances where a diagnosis of genital warts, bacterial vaginosis, candidosis or genital herpes was made).

Figure 4-6: Percentage testing positive by year and gender, stratified by age group (a), sexual risk group (b), and venue of test (c) (NCSP dataset, 15 to 24 yea-old women and men, 2008 to 2011)



[x]*Sexual risk group: High: more than 1 sexual partner in the last year and at least one new sexual partner in the last 3 months; Medium: either more than 1 sexual partner in the last year or at least one new sexual partner in the last 3 months; Low: neither more than 1 sexual partner in the last year nor at least one new sexual partner in the last 3 month;* [y]*SRH: Sexual and reproductive health services; Outreach: tests performed in non-clinical settings including entertainment and leisure venues; Remote testing: tests performed without face to face contact with a health professional at the time of test, includes tests performed through the internet.*

Figure 4-7: Percentage testing positive by year and gender, stratified by age group. (GUMCAD, 15 to 24 year-olds)



[x] *Among attendances where a chlamydia test and one of the specified symptomatic conditions were recorded on the same date. For genital warts and genital herpes, data are presented for first episodes (as recurrences are possible).*

4.4.5 Trends by calendar quarter

Quarterly trends in the percentage testing positive varied by dataset and venue type (Figure 4-8). In 2009 to 2011, there was a peak in numbers of testing episodes reported through the NCSP dataset between January and March of each year, which corresponded to a simultaneous drop in the percentage testing positive. This was also accompanied by a nadir in the proportion of tests coming from women in the ‘high risk’ sexual behaviour category (Figure 4-9). Among women, this seasonality in patterns of testing and of percentage testing positive was evident for tests in education settings, but was not seen in testing performed in sexual and reproductive health services or GP settings or in tests reported through GUMCAD.

Figure 4-8: Numbers of tests and percentage testing positive by calendar quarter, dataset and location of testing (15-24 year-old women and men)

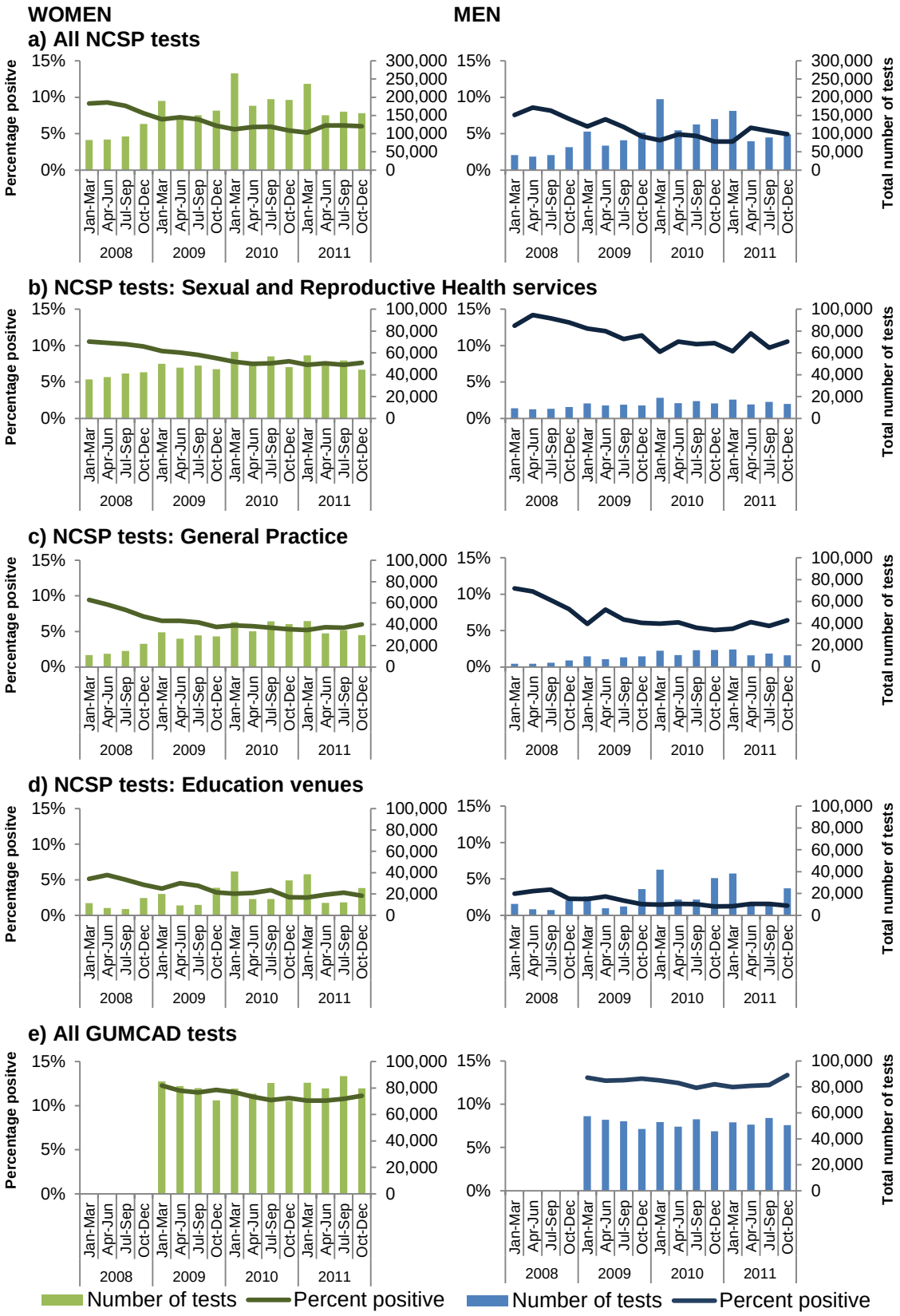
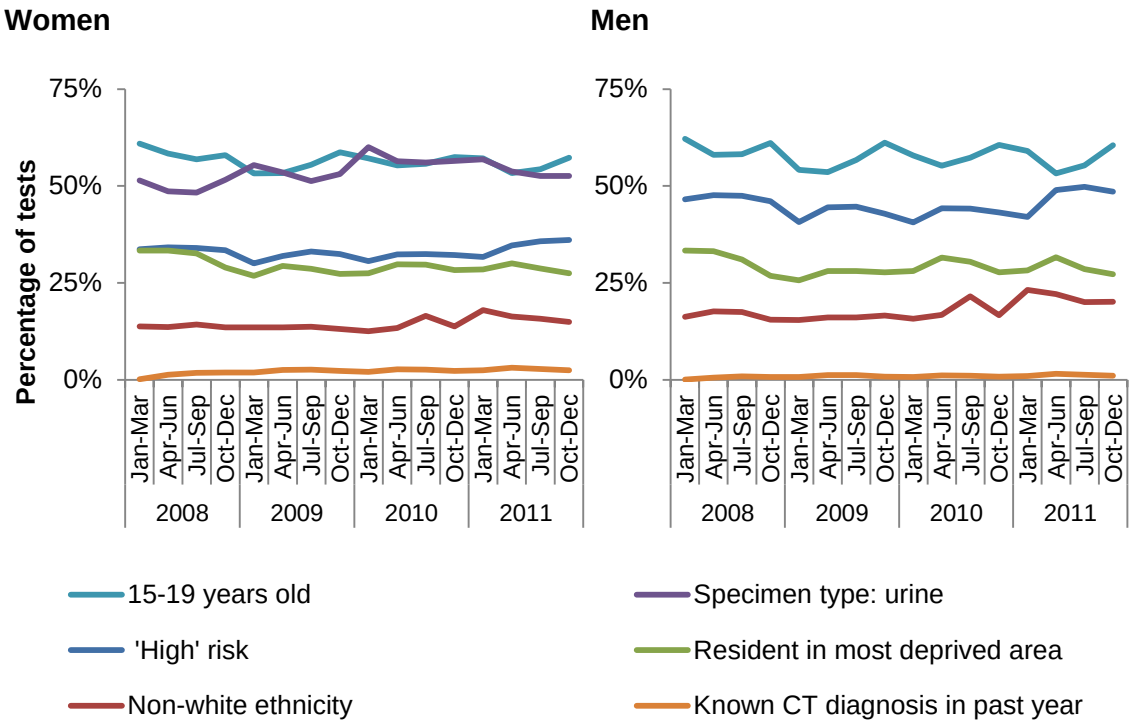


Figure 4-9: Trends in reported characteristics by calendar quarter, NCSP dataset (15 to 24 year-old women and men, 2008 to 2011)



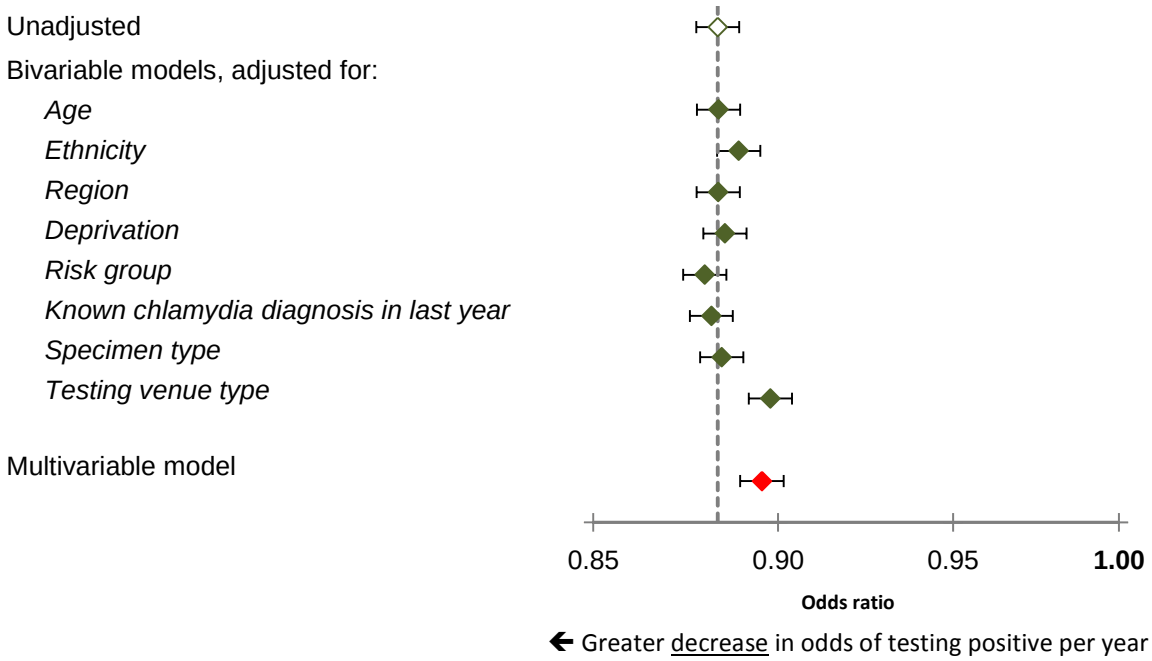
4.4.6 Assessing the selection effects introduced by changes in risk factor variables over time

Figure 4-10 and Figure 4-11 show the estimated annual change in the percentage testing positive among NCSP and GUMCAD testing episodes before adjusting for other variables (unadjusted), after adjusting for one additional variable at a time (age, ethnicity, region, deprivation, sexual risk group, known chlamydia diagnosis in the last year, testing venue type and, for women, specimen type; the bivariable models) and after adjusting for all variables (multivariable analyses).

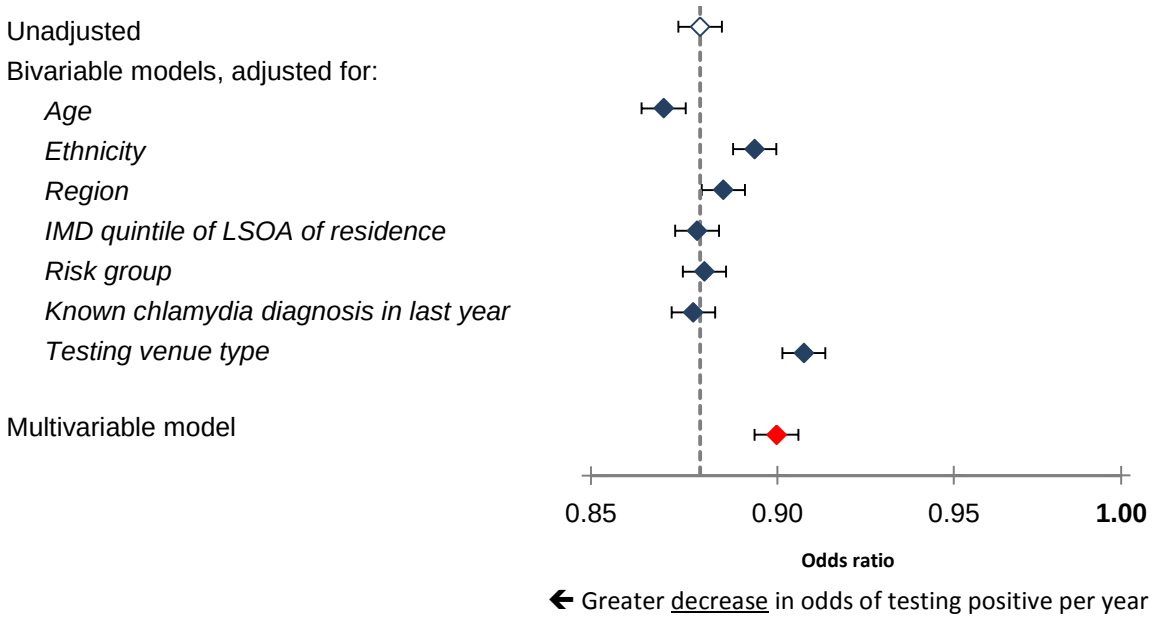
Figure 4-10: Unadjusted and adjusted odds ratios (and 95%CI) of testing positive per additional year, estimated from univariable, bivariable and multivariable models (NCSP tests, 15 to 24 year-olds 2008 to 2011)*

Open diamonds show the unadjusted odds ratio (OR) of testing positive per year, without adjusting for any other variables; closed diamonds show the adjusted OR of testing positive per year after including the stated risk factor variable of interest in the logistic regression model, either one additional variable at a time (bivariable analysis) or with all variables included (multivariable analysis). The dashed line shows the unadjusted OR.

Women



Men



Analyses are limited to tests with complete data on all variables included in the multivariable analysis. IMD: Index of Multiple Deprivation; Risk group: High: more than 1 sexual partner (SP) in the previous year and at least one new SP in the previous 3 months; Medium: either more than 1 SP in the previous year or at least one new SP in the previous 3 months; Low: neither more than 1 SP in the previous year nor at least one new SP in the previous 3 months.

Among NCSP testing episodes, unadjusted and adjusted ORs of testing positive were less than 1. Thus between 2008 and 2011, there was a reduction in the percentage testing positive, even after adjusting for all available demographic and behaviour variables (Figure 4-10).

In the bivariable models, adjusting for venue type had the largest and only notable effect on the estimated trend in percentage testing positive. Among women, a 14% annual decline was observed before adjustment (OR 0.86, 95%CI 0.86-0.87), compared to an 11% annual decline after adjusting for venue type of test (AOR 0.89, 95%CI 0.88-0.89). Among men, a 16% annual decline was observed in the unadjusted analysis, compared to a 12% decline after adjustment for venue testing type (unadjusted OR 0.84, 95%CI 0.83-0.84; AOR 0.88, 95%CI 0.83-0.84).

In the multivariable models, (adjusting for age, ethnicity, sexual risk group, IMD quintile of LSOA, having a known chlamydia diagnosis in the past year, testing venue type and specimen type [women only]), among women, there was a 12% annual decline before adjustment, and an 11% annual decline after adjustment (unadjusted OR 0.88, 95%CI 0.88-0.89; AOR 0.89, 95%CI 0.88-0.90). Among men there was a 12% annual decline before controlling for the other variables, and a 10% annual decline after adjustment (unadjusted OR 0.88, 95%CI 0.87-0.89; AOR 0.90, 95%CI 0.89-0.91).

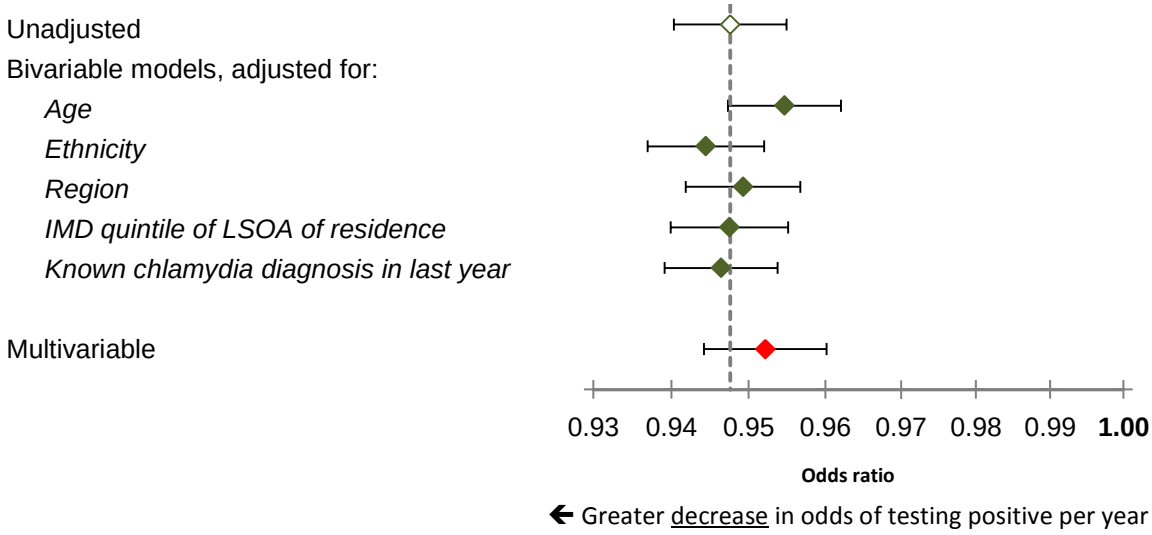
Sensitivity analyses using those NCSP testing episodes with complete data on each variable showed similar patterns, whereby adjusting for venue type of test was the most important variable, and changes in other variables led to little difference between unadjusted and adjusted ORs (data not shown).

Among tests reported to GUMCAD, all unadjusted and adjusted ORs were less than 1 among women and men, indicating a decline in the percentage testing positive during the analysis period (2009 to 2011). All ORs of testing positive among MSM were >1, indicating an increase in the percentage testing positive per year (Figure 4-11 (a-b)). Adjustment made a negligible difference to the measured trend in positivity among GUMCAD testing episodes in any of the bivariable or multivariable analyses (Figure 4-11 (c)).

Figure 4-11: Unadjusted and adjusted odds ratios (and 95%CI) of testing positive per additional year, estimated from univariable, bivariable and multivariable models (GUMCAD tests, 15 to 24 year-olds 2009 to 2011)

Open diamonds show the unadjusted odds ratio (OR) of testing positive per year, without adjusting for any other variables; closed diamonds show the adjusted OR of testing positive per year after including the stated risk factor variable of interest in the logistic regression model, either one additional variable at a time (bivariable analysis) or with all variables included (multivariable analysis). The dashed line shows the unadjusted OR.

Women



Men

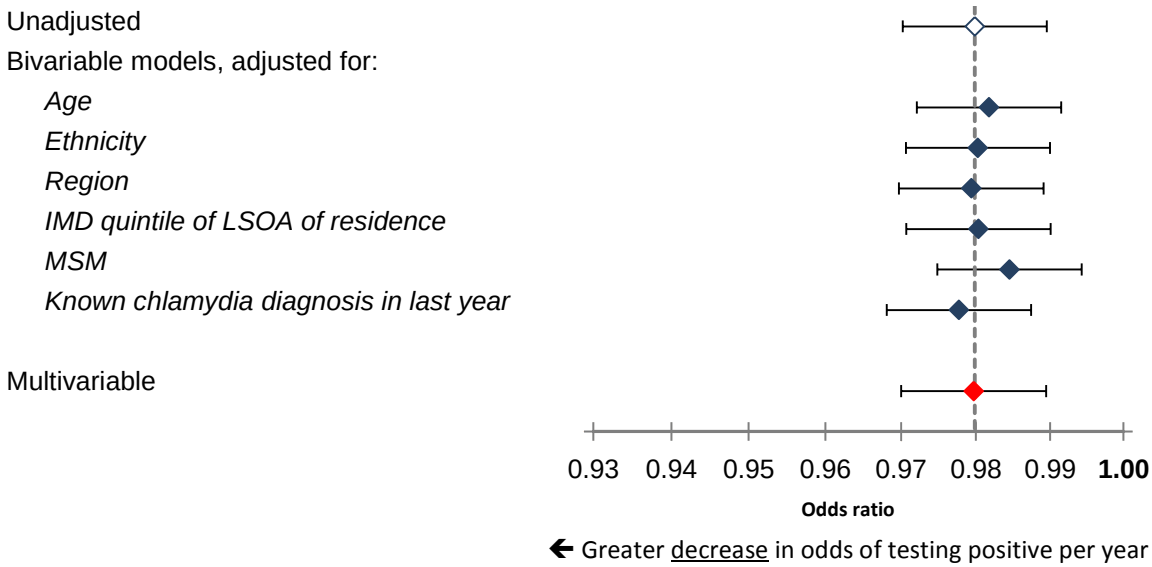
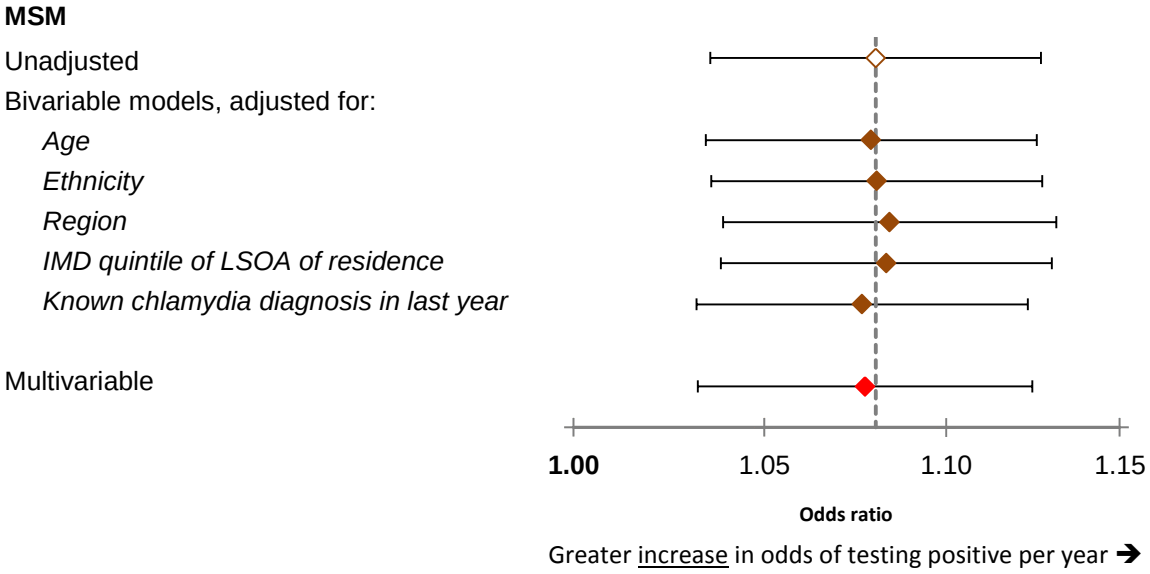


Figure 4-11continued



**Analyses are limited to tests with complete data on all variables included in the multivariable analysis.*

4.5 Discussion

4.5.1 Key findings

The number of 15 to 24 year-olds who tested for chlamydia increased between 2008 and 2011, while the percentage testing positive decreased. There was considerable variation over time in the relative contributions made by different testing venue types. Among those tested, people reporting more sexual partners and those reporting a previous chlamydia diagnosis were more likely to test positive, as were those living in more deprived areas.

Testing venue type was an important confounder in the relationship between test result and year among the tests reported to the NCSP. In men tested through the NCSP, there was evidence of confounding of the relationship between year and test result arising from differences in the distribution of age

and ethnicity in each year. In women and in men tested in GUM clinics, there was no evidence of confounding arising from changes in other demographic or sexual behaviour variables for which data are available among those who tested as part of the NCSP or in GUM clinics, suggesting that these variables did not change sufficiently over time to introduce substantial error.

4.5.2 Strengths and limitations

The main strength of this analysis is that it used two large datasets with national coverage and individual-level data that allowed investigation of the relationship between testing positive for chlamydia and trends in percentage testing positive and the characteristics of those tested. However it should be noted that the size of the datasets means that even small differences would likely be statistically significant, thus the size and direction of the associations should be considered when determining public health significance.

The analysis was limited by the completeness of data reporting. A large proportion of NCSP tests had missing data on one or more variable of interest and the primary analysis looking at the impact of changes in the population tested on trends in percentage testing positive had to be limited to tests with complete data. However, sensitivity analysis showed that the same patterns were seen among tests with complete data on each variable as when the limited dataset was used. The analysis was also limited as individuals could not be linked between datasets, meaning that the number with a previous known diagnosis is likely to be underestimated. It was interesting to note that the percentage of women and men with a known diagnosis in the last year increased in the NCSP dataset but decreased in GUMCAD between 2010 and 2011. While re-infections have a potentially important part to play in the

transmission, these divergent trends likely reflect changing patterns of service use with under 25 year-olds increasingly accessing testing outside of GUM services.

As described in Chapter 3, previous studies in the US, Scotland and the Netherlands have shown that trends in percentage testing positive for chlamydia among sentinel and clinic populations can be particularly affected by changes in test technology.[203-205,223] This is unlikely to have been influential in this analysis, as NAATs were universally in use during the analysis period[128]. It is feasible however that differences in the exact test used may have had a minor effect on the data which has not been accounted for in this analysis.

4.5.3 Implications for evaluation of chlamydia control

Changes in the distribution of venue testing types can explain some, but not all, of the observed decline in percentage testing positive for chlamydia among 15 to 24 year-olds tested within the NCSP between 2008 and 2011. Thus this analysis of surveillance data up to 2011 provide some support for there having been a decrease in chlamydia infection over this period. However, this analysis also demonstrates that trends in the percentage testing positive in England are subject to measured and, potentially, unmeasured confounding. Specifically, venue type remained significantly associated with testing positive even after adjusting for all other available demographic and sexual behaviour variables. This demonstrates that the available data were not able to fully capture risk of testing positive for chlamydia. Thus, even after adjusting for sexual behaviour, trends in percentage testing positive will still be subject to unmeasured confounding and cannot be reliably attributed to there having been a change in the incidence or prevalence of infection. Stratifying analyses by venue of test

will reduce some of this potential error, but it is not possible with the available data to know whether this will fully eliminate the potential for confounding of trend estimates.

This raises the question as to what other data would be needed to improve the utility of surveillance data for monitoring the impact of chlamydia control programmes.

Firstly, more detailed sociodemographic and sexual behaviour variables may be useful. Only limited data were included in each dataset meaning it is possible that there were changes in the risk profile of those tested that were not captured. In the NCSP dataset, number of partners was recorded as a binary variable (<1 / ≥2). Thus people with 2 partners in the last year could not be distinguished from those with many more sexual partners in the last year, even though their risk of infection would be very different.[133] A greater level of detail about sexual risk would be useful to allow adjustment for differences in characteristics of the population tested, which arise from changes in service use patterns or from underlying changes in sexual behaviour.

Secondly, data were not available on whether tests had been carried out as a result of partner notification. More recently-available data suggest that around 35% of people who attend GUM clinics as a result of partner notification (i.e. informed of having an infected partner) test positive for chlamydia.[224] Thus changes in partner notification rates over this period could also have had an effect on trends in percentage testing positive. Since 2012, GUMCAD has included a variable on whether tests were carried out as a result of partner notification. This variable should be incorporated into any future analyses of

trends in percentage testing positive using GUMCAD data. Data on numbers of partners tested were collected for tests performed through the NCSP up to 2012. However, these data were collected in a separate, aggregate dataset and as such could not be linked to data on tests and diagnoses. The data were also subject to considerable data quality issues and under-reporting (personal communication Alireza Talebi) and as such have not been reported in this chapter and were not incorporated into this analysis.

It was not possible to measure uptake of testing (i.e. number tested / number attending) among those attending all venues. This would have been possible with data from GUM clinics as a clinic-attending denominator is available. However as the offer and uptake of a chlamydia test is less likely to vary in GUM settings this was not investigated in this analysis. Developments in the GUMCADv2 surveillance system, whereby comparable information to that collected in GUM clinics is now being collected for other commissioned non-GUM sexual health services, mean that a measure of uptake of testing within sexual and reproductive health services and some GP clinics will be available in coming years. The extent to which percentage testing positive varies with test uptake within a setting would be useful to explore in future analyses.

4.5.4 Summary

In summary, given the potential for residual unmeasured confounding, the observed decreases in percentage testing positive in the NCSP dataset or GUMCAD do not provide strong evidence of there having been a decrease in chlamydia incidence or prevalence between 2008 and 2011, in years with relatively high levels of screening among under 25 year-olds. While useful to identify volumes of testing and diagnoses and factors associated with being

infected at the time of testing, these surveillance data alone do not provide sufficiently reliable measures of chlamydia infection over time for the purposes of evaluating chlamydia screening. More robust outcome measures are needed to evaluate the impact of chlamydia screening. In the next three chapters, I turn to measures of chlamydia prevalence among general population samples.

5 Pilot of a postal survey designed to measure the population prevalence of chlamydia among young women

In the previous chapter I investigated the use of surveillance data for monitoring trends in percentage testing positive for chlamydia. I showed that such data alone are unsuitable for evaluating the impact of chlamydia screening, in part due to the potential for unmeasured confounding arising from changing patterns of service use over time that could not be adjusted for using the available data. One option to address this issue is to establish repeated cross-sectional surveys among young adults, as the population targeted by the NCSP. In this chapter I present a pilot study which I carried out to investigate the feasibility of a repeated postal survey of chlamydia prevalence with anonymous testing for chlamydia in England. The pilot was conducted between June and August 2011 in two primary care trusts (PCTs) in England and was carried out in conjunction with the Health Protection Agency (HPA)[14].

5.1 Aims & objectives

The aim of the study presented in this chapter was to determine whether repeat cross-sectional surveys using postal invitations and anonymous testing (i.e. without return of test result) could be a feasible method of population-based chlamydia prevalence monitoring in England. This aim was addressed through the following objectives:

[14] Part of Public Health England since 2013.

- To design and pilot a cross-sectional survey of chlamydia prevalence using postal invitations and anonymous testing in two primary care trusts (PCTs) in England.
- To compare participation rates using different invitation approaches (+/- provision of a test kit; +/- offer of small financial incentive).
- To investigate selection bias and costs associated with the different approaches.

5.2 Methods

5.2.1 Participants

Women aged 17 or 18 and resident in two PCTs (NHS Northamptonshire and NHS Sutton & Merton) were eligible for inclusion in the study.

This age group was selected for a number of reasons. Firstly, a high proportion of this age group would be expected to be sexually active[133] and thus be an appropriate target group for monitoring changes in prevalence. Secondly, the proportion of young adults living with their parents declines steeply with age over 16 years[225] meaning the reliability of address data reduces with age. Thirdly, chlamydia prevalence was expected to be relatively high among this age group,[123] thus providing a good opportunity to detect small changes in prevalence over time that might be expected from mathematical models[81]. However, only 18 year-old women were included in NHS Northamptonshire in order to comply with local guidance about research involving children (see section 5.2.4).

The sample was limited to women as levels of chlamydia screening are higher in women than men.[226,227] Any direct impact of screening on prevalence is

therefore likely to be greater in women. Furthermore, the most serious complications of chlamydia such as PID, ectopic pregnancy and infertility, occur in women, making monitoring of prevalence in women arguable more important. Trends in chlamydia prevalence in women should be indicative of changes in prevalence among heterosexual men.

The two pilot sites were chosen for pragmatic purposes, to include one site in London and one outside of London and to include areas with different levels of screening activity. Table 5-1 shows the estimated proportion of 15-24 year-olds tested, the diagnosis rate (diagnoses per 100,000 population) and percentage testing positive in the two participating PCTs compared to England.

Table 5-1: Opportunistic screening uptake, diagnosis rates and PCT characteristics in the participating PCTs, 2011/12[228]

	Northamptonshire	Sutton & Merton	England
Estimated coverage (number of tests per 100 population of 15-24 year-olds)	34%	24%	29%
Rank (1=PCT with highest coverage)	35/151	108/151	N/A
Diagnosis rate (diagnoses per 100,000 population of 15-24 year-olds)	2,457	2,008	2,090
Rank (1=PCT with highest diagnosis rate)	38/151	85/151	N/A
Percentage testing positive	7.2%	8.3%	7.3%
Classification	Rural	Urban	N/A

**Urban: PCTs with 50 percent of their population in one of the 17 urban areas with a population of at least 250,000; *Rural: PCTs with more than 26 percent of their population in rural settlements and larger market towns.*

Eligible individuals were identified using lists of people registered with a GP in the two participating PCTs. A total of 3,857 women in NHS Sutton & Merton and

3,687 women in Northamptonshire were eligible.[15] The study aimed to establish a sampling frame that could be used to send postal invitation to a random sample representative of the general population of young women in England. The sampling frame therefore needed to have current address information for named individuals, of known age. As discussed in section 3.2.2.2, GP lists are known to be limited by potential inaccuracies. However GP lists were chosen as the most comprehensive source of this information in England that was available for use, and as sampling via household lists was considered too resource intensive.

5.2.2 Study procedures

As described in the Chapter 3, response rate would likely be a key issue in determining feasibility and bias of any survey estimates. Participants in the pilot were therefore allocated into three different groups to allow comparison of response rates using different recruitment approaches (Table 5-2). All of the selected women were sent an invitation letter by post. Group A were sent a test kit with their invitation. The test kit included: an invitation letter; a cover letter from the participating PCT; a study information leaflet; a short questionnaire including questions on sexual behaviour; a vulvovaginal swab (VVS); an instruction leaflet on how to use the swab and return the sample and a pre-paid return envelope. Group B were sent a test kit and also offered a £5 voucher for high-street shops on return of sample. Group C were not sent a test kit but instead were invited to contact the study team by text message, email or return

[15] In order to comply with regulatory approvals (section 5.2.4), invitations were sent out by staff at the participating PCTS; none of the study personnel at the HPA had access to name or address information of those invited.

of postcard to request a kit. A reminder letter was sent to non-responders three weeks after the initial invitation. Individuals who did not wish to participate in the survey were asked to complete and return a pre-paid postcard to the research team, indicating the reason they did not want to participate.

Table 5-2: Invitations sent by randomisation group

	Minimum number of invitations required*	Number of invitations sent per PCT	Number of invitations sent in total
Group A: Kit	968	500	1,000
Group B: Kit + voucher	484	250	500
Group C: No kit	484	250	500

**Sufficient to estimate the difference in response rate of 5 percentage points with 95% confidence. Randomised in a ratio of 1:2 (B:A and C:A).*

The study questionnaire was designed to include questions that matched those in the Natsal-2 as closely as possible, to allow comparisons between the surveys (see Appendix 1). In order to maximise the acceptability of the study invitations, feedback was obtained on draft versions of the study paperwork (invitation letter and patient information leaflet) using two focus groups among a total of 17 women aged 16 to 18 years old. Focus group participants were recruited from a local higher education college and groups were facilitated by two female facilitators (Woodhall and Collander-Brown). Participants were provided with a £20 voucher as a token of appreciation. Feedback from the focus groups led to the information leaflet being redesigned to make it brighter, and more eye-catching, to reduce the amount of text in the leaflet, and to revise the invitation letter and information leaflet to emphasise that the invitation was being sent only on the basis of the age of the participant, and was not linked to any knowledge about the invitee's sexual activity.

A total of 1,000 individuals from each PCT were selected at random for invitation, and were subsequently allocated to three study arms using simple randomisation.[16] The sample size was sufficient to identify a minimum 5% difference in response rate between three different types of postal invitation (Table 5-2). Group B was expected to have higher costs per invitation due to the offer of the £5 voucher. The main comparison was planned between group A and B and group A and C. The groups were therefore randomised in a ratio of 1:2 (B:A and C:A) for the purposes study costs and logistics.

5.2.2.1 Return of biological sample for anonymous testing

Consenting participants returned the questionnaire and self-taken vulvovaginal swab to the HPA. The vulvovaginal swabs were sent to the Sexually Transmitted Bacteria Reference Unit (STBRU) for unlinked anonymous testing. Samples were tested using the APTIMA COMBO 2 assay for both chlamydia and gonorrhoea (Gen-probe Inc., San Diego, CA). Reactive samples were confirmed according to the manufacturers' instructions.

Test results could not be linked to any personal identifiable information, and participants were not sent any test results. Testing was carried out anonymously for a number of reasons. Firstly, as discussed in the Chapter 3, it is reasonable to expect that propensity to participate in a survey of chlamydia prevalence may be related to risk of having chlamydia. If test results had been

[16] Random selection and allocation was performed by the local lead at the PCT using an Excel spreadsheet and written procedure to standardise the process across participating sites. Study sites entered the eligible participants into the spreadsheeet which assigned a random number to each eligible participant. Participants were then re-ordered by random number and the first 1,000 were selected. The first 500 were allocated to group A, the second 250 to group B and the third 250 to group C.

provided then it was expected that those who had taken a test recently or who did not consider themselves to be at risk from having chlamydia would be less likely to participate. There were also logistical considerations. In returning results to participants, it would have been necessary to adhere to governance standards for clinical testing, including timely return of results, and arranging partner notification and treatment.[229] It was not considered practical to try to achieve these standards within the resources of the pilot or future surveys. This aspect of the methodology formed an important part of the ethical review of the study (see section 5.2.4). The study was conducted in the context of widespread availability of chlamydia screening and testing. The study information leaflet provided detailed information on where a named test could be obtained locally. The Natsal-3 survey provided an important precedent for this decision, where anonymous testing for STIs without return of results was found to be an acceptable approach.[230]

5.2.3 Analysis

Participation rates were defined as the number of samples returned with consent for testing divided by the number of invitations sent and were measured in each PCT and in each randomisation group. Reasons for non-response derived from the pre-paid postcard were compiled.

Reported sexual behaviours were compared between randomisation groups using a chi-squared test. In order to assess whether the recruited sample was comparable to the general population, I also compared reported sexual behaviours among study participants in each randomisation group to responses

from 17 and 18 year-old female participants in Natsal-2 (n=359) and the Health Survey for England conducted in 2010 (HSE2010, n=108).[17] Sampling weights were applied according to the data analysis guides for each survey. The complex survey function in Stata was used to calculate standard errors, in order to allow for clustering and stratification.

In order to identify whether the population tested through this population-based postal survey with anonymous testing was different to the population being tested through the NCSP, the reported sexual behaviour in the pilot survey was compared to information from same-aged women (17 to 18 in Sutton & Merton, 18 in Northamptonshire), tested through the NCSP in the two participating PCTs in 2011 (n=3,485). Table 5-3 shows the variables that were available in each of the comparator datasets, and were used for analysis. All statistical analyses were performed using Stata version 12.0 (StataCorp, College Station, Texas, USA).

[17] Although data from Natsal-3 would provide more timely results for comparison, the data were not available at the time of this analysis.

Table 5-3: Sexual behaviour variables available in the pilot survey and comparator samples

Variable	Pilot survey	Natsal-2	HSE 2010	NCSP 2011
Ever had chlamydia test	✔	✖	✔	✖
Ever had sex	✔	✔	✔	✖
More than one sexual partner in the past year*	✔	✔	✔	✔
At least one new sexual partner in the past year*	✔	✔	✖	✖
More than one sexual partner in the past three months*	✔	✔	✖	✖
At least one new sexual partner in the past three months*	✔	✖	✖	✔
Condom used at last intercourse	✔	✔	✖	✖

**Variables were collected as continuous variables in the pilot questionnaire (number of sexual partners in past year, number of new sexual partner per year etc). Due to the small numbers available, responses were categorised into binary variables for the purposes of comparison.*

An area-level indicator of socioeconomic deprivation (IMD[220]) was assigned to all invited individuals by mapping postcodes of residence to LSOA of residence. Ranks of IMD scores were grouped into quintiles. The distribution of IMD quintiles was then compared between participants and the invited population.

The marginal costs per invitation and per sample received for each randomisation group were estimated (defined as the total of the unit costs of all consumables, postage and testing, divided by the number of invitations sent or the number of samples returned with consent for testing (Table 5-4). Staff and overhead costs were not included, as these were assumed to be equivalent for all recruitment methods.

Table 5-4: Unit costs of consumables

Item	Cost per unit
PRINTING: Letters & information sheets	
Printing of invitation letter	£0.05
Printing of PCO cover letter	£0.05
Printing of participant information	£0.10
Printing of participant instruction leaflet	£0.10
Printing of sample collection kit request card/voucher request card	£0.02
Printing of questionnaire	£0.11
Letter to accompany requested sample collection kits	£0.05
Reminder letters	£0.05
Letter to accompany music voucher	£0.05
ENVELOPES: Addressed envelopes for:	
Invitations (group C) (size: A5)	£0.01
Reminder letters (size: A5)	£0.01
Gift voucher/Kit request card (size: DL)	£0.01
Address label	£0.02
POSTAGE	
Invitation - without kit (2nd class letter)	£0.25
Invitation - with kit @ £0.44 (2nd class Large letter)	£0.44
Sample collection kits @ £0.44 (2nd class Large letter)	£0.44
Reminder letters (2nd class letter)	£0.28
Gift voucher (2nd class letter)	£0.28
Freepost for test request slip return (2nd class Freepost, standard response)	£0.32
Freepost for sample return (1st class Freepost, standard response)	£0.42
INCENTIVES	
Gift voucher (£5 each)	£5.00
SAMPLE COLLECTION KITS	
Rigid container+absorbent pad	£0.25
Outer envelope	£0.07
Return envelope	£0.15
Tube label	£0.06
Collection kits @ 1.39 plus VAT	£1.63
LABORATORY TESTING	
Testing (includes sample collection kit) @ £5 plus VAT	£5.88

5.2.4 Regulatory approval

Participants indicated their consent for testing and storage of samples using a tick box on the questionnaire. Signed consent was not requested in order to maintain anonymity of participants.

The study was approved by North London Research Ethics Committee.[18] Research governance approval was obtained from both participating PCTs. Research governance approval was sought to invite both 17 and 18 year-olds. This age group was approved by the Research Ethics Committee. However research governance approval for NHS Northamptonshire was only granted for 18 year-olds due to local guidance on the use of personal information for under-18 year-olds.

National Information Governance Board (NIGB) approval was originally sought to obtain lists of names and addresses of eligible participants from the PCTs, to enable the study team to send invitations directly from the HPA. Approval was not granted, meaning that the initial invitation letter was sent by the PCT, and the HPA study team did not have access to any personal identifiable information from the women invited to the study.[19]

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[18] REC reference number: 10/H0717/57

19 Except personal identifiable information provided by participants, in order to request kits or vouchers. This information was not linked to any test result or study information

5.3 Results

5.3.1 Participation rates

A total of 155/2,000 (7.8%) samples were returned with consent, 33 of which were returned after receipt of a reminder letter (Table 5-5). Consent was declined by a further 48 women, and 30 invitations were returned as undelivered. Participation rates were higher in Northamptonshire (90/1,000; 9.0%) than Sutton & Merton (65/1,000; 6.5%) (p=0.04). Participation rates varied by randomisation group; 78/1,000 (7.8%) of those in Group A, 72/500 (14.4%) in Group B and 5/500 (1%) in Group C returned a sample and provided consent (A v B: p<0.001). All received samples had sufficient material for testing; 3/155 (2%) tested positive for chlamydia (1 in Group A, 2 in Group B).

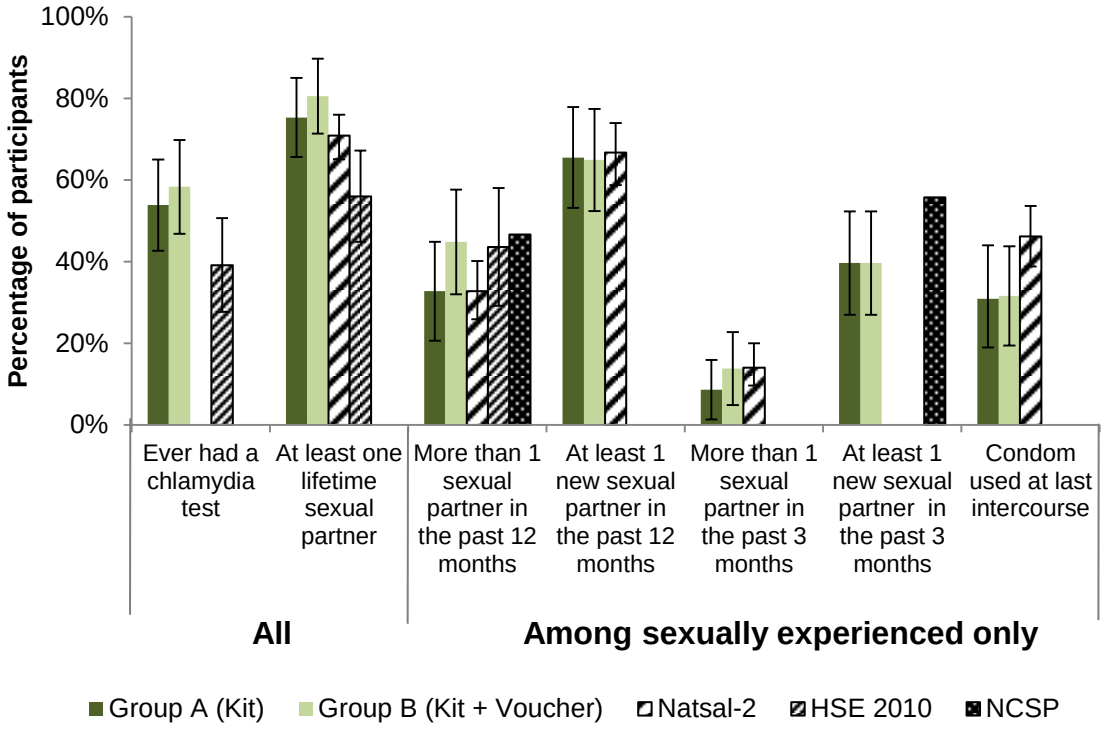
Table 5-5: Participation rates by randomisation group

Participation rates	Randomisation Group						Overall	
	A: Kit (n=1,000)		B: Kit + voucher (n=500)		C: No kit (n=500)		(n=2,000)	
	n	%	n	%	n	%	n	%
NHS Northamptonshire	47/500	9.4%	41/250	16%	2/250	0.8%	90/1,000	9.0%
NHS Sutton & Merton	31/500	6.2%	31/250	12%	3/250	1.2%	65/1,000	6.5%
Overall	78/1,000	7.8%	72/500	14%	5/500	1.0%	155/2,000	7.8%

5.3.2 Assessment of selection bias

Figure 5-1 shows the reported characteristics among Groups A and B compared to 17 and 18 year-old participants in Natsal-2 and HSE2010, as well as data for 17 and 18 year-old females tested through the NCSP in the two participating PCTs in 2011.

Figure 5-1: Reported sexual behaviours among pilot survey participants, same aged Natsal-2 participants, HSE 2010 participants and NCSP test carried out in participating PCTs in 2011



**Comparable questions are not available from all sources. Bars show proportions, with 95% confidence intervals shown as error bars. Everyone tested through the NCSP was assumed to be sexually experienced.*

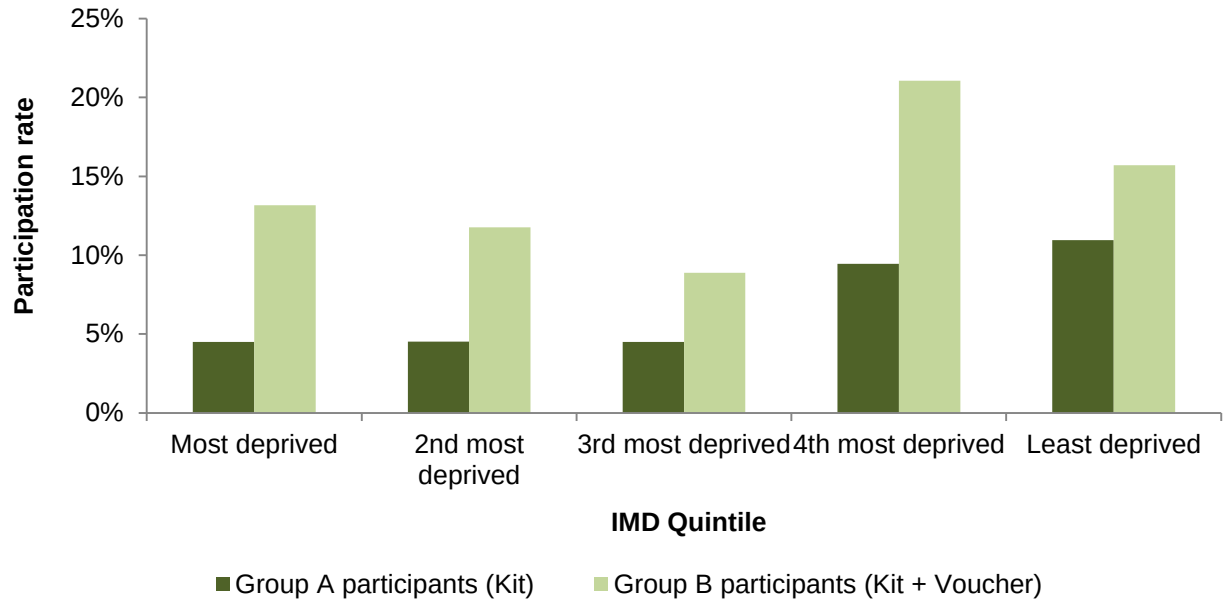
A total of 78% participants were sexually-experienced (reported at least one lifetime sexual partner, Figure 5-1). Due to the small sample size in Group C (n=5), no comparisons of reported behaviour or demographic characteristics are reported for this group. A higher proportion of participants in Group B than Group A were sexually-experienced (81% in Group B versus 75% in Group A, p=0.47), reported ever having had a chlamydia test (58% versus 54%, p=0.58) and reported more than one sexual partner in the past 12 months (45% versus 33% among sexually active participants, p=0.18). None of the observed differences were statistically significant (at the 0.05 level).

Responses from participants in the pilot survey were broadly similar to Natsal-2 responses, although there was some heterogeneity. A higher proportion of same-aged sexually experienced Natsal-2 participants reported condom use at last intercourse compared to pilot study participants (46% versus 31% in Group A, p=0.048; and versus 32% in Group B, p=0.045). The percentages of participants who reported ever having had a chlamydia test and who reported being sexually-experienced were higher than those reported among HSE2010 participants (Figure 5-1).

The percentage of participants who reported having had at least one new sexual partner in the last three months was lower than that reported among same-aged women tested through the NCSP in 2011 (40% in both Groups A and B versus 56% in NCSP tests. p=0.02).

The low response rates prevented a subgroup analysis of response rates by IMD quintile. However in both groups A and B, participation rates were higher among those living in less deprived areas (Figure 5-2). Participation rates varied less by IMD quintile in Group B.

Figure 5-2: Participation rates by IMD quintile and randomisation group



IMD: Index of multiple deprivation, quintile based on lower super output area of residence.

5.3.3 Cost per invitations and cost per sample received

The marginal cost per initial invitation was £3.00 for group A, £3.10 for Group B and £0.50 for Group C. The marginal cost per sample received was £51 for Group A, £36 for Group B and £93 for Group C (Table 5-6).

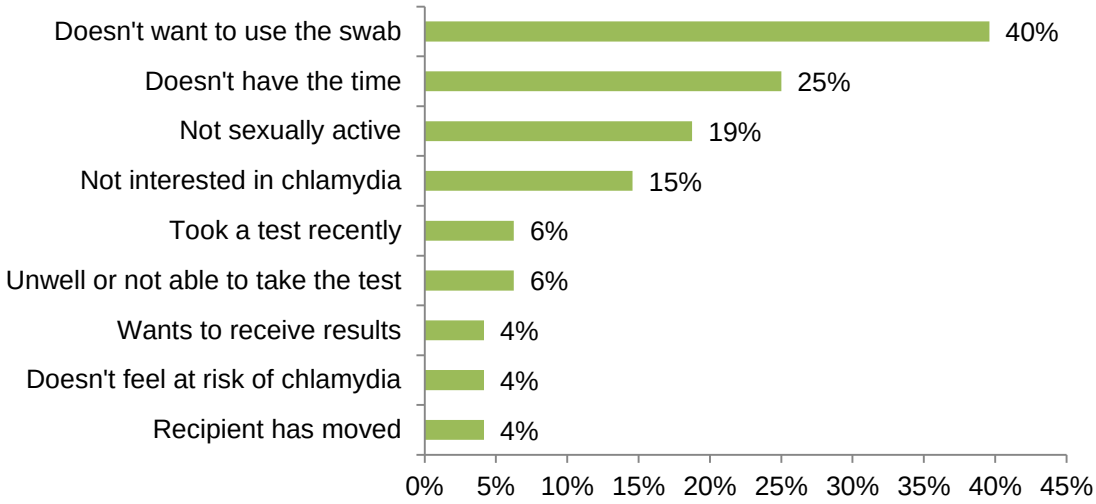
Table 5-6: Costs per invitation sent and sample received by randomisation group

	Group A (Kit)	Group B (Kit + voucher)	Group C (No kit)
Per invitation	£3.00	£3.10	£0.50
Per sample	£51	£36	£93

5.3.4 Reasons for non-participation

A total of 48 women declined consent by returning the pre-paid postcard (3% of all women who did not return a sample). The most commonly cited reasons for non-participation were that women did not want to use the swab (19/48, 40%), did not have the time (12/48, 25%), were not sexually active (9/48, 19%) or were not interested in chlamydia (7/48, 15%). Two respondents (4%) indicated that they wanted to receive their results (Figure 5-3).

Figure 5-3: Reported reasons for non-participation (n=48)



*Respondents could choose more than one option. Responses marked * were derived from free-text responses.*

5.4 Discussion

5.4.1 Key findings

This pilot of a postal survey of young women with anonymous testing for chlamydia achieved a maximum response rate of 14%. Given this low response rate, the piloted methodology is not a feasible approach for obtaining regular measures of chlamydia prevalence among young women.

5.4.2 Strengths and limitations

The main strength of this pilot study was that invitations were randomly allocated into different groups to allow investigation of the response rates that could be expected given different approaches. This showed that offering a small financial incentive slightly increased participation, and reduced the cost per sample received, although none of the piloted approaches achieved an acceptable response rate.

The study was subject to limitations. Firstly, it was not possible to determine whether participation rates would have been higher if participants had been offered their results. People who take part in named chlamydia testing are, on average, at higher risk of infection than the general population[182]. Therefore participants were not provided with their test results to reduce potential non-response bias (section 3.2.2.1). Among the 48 individuals who provided a reason for non-participation using the pre-paid postcard, only 2 respondents stated that they did not take part because they wanted to receive their test results. Although this is a small sample and only indicative of potential reasons for non-participation in the overall population, this suggests that providing test results would not have led to substantially higher response rates. This is consistent with the low participation rates in other recent postal chlamydia screening studies, where named testing was used[88,158]. However it is possible that offering test results may have led to a larger sample size.

A further limitation is that the age of those eligible and of participants was not known, meaning that not possible to determine whether the difference in participation rates between Northamptonshire and Sutton & Merton was associated with age or whether this was more likely to be due to local variation

in the willingness to participate or completeness of the GP registers. It was originally envisaged that year and month of birth would be provided from the participating PCTs, but this was unavailable. A lower response rate in the London PCT (Sutton & Merton) would be consistent with other studies that have shown lower participation rates within London compared to the rest of the country[171].

The GP registers may not have been accurate in terms of registered patients' addresses. A total of 30/1,845 (1.6%) invitations among non-participants were returned to sender, indicating that they never reached the intended participant. This is unlikely to be the total number of undelivered invitations. These undelivered invitations were included in the denominator for participation rates. If the proportion of 'ghost' patients seen in the ClaSS study (26%, see section 3.2.2.2)[10] is applied to the results of this pilot, then the participation rate among those likely to have received the sample would be higher, but still low (11% in Group A, 19% in Group B, 1% in Group C).

The most commonly stated reason for non-participation was not wanting to use the self-taken VVS. While VVS have been found to be an acceptable method of sampling for diagnostic tests or chlamydia screening, as no clinical result was being returned, this may have reduced the willingness to use the swab. Urine samples are possible alternatives, but the sensitivity of NAAT tests among women is lower using urine compared to VVS samples[231].

5.4.3 Implications for evaluation of chlamydia control

Low response rates do not necessarily lead to biased estimates of outcome measures; bias will only occur if participants and non-participants differ in

respect to the outcome of interest. In order to gain some insight into the non-response bias in this survey, participation rates were compared by residence based deprivation, and responses from the pilot were compared to three other samples (Natsal-2, HSE2010 and women tested through the NCSP). Participation rates were higher among those in less deprived areas. As residence-based deprivation measures have been found to be a risk factor for chlamydia infection,[133] this suggests there may have been some important differences between participants and non-participants that may have introduced bias. Although limited by sample size, there was some evidence to suggest that these differences (and the potential resulting bias) were reduced with the offer of a voucher. There were minimal differences between our participants and the same aged Natsal-2 or HSE respondents. While this suggests that the findings from these three sources may be consistent, the utility of these comparisons is limited by the sample size in Natsal-2 and HSE for 17 and 18 year-old women and as Natsal-2 and HSE2010 provide national estimates that would mask local variation. Furthermore, Natsal-2 was carried out over 10 years ago, which may limit comparability of findings. Results from the more-recently conducted Natsal (Natsal-3, conducted 2010-12) were not available at the time of the pilot study. One alternative approach to explore the non-response bias would be to compare those who responded before or after a reminder was sent. If differences between groups are seen, then it is also reasonable to assume there to be important differences between participants and non-participants[232]. However numbers were too small for meaningful comparisons within this pilot survey.

Although it was not possible in this pilot to establish with certainty whether participants and non-participants had the same risk of having chlamydia, given

the low participation rates, a survey using the piloted methodology would be open to substantial, and potentially variable, selection bias. Even if the prevalence of infection among participants and non-participants did not differ, the costs of implementing repeated cross-sectional surveys would be prohibitively large, due to the number of invitations needed to achieve the sample size needed to measure relatively small changes in prevalence between surveys.

5.4.4 Summary

In summary, this pilot study showed that repeated cross-sectional studies of chlamydia prevalence using postal invitations with anonymous testing for chlamydia is not a suitable method for measuring chlamydia prevalence in the general population. Other methods for measuring chlamydia prevalence are therefore required, and in the next chapter I explore the use of data from large nationally-representative sexual behaviour surveys as an alternative to chlamydia-specific surveys.

6 Chlamydia prevalence measured in the second and third National Surveys of Sexual Attitudes and Lifestyles (Natsal-2 and Natsal-3)

The results of the previous chapter show that a postal survey of chlamydia prevalence is unfeasible, would incur unjustifiably high costs and would be open to considerable selection bias. Repeated cross-sectional postal surveys are not suitable for population-based monitoring of chlamydia prevalence among young women in England. Other methods for monitoring chlamydia prevalence over time are therefore required. In the following two chapters I investigate the use of the National Surveys of Sexual Attitudes and Lifestyles (Natsal) as a means of comparing age-specific chlamydia prevalence among a sample of the general population at different time points (presented in this chapter) and to explore how chlamydia screening had been delivered up to 2012, and what the epidemiology of infection in relation to testing can tell us about the actual or expected impact of chlamydia screening (Chapter 7).

6.1 Background

The analyses in this and the subsequent chapter use data from the second and third National Surveys of Sexual Attitudes and Lifestyles (Natsal-2 and Natsal-3 respectively). Natsal are three, stratified probability sample surveys of the British general population. The first survey (Natsal-1) was conducted in 1990-1991,[170] Natsal-2 in 1999-2001[171] and Natsal-3 in 2010-12.[172] In both Natsal-2 and Natsal-3, chlamydia prevalence was estimated from urine samples among a subset of participants.[23] The surveys also provide a wealth of information on sexual behaviour, attitudes and lifestyles, experience of STI diagnoses (including chlamydia) and, in Natsal-3, chlamydia testing.

As both Natsal-2 and Natsal-3 measured the prevalence of *C. trachomatis* detected in urine (hereafter termed 'prevalent infection'), the surveys provide a unique opportunity to compare estimates of chlamydia prevalence among the general population of young adults before and after the widespread implementation of chlamydia screening. However, as described in detail below, there were differences in the detection strategy used in each survey, meaning that such comparisons should be made with caution. The analyses presented in this chapter were conducted to explore how this and other differences between the surveys might affect the conclusions that can be made about changes in chlamydia prevalence among young adults using a series of adjustments and counterfactual scenarios.

6.2 Aims & objectives

To investigate whether the Natsal surveys can be used to compare chlamydia prevalence before and after the implementation of the NCSP and determine how differences between the surveys and underlying changes in sexual behaviour affect the conclusions that can be made about change in chlamydia prevalence between 1999-2001 and 2010-12. This aim was addressed through the following objectives:

- To compare chlamydia prevalence among 18 to 24 year-old participants in the Natsal-2 and Natsal-3 surveys.
- To adjust Natsal-2 and Natsal-3 prevalence estimates and comparisons for known and possible differences between the surveys.
- To describe differences in reported sexual behaviour and markers of sexual behaviour between the surveys and their potential impact on chlamydia prevalence.

6.3 Methods

6.3.1 Summary of survey methodology and testing of biological specimens in Natsal-2 and Natsal-3

Full details of the survey methods and questionnaire have been described elsewhere.[172] In summary, both surveys used an independently designed, multi-stage, clustered, stratified probability sample, using the 'small-user' Postcode Address File, a list of all addresses (delivery points) in the Britain, as the sampling frame. Postcode sectors were selected as the primary sampling units, addresses within them were selected at the second stage, and finally one eligible adult per address was randomly selected at the final stage. In both surveys, participants were interviewed in their own homes using computer-assisted face-to-face and computer-assisted self-interview for the most sensitive questions.[4,5] Most questions in Natsal-3 were identical in wording to those used in Natsal-2. However, there were some questions used in Natsal-3 that were not used in Natsal-2, including whether someone had been tested for chlamydia in the last year and reason for testing. Some questions had slightly altered in wording, the only relevant one for the analyses presented in this thesis being the wording for self-reported diagnosis in the last year (see Box 6-1). A summary of the key features and differences between Natsal-2 and Natsal-3 is provided in Table 6-1.

Table 6-1: Key features of the second and third National Surveys of Sexual Attitudes and Lifestyles[5,172]

	Natsal-2	Natsal-3
Age range	16 to 44 years	16 to 74 years*
Number of participants	11,161[$]	15,162
Survey method	Computer-assisted personal interviewing (CAPI) including computer-assisted self-interview (CASI)	
Response rate[^]	65%	58%
Self-reported chlamydia test in the last year collected?	No	Yes
Self-reported chlamydia diagnosis in the last year collected?	Yes – calendar year of last diagnosis.	Yes
Eligibility to provide a urine sample	A subset of sexually-experienced participants[133]	All 16 to 17 year-olds (regardless of reported sexual activity); all sexually-experienced 18 to 24 year-olds; a random subsample of 25 to 44 year-olds[23].
Urine collection device	Urine cup	'FirstBurst' urine collection device
Diagnostic assay	Ligase Chain Reaction (LCx) (Abbott Diagnostics) [133]	Aptima Combo 2 (AC2) (Hologic Gen-Probe) [23]
Did participants receive their chlamydia test results?	Yes	No

** Younger adults aged 16 to 34 years were oversampled to increase statistical analysis power for this group.*
[^]As eligibility within households was not known for those households not contacted, these calculated response rates use an estimated denominator of eligible using data from households that could be contacted.[4,5]
[$] Natsal-2 also included a boost sample of adults of Black and Asian ethnicity, but these data were not included in the analyses presented in this thesis.

In both surveys, a subset of participants was invited to provide a urine sample for testing for *C. trachomatis* testing. In Natsal-2, consenting participants were asked to collect a first-catch urine specimen in a plastic urine cup and transfer this to a 20ml universal container (containing 1 mg boric acid as a stabilising agent) for posting to the laboratory where they were tested for chlamydia using the ligase chain reaction test by Abbott Diagnostics (hereafter termed LCx)[133].

Positive samples were confirmed through a repeat test using the LCx on the same sample (personal correspondence, C Carder. 2013). In Natsal-3, participants were asked to collect a urine specimen using a 'FirstBurst' urine collection device, which diverts the first 4-5mls of urine flow into specimen collection tube, without dilution from subsequent urine flow. This device increases the bacterial load in the specimen held in the specimen collection tube compared to a first catch specimen using a urine cup.[233] Urine samples were posted to Public Health England (PHE) where they were tested for *Chlamydia trachomatis* using the Aptima Combo 2 assay (Hologic Gen-Probe); all positive and equivocal results were confirmed with the Aptima chlamydia monospecific assay.[23]

In Natsal-2, participants received their chlamydia test results if they were positive whereas testing in Natsal-3 was carried out anonymously (i.e. without return of results) and participants did not receive their results for any of the other STI tests. The rationale for STI test results not being provided in Natsal-3 has been provided elsewhere.[230] Briefly, this was deemed appropriate and ethical for Natsal-3 given the availability of free STI testing and advice at the time of the survey. Furthermore, urine samples were tested for other STI (HPV, gonorrhoea, *Mycoplasma genitalium* and HIV), and for some of these (HPV and *Mycoplasma genitalium*) the result would be of uncertain clinical value. Timeliness of testing and in some cases test accuracy were also limited given the constraints of the survey conditions and specimen type meaning that STI testing would not be fully compliant with clinical standards. Participants were given information about where to obtain free diagnostic STI and HIV testing and sexual health advice.

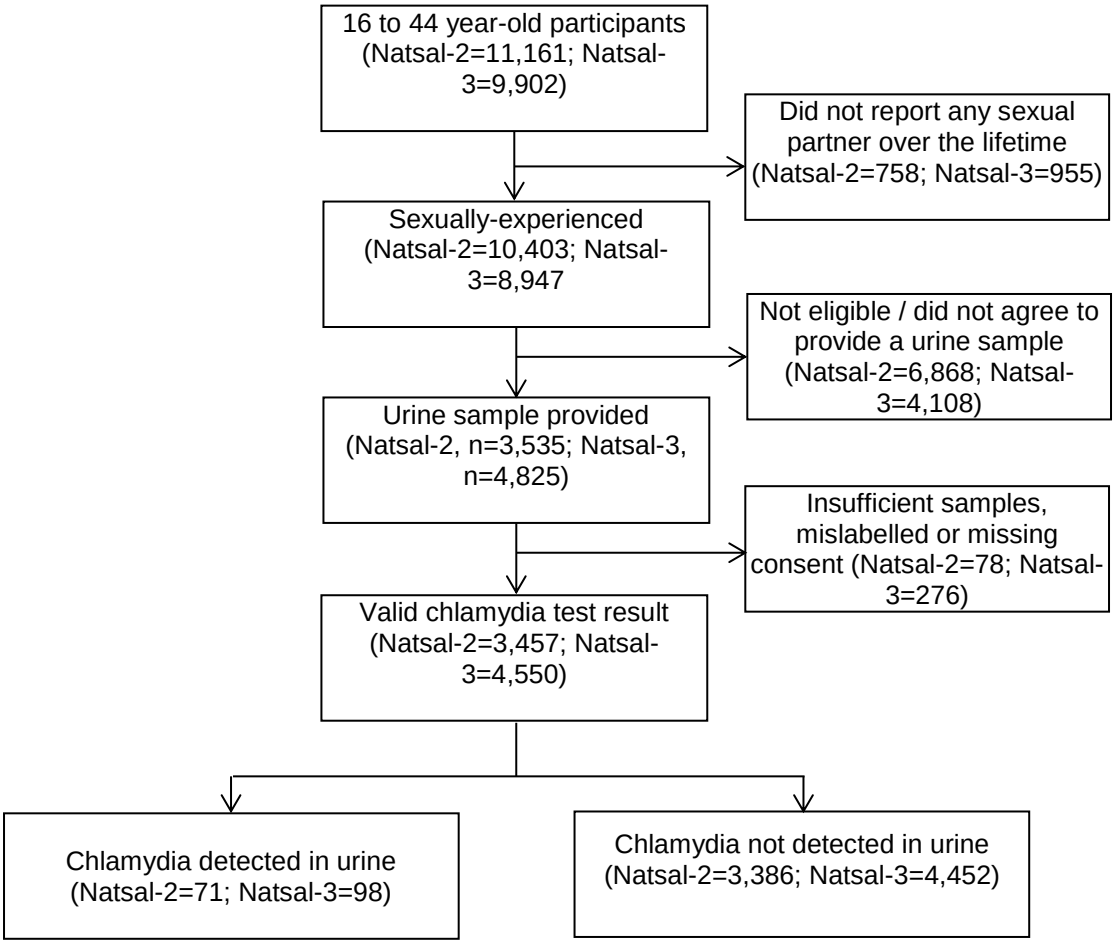
In both surveys, urine specimens were also tested for HPV using an in-house Luminex-based genotyping assay for detection of HPV types 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73 and 82. In Natsal-2, this testing was carried out following storage at -80C as part of a separate, ethically-approved study[234]. In Natsal-3, participants consented to their specimen being anonymously tested for HPV, and testing was carried out shortly after collection.[23,234]

6.3.2 Participants

All analyses in this chapter are based on data from sexually-experienced participants in Natsal-2 or Natsal-3. Apart from summary estimates of the key outcome measures (see below), which were produced for 16 to 44 year-olds, all analyses were conducted among women and men aged 18 to 24 year-old as the age group targeted for chlamydia screening by the NCSP and as urine samples were not collected from 16 to 17 year-old participants in Natsal-2.

The key outcomes of interest were prevalent infection, self-reported chlamydia diagnosis in the last year ('recent diagnosis'), self-reported chlamydia diagnosis at any time prior to the interview date ('ever diagnosed') and, for analyses among Natsal-3 participants, self-report of a chlamydia test in the last year ('recent testing').

Figure 6-1: Flow chart showing participants included (16 to 44 year-old Natsal-2 & Natsal-3)



6.3.3 Statistical analysis

6.3.3.1 Complex survey sampling and weighting

All analyses were carried out using Stata 12.1, accounting for the weighting, clustering and stratification of the Natsal data.[23,172,235] In both surveys, weights constructed and provided by the survey team were applied to adjust for unequal probability of selection and non-response to ensure the sample data were broadly representative of the British general population, according to the most recent census, in terms of gender, age group and Government Office

Region[236,237] and the differential provision of urine samples by demographic and selected sexual behaviours.[5,172]

Questions about self-reported diagnosis of chlamydia differed slightly between surveys. For estimates of diagnoses in the last year among Natsal-2 participants, I therefore constructed an additional weight to correct for the overestimate of recent diagnosis in the last year and to allow comparisons between the surveys (Box 6-1).

Box 6-1: Construction of additional weight for diagnosis in the last year

In Natsal-2, participants were asked the calendar year of their most recent chlamydia diagnosis, whereas in Natsal-3, participants were asked whether they had been diagnosed in the 12 months before the interview. A further weighting was therefore applied when estimating self-reported diagnosis in the last year in Natsal-2 to allow comparisons between the surveys. These additional 'diagnosis weights' were constructed as the number of days in the year specified that would have been in the 12 months before the interview. Weights were constructed for each month, assuming the date of interview was at the midpoint of the month (15th of the month, apart from February, where 14th was used).

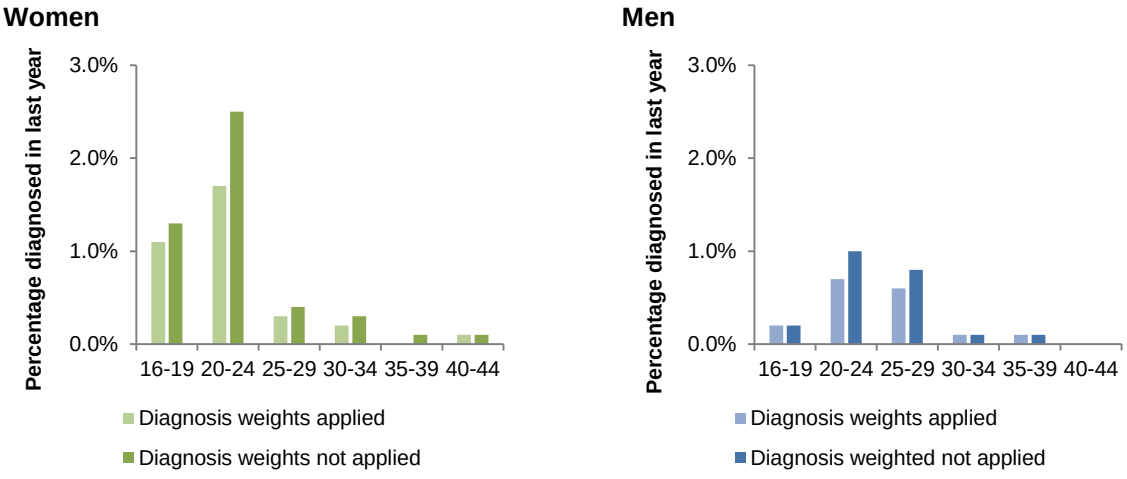
For example, for a participant interviewed on the 15th of January 2000 who reported their last diagnosis was in 1999, 351 of the 365 days in 1999 would have been within the 12 months preceding the interview, thus the 'diagnosis weight' was 351/365=0.96. For a participant interviewed on the 15th of December 2000, only 16/365 days in 1999 would have been within the 12 months before the interview, resulting in a weight of 0.04. Table 6-2 below shows diagnosis weights calculated for each month. Diagnosis weights were then multiplied by the urine weights (which incorporate unequal probability of selection, nonresponse to main survey and urine sub-study), and used as final weights for estimate of diagnosis in the last year in Natsal-2. Figure 6-2 shows the difference in the estimated proportion with a chlamydia diagnosis in the last year by gender and age group.

Table 6-2: Diagnosis weights by month of interview

Month of interview	January	February	March	April	May	June	July	August	September	October	November	December
Days within preceding year	351	321	291	260	230	199	169	138	107	77	46	16
'Diagnosis weight'*	0.96	0.88	0.8	0.71	0.63	0.55	0.46	0.38	0.29	0.21	0.13	0.04

**Number of days within preceding year / 365. Presented to 2 decimal places.*

Figure 6-2: Impact of 'diagnosis weights' on estimated proportion diagnosed in the last year by age group (Natsal-2)



6.3.3.2 Comparison of chlamydia prevalence and diagnoses in Natsal-3 versus Natsal-2 among under-25 year-olds

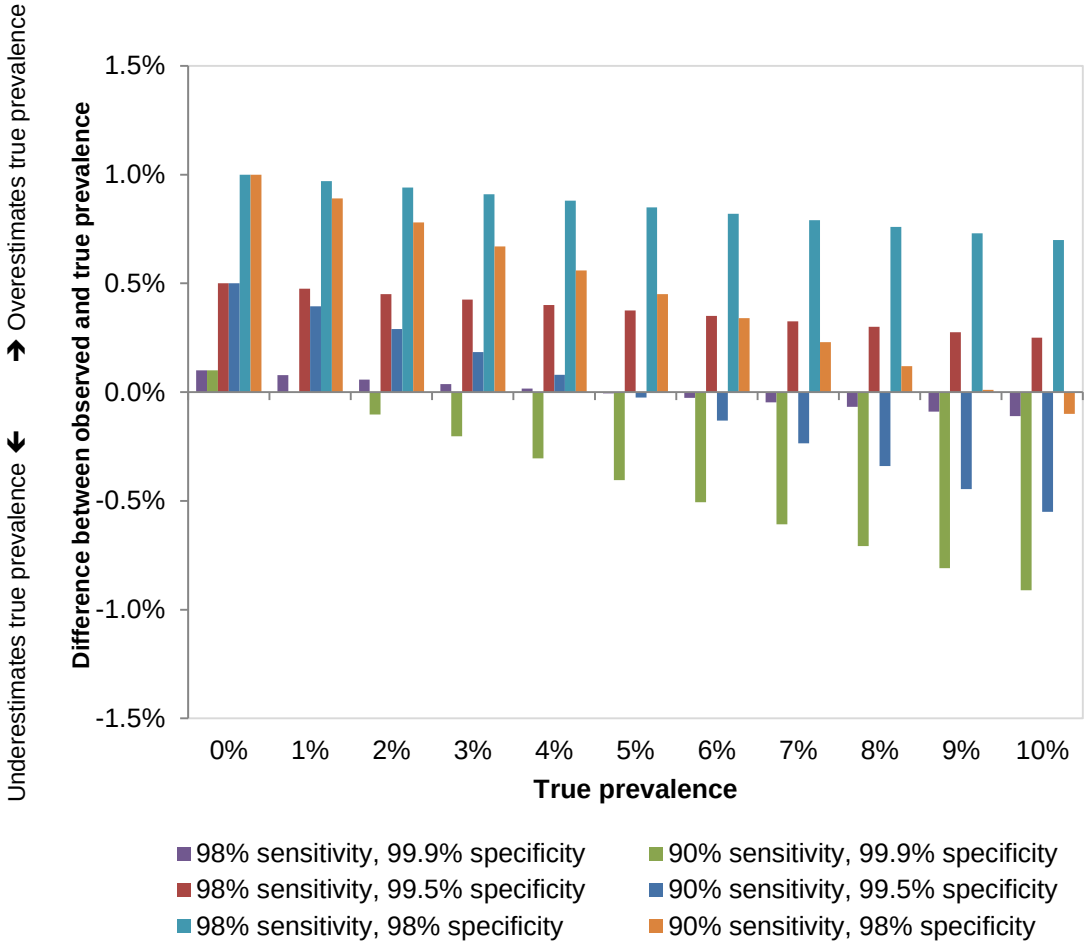
The prevalence of infection and of self-reported diagnoses (ever or in the last year) in Natsal-3 was compared to Natsal-2 using univariable logistic regression with survey (i.e. Natsal-2 or Natsal-3) entered as the independent variable.

These comparisons were further explored by setting up a series of counterfactual scenarios to investigate the impact of differences between surveys on comparisons of chlamydia prevalence between them.

6.3.3.3 Correction for measurement error arising from imperfect diagnostic tests

As set out in section 6.3.1 above, different specimen collection devices and diagnostic tests were used in Natsal-2 and Natsal-3, reflecting changes in technologies between them. Differences in the detection strategy (i.e. the combination of tests, confirmation procedures and specimen collection devices) used in each survey may affect prevalence estimates and their comparability.[140,238,239] Imperfect tests lead to misclassification bias, whereby tests with <100% sensitivity result in individuals with an infection being incorrectly classified as negative ('false negatives') and tests with <100% specificity in individuals without an infection being categorised as having an infection ('false positives'). Thus imperfect tests can over or underestimate 'true' prevalence.[240-243] The extent and direction of this error will depend on both the sensitivity and specificity of the test used and the true prevalence of infection within the population (Figure 6-3).

Figure 6-3: Difference between observed and true prevalence with different test characteristics



Where the sensitivity and specificity of a diagnostic test is known, the 'true' prevalence of infection (i.e. that would have been measured, had a perfect test been used), can be calculated using the following formula set out by Rogan and Gladen:[243]

$$\text{Prevalence}_{\text{adjusted}} = \frac{\text{Prevalence}_{\text{observed}} + \text{specificity} - 1}{\text{sensitivity} + \text{specificity} - 1} \quad [1]$$

By applying this equation to observed prevalence estimates, the 'true' prevalence can be calculated. However this relies on knowing the true

sensitivity and specificity of the test, which in turn relies on having a perfect 'gold standard' test, i.e. a test (or combination of tests, also termed a 'reference standard') that is capable of classifying individuals into those who do and do not have an infection. Estimates of the sensitivity and specificity of chlamydia NAATs have been shown to vary according to the gold standard used.[238,240,244] Estimated performance characteristics of earlier NAATs (such as LCx) are particularly subject to error, where less sensitive assays (i.e. culture or enzyme immunoassays) have been used as the gold standard, or when discrepant analysis[20] has been applied.[238,240,245-247] Adjusting prevalence estimates to achieve a true prevalence is therefore problematic. To address this, the prevalence estimated in Natsal-2 was adjusted to estimate the prevalence of chlamydia that *would have been measured*, had the same detection strategy been used in Natsal-2 as was used in Natsal-3, thereby increasing the comparability of the prevalence estimates while acknowledging that they both may remain imperfect estimates of true prevalence.

To do this, firstly the 'test-adjusted' prevalence was calculated by applying the Rogan & Gladen formula [1] to the prevalence estimates and 95% confidence intervals[248] in Natsal-2, using the sensitivity (91.1%) and specificity (99.1%) of the LCx compared to the AC2 NAAT from a head to head study of the two assays reported by Gaydos et al[249] (Box 6-2). A 'detection strategy-adjusted' prevalence was then calculated by applying this formula [1] to the 'test-adjusted' prevalence. The sensitivity (97.1%) and specificity (100%) estimates for the

[20] A method introduced to overcome problems of the gold standard being less sensitive than the test under evaluation. Specimens that were positive for chlamydia on the assay under evaluation but negative by the gold standard (usually culture) were tested using an additional assay. This 'discrepant analysis' approach was subsequently discredited as it leads to systematic overestimation of the sensitivity and specificity of the test under evaluation.[240]

FirstBurst were taken from a study of urine specimens collected from 534 men using both a urine cup and the FirstBurst device and tested using the Amplicor CT/NG PCR assay (Roche Molecular Systems, Branchburg, NJ).[233]

As Natsal-2 and Natsal-3 are complex surveys, the standard errors are estimated using the complex survey function in Stata to account for the stratification and clustering of the surveys. However, as the 'detection strategy-adjusted' estimates were calculated based on the previously estimated point estimates (and 95%CIs) of chlamydia prevalence, the complex survey analysis function in Stata could not be applied. An approximate method was therefore used to compare the adjusted Natsal-2 prevalence estimates to Natsal-3 prevalence, while also taking into account the original clustering of the sample. Firstly, the effective sample size (the sample size which equates to the given confidence intervals, if the survey had been conducted as a simple random sample), was derived using the adjusted prevalence estimates, and the design effects for each age group.[250] A simulated dataset was then created where the number of observations was equal to the effective sample size and the number with a positive chlamydia test result corresponded to the 'detection strategy-adjusted' point estimates. The simulated dataset was then used to calculate the odds ratio for prevalence in Natsal-3 versus 'detection strategy adjusted' prevalence in Natsal-2 using logistic regression.

Box 6-2: Literature review of sensitivity and specificity of ligase chain reaction (LCx) and Aptima Combo 2 (AC2) assays for *Chlamydia trachomatis* detection

In order to adjust the Natsal-2 prevalence to determine the prevalence that would have been observed had the same detection strategy been used as was used in Natsal-3, the relative sensitivity and specificity of the LCx compared to the AC2 was needed. A literature review was therefore carried out to identify i) systematic reviews of the sensitivity and specificity of the LCx and AC2 and ii) studies where the LCx had been compared directly to the AC2. Along with a search of an electronic database (MEDLINE), unpublished data were obtained via contact with experts in the field (personal communication, Prof Catherine Ison).

Two reviews were identified that provide summary estimates of the sensitivity and specificity of the LCx and AC2. In a systematic review by Nelson *et al*[251] estimated sensitivity of LCx among non-pregnant women ranged from 70% to 96% and specificity between 99% and 100%. In a review of non-invasive testing for chlamydia and gonorrhoea, Cook *et al*[252] included studies which compared urine to other sample types and reported pooled estimates for TMA (ACT or AC2) in urine of 92.5% (95%CI 88.0%-97.0%) sensitivity and 98.6% (95%CI 97.7%-99.6%) specificity in women and 87.7% (95%CI 80.1%-95.2%) sensitivity and 99.4% (95%CI 98.7% - 100%) specificity in men. However the gold standards used for the studies included in these reviews vary considerably, with earlier studies of the LCx often comparing to culture.

Five studies were identified which included a head to head comparison of LCx and AC2.[249,253-256] However only in the study by Gaydos et al, where 506 first catch urine samples were tested with both the LCx and AC2, can the performance characteristics of LCx in relation to AC2 (i.e. using AC2 as a gold standard) be calculated from the results reported.[249] In this study, 506 first catch urine samples from women and men aged 12 to 20 years old attending school-based clinics for routine screening were tested with both the LCx and AC2.[249] This resulted in a sensitivity and specificity of the LCx compared to the AC2 of 91.1% and 99.1% respectively.

Table 6-3: Comparison of results from LCx and AC2 from 506 urine specimens
(Based on Table 1, Gaydos et al 2004[249])

		AC2 ('gold standard)		
		Positive	Negative	Total
LCx	Positive	72	4	76
	Negative	7	423	430
	Total	79	427	**506**

Sensitivity of LCx relative to AC2: 91.1%
Specificity of LCx relative to AC2: 99.1%

Samples that were positive only on the AC2 were retested using the APTIMA chlamydia monospecific assay (ACT) [249]. Results shown for the AC2 are based on AC2 plus confirmation with ACT where both tests were available as this is closest to the detection strategy used in Natsal-3.[23]

AC2: Aptima Combo 2; LCx: Ligase chain reaction; ACT: Aptima chlamydia monospecific assay

6.3.3.4 Combining urine infections with recent screen-detected diagnoses

The average duration of an untreated, asymptomatic chlamydia infection is estimated to be in the region of 16 months.[18] Therefore in both surveys, a proportion of the individuals who had been diagnosed with chlamydia in the last year might have had an infection at the time of the survey had they not been tested and appropriately treated (i.e., had their duration of infection not been shortened by treatment). A hypothetical scenario was constructed to estimate what the prevalence of infection would have been in Natsal-3, had there been no asymptomatic screening among young adults in the year before the survey.

In order to do this, diagnoses were categorised as being either 'screen-detected' or not, based on the reason reported for most recent test. The Natsal-3 questionnaire did not ask where an individual was last diagnosed or why they had been tested. Reason of most recent test among those diagnosed in the last year was therefore assumed to refer to the test associated with the diagnosis. Reported tests in the last year were considered to be 'clinically-indicated' where the reason for last test was reported as either having had symptoms, having a partner diagnosed with chlamydia or who had symptoms, or a repeat test after a previous positive result. Individuals who reported having been diagnosed with chlamydia in the last year were considered to have a 'screen-detected' diagnosis if they reported a non-clinically indicated reason for their last test ("wanted a check-up"; "offered a test" or "worried about risk"). Reason for test was not collected in Natsal-2. For the purposes of this analysis, all reported diagnoses in Natsal-2 were considered to be a result of clinically-indicated testing, as the survey was carried out before the implementation of widespread chlamydia screening.

The proportion of Natsal-3 participants who had a 'screen-detected' diagnosis in the last year was estimated. As the simplest scenario, it is assumed that all of these 'screen-detected' infections would have persisted to the time of the Natsal-3 interview in the absence of screening. The estimated prevalence in Natsal-2 was then compared to the combined prevalence of infection and/or 'screen-detected' diagnoses in Natsal-3 using logistic regression.[21]

6.3.3.5 Adjustment for hypothetical and unmeasured differences between participants and non-participants

Survey estimates may be biased where participants and non-participants differ with regard to the outcome of interest. As described in section 6.3.3, the weights applied to the Natsal-2 and Natsal-3 data were designed to minimise such participation bias arising firstly for non-response in the Natsal survey, and secondly for differential participation in the biological sampling part of the survey. In the weights to address the former, adjustments could be made to ensure the achieved sample was representative of the British population with regard to gender, age group and Government Office Region.[236,237] Weights could not adjust for differences in sexual behaviour, as no information was available from non-participants. As detailed demographic and behavioural data were available from survey participants who did and did not consent to provide a urine sample for chlamydia testing, survey weights could provide a more detailed adjustment for non-participation bias.[5,172] However it is feasible that participation bias remains in each survey due to unmeasured differences between participants and non-participants.

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[21] With additional weights applied for estimation of recent diagnoses in Natsal-2 as described in Box 6-1.

The potential impact of unmeasured/uncorrected-for participation bias was explored by calculating a range of 'participation-adjusted' prevalence estimates for Natsal-2 and Natsal-3, by varying the (hypothetical) participation bias in each survey from the estimated chlamydia prevalence being 50% lower to being 50% higher than among non-participants. The resulting odds ratios for each combination were then calculated and plotted against the participation bias in Natsal-2 and Natsal-3. In all scenarios response rates were assumed to be equivalent to those seen in each survey.[22] The resulting scenarios represent hypothetical differences between participants and non-participants which have not been captured by either the post-stratification weighting to account for non-participation in the main survey, or by the weights applied for differential provision of urine samples by demographic and behavioural characteristics.

6.3.3.6 Indicators of change in sexual behavioural risk of transmission

Identification and treatment of chlamydia infections is only one of the factors that affect chlamydia transmission and prevalence. If sexual behaviours changed in the ten year period between the Natsal surveys, then in the absence of widespread screening, chlamydia prevalence may have either increased or decreased. In order to explore whether there is any evidence for a change in the behavioural risk of STI transmission, the estimated prevalence of reported sexual behaviours (condom use at last sex; numbers of new or condomless sexual partners in the last year; number of lifetime sexual partners) was compared between 18-24 year-old participants in Natsal-2 and Natsal-3. The proportion of Natsal-3 participants who reported having had their first

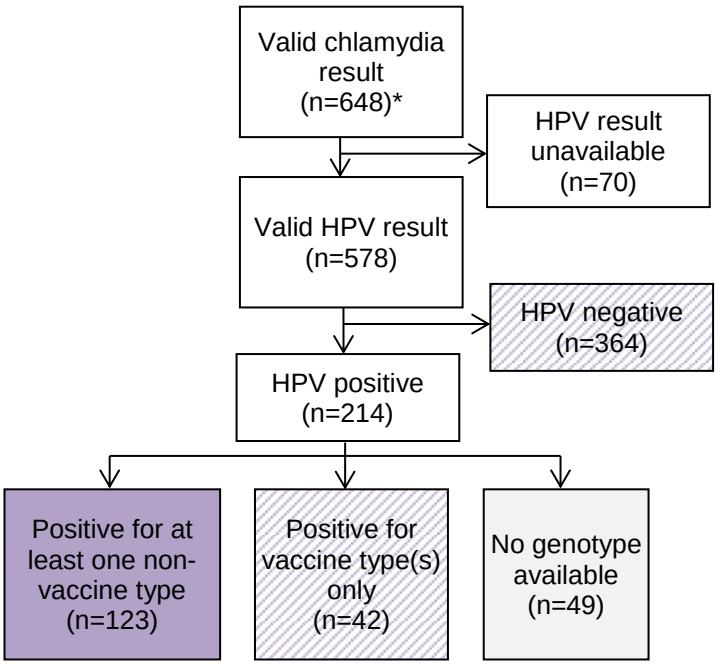
[22] Overall participation rate in Natsal-2 (65.4%)[171]; 16-29 year-old boost sample in Natsal-3 (67.3%)[5].

heterosexual sexual intercourse before the age of 16 was estimated and plotted by year the participant turned 16.

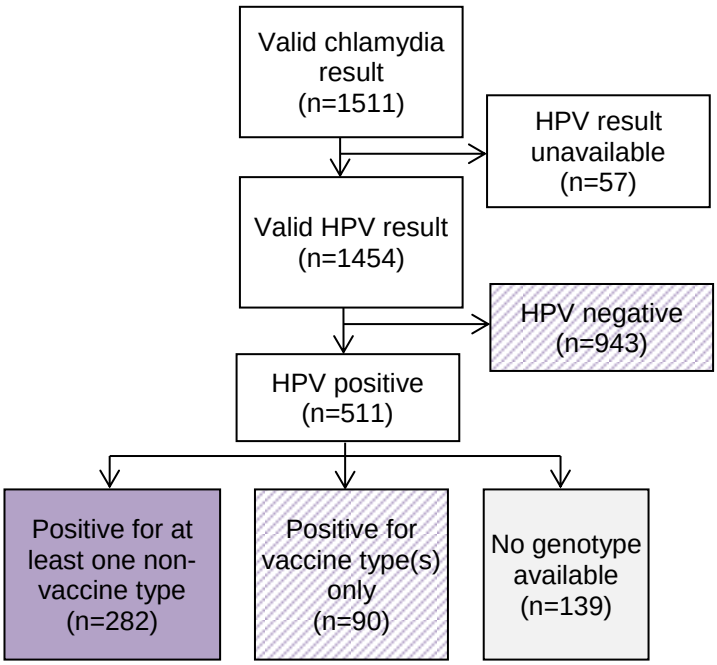
The prevalence of non-vaccine-HPV types detected in urine was also compared between the surveys, as a biological marker of sexual behaviour change. Non-vaccine types comprised high-risk HPV types other than those included in the bivalent HPV vaccine (HPV 16, 18) and those with evidence of cross-protection (HPV 31, 33, 45).[257] HPV 6 and 11, which were also tested for, were considered non-vaccine types for the purposes of this analysis as although a quadrivalent vaccine is available that protects against HPV 6 and 11, the bivalent vaccine was used within the national vaccination campaign up to 2012.[258] Thus Natsal-3 participants would not have been eligible for quadrivalent vaccination. Participants who were HPV positive but where no type-specific data were available were excluded (Figure 6-4).

Figure 6-4: Flowchart showing samples included in analysis of non-vaccine HPV prevalence (18-24 year-old sexually-experienced women and men)

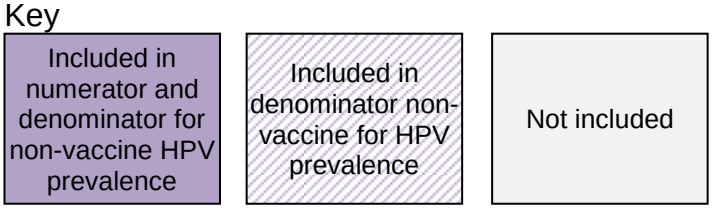
Natsal-2



Natsal-3



Key



6.3.4 Regulatory approval

Natsal-2 obtained ethical approval from University College Hospital, North Thames Multicentre, and all local research ethics committees in Britain.[133] Natsal-3 was approved by Oxfordshire Research Ethics Committee A (reference 09/ H0604/27). Approval for use of these data for this analysis was granted by the Natsal-3 Project Management Team.

6.4 Results

6.4.1 Summary of prevalence, diagnosis and testing by age group and gender (Natsal-3)

Table 6-4 shows the prevalence of chlamydia infection and of self-reported chlamydia testing and diagnosis in the last year among sexually-experienced 16 to 44 year-olds. Chlamydia prevalence and recent diagnoses peaked among 20 to 24 year-olds in men, and among 16 to 19 year-olds in women. No prevalent infections were detected among 16 to 18 year-old men.[23] Testing was highest in 16 to 19 year-olds among both men and women. The proportion who had ever been diagnosed with chlamydia peaked in an older age group than the peak for recent diagnoses (i.e in 25 to 29 year-olds in men and 20 to 24 year-olds in women). Reported diagnoses and testing were higher among women than men across all age groups.

Among 16 to 24 year-olds, 3.1% of women and 2.3% of men had a prevalent chlamydia infection, 62.5% of women and 43.2% of men had either been tested, or offered a chlamydia test in the last year and 12.3% of women and 5.3% men had ever been diagnosed with chlamydia.

Table 6-4: Prevalence of chlamydia (detected in urine), and self-reported testing and diagnosis by age group and sex (sexually-experienced 16-44 year-olds, Natsal-2 and Natsal-3)

Age group (years)	Prevalent infection**		Ever diagnosed with chlamydia		Diagnosed with chlamydia in the last year		Tested in the last year	Offered, not tested in last year	Bases, Wt, Unwt					
									Prevalent infection		Tested/offered/ ever diagnosed		Diagnosed in the last year	
	Natsal-2	Natsal-3	Natsal-2	Natsal-3	Natsal-2*	Natsal-3*	Natsal-3	Natsal-3	N2	N3	N2	N3	N2	N3
Women														
16-19	3.9% (1.4-10.3)	3.8% (2.2-6.3)	1.3% (0.6-3.2)	7.4% (5.5-9.9)	1.1% (0.5-2.8)	3.4% (2.2-5.2)	56.6% (52.5-60.6)	10.4% (8.2-13.1)	86, 73	234, 343	451, 387	374, 582	451, 387	374, 582
20-24	2.8% (1.5-5.2)	2.7% (1.7-4.3)	5.3% (3.9-7.2)	14.9% (12.7-17.5)	1.7% (1.0-2.9)	2.7% (1.8-4.1)	52.8% (49.2-56.4)	7.1% (5.5-9.2)	271, 209	391, 497	773, 598	629, 793	771, 598	629, 793
25-29	2.1% (1.1-4.0)	2.2% (1.2-4.0)	3.5% (2.6-4.8)	12.3% (10.5-14.3)	0.3% (0.1-0.6)	0.9% (0.5-1.6)	30.0% (27.2-32.9)	3.9% (2.9-5.3)	328, 256	422, 419	869, 777	651, 826	867, 777	651, 826
30-34	1.4% (0.6-3.0)	0.8% (0.4-1.9)	3.8% (2.8-5.0)	9.3% (7.6-11.3)	0.2% (0.1-0.5)	0.1% (0.0-0.5)	16.5% (14.2-19.2)	0.6% (0.3-1.3)	375, 318	385, 274	1008, 950	654, 630	1008, 950	654, 630
35-39	1.0% (0.4-2.5)	0.6% (0.1-2.6)	3.2% (2.4-4.3)	5.0% (3.5-7.1)	0.0% (0.0-0.1)	0.0% -	10.1% (7.8-12.9)	0.9% (0.4-2.2)	384, 311	393, 167	1059, 881	671, 382	1059, 881	671, 382
40-44	0.2% (0.0-1.4)	0.0% -	1.5% (0.9-2.5)	4.6% (3.2-6.7)	0.1% (0.0-0.3)	0.0% -	8.3% (6.3-10.8)	0.2% (0.0-1.1)	305, 269	441, 185	946, 798	724, 408	946, 798	724, 408
Men														
16-19	2.8% (0.7-11.1)	0.3% (0.1-1.4)	0.2% (0.0-1.4)	3.5% (2.2-5.7)	0.2% (0.0-1.4)	1.9% (1.0-3.7)	40.4% (35.9-45.1)	8.0% (5.9-10.8)	94, 94	214, 395	455, 410	344, 675	454, 410	344, 675
20-24	2.9% (1.1-7.4)	3.4% (2.2-5.2)	1.9% (0.9-3.8)	6.3% (4.8-8.4)	0.7% (0.2-2.0)	2.1% (1.2-3.5)	31.1% (27.8-34.7)	8.9% (6.8-11.4)	254, 272	383, 597	791, 778	624, 1065	785, 778	624, 1065
25-29	4.6% (2.3-9.0)	0.8% (0.3-1.9)	2.1% (1.2-3.4)	10.2% (8.2-12.7)	0.6% (0.2-1.5)	0.8% (0.3-2.0)	19.4% (16.6-22.5)	3.0% (1.9-4.6)	313, 398	412, 650	920, 1143	670, 1364	918, 1143	670, 1364
30-34	1.4% (0.5-3.5)	1.2% (0.5-3.0)	1.8% (1.1-2.9)	9.2% (7.0-12.1)	0.1% (0.0-0.4)	0.4% (0.1-1.4)	9.5% (7.2-12.3)	0.7% (0.3-1.7)	368, 466	397, 496	1065, 1325	653, 1033	1063, 1325	653, 1033
35-39	1.4% (0.5-4.0)	0.6% (0.1-4.4)	1.4% (0.8-2.4)	4.4% (2.7-7.1)	0.1% (0.0-0.4)	0.1% (0.0-0.9)	4.7% (3.1-7.2)	0.0% -	344, 415	421, 268	1085, 1252	673, 591	1084, 1252	673, 591
40-44	0.5% (0.1-3.3)	0.0% -	0.6% (0.2-1.6)	2.8% (1.5-5.1)	0.0% -	0.6% (0.2-1.6)	3.5% (2.1-5.9)	0.5% (0.1-3.2)	309, 376	457, 259	966, 1104	751, 598	965, 1104	751, 598

**Estimates of proportion diagnosed in last year in Natsal-2 have been calculated using additional weights to adjust for over-estimation and to make comparable between surveys. See Box 6-1 for details. **Natsal-2 prevalence estimates in the youngest age group are among 18-24 year-olds, as 16-17 year-olds were not tested for chlamydia.*

6.4.2 Comparison of chlamydia prevalence and diagnoses in Natsal-3 versus Natsal-2 among under-25 year-olds

Table 6-5 compares the prevalence of self-reported chlamydia diagnoses (ever and in the last year) for 16 to 24 year-olds in Natsal-2 and Natsal-3 and the corresponding estimates of chlamydia prevalence for 18 to 24 year-olds. In univariable analyses, there was no significant difference between the prevalence of chlamydia among 18 to 24 year-olds in Natsal-3 compared to Natsal-2 (OR 1.04, 0.53-2.01 in women; OR 0.91, 0.36-2.27 in men). Among 16 to 24 year-olds, there was at least a three-fold increase in the odds of ever having been diagnosed with chlamydia (OR in women: 3.52, 2.47-5.01; OR in men: 4.40, 2.11-9.16), and at least a two-fold increase in the odds of having been recently diagnosed (OR in women 1.99, 1.12-3.54; OR in men 4.08, 1.40-11.8). There was no notable difference in these comparisons when limiting to participants resident in England (data not shown).

Table 6-5: Percentage with a prevalent chlamydia infection, ever diagnosed with chlamydia and recently diagnosed with chlamydia by survey and odds ratio (OR) for difference between surveys (sexually-experienced 16-24 year-olds)

	Natsal-2		Natsal-3		Natsal-3 v Natsal-2			Bases (W,UW)	
	%	95%C.I	%	95%C.I	OR	95%CI	p	Natsal-2	Natsal-3
Women									
Ever diagnosed with chlamydia	3.8%	(2.8-5.2)	12.3%	(10.6-14.1)	3.52	(2.47 - 5.01)	<0.001	1246, 1188	968, 1740
Diagnosed with chlamydia in the last year	1.5%	(0.9-2.4)	3.0%	(2.2-4.0)	1.99	(1.12 - 3.54)	0.019	1239, 1188	968, 1740
Prevalent chlamydia infection[a]	3.1%	(1.8-5.2)	3.2%	(2.2-4.6)	1.04	(0.53 - 2.01)	0.92	348, 366	513, 821
Men									
Ever diagnosed with chlamydia	1.3%	(0.6-2.5)	5.3%	(4.1-6.7)	4.40	(2.11 - 9.16)	<0.001	1224, 985	1003, 1375
Diagnosed with chlamydia in the last year	0.5%	(0.2-1.3)	2.0%	(1.3-3.0)	4.08	(1.40 - 11.84)	0.010	1222, 985	1003, 1375
Prevalent chlamydia infection[a]	2.9%	(1.3-6.3)	2.6%	(1.7-4.0)	0.91	(0.36 - 2.27)	0.83	357, 282	533, 690

[a] *18 to 24 year-olds*

6.4.2.1 Correction for measurement error arising from imperfect diagnostic tests

The difference between the 'test-adjusted' (i.e. adjusted for assay used) and the 'detection strategy-adjusted' (i.e. adjusted for assay and specimen collection device) prevalence estimates was negligible (<0.1% difference among men; 0.1% difference among women). This is to be expected, as nucleic acid amplification tests (NAATs) can detect chlamydia at very low organism loads,[259,260] thus the additional urine concentration provided by the FirstBurst device makes little difference to the results achieved using NAATs.[233] Given this negligible difference, the 'detection strategy-adjusted' estimates are presented for completeness.

The point estimate of the ‘detection strategy-adjusted’ prevalence was slightly lower than the unadjusted prevalence estimate in Natsal-2 among both women and men aged 18 to 24 (Figure 6-5). This might seem initially counterintuitive, as there is often a tendency to focus on imperfect sensitivity of tests and resultant false-negatives, thus creating an expectation that the lower sensitivity of LCx compared to AC2 would have underestimated chlamydia prevalence in Natsal-2. However, at such low levels of prevalence, small differences in the specificity dominate the direction of the measurement error.

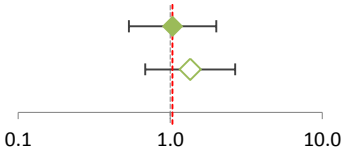
After adjustment for differences in the detection strategy, the prevalence in Natsal-3 was non-significantly higher than the adjusted prevalence in Natsal-2 among both men (2.6% vs 2.2%, OR 1.12, 0.38-3.28) and women (3.2% vs 2.5%, OR 1.35, 0.69-2.68). Thus, all else being equal, if Natsal-2 tests had been carried out using the same detection strategy as in Natsal-3 the estimated prevalence in Natsal-3 would likely have been higher than that of Natsal-2, but this would not have amounted to a statistically significant difference.

Figure 6-5: Odds ratio of chlamydia prevalence in Natsal-3, compared to unadjusted and 'detection strategy adjusted' prevalence in Natsal-2 (sexually-experienced 18-24 year-old women and men)

The solid markers and red dashed lines, show the unadjusted OR for prevalence in Natsal-3 compared to Natsal-2. Each open marker shows the OR of the unadjusted Natsal-3 prevalence compared to the 'detection strategy adjusted' prevalence in Natsal-2.

Women aged 18-24

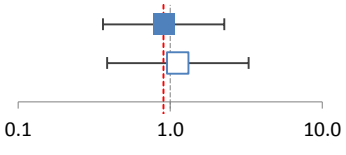
Natsal-2 comparison prevalence	Natsal-2 'prevalence'	Natsal-3 prevalence	Odds ratio (Natsal-3 v Natsal-2)
Unadjusted	3.1% (1.8-5.2)	3.2% (2.2-4.6)	1.04 (0.53-2.01)
Natsal-2 adjusted for test and specimen-collection	2.5%(1.0-4.9)	3.2% (2.2-4.6)	1.35 (0.69-2.68)



Prevalence lower in Natsal-3 ← → Prevalence higher in Natsal-3

Men aged 18-24

Natsal-2 comparison prevalence	Natsal-2 'prevalence'	Natsal-3 prevalence	Odds ratio (Natsal-3 v Natsal-2)
Unadjusted	2.9% (1.3-6.3)	2.6% (1.7-4.0)	0.91 (0.36-2.27)
Natsal-2 adjusted for test and specimen-collection	2.2% (0.4-6.2)	2.6% (1.7-4.0)	1.12 (0.38-3.28)



Prevalence lower in Natsal-3 ← → Prevalence higher in Natsal-3

6.4.2.2 Combining urine infections with recent screen-detected diagnoses

In Natsal-3, 0.9% of men and 1.6% of women aged 18 to 24 with a valid chlamydia test result had a 'screen-detected' diagnosis (i.e. reported a non-clinically indicated reason for their last test) in the last year. Thus in Natsal-3, 4.4% of women and 3.5% of men aged 18 to 24 years had a prevalent chlamydia infection and/or a screen-detected diagnosis in the last year. The proportion of Natsal-3 participants who had either a screen-detected diagnosis or a prevalent infection was non-statistically significantly higher than the proportion with a prevalent infection in Natsal-2 among both women (4.4% versus 3.1%, OR 1.45 95%CI 0.75-2.80) and men (3.5% versus 2.9%, OR 1.21

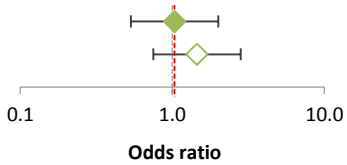
95%CI 0.49-2.97) (Figure 6-6). Thus, all else being equal, and assuming a) that in the absence of screening all these 'screen-detected' infections would have persisted to the point of the Natsal-3 interview and b) that there were no screen-detected infections in Natsal-2, there would have been a greater increase in prevalence between surveys than was observed. This would not have been detectable as a significant difference.

Figure 6-6: Hypothetical scenario, showing odds ratio of chlamydia prevalence plus 'screen-detected' diagnosis in Natsal-3, compared to unadjusted prevalence in Natsal-2 (sexually experienced 18-24 year-old women and men).

The solid markers and red dashed lines, show the unadjusted OR for prevalence in Natsal-3 compared to Natsal-2. Each open marker shows the OR of the 'screen-detected diagnoses'-adjusted prevalence in Natsal-3 compared to the unadjusted Natsal-2 prevalence.

Women aged 18-24

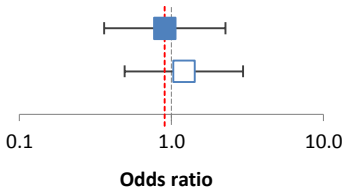
Natsal-3 comparison prevalence	Natsal-2 prevalence	Natsal-3 'prevalence'	Odds ratio (Natsal-3 v Natsal-2)
Unadjusted	3.1% (1.8-5.2)	3.2% (2.2-4.6)	1.04 (0.53-2.01)
Natsal-3 adjusted for recent, 'screen-detected' diagnoses	3.1% (1.8-5.2)	4.4% (3.1-6.3)	1.45 (0.75-2.80)



Prevalence lower in Natsal-3 ← → Prevalence higher in Natsal-3

Men aged 18-24

Natsal-3 comparison prevalence	Natsal-2 prevalence	Natsal-3 'prevalence'	Odds ratio (Natsal-3 v Natsal-2)
Unadjusted	2.9% (1.3-6.3)	2.6% (1.7-4.0)	0.91 (0.36-2.27)
Natsal-3 adjusted for recent, 'screen-detected' diagnoses	2.9% (1.3-6.3)	3.5% (2.4-5.0)	1.21 (0.49-2.97)



Prevalence lower in Natsal-3 ← → Prevalence higher in Natsal-3

6.4.2.3 Adjustment for hypothetical unmeasured differences between participants and non-participants

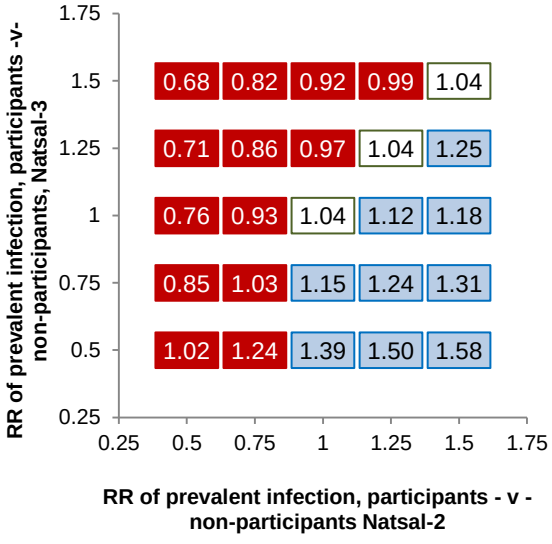
Figure 6-7 shows the 'participation-adjusted' OR across the range of hypothetical combinations of participation bias in Natsal-2 and Natsal-3 specified in section 6.3.3.5 for 18 to 24 year-old women and men. ORs

presented in red boxes are those where the comparison of ‘participation-adjusted’ prevalence estimates (Table 6-6) resulted in an OR smaller than that using the unadjusted prevalence estimates; those in blue are where the participation-adjusted OR are greater than the unadjusted OR and those which are unshaded indicate where the participation-adjusted and unadjusted OR where equivalent (to 2 decimal places). Under the applied assumptions, the ‘participation-adjusted’ OR of prevalent infection in Natsal-3 compared to Natsal-2 ranged from 0.68 to 1.58 for women and 0.59 to 1.37 for men.

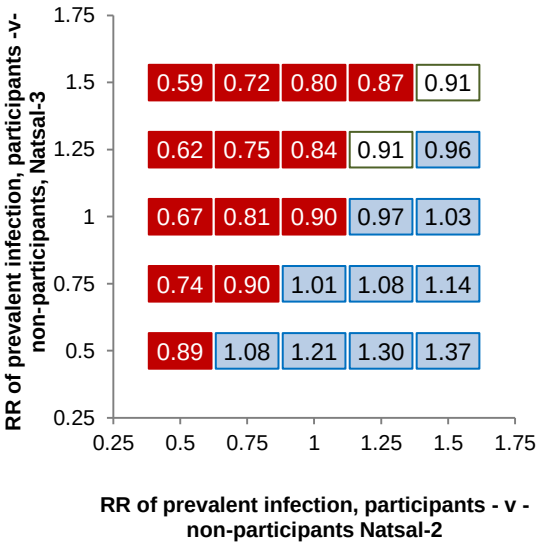
Figure 6-7 Hypothetical odds ratio of prevalent infection in Natsal-3 versus Natsal-2 under different assumptions of unmeasured participation bias (sexually-experienced 18-24 year-olds)

Figures show hypothetical, 'participation-adjusted' odds ratios of prevalent infection in Natsal-3 versus Natsal-2 using a weighted prevalence under different assumptions of the relative risk of having a prevalent infection in participants versus non-participants in each survey (see Table 6-6). The colours of the boxes show whether the participation-adjusted' OR is smaller (red boxes), larger (blue boxes) or the same (unshaded boxes) as the OR estimated using the unadjusted prevalence estimates.

Women



Men



Key:

1.00	OR of 'participation-adjusted prevalence is smaller than that using unadjusted prevalence (i.e. OR of difference between surveys would have been underestimated)
1.00	OR of 'participation-adjusted prevalence is equivalent to that using unadjusted prevalence (i.e. OR of difference between surveys would not have been affected.)
1.00	OR of 'participation-adjusted prevalence is larger than unadjusted prevalence (i.e. OR of difference between surveys would have been overestimated)

Table 6-6: Hypothetical effect of unmeasured participation biases on estimates of difference in prevalence in Natsal-2 and Natsal-3 (sexually-experienced 18-24 year-olds)

Natsal-2			Natsal-3		
(a) Relative risk of prevalent infection, participants v non-participants	(b) Hypothetical prevalence in non-participants	(c)Hypothetical 'participation-adjusted' prevalence	(d Relative risk of prevalent infection, participants v non-participants	(e) Hypothetical prevalence in non-participants	(f) Hypothetical 'participation-adjusted' prevalence
0.5	6.2%	4.2%	0.5	6.4%	4.3%
0.5	6.2%	4.2%	0.75	4.3%	3.6%
0.5	6.2%	4.2%	1	3.2%	3.2%
0.5	6.2%	4.2%	1.25	2.6%	3.0%
0.5	6.2%	4.2%	1.5	2.1%	2.9%
0.75	4.1%	3.5%	0.5	6.4%	4.3%
0.75	4.1%	3.5%	0.75	4.3%	3.6%
0.75	4.1%	3.5%	1	3.2%	3.2%
0.75	4.1%	3.5%	1.25	2.6%	3.0%
0.75	4.1%	3.5%	1.5	2.1%	2.9%
1	3.1%	3.1%	0.5	6.4%	4.3%
1	3.1%	3.1%	0.75	4.3%	3.6%
1	3.1%	3.1%	1	3.2%	3.2%
1	3.1%	3.1%	1.25	2.6%	3.0%
1	3.1%	3.1%	1.5	2.1%	2.9%
1.25	2.5%	2.9%	0.5	6.4%	4.3%
1.25	2.5%	2.9%	0.75	4.3%	3.6%
1.25	2.5%	2.9%	1	3.2%	3.2%
1.25	2.5%	2.9%	1.25	2.6%	3.0%
1.25	2.5%	2.9%	1.5	2.1%	2.9%
1.5	2.1%	2.7%	0.5	6.4%	4.3%
1.5	2.1%	2.7%	0.75	4.3%	3.6%
1.5	2.1%	2.7%	1	3.2%	3.2%
1.5	2.1%	2.7%	1.25	2.6%	3.0%
1.5	2.1%	2.7%	1.5	2.1%	2.9%

Notes on calculations
(b) Measured prevalence in participants (3.1%) x (a)
(c) Weighted prevalence of (b) and 3.1% using response rate (65.4%)[171]
(e) Measured prevalence in participants (3.2%) x (d)
(f) Weighted prevalence of (b) and 3.2% using response rate (67.3%)[5]

Figure 6-7 shows that where the extent and direction of the hypothetical participation bias was similar in each year, even though each estimate of prevalence may itself be biased, the impact on comparisons between the years was minimal. For example, if in both Natsal-2 and Natsal-3, the relative risk of

having a prevalent infection in participants v non-participants in 18 to 24 year-old women was 1.25 in each year, the 'participation-adjusted' prevalence would have been 2.9% in Natsal-2, compared to the 3.1% that was actually estimated in the survey; in Natsal-3, the 'participation-adjusted' prevalence would have been 3.0%, compared to the 3.2% actually measured. Although in this scenario the actual estimates in both Natsal-2 and Natsal-3 would have been biased towards a higher prevalence, the resulting ORs of testing positive in Natsal-3 versus Natsal-2 are equivalent (to 2 decimal places), being 1.04 for both the 'participation-adjusted' OR and the unadjusted OR.

Figure 6-7 also shows that the potential for comparisons between surveys to be affected was greater where the direction of the hypothetical bias was the same, but the extent was different. Again taking the example of 18 to 24 year-old women, if the relative risk of having a prevalent infection in participants v non-participants was 1.25 in Natsal-2 but 1.5 in Natsal-3, the 'participation-adjusted' OR would be 0.99, compared to the unadjusted OR of 1.04. The most extreme impact on comparisons between surveys arose from where the direction of bias was assumed to be different in each survey, and the difference between participants and non-participants in each year was large.

6.4.2.4 Indicators of change in sexual behavioural risk of transmission

Reported numbers of sexual partners, non-condom use and prevalence of non-vaccine HPV types (see section 6.3.3.6), tended to be similar or slightly higher for women and lower for men in Natsal-3 compared to Natsal-2 (Figure 6-8), although none of the observed differences were statistically significant. In both women and men, the proportion reporting non-use of condoms at last sex was very similar between the surveys. However, after stratifying by partnership type,

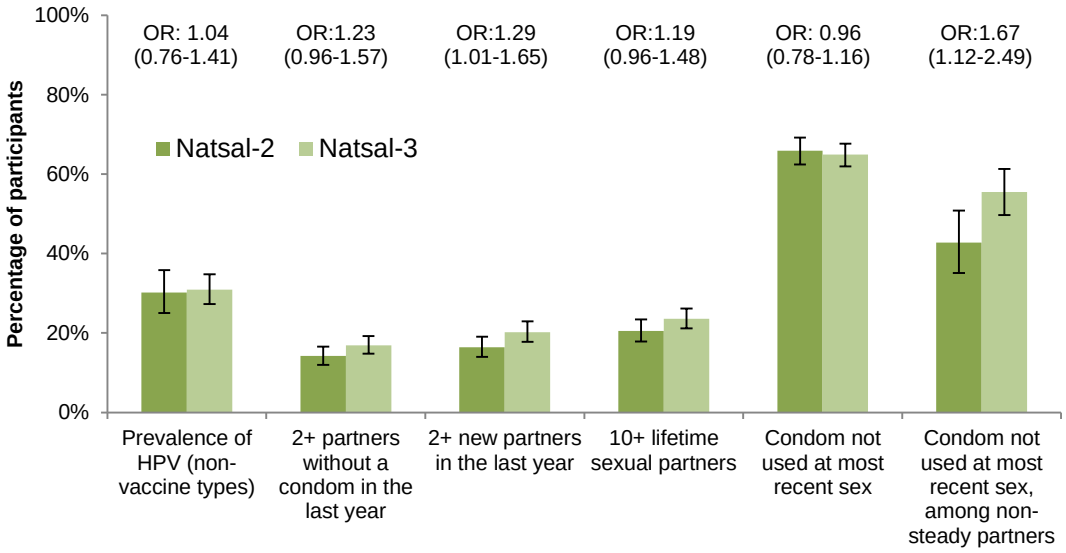
the percentage who reported not having used a condom at last sex increased between surveys from 43% to 56% in women and 34% to 38% in men whose last sex was with a non-steady partner. This was not a statistically significant difference.

There was no change in the median age at first intercourse among sexually-experienced 18 to 24 year-olds between Natsal-3 and Natsal-2 (16 years among women and men). However, among Natsal-3 participants, the proportion who reported having had sex by the age of 16 increased with decreasing age. The proportion of women who reported having sex by age 16 increased by an average of 3% per year (relative to that measured in the previous year) from 2000 to 2012 in both women (prevalence ratio 1.03, 1.02-1.05, $p<0.001$) and men (prevalence ratio 1.03, 1.01-1.06, $p=0.003$) (Figure 6-9).

Figure 6-8: Prevalence of non-vaccine HPV and selected sexual behaviours among sexually experienced 18-24 year-olds in Natsal-2 and Natsal-3

Error bars show 95% confidence intervals on the prevalence of non-vaccine HPV or reported sexual behaviour. OR: Unadjusted odds ratio (95%CI shown in parentheses) for Natsal-3 versus Natsal-2, derived using logistic regression. Reference groups are those without the reported characteristic.

Women



Men

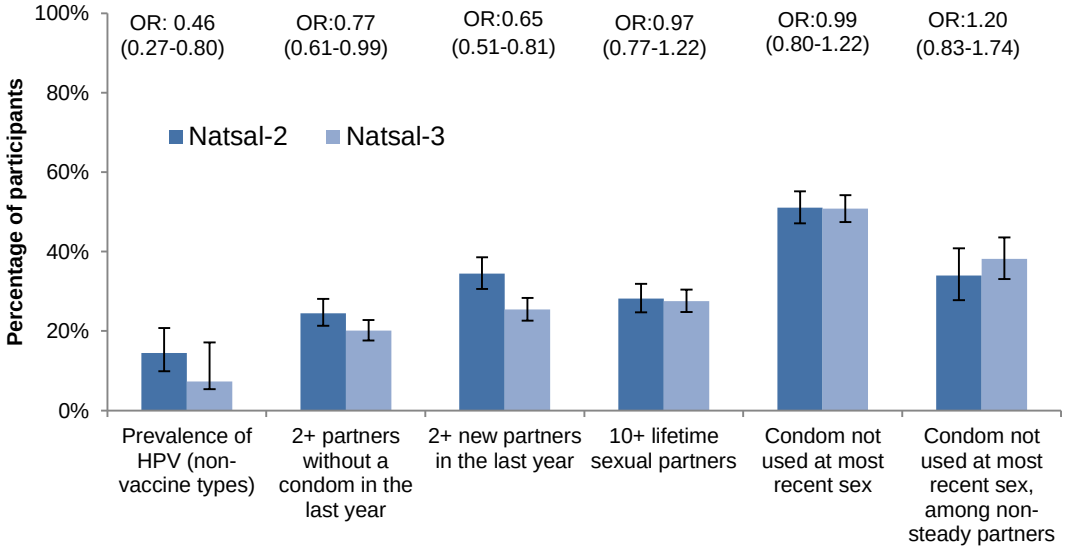
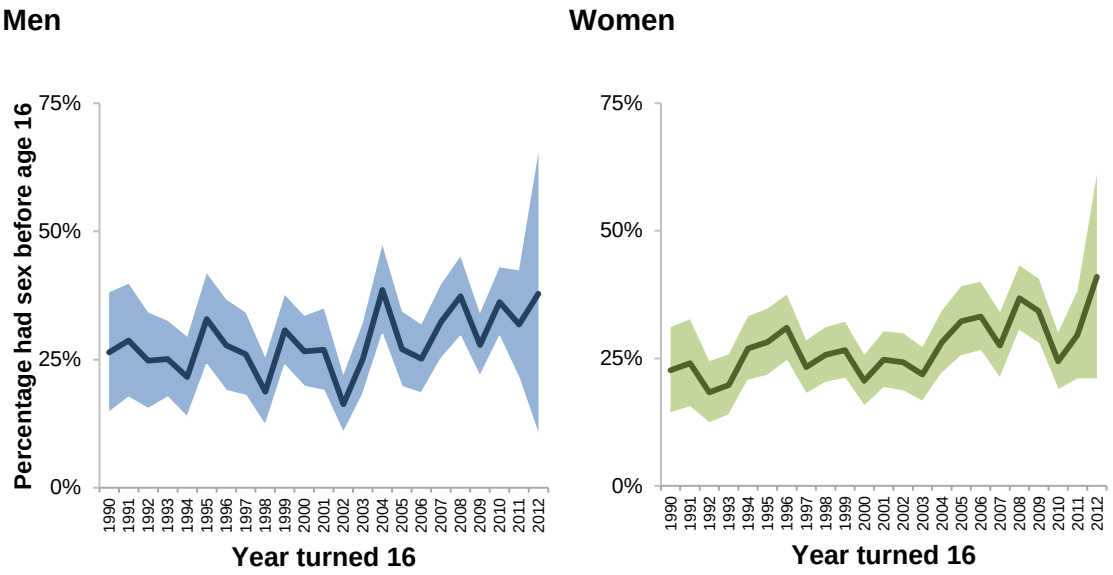


Figure 6-9: Proportion reporting having had heterosexual sex before the age of 16 by year turned 16 (Natsal-3)

The shaded area shows 95% confidence intervals. Participants who report having had sex before the age of 13 are excluded from the denominator.



6.5 Discussion

6.5.1 Key findings

There was no significant difference in chlamydia prevalence, as measured in the second and third Natsal surveys, in 2010-12 compared to that in 1999-2001. Adjusting for the different tests used in each survey did not alter the conclusions that can be made about the difference in chlamydia prevalence.

6.5.2 Strengths and limitations

The main strength of this analyses was that it used data from two probability surveys with high response rates, with the two surveys having been carried out before (Natsal-2) and after (Natsal-3) the implementation of the NCSP.

The sample size available was the main limitation for the comparisons of prevalence for each year. As a result, the Natsal surveys were consistent with a wide range of scenarios, from at least a halving of the odds of infection to more than doubling of the odds of infection between surveys (unadjusted 95%CIs ranged from at least 0.5 to 2 in both women and men). None of the adjusted estimates (i.e. adjusted for detection strategy, for screen-detected diagnoses or for hypothetical unmeasured participation bias) approached statistical significance, although the direction of the adjustments was informative. This analysis showed that in some scenarios, unmeasured participation bias may affect comparisons between surveys. However even after adjustment for a wide range of scenarios, the point estimates for prevalence differences lay within the 95% confidence intervals for odds ratios based on the unadjusted Natsal estimates, again emphasising the limitations arising from the available sample size. One alternative to investigating change in chlamydia prevalence relative to HPV prevalence and sexual behaviours would have been to include these variables as confounders in a regression model. The small absolute numbers of prevalent infections meant results from such an analysis would be subject to considerable error, so this was not pursued.

Adjustment for the differences in the detection strategy used in each survey was limited by the data available on the sensitivity and specificity of the LCx and the AC2 and the urine cup compared to the FirstBurst urine collection device. As the adjusted prevalence used the AC2 as the gold standard, this may be a biased estimator of the 'true' prevalence of infection in the population if the AC2 is not a perfect test. An alternative approach would have been to also adjust the Natsal-3 prevalence for AC2 performance characteristics. However this approach would introduce substantial uncertainty, as measuring the sensitivity

and specificity of diagnostic tests is highly dependent on the gold standard used, and there is no agreed reference standard for chlamydia NAATs.[244] The use of the point estimate of the sensitivity and specificity LCx versus AC2 is also an oversimplification, which did not incorporate the error within the sensitivity and specificity measurement. However as there was no significant difference when using these adjusted estimates, even wider confidence intervals would not alter the interpretation. There is only one published study which compares the FirstBurst to the urine cup. This was limited to samples from men and used a different NAAT (Amplicor CTY/NG PCR)[233]. However additional studies are unlikely to have affected these findings as low prevalences are more subject to error arising from imperfect specificity rather than sensitivity, and only marginal additional benefit would be expected from increased organism load when measuring chlamydia prevalence among the general population.

In comparing the prevalence plus 'screen-detected' diagnoses, it was assumed that all diagnoses in Natsal-2 had come about as a result of clinically-indicated testing. As no data were collected on reason for test, this is a simplification and it is feasible that a proportion of diagnoses may have come about as a result of asymptomatic screening activity.

The analysis did not account for all of the differences between the surveys. Degradation of specimens during transit (and storage, for HPV) may also have led to prevalence having been underestimated in Natsal-2 and Natsal-3. This was not investigated in detail, as quantitative estimates of the loss of precision were not available. This was acknowledged at the time of the Natsal-2 survey as a potential cause of underestimating prevalence.[133,234] Degradation is also

feasible in Natsal-3, although all specimens were transported in accordance with the manufacturer's instructions, and AC2 specimens are considered to be stable at room temperature for several months. Given the large confidence intervals on the unadjusted and adjusted estimates of prevalence difference, this potential difference is again unlikely to materially affect conclusions which can be made based on the Natsal surveys.

Prevalent chlamydia infection was measured in urine samples. This may have missed some infections in women among whom vulvovaginal swabs demonstrate marginally higher sensitivity.[261] Urine sampling will also have missed rectal infections, leading to underestimation of the total currently infected with chlamydia. However, the impact on our findings is likely minimal as men who have sex with men made up a small proportion of this sample of Natsal participants.[235]

6.5.3 Implications for evaluation of chlamydia control

Although comparisons between the surveys had limited power due to the sample size available, there was no evidence to support there having been a decrease in prevalence between the surveys. However, there was some indication that risk behaviours relating to transmission risk may have increased among young women, but not in men. Additionally, the analysis that combined 'screen-detected' diagnoses with prevalent infections in Natsal-3 suggested that if all screen-detected infections in Natsal-3 had persisted to the time of the interview, then the prevalence in Natsal-3 would have been higher. Thus, in the absence of widespread chlamydia screening, chlamydia incidence and prevalence might have been expected to increase. However this remains an unproven hypothesis, as there is no evidence to determine how many, if any of

the ‘screen-detected’ infections would have persisted to the point of the interview and an increase in risk behaviours was not seen in all groups, or consistently across several behaviours, and there was no increase seen in non-vaccine high risk HPV types among women.

6.5.4 Summary

In summary, there is no definitive evidence from the Natsal surveys to suggest that chlamydia prevalence has changed in either absolute terms or relative to indicators of sexual behavioural risk during a period of increased chlamydia testing and screening. Returning to the notion of process monitoring described in Chapter 2, it is important to understand how chlamydia screening has been delivered to consider whether we would have expected prevalence to have decreased over this period. In the next chapter, I use data from Natsal-3 to investigate the implementation of chlamydia screening in relation to risk of infection in more detail.

7 Chlamydia prevalence, diagnosis and testing among 16 to 24 year-old participants in the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3)

In the previous chapter I compared the prevalence of chlamydia estimated in the second and third Natsal surveys, which were conducted before and after the implementation of the NCSP, and found no definitive evidence to suggest that chlamydia prevalence had decreased in the ten years between the surveys. In this chapter I use Natsal-3 data to further our understanding of how chlamydia screening had been delivered in practice up to 2012.

7.1 Background

As Natsal-3 measured prevalent infection and also collected data on self-reported chlamydia testing and diagnoses, the survey presents a unique opportunity to explore factors associated with testing and infection within the same population, three to five years after the NCSP had been nationally-implemented. Sonnenberg *et al* have previously reported an overview of STI prevalence and service use using data from Natsal-3, including chlamydia prevalence and self-reported testing in the last year among 16 to 24 year-olds.[23] Although Sonnenberg *et al* reported prevalence by age group, factors associated with prevalent infection were assessed among all 16 to 44 year-olds and only a limited number of factors associated with chlamydia prevalence and testing were explored (age group, area-level deprivation, number of sexual partners in the last year, sexual partners in the last year without a condom [investigated for prevalence only], age at first sex and any same-sex experience). In this chapter, a detailed analysis of 16 to 24 year-olds in Britain (as the age group targeted by the NCSP) is presented. Factors associated with

prevalent chlamydia infection, previous chlamydia diagnosis and chlamydia testing are described and compared to assess the extent to which, up to 2012, opportunistic chlamydia screening was reaching 16 to 24 year-olds at risk of chlamydia.

7.2 Aims & objectives

To investigate whether chlamydia screening patterns indicate that chlamydia screening has been delivered in such a way that we would expect it to effect a reduction in the incidence or prevalence of infection. This aim was addressed through the following objectives:

- Using data from Natsal-3, to describe self-reported chlamydia testing, self-reported diagnosis and prevalent infection (detected in urine) among 16 to 24 year-olds living in Britain in 2010-12 by sociodemographic, clinical and behavioural variables.
- To compare factors associated with self-reported chlamydia testing, self-reported diagnosis and prevalent infection (detected in urine) among 16 to 24 year-olds in Natsal-3.

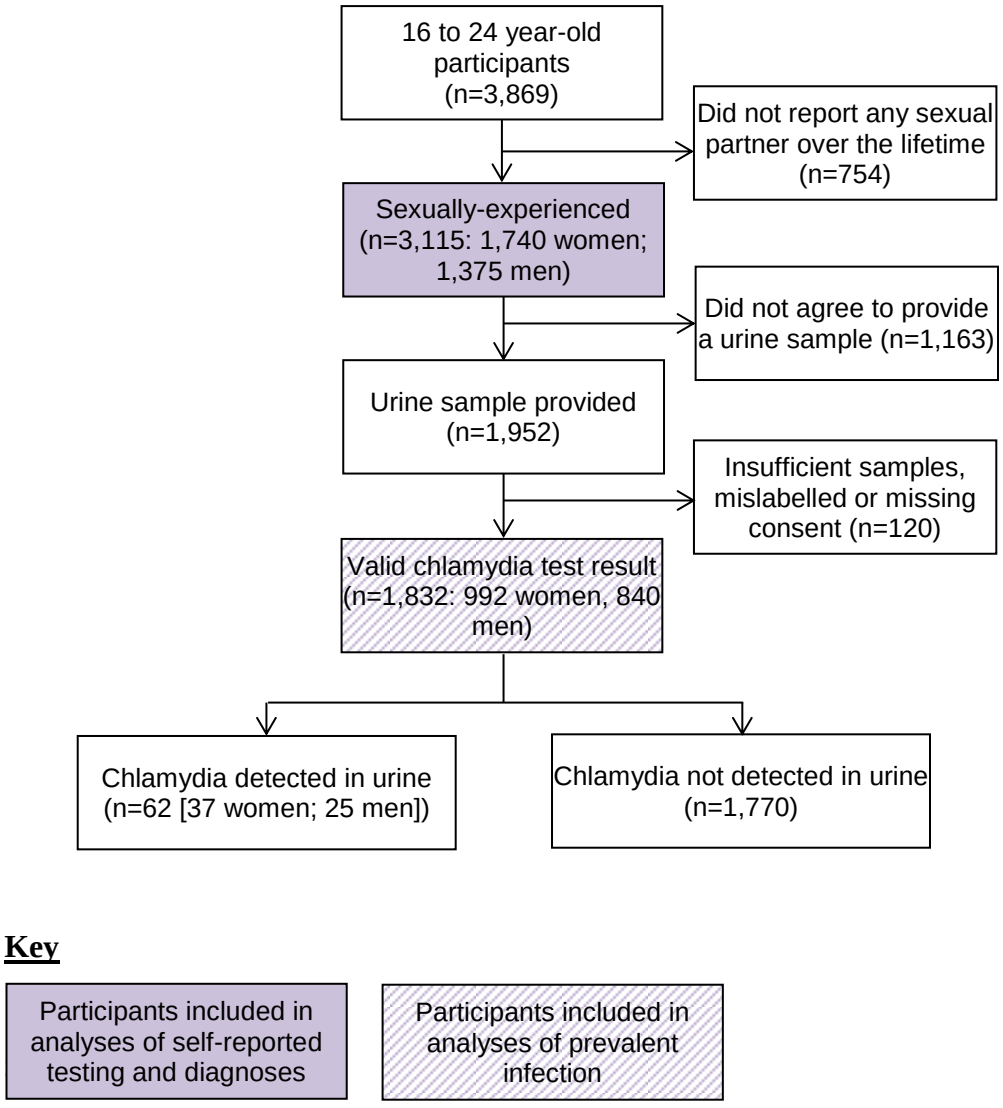
7.3 Methods

7.3.1 Participants

A flow chart of participants included in this analysis is presented in Figure 7-1. Analyses of recent testing (self-reported testing in the last year) and recent diagnosis (self-reported diagnosis in the last year) were based on sexually-experienced 16 to 24 year-olds (n=3,115). Analyses of prevalent infection (*C. trachomatis* detected in urine) were among those who provided a urine sample

for STI testing and for whom a valid chlamydia test result is available (n=1,832, 62 of whom had a prevalent chlamydia infection detected in urine).

Figure 7-1: Flow chart showing participants included in analyses of self-reported chlamydia testing, self-reported diagnosis and prevalent infection detected in urine (16 to 24 year-old Natsal-3 participants)



7.3.2 Statistical analysis

Analyses were carried out using Stata 12.1, accounting for the weighting, clustering and stratification of the Natsal data[23,172,235] as set out in the previous chapter (section 6.3.3).

Factors associated with prevalent infection, recent diagnosis and recent testing were investigated using univariable and multivariable logistic regression, for women and men separately. While the overall percentage of 16 to 24 year-olds who reported having been diagnosed with chlamydia (ever or in the last year) is reported among the sexually-experienced population, risk factors for recent diagnosis were investigated among those with a recent test so that results represent associations with infection at the time of test and not with testing per se. Sociodemographic and behavioural factors reported to be associated with STI risk were included as predictor variables.[133,262,263] Associations with deprivation were explored using both residence-based (quintile of IMD for the LSOA of residence) and individual-based (age left school) measures. Sexual behaviours investigated included numbers of sexual partners in the last year (total, new, without a condom), number of lifetime sexual partners and condom use at last sex. Frequency of binge drinking (>6/8 units on one occasion in women/men) was included as a proxy for sexual risk behaviour that may not be captured in reported numbers of sexual partners.

Two approaches to multivariable modelling were explored; maximal and parsimonious models were constructed for all outcomes of interest. To fit parsimonious models, variables found significant at $p<0.1$ in univariable analyses were entered into a multivariable model selection process based on backwards selection whereby variables were removed from the model if the

statistical significance of their association with the outcome had an associated p value of >0.05. Only those variables significantly associated with the outcome were retained in the final parsimonious models. For maximal models, all variables included in univariable models were included with two exceptions: number of sexual partners in the last year was not included due to collinearity with other sexual partnership variables; age left school was not included as data were unavailable for 16 year-olds. The results from the two models were largely comparable (see Appendix 2 for a detailed comparison). Results from the maximal models are therefore presented in the results section below to provide odds ratios (OR) adjusted for potential confounders.

In order to explore how chlamydia infections were distributed across different risk groups, the proportion reporting different demographic and behavioural factors was calculated among a) individuals with a prevalent infection, b) individuals with a recent diagnosis and c) the sexually-experienced population.

Sub-group analyses by country (England, Scotland and Wales) were performed when the difference in screening practice between countries was of potential relevance.

7.4 Results

7.4.1.1 Reason and location for last test (Natsal-3)

Among 16 to 24 year-olds who reported recently testing, fewer than 10% reported a clinical indication (symptoms; a partner with chlamydia/symptoms; check-up after a previous diagnosis) for their last test (Table 7-1). Around three-quarters of women and half of men had last been tested in either a sexual

health clinic, GP surgery, or a family planning clinic. When limiting to women and men recently diagnosed, 29.0% had last been tested due to having symptoms and 20.9% due to having a partner diagnosed with chlamydia or with symptoms (Table 7-1). Almost all of (95.4%) of those recently diagnosed had been most recently tested in a sexual health clinic, family planning clinic, or GP surgery. Whereas 17% of all recent tests had been carried out in educational settings, only 1.7% of those recently diagnosed reported their last test in this setting.

Table 7-1: Reason and location of most recent chlamydia test, among those tested for chlamydia in the last year, by whether diagnosed in last year (16-24 year-old sexually-experienced women and men)

	By sex				By whether diagnosed in the last year[a]			
	Women		Men		Diagnosed in the last year		Not diagnosed in the last year	
	Percent	95%CI	Percent	95%CI	Percent	95%CI	Percent	95%CI
Denominator (W,UW)	523, 943		347, 475		48, 81		816, 1330	
Reason for most recent test								
Had symptoms	4.2%	(3.0-5.8)	4.2%	(2.7-6.5)	29.0%	(19.0-41.5)	2.7%	(1.9-3.8)
Partner diagnosed with chlamydia or had symptoms	2.8%	(1.7-4.5)	3.8%	(2.4-6.1)	20.9%	(12.8-32.2)	2.2%	(1.4-3.4)
Check up after a previous positive	1.3%	(0.63-2.6)	0.95%	(0.33-2.7)	8.6%	(3.2-21.1)	0.7%	(0.4-1.4
Wanted a check-up / offered a test / worried about risk	84.9%	(82.1-87.4)	87.3%	(83.8-90.1)	37.2%	(26.2-49.86)	88.7%	(86.8-90.4)
Other	6.8%	(5.3-8.7)	3.7%	(2.3-6.0)	4.3%	(1.5-12.0)	5.7%	(4.5-7.1)
Location of most recent chlamydia test								
Sexual health clinic	28.9%	(25.5-32.6)	30.5%	(25.9-35.5)	62.9%	(50.4-73.9)	27.6%	(25.0-30.4)
GP surgery	35.1%	(31.7-38.6)	17.0%	(13.6-20.9)	27.1%	(17.7-39.1)	28.0%	(25.3-30.8)
NHS FP clinic	9.2%	(7.4-11.4)	4.3%	(2.7-6.8)	5.4%	(1.6-16.3)	7.3%	(6.0-8.9)
School, college or university	11.6%	(9.4-14.2)	24.5%	(20.4-29.1)	1.7%	(0.4-7.2)	17.5%	(15.2-20.1)
Elsewhere	15.2%	(12.9-17.8)	23.8%	(19.3-28.9)	2.9%	(1.0-8.1)	19.6%	(17.2-22.2)

GP: General practice; FP: Family planning. [a]Women and men were combined due to small denominator for diagnosed in the last year.

7.4.1.2 Factors associated with infection, diagnosis and testing

Table 7-2 explores associations between sociodemographic and behavioural variables and prevalent infection, recent testing and recent diagnosis. In univariable analyses, higher numbers of sexual partners (total/new/without a condom) in the last year were significantly ($p<0.05$) associated with prevalent infection among women and men. In women, area-level deprivation and frequency of binge drinking were also associated with prevalent infection. Among men, number of lifetime sexual partners, age group, age left school, age at first sex, and condom non-use at last sex were significantly associated with prevalent infection. Similar factors were associated with recent diagnosis among those tested. In multivariable analyses, living in more deprived areas and more frequent binge drinking remained significantly associated with having a prevalent infection in women (AOR 4.23, 95%CI 1.53-11.6, p=0.01; AOR 2.51, 95%CI 1.08-5.76, p=0.01 respectively). Being aged 20 to 24 years (AOR 7.54, 95%CI 1.37-41.3, p=0.02), living in more deprived areas (AOR 3.75, 95%CI 1.11-12.5, p=0.04) and higher numbers of lifetime sexual partners ($\geq$10 versus 1-4, AOR 8.69, 1.21-62.0, p=0.03) remained significantly associated with prevalent infection in men.

Table 7-2a: Percentage, unadjusted and adjusted odds (OR/AOR) ratios for prevalent chlamydia infection, self-reported diagnosis in the last year and self-reported testing by sociodemographic and behavioural factors (16-24 year-old sexually-experienced women, Natsal-3)

	Prevalent chlamydia infection detected in urine (n=992)								Diagnosed with chlamydia in the last year (among those tested in the last year) (n=940)								Tested for chlamydia in the last year (n=1,736)								Denominator (weighted, unweighted) [a]		
	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	Infection	Diagnosis	Tested
Age group																											
16-19	3.8%	(2.2-6.3)	1.00	-	0.36	1.00	-	0.50	6.0%	(3.8-9.2)	1.00	-	0.62	1.00	-	0.58	56.6%	(52.5-60.6)	1.00	-	0.16	1.00	-	0.15	214, 395	193, 375	343, 672
20-24	2.7%	(1.7-4.3)	0.71	(0.35-1.46)		0.71	(0.27-1.87)		5.1%	(3.4-7.6)	0.86	(0.46-1.60)		0.80	(0.35-1.78)		52.8%	(49.2-56.4)	0.86	(0.69-1.06)		0.82	(0.62-1.07)		383, 597	329, 565	623, 1064
Country[c]																											
England	2.9%	(2.0-4.3)	1.00	-	0.53	1.00	-	0.48									57.1%	(54.1-60.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	504, 817	469, 832	823, 1452
Scotland	3.1%	(1.1-8.6)	1.08	(0.35-3.33)		1.34	(0.43-4.14)										32.4%	(24.4-41.5)	0.36	(0.24-0.54)		0.29	(0.18-0.45)		56, 103	30, 58	91, 178
Wales	5.3%	(1.9-13.8)	1.87	(0.63-5.60)		1.88	(0.63-5.54)										45.6%	(36.2-55.4)	0.63	(0.42-0.94)		0.53	(0.32-0.85)		37, 72	24, 50	52, 106
IMD quintile of LSOA of residence[d]																											
2 least deprived	1.3%	(0.5-3.4)	1.00	-	**0.01**	1.00	-	**0.01**	4.8%	(2.8-8.1)	1.00	-	0.23	1.00	-	0.36	54.2%	(49.5-58.8)	1.00	-	0.99	1.00	-	0.94	213, 355	183, 319	338, 595
Middle quintile	1.8%	(0.8-4.2)	1.37	(0.38-4.90)		1.40	(0.39-4.98)		3.5%	(1.6-7.3)	0.71	(0.27-1.86)		1.06	(0.37-3.04)		54.4%	(48.0-60.7)	1.01	(0.74-1.38)		1.03	(0.71-1.48)		111, 174	102, 176	189, 324
2 most deprived	4.9%	(3.3-7.3)	3.82	(1.35-10.8)		4.23	(1.53-11.6)		6.8%	(4.6-10.0)	1.46	(0.73-2.93)		1.70	(0.73-3.91)		54.0%	(49.8-58.2)	0.99	(0.77-1.27)		0.97	(0.73-1.29)		273, 463	236, 445	439, 817
Age left school[e]																											
17+	3.2%	(2.1-4.8)	1.00	-	0.88				5.2%	(3.6-7.5)	1.00	-	0.58				54.3%	(51.0-57.6)	1.00	-	0.70				445, 700	387, 658	715, 1217
16	3.4%	(1.9-6.0)	1.06	(0.50-2.22)					6.2%	(3.7-10.5)	1.21	(0.62-2.37)					55.5%	(50.1-60.8)	1.05	(0.82-1.35)					120, 229	109, 228	196, 405
Frequency of binge drinking																											
Never / <monthly	2.5%	(1.5-4.1)	1.00	-	**<0.01**	1.00	-	**0.01**	3.7%	(2.4-5.7)	1.00	-	**0.03**	1.00	-	0.28	52.1%	(48.7-55.5)	1.00	-	**0.01**	1.00	-	0.08	373, 598	312, 561	601, 1085
Monthly	1.2%	(0.5-3.3)	0.49	(0.16-1.52)		0.46	(0.13-1.51)		6.6%	(3.6-11.8)	1.85	(0.85-4.01)		1.91	(0.74-4.89)		52.4%	(46.6-58.2)	1.01	(0.78-1.32)		0.75	(0.54-1.02)		130, 226	112, 200	214, 375
>weekly	7.9%	(4.7-13.1)	3.35	(1.55-7.25)		2.51	(1.08-5.76)		9.4%	(5.2-16.3)	2.69	(1.25-5.80)		2.06	(0.75-5.61)		64.4%	(57.6-70.7)	1.66	(1.22-2.27)		1.16	(0.81-1.64)		95, 168	97, 177	151, 274
Age at first heterosexual sex																											
17+	1.6%	(0.7-3.7)	1.00	-	0.15	1.00	-	0.42	4.1%	(1.8-8.9)	1.00	-	0.37	1.00	-	0.93	43.9%	(38.7-49.1)	1.00	-	**<0.01**	1.00	-	0.05	188, 246	137, 215	313, 489
16	3.9%	(2.1-6.9)	2.52	(0.86-7.36)		2.20	(0.67-7.17)		5.0%	(2.8-8.9)	1.24	(0.44-3.55)		0.80	(0.26-2.42)		56.4%	(51.6-61.1)	1.66	(1.25-2.20)		1.39	(0.99-1.92)		178, 304	154, 272	273, 503
<16	4.0%	(2.4-6.6)	2.65	(0.95-7.36)		1.82	(0.60-5.42)		6.9%	(4.8-9.9)	1.76	(0.70-4.41)		0.89	(0.35-2.25)		63.9%	(59.8-67.9)	2.27	(1.75-2.94)		1.44	(1.05-1.97)		213, 415	220, 429	344, 680
Condom used for most recent sex with most recent partner																											
Yes	2.8%	(1.5-5.3)	1.00	-	0.53	1.00	-	0.29	3.4%	(1.6-7.0)	1.00	-	0.14	1.00	-	0.14	51.6%	(46.9-56.3)	1.00	-	**0.03**	1.00	-	0.97	202, 314	170, 303	330, 586
No	3.6%	(2.4-5.4)	1.28	(0.59-2.80)		1.59	(0.67-3.74)		6.3%	(4.4-8.9)	1.90	(0.81-4.49)		1.88	(0.81-4.32)		58.0%	(54.6-61.3)	1.30	(1.03-1.63)		1.01	(0.74-1.35)		352, 613	328, 592	567, 1027
Number of sexual partners in the last year																											
0 or 1	2.5%	(1.5-4.0)	1.00	-	**0.03**				3.0%	(1.7-5.4)	1.00	-	**0.01**				46.6%	(43.3-50.0)	1.00	-	**<0.01**				387, 600	291, 507	624, 1096
2	3.9%	(1.8-8.5)	1.62	(0.63-4.15)					6.6%	(3.7-11.6)	2.25	(0.98-5.18)					65.2%	(58.8-71.1)	2.15	(1.59-2.89)					90, 161	93, 178	143, 275
3 to 4	1.9%	(0.7-5.1)	0.75	(0.24-2.33)					8.8%	(5.2-14.6)	3.08	(1.34-7.05)					69.7%	(62.0-76.4)	2.63	(1.82-3.80)					63, 127	76, 146	111, 210
5+	8.3%	(3.9-16.8)	3.57	(1.39-9.17)					11.6%	(6.2-20.8)	4.19	(1.69-10.4)					74.8%	(64.4-83.0)	3.40	(2.05-5.65)					49, 93	58, 101	77, 135

Table 7-2a continued.

Number of new sexual partners in the last year																						
0	2.2% (1.3-3.7)	1.00	-	**0.03**	1.00	-	0.70	2.8%(1.5-5.0)	1.00	-	**<0.01**	1.00-	0.11	45.6%(41.9-49.3)	1.00	-	**<0.01**	1.00	-	**<0.01**	313, 495	226, 397	495, 873
1	2.8% (1.2-6.3)	1.26	(0.47-3.41)		1.17	(0.38-3.52)		4.8%(2.5-9.1)	1.76	(0.71-4.38)		1.89(0.69-5.16)		59.2%(54.0-64.2)	1.73	(1.34-2.23)		1.69	(1.25-2.27)		160, 263	156, 287	264, 485
2+	5.9% (3.5-9.8)	2.73	(1.26-5.93)		1.65	(0.50-5.39)		10.7%(7.3-15.6)	4.23	(2.04-8.79)		3.09(1.07-8.86)		70.0%(63.8-75.6)	2.79	(2.03-3.84)		1.46	(0.95-2.21)		118, 225	137, 249	197, 359
Number of sexual partners in the last year without a condom																						
0	2.9% (1.2-7.1)	1.00	-	**0.03**	1.00	-	0.18	4.2%(1.5-11.6)	1.00	-	**<0.01**	1.00-	0.84	36.4%(30.8-42.3)	1.00	-	**<0.01**			0.05	120, 173	76, 130	210, 361
1	2.2% (1.4-3.6)	0.76	(0.26-2.17)		0.34	(0.10-1.10)		3.8%(2.4-6.1)	0.90	(0.27-2.94)		0.72(0.15-3.21)		54.7%(51.4-58.0)	2.11	(1.61-2.78)		1.52	(1.03-2.24)		368, 606	319, 567	585, 1049
2+	6.3% (3.5-11.2)	2.25	(0.73-6.93)		0.49	(0.12-1.83)		10.3%(7.0-15.0)	2.60	(0.80-8.46)		0.90(0.18-4.49)		74.2%(68.3-79.4)	5.04	(3.47-7.32)		1.86	(1.09-3.15)		108, 212	126, 241	169, 322
Concurrent partnerships in last year[f]																						
No	2.7% (1.8-4.2)	1.00	-	0.19	1.00	-	0.85	4.3%(2.9-6.4)	1.00	-	0.13	1.00-	0.46	51.0%(47.8-54.2)	1.00	-	**<0.01**	1.00	-	0.05	439, 706	361, 639	710, 1256
Yes	6.3% (2.9-13.4)	2.40	(0.94-6.15)		1.34	(0.48-3.70)		8.1%(4.1-15.3)	1.95	(0.84-4.54)		0.75(0.27-2.00)		74.6%(67.1-80.8)	2.81	(1.93-4.09)		1.46	(0.93-2.28)		66, 134	78, 146	105, 196
Unknown	3.1% (1.3-7.2)	1.14	(0.43-3.04)		1.13	(0.38-3.31)		7.8%(4.3-13.9)	1.88	(0.90-3.94)		1.46(0.62-3.38)		64.6%(57.5-71.2)	1.76	(1.27-2.42)		1.53	(1.02-2.28)		73, 127	76, 144	117, 226
Number of lifetime sexual partners																						
1 to 4	2.4% (1.4-4.2)	1.00	-	0.14	1.00	-	0.67	2.1%(1.1-4.0)	1.00	-	**<0.01**	1.00-	0.08	43.5%(40.0-47.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	321, 482	218, 391	503, 894
5 to 9	2.8% (1.4-5.2)	1.15	(0.48-2.75)		0.87	(0.32-2.32)		6.2%(3.7-10.3)	3.07	(1.33-7.07)		2.40(0.90-6.37)		63.8%(58.5-68.7)	2.29	(1.76-2.96)		1.96	(1.43-2.69)		150, 267	161, 289	252, 453
10+	5.4% (2.9-9.7)	2.29	(0.97-5.39)		1.39	(0.45-4.18)		9.9%(6.5-14.7)	5.12	(2.31-11.3)		3.76(1.19-11.8)		69.6%(63.9-74.7)	2.97	(2.22-3.98)		2.11	(1.41-3.13)		121, 234	141, 254	202, 373
Ever had any same sex experience/contact																						
No	3.1% (2.1-4.4)	1.00	-	0.92	1.00	-	0.49	5.3%(3.7-7.5)	1.00	-	0.72	1.00-	0.44	51.9%(48.8-55.0)	1.00	-	**<0.01**	1.00	-	0.24	473, 750	388, 704	749, 1352
Yes	3.2% (1.4-7.1)	1.05	(0.42-2.63)		0.74	(0.30-1.76)		5.9%(3.5-10.0)	1.13	(0.57-2.24)		0.71(0.30-1.68)		61.9%(56.0-67.5)	1.51	(1.15-1.98)		1.21	(0.88-1.65)		124, 242	134, 236	218, 384

Table 7-2b: Proportion, unadjusted and adjusted odds ratios for prevalent chlamydia infection, self-reported diagnosis in the last year and self-reported testing by sociodemographic and behavioural factors (16-24 year-old sexually-experienced men, Natsal-3)

	Prevalent chlamydia infection detected in urine (n=840)								Diagnosed with chlamydia in the last year (among those tested in the last year) (n=471)								Tested for chlamydia in the last year (n=1,375)								Denominator (weighted, unweighted)[a]		
	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	Infection	Diagnosis	Tested
Age group																											
16-19	0.3%	(0.1-1.4)	1.00	-	**<0.01**	1.00	-	**0.02**	4.7%	(2.4-9.0)	1.00	-	0.41	1.00	-	0.61	40.4%	(35.9-45.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	234, 343	151, 226	374, 582
20-24	3.4%	(2.2-5.2)	10.6	(2.40-46.3)		7.54	(1.37-41.3)		6.7%	(3.9-11.1)	1.46	(0.59-3.58)		0.76	(0.26-2.15)		31.1%	(27.8-34.7)	0.67	(0.52-0.86)		0.53	(0.37-0.73)		391, 497	192, 245	629, 793
Country[c]																											
England	1.9%	(1.2-3.0)	1.00	-	0.12	1.00	-	0.27									37.3%	(34.3-40.3)	1.00	-	**<0.01**	1.00	-	**<0.01**	532, 719	316, 440	859, 1181
Scotland	5.7%	(2.1-14.3)	3.13	(1.04-9.45)		3.16	(0.78-12.8)										22.2%	(14.0-33.5)	0.48	(0.27-0.85)		0.33	(0.16-0.64)		60, 72	20, 22	89, 111
Wales	1.7%	(0.2-12.1)	0.88	(0.11-7.02)		1.20	(0.18-7.63)										12.8%	(6.9-22.3)	0.25	(0.13-0.48)		0.19	(0.08-0.40)		33, 49	7, 9	55, 83
IMD quintile of LSOA of residence[d]																											
2 least deprived	1.3%	(0.4-3.6)	1.00	-	0.14	1.00	-	**0.04**	5.2%	(2.5-10.5)	1.00	-	0.85	1.00	-	0.85	34.5%	(30.0-39.2)	1.00	-	0.89	1.00	-	0.75	241, 315	127, 180	369, 509
Middle quintile	1.6%	(0.6-4.4)	1.24	(0.26-5.88)		1.01	(0.15-6.68)		5.0%	(1.7-13.8)	0.96	(0.26-3.58)		0.68	(0.15-2.97)		33.3%	(27.4-39.9)	0.95	(0.67-1.35)		1.04	(0.70-1.52)		114, 164	60, 86	183, 263
2 most deprived	3.4%	(2.1-5.6)	2.71	(0.83-8.82)		3.75	(1.11-12.5)		6.5%	(3.6-11.4)	1.26	(0.48-3.33)		1.06	(0.42-2.64)		35.2%	(31.1-39.5)	1.03	(0.78-1.36)		1.13	(0.82-1.53)		269, 361	155, 205	450, 603
Age left school[e]																											
17+	1.6%	(0.9-2.7)	1.00	-	**0.01**				5.3%	(3.1-9.0)	1.00	-	0.49				33.6%	(30.4-37.1)	1.00	-	0.21				439, 568	233, 304	703, 927
16	5.0%	(2.7-9.2)	3.28	(1.38-7.82)					7.2%	(3.6-13.8)	1.38	(0.55-3.45)					37.8%	(32.3-43.5)	1.20	(0.91-1.58)					143, 206	87, 134	230, 334
Frequency of binge drinking																											
Never / <monthly	1.1%	(0.4-2.7)	1.00	-	0.08	1.00	-	0.62	3.5%	(1.6-7.7)	1.00	-	0.07	1.00	-	0.46	28.1%	(24.6-32.0)	1.00	-	**<0.01**	1.00	-	**0.04**	322, 421	146, 204	527, 715
Monthly	3.0%	(1.4-6.2)	2.79	(0.85-9.18)		1.47	(0.33-6.48)		4.0%	(1.5-10.3)	1.15	(0.31-4.18)		0.60	(0.13-2.67)		39.9%	(33.4-46.7)	1.69	(1.21-2.37)		1.48	(1.01-2.16)		125, 177	80, 113	202, 289
>weekly	3.8%	(2.0-7.0)	3.58	(1.17-11.0)		2.03	(0.49-8.38)		9.8%	(5.6-16.6)	2.98	(1.07-8.34)		1.23	(0.48-3.14)		43.2%	(37.5-49.1)	1.94	(1.44-2.62)		1.50	(1.04-2.15)		177, 241	117, 154	273, 370
Age at first heterosexual sex																											
17+	1.0%	(0.3-2.8)	1.00	-	**0.03**	1.00	-	0.67	2.8%	(0.7-9.9)	1.00	-	0.26	1.00	-	0.74	25.6%	(21.4-30.3)	1.00	-	**<0.01**	1.00	-	0.05	210, 245	87, 112	340, 431
16	1.5%	(0.5-4.6)	1.49	(0.31-7.15)		1.14	(0.27-4.74)		4.7%	(1.8-11.8)	1.75	(0.33-9.27)		1.14	(0.24-5.30)		33.4%	(27.9-39.4)	1.46	(1.03-2.06)		1.13	(0.75-1.67)		148, 205	84, 108	253, 351
<16	4.0%	(2.4-6.5)	4.18	(1.31-13.3)		1.65	(0.55-4.90)		7.8%	(4.7-12.6)	2.99	(0.70-12.7)		1.58	(0.37-6.62)		45.3%	(40.7-49.9)	2.40	(1.78-3.23)		1.53	(1.07-2.19)		238, 352	167, 243	376, 539
Condom used for most recent sex with most recent partner																											
Yes	0.7%	(0.2-2.0)	1.00	-	**<0.01**	1.00	-	0.10	4.3%	(2.0-8.9)	1.00	-	0.22	1.00	-	0.91	33.5%	(29.7-37.6)	1.00	-	0.13	1.00	-	0.87	301, 391	163, 221	491, 671
No	4.1%	(2.6-6.4)	6.03	(1.87-19.4)		3.59	(0.77-16.6)		7.4%	(4.5-12.0)	1.79	(0.70-4.59)		1.06	(0.35-3.21)		38.0%	(33.9-42.4)	1.22	(0.95-1.56)		0.97	(0.70-1.34)		283, 398	172, 237	458, 621
Number of sexual partners in the last year																											
0 or 1	1.5%	(0.7-3.0)	1.00	-	**0.01**				3.4%	(1.5-7.8)	1.00	-	**<0.01**				26.0%	(22.6-29.7)	1.00	-	**<0.01**				359, 466	145, 196	568, 768
2	1.3%	(0.4-4.2)	0.86	(0.21-3.56)					0.9%	(0.2-3.9)	0.27	(0.05-1.41)					40.3%	(33.2-47.7)	1.92	(1.34-2.75)					123, 159	74, 99	185, 251
3 to 4	3.1%	(1.1-8.5)	2.16	(0.60-7.78)					1.5%	(0.4-6.2)	0.44	(0.08-2.30)					43.0%	(35.5-50.9)	2.15	(1.49-3.10)					70, 110	57, 83	134, 194
5+	7.5%	(3.7-14.6)	5.47	(1.89-15.9)					21.2%	(12.9-32.7)	7.54	(2.66-21.3)					60.9%	(51.8-69.3)	4.42	(2.93-6.67)					67, 100	63, 89	103, 146

Table 7-2b continued.

Number of new sexual partners in the last year																						
0	1.8%	(0.9-3.8)	1.00	-	**0.01**	1.00	-	0.49	5.5%	(2.3-12.6)	1.00	-	0.37	1.00	-	0.31	26.0%	(22.0-30.5)	1.00	-	**<0.01**	1.00	-	0.37	263, 335	108, 136	416, 540
1	0.8%	(0.2-2.5)	0.42	(0.10-1.72)		0.33	(0.05-2.06)		4.0%	(1.7-9.0)	0.71	(0.21-2.47)		1.13	(0.09-13.9)		36.7%	(31.8-41.8)	1.64	(1.21-2.24)		1.28	(0.88-1.85)		203, 270	115, 161	323, 452
2+	5.1%	(2.9-8.8)	2.87	(1.08-7.63)		0.47	(0.09-2.45)		8.0%	(4.5-13.7)	1.48	(0.50-4.35)		2.87	(0.26-30.7)		46.3%	(40.7-52.0)	2.45	(1.78-3.37)		1.06	(0.67-1.68)		152, 229	115, 170	251, 366
Number of sexual partners in the last year without a condom																										
0	0.3%	(0.1-1.3)	1.00	-	**<0.01**	1.00	-	0.09	1.8%	(0.4-8.4)	1.00	-	**0.04**	1.00	-	0.45	27.0%	(22.4-32.1)	1.00	-	**<0.01**	1.00	-	0.49	205, 248	88, 115	331, 450
1	1.7%	(0.8-3.6)	5.26	(1.05-26.2)		1.23	(0.09-15.2)		4.9%	(2.6-8.9)	2.75	(0.50-15.0)		0.78	(0.19-3.15)		34.3%	(30.2-38.7)	1.41	(1.02-1.96)		1.12	(0.72-1.71)		287, 396	160, 222	475, 640
2+	6.5%	(3.9-10.9)	21.3	(4.67-97.2)		4.95	(0.42-57.9)		10.9%	(6.0-19.0)	6.51	(1.19-35.6)		0.46	(0.11-1.83)		48.8%	(42.3-55.4)	2.59	(1.81-3.70)		1.37	(0.80-2.34)		130, 194	95, 134	194, 281
Concurrent partnerships in last year[f]																										
No	2.6%	(1.6-4.2)	1.00	-	0.74	1.00	-	0.05	6.7%	(4.1-10.8)	1.00	-	0.10	1.00	-	0.07	32.9%	(29.6-36.3)	1.00	-	**<0.01**	1.00	-	0.24	418, 557	219, 298	676, 916
Yes	2.0%	(0.7-5.4)	0.75	(0.24-2.37)		0.18	(0.04-0.71)		6.5%	(2.7-14.8)	0.96	(0.34-2.72)		0.60	(0.19-1.79)		49.7%	(41.0-58.4)	2.02	(1.37-2.96)		1.52	(0.92-2.50)		82, 121	67, 92	136, 188
Unknown	1.7%	(0.5-5.6)	0.64	(0.17-2.37)		0.60	(0.11-3.00)		1.3%	(0.3-5.5)	0.19	(0.04-0.88)		0.06	(0.00-0.71)		38.5%	(30.9-46.7)	1.28	(0.88-1.86)		1.18	(0.77-1.80)		92, 122	52, 75	137, 193
Number of lifetime sexual partners																										
1 to 4	0.4%	(0.1-1.5)	1.00	-	**<0.01**	1.00	-	**0.03**	1.0%	(0.3-3.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	25.3%	(21.8-29.2)	1.00	-	**<0.01**	1.00	-	**<0.01**	332, 412	133, 176	524, 706
5 to 9	1.2%	(0.3-4.0)	3.21	(0.47-21.9)		1.78	(0.20-15.5)		3.8%	(1.3-10.8)	4.15	(0.82-21.0)		4.87	(0.58-40.2)		39.6%	(33.6-45.9)	1.93	(1.39-2.69)		1.50	(1.01-2.21)		141, 200	84, 123	222, 314
10+	7.6%	(4.8-11.7)	22.6	(4.92-104)		8.69	(1.21-62.0)		12.3%	(7.6-19.2)	14.6	(3.89-54.5)		19.80	(3.03-129.)		49.2%	(43.2-55.2)	2.86	(2.09-3.92)		2.23	(1.45-3.42)		148, 224	121, 167	247, 342
Ever had any same sex experience/contact																										
No	2.3%	(1.5-3.5)	1.00	-	0.89	1.00	-	0.37	5.8%	(3.8-8.9)	1.00	-	0.87	1.00	-	0.82	33.9%	(31.1-36.8)	1.00	-	0.11	1.00	-	**0.02**	577, 762	311, 427	922, 126
Yes	2.0%	(0.4-9.0)	0.90	(0.18-4.48)		0.31	(0.02-4.16)		5.1%	(1.0-22.0)	0.87	(0.17-4.54)		0.79	(0.10-6.09)		42.4%	(32.2-53.4)	1.44	(0.92-2.26)		2.08	(1.12-3.84)		47, 78	31, 44	80, 115

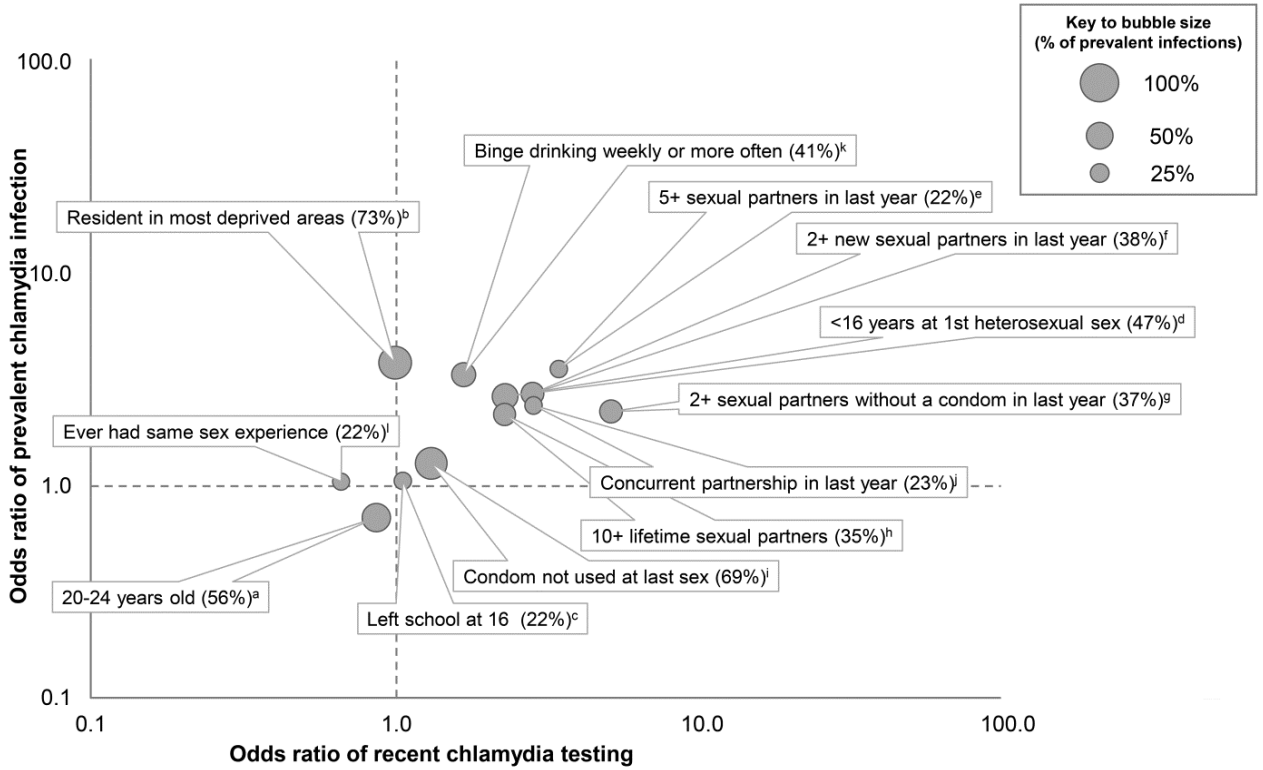
[a]N in column headings shows unweighted denominators. Total denominators by characteristic and in multivariable models vary due to item-missingness. [b]AOR: Adjusted odds ratios, adjusted for all variables shown. [c]Results for recent diagnosis are not reported due to small sample size in Scotland and Wales when limited to those tested. [d]IMD: Index of multiple deprivation of LSOA (lower super output area) of residence. IMD scores for England, Scotland and Wales were adjusted before being combined and assigned to quintiles, using the method described by Payne and Abel[264]. [e]Excludes 16 year-olds. [f]Among those with ≥1 sexual partner in last year.

Figure 7-2 shows the unadjusted OR for prevalent infection and for recent testing by sociodemographic and behavioural factors. Groups in the upper right hand quadrant are those where both the odds of prevalent infection and of testing were higher than the reference group. Groups in the upper left hand quadrant show those where the odds of prevalent infection were higher, but odds of testing were lower than the reference group. The demographic and behavioural factors associated with recent testing were broadly similar to those associated with prevalent infection and with recent diagnosis, with some exceptions. Notably, whereas women living in one of the two most deprived IMD quintiles had almost a four-fold increase in the odds of prevalent infection compared to those living in less deprived areas (OR 3.82, 95%CI 1.35-10.79), the odds of recent testing did not differ by deprivation (OR 0.99, 95%CI 0.77-1.27). Among men, the odds of prevalent infection were higher among 20 to 24 versus 16 to 19 year-olds (OR 10.6, 95%CI 2.40-46.3), but odds of recent testing were lower in the older age group (OR 0.67, 0.44-0.84). In men, not having used a condom at last sex was associated with a six-fold increase in the odds of prevalent infection (OR 6.03, 95%CI 1.87-19.42), but was not associated with recent testing (OR 1.22, 95%CI 0.95-1.56). Similar patterns were seen when comparing adjusted ORs from multivariable models (Table 3).

Although the proportion recently tested was generally higher in those reporting risk factors for chlamydia, recent testing remained well below 100% in all sociodemographic and behavioural subgroups. For example, 25% (95%CI 20%-31%) of women and 47% (95%CI 41%-53%) of men with two or more new sexual partners in the last year, and 20% (95%CI 16%-27%) and 45% (95%CI 38%-51%) with two or more sexual partners without a condom in the last year had not been either recently tested or offered a test. There was evidence of

both repeat (or persistent) and incident infections. Among individuals with a prevalent chlamydia infection, 14% (95%CI 7%-14%) had ever been diagnosed with chlamydia and 5% (95%CI 2%-17%) reported a diagnosis in the last year (indicating either repeat or persistent infections). Fifty percent (95%CI 35%-64%) of those with a prevalent infection reported a recent chlamydia test (89% of whom did not report a recent diagnosis, thus indicating incident rather than repeat/persistent infections within the last year).

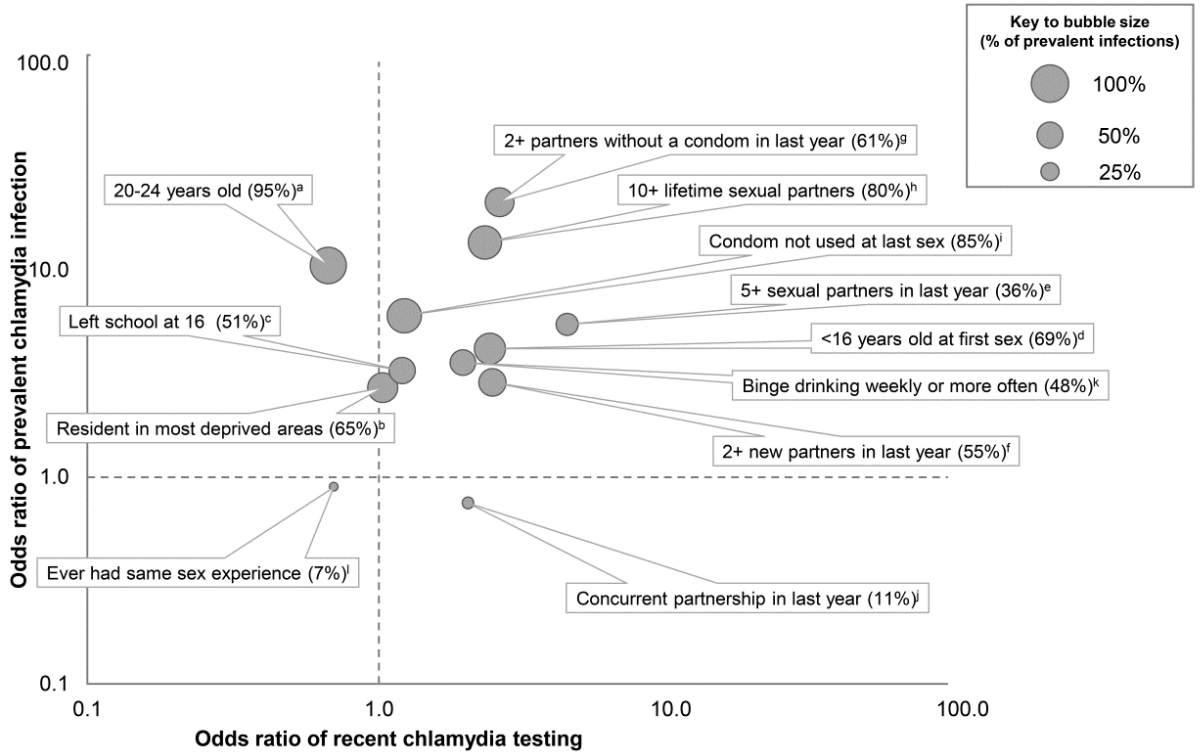
Figure 7-2a: Bubble plot showing unadjusted odds ratios for prevalent chlamydia infection versus recent testing by sociodemographic and behavioural factors, and percentage of prevalent infections in each group (sexually-experienced 16-24 year-old <u>women</u>)



The area of the bubble represents the percentage of those with a prevalent infection in each group (percentage shown in parentheses). Factors in the upper right hand quadrant are those where both the odds of prevalent infection and of testing were higher than the reference group. Factors in the upper left hand quadrant show those where the odds of prevalent infection were higher, but odds of testing were lower than the reference group.

Letters indicate reference groups: [a] 16-19 years old; [b] Resident in lower super output area in the 2 least deprived quintiles, as measured by Index of Multiple Deprivation (IMD); [c] Left school at 17+ (among those aged ≥16); [d] 17+ years at first heterosexual sex; [e] 0 or 1 sexual partners in the last year; [f] 0 new sexual partners in the last year; [g] 0 sexual partners in the last year without a condom; [h] 1 to 9 lifetime sexual partners; [i] Condom used at last sex; [j] No concurrent partnership in last year (among those with 1+ more sexual partners in last year); [k] Reports binge drinking never or less than monthly; [l] Never had same sex contact/experience.

Figure 7-2b: Bubble plot showing unadjusted odds ratios for prevalent chlamydia infection versus recent testing by sociodemographic and behavioural factors, and percentage of prevalent infections in each group (sexually-experienced 16-24 year-old men)



The area of the bubble represents the percentage of those with a prevalent infection in each group (percentage shown in parentheses). Factors in the upper right hand quadrant are those where both the odds of prevalent infection and of testing were higher than the reference group. Factors in the upper left hand quadrant show those where the odds of prevalent infection were higher, but odds of testing were lower than the reference group.

Letters indicate reference groups: [a] 16-19 years old; [b] Resident in lower super output area in the 2 least deprived quintiles, as measured by Index of Multiple Deprivation (IMD); [c] Left school at 17+ (among those aged ≥16); [d] 17+ years at first heterosexual sex; [e] 0 or 1 sexual partners in the last year; [f] 0 new sexual partners in the last year; [g] 0 sexual partners in the last year without a condom; [h] 1 to 9 lifetime sexual partners; [i] Condom used at last sex; [j] No concurrent partnership in last year (among those with 1+ more sexual partners in last year); [k] Reports binge drinking never or less than monthly; [l] Never had same sex contact/experience.

7.4.1.3 Distribution of infections by demographic and behavioural characteristics

Table 7-3 shows the distribution of demographic and behavioural characteristics among individuals with a prevalent infection, those with a recent diagnosis and the sexually-experienced population. Among both women and men, prevalent infections were detected in those reporting no new sexual partners in the last year, and those reporting no condomless sexual partners in the last year. Infections in women tended to be more evenly distributed according to numbers of sexual partners and other risk factors than in men. For example, among the 62 individuals (37 women, 25 men) with a prevalent infection 38% of women and 55% of men reported two or more new sexual partners in the last year (versus 21% and 25% of the sexually-experienced population); 37% of women and 61% of men reported two or more condomless sexual partners in the last year (versus 18% and 19% of the population). Living in one of the 40% most deprived LSOA accounted for 73% and 65% of prevalent infections in women and men respectively. This difference in distribution of infections by sex is also illustrated in Figure 7-2, where the size of the markers indicates the proportion of prevalent infections found in that risk group. Reporting that no condom had been used at last sex was common among this age group (63% of sexually-experienced women and 48% of men), and among both women and men with a prevalent infection (69% in women and 85% in men).

Table 7-3a: Distribution of demographic and behavioural characteristics among a) individuals with a prevalent chlamydia infection, b) individuals with a recent chlamydia diagnosis and c) the sexually-experienced population (16-24 year-old sexually-experienced <u>women,</u> Natsal-3).

	(a) Prevalent infection detected in urine (n=37)		(b) Diagnosed with chlamydia in the last year (n=54)		(c) Sexually-experienced population (n=1,740)	
	Percent	95%CI	Percent	95%CI	Percent	95%CI
Age group						
16-19	43.6%	(26.7-62.1)	40.5%	(26.6-56.2)	35.6%	(33.2-38.0)
20-24	56.4%	(37.9-73.3)	59.5%	(43.8-73.4)	64.4%	(62.0-66.8)
Country						
England	79.8%	(62.5-90.3)	92.1%	(80.8-97.0)	85.1%	(83.1-86.9)
Scotland	9.5%	(3.3-24.5)	3.4%	(0.7-14.3)	9.5%	(8.0-11.2)
Wales	10.8%	(3.8-27.0)	4.5%	(1.3-14.3)	5.4%	(4.4-6.7)
IMD quintile of LSOA of residence[a]						
2 least deprived quintiles	15.6%	(5.9-35.2)	30.9%	(18.4-46.9)	35.1%	(32.3-38.0)
middle quintile	11.0%	(4.5-24.7)	12.5%	(5.6-25.4)	19.5%	(17.3-21.9)
2 most deprived quintiles	73.4%	(54.9-86.3)	56.7%	(40.8-71.3)	45.4%	(42.5-48.4)
Age left school[b]						
17+	77.9%	(62.0-88.3)	74.9%	(60.2-85.4)	78.5%	(76.3-80.6)
16	22.1%	(11.7-38.0)	25.1%	(14.6-39.8)	21.5%	(19.4-23.7)
Age at first heterosexual sex						
17+	16.0%	(6.5-34.3)	19.5%	(8.9-37.7)	33.6%	(31.0-36.3)
16	37.3%	(21.0-57.1)	27.0%	(15.1-43.3)	29.5%	(27.0-32.0)
<16	46.8%	(28.8-65.6)	53.5%	(38.0-68.4)	36.9%	(34.3-39.6)
Number of sexual partners in the last year						
0 or 1	52.1%	(33.7-69.9)	31.10%	(18.2-47.9)	65.3%	(62.7-67.9)
2	19.4%	(8.6-38.0)	21.70%	(12.3-35.5)	15.0%	(13.3-17.0)
3 to 4	6.4%	(2.1-17.5)	23.60%	(13.6-37.7)	11.6%	(10.1-13.2)
5+	22.2%	(9.8-42.7)	23.60%	(12.2-40.6)	8.1%	(6.6-9.9)
Number of new sexual partners in the last year						
0	38.0%	(22.4-56.6)	21.9%	(12.0-36.7)	51.8%	(49.0-54.5)
1	24.4%	(10.9-46.0)	26.1%	(13.9-43.7)	27.6%	(25.2-30.1)
2+	37.6%	(21.7-56.6)	51.9%	(36.4-67.1)	20.6%	(18.4-23.1)
Number of sexual partners in the last year without a condom						
0	18.9%	(7.5-40.1)	11.4%	(3.9-28.6)	21.8%	(19.7-24.1)
1	44.1%	(26.9-62.9)	43.0%	(28.6-58.6)	60.6%	(58.0-63.2)
2+	36.9%	(20.6-57.0)	45.7%	(31.5-60.6)	17.5%	(15.6-19.6)
Number of sexual partners over the lifetime						
1 to 4	42.2%	(25.1-61.4)	16.1%	(8.3-28.8)	52.6%	(49.9-55.3)
5 to 9	22.6%	(11.3-40.1)	35.0%	(21.6-51.2)	26.3%	(24.0-28.8)
10+	35.2%	(19.2-55.3)	48.9%	(33.5-64.5)	21.1%	(19.0-23.4)
Condom used for most recent sex with most recent partner						
Yes	31.1%	(16.6-50.5)	21.9%	(10.7-39.7)	36.8%	(34.2-39.6)
No	68.9%	(49.5-83.4)	78.1%	(60.3-89.3)	63.2%	(60.4-65.8)
Concurrent partnerships in last year [c]						
No	65.0%	(45.4-80.6)	56.0%	(40.5-70.4)	76.2%	(73.9-78.3)
Yes	22.6%	(10.0-43.5)	22.8%	(11.8-39.5)	11.3%	(9.7-13.1)
Unknown	12.4%	(5.0-27.6)	21.2%	(11.7-35.4)	12.6%	(10.9-14.4)
Frequency of binge drinking						
never / less than monthly	50.5%	(32.4-68.6)	41.2%	(27.0-57.0)	62.3%	(59.7-64.9)
monthly	8.7%	(3.0-22.9)	26.4%	(14.7-43.0)	22.1%	(19.9-24.5)
weekly or more often	40.7%	(24.2-59.6)	32.4%	(18.8-49.8)	15.6%	(13.7-17.6)
Ever had any same sex experience/contact						
Yes	21.6%	(9.4-42.2)	28.1%	(16.5-43.6)	22.5%	(20.3-24.8)
No	78.4%	(57.8-90.6)	71.9%	(56.4-83.5)	77.5%	(75.2-79.7)
Bases (wt, unwt)	18, 37		28, 54		968, 1740	

Table 7-3b: Distribution of demographic and behavioural characteristics among a) individuals with a prevalent chlamydia infection, b) individuals with a recent chlamydia diagnosis and c) the sexually-experienced population (16-24 year-old sexually-experienced men, Natsal-3).

	(a) Prevalent infection detected in urine (n=25)		(b) Diagnosed with chlamydia in the last year (n=27)		(c) Sexually-experienced population (n=1,375)	
	%	95%CI	%	95%CI	%	95%CI
Age group						
16-19	5.5%	(1.2-22.5)	35.6%	(17.9-58.3)	37.3%	(34.4-40.2)
20-24	94.5%	(77.5-98.8)	64.4%	(41.7-82.1)	62.7%	(59.8-65.6)
Country						
England	71.8%	(47.3-87.9)	78.8%	(55.5-91.7)	85.7%	(82.7-88.2)
Scotland	24.2%	(9.5-49.3)	19.2%	(7.0-43.1)	8.8%	(6.8-11.4)
Wales	3.9%	(0.5-26.9)	2.0%	(0.2-14.5)	5.5%	(4.0-7.5)
IMD quintile of LSOA of residence[a]						
2 least deprived quintiles	22.0%	(7.3-50.1)	33.7%	(16.4-56.7)	36.9%	(33.6-40.2)
middle quintile	12.9%	(4.1-34.1)	15.3%	(5.1-38.0)	18.2%	(15.9-20.7)
2 most deprived quintiles	65.1%	(41.5-83.1)	51.0%	(29.9-71.8)	44.9%	(41.4-48.5)
Age left school[b]						
17+	49.3%	(27.7-71.1)	66.5%	(43.5-83.6)	75.4%	(72.6-77.9)
16	50.7%	(28.9-72.3)	33.5%	(16.4-56.5)	24.6%	(22.1-27.4)
Age at first heterosexual sex						
17+	15.1%	(4.9-37.9)	12.3%	(3.1-38.4)	35.1%	(32.1-38.2)
16	15.7%	(4.5-42.3)	20.6%	(7.7-44.7)	26.1%	(23.5-28.8)
<16	69.2%	(44.9-86.1)	67.1%	(43.1-84.6)	38.8%	(35.8-41.8)
Number of sexual partners in the last year						
0 or 1	37.4%	(18.2-61.6)	25.2%	(10.7-48.7)	57.30%	(54.3-60.3)
2	11.0%	(3.0-33.3)	3.5%	(0.7-15.0)	18.70%	(16.5-21.2)
3 to 4	15.6%	(5.1-38.5)	4.4%	(1.0-18.0)	13.60%	(11.7-15.7)
5+	36.1%	(17.6-59.8)	66.9%	(44.4-83.6)	10.40%	(8.8-12.2)
Number of new sexual partners in the last year						
0	34.1%	(16.0-58.5)	30.3%	(13.1-55.4)	42.1%	(39.0-45.2)
1	11.1%	(3.0-33.2)	23.3%	(9.8-45.9)	32.6%	(29.7-35.6)
2+	54.8%	(32.0-75.7)	46.5%	(26.3-67.9)	25.3%	(22.8-28.0)
Number of sexual partners in the last year without a condom						
0	4.8%	(1.0-19.9)	8.2%	(1.6-33.0)	33.1%	(30.2-36.1)
1	34.7%	(16.1-59.5)	39.7%	(21.1-61.8)	47.5%	(44.4-50.5)
2+	60.5%	(36.7-80.2)	52.1%	(30.7-72.8)	19.4%	(17.2-21.8)
Number of sexual partners over the lifetime						
1 to 4	8.50%	(1.8-32.5)	6.5%	(1.8-21.3)	52.70%	(49.8-55.7)
5 to 9	11.60%	(3.0-35.8)	16.7%	(5.5-41.1)	22.40%	(20.0-25.0)
10+	79.90%	(55.8-92.6)	76.7%	(53.8-90.3)	24.90%	(22.5-27.4)
Condom used for most recent sex with most recent partner						
Yes	15.5%	(4.9-39.3)	35.3%	(17.2-58.9)	51.7%	(48.6-54.8)
No	84.5%	(60.7-95.1)	64.7%	(41.1-82.8)	48.3%	(45.2-51.4)
Concurrent partnerships in last year[c]						
No	77.6%	(55.8-90.5)	74.5%	(52.3-88.7)	71.2%	(68.4-74.0)
Yes	11.4%	(3.7-30.3)	22.0%	(9.0-44.6)	14.3%	(12.3-16.6)
Unknown	11.0%	(3.0-33.3)	3.5%	(0.7-15.0)	14.5%	(12.5-16.7)
Frequency of binge drinking						
never / less than monthly	25.1%	(9.9-50.6)	25.9%	(11.2-49.1)	52.6%	(49.6-55.5)
monthly	26.7%	(12.0-49.5)	16.2%	(5.8-37.7)	20.2%	(17.9-22.6)
weekly or more often	48.2%	(26.6-70.4)	57.9%	(35.8-77.3)	27.3%	(24.7-30.0)
Ever had any same sex experience/contact						
Yes	6.8%	(1.3-29.3)	8.2%	(1.6-33.0)	8.0%	(6.5-9.8)
No	93.2%	(70.7-98.7)	91.8%	(67.0-98.4)	92.0%	(90.2-93.5)
Bases (wt, unwt)		14, 25		20, 27		1003, 1375

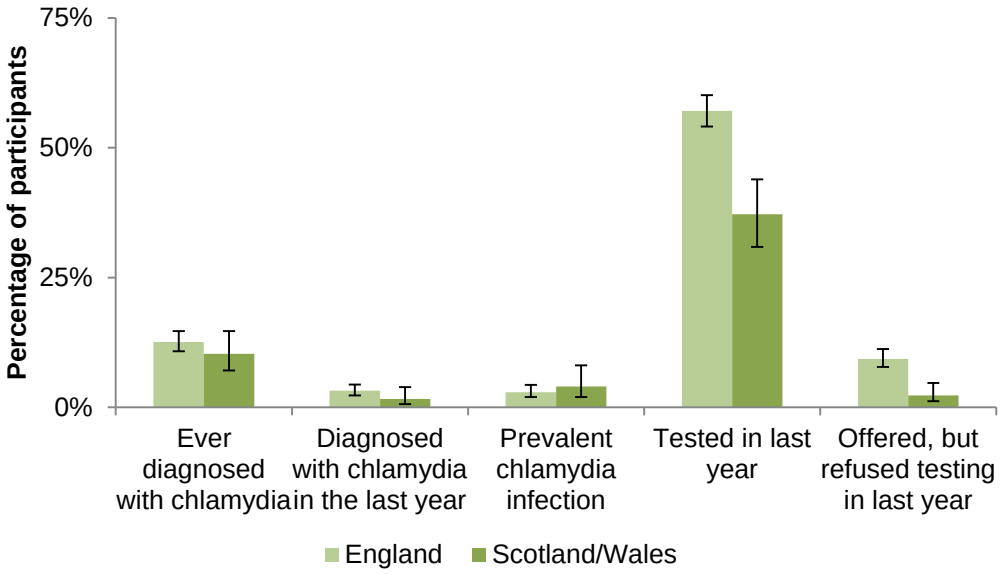
[a]IMD: Index of multiple deprivation of LSOA (lower super output area) of residence. IMD scores for England, Scotland and Wales were adjusted before being combined and assigned to quintiles, using the method described by Payne and Abel[39]; [b]Excludes 16 year-olds;[c]Among those with 1+ more sexual partners in last year

7.4.1.4 England versus Scotland/Wales

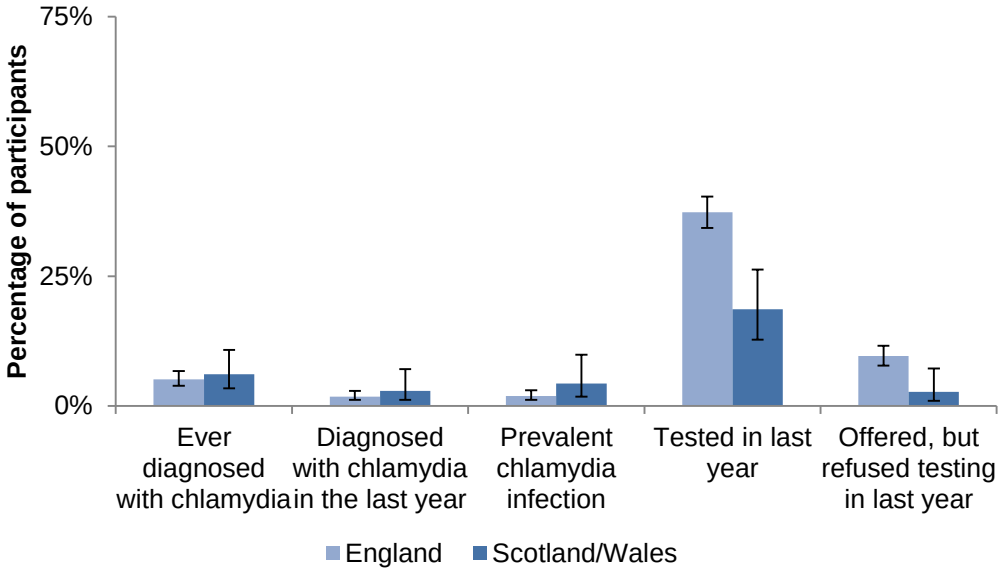
Women and men living in England were significantly more likely to have been recently tested than those living in Scotland or Wales (OR: 2.25, 95%CI 1.66-3.05 in women; 2.60, 1.64-4.12 in men, Figure 7-3). There was no significant difference in the prevalence of infection or proportion recently diagnosed by country of residence. When limiting to participants resident in England, there were no notable differences in either the factors associated with prevalent infection, recent diagnosis or recent testing, or in the relationships between these factors (Appendix 3).

Figure 7-3: Percentage with a prevalent chlamydia infection, ever diagnosed with chlamydia, recent diagnosis of chlamydia and recently tested for chlamydia by country of residence (sexually-experienced 16-24 year-olds, Natsal-3)

Women



Men



7.5 Discussion

7.5.1 Key findings

In 2010-12 chlamydia was a common, and commonly diagnosed, infection among young adults in Britain. Prevalent infections in women were more evenly distributed according to numbers of sexual partners than in men. Diagnoses had arisen following both opportunistic screening and clinically-indicated testing in roughly equal numbers. Living in more deprived areas was significantly associated with prevalent infection after adjusting for sociodemographic and behavioural factors. The proportion reporting chlamydia testing was generally greater among those reporting factors associated with chlamydia. However, substantial proportions of young adults reporting risk factors for chlamydia had not been recently tested and incident infections in the last year were evident.

7.5.2 Strengths and limitations

The major strength of this analysis is that it used individual-level data from a nationally-representative sample. Behavioural and biological data were linked to examine a range of risk factors for different outcomes within the same survey.

Investigations using the Natsal-3 data were reliant on the questions asked in the survey. For example the survey asked about the location of the most recent test, but not of the most recent diagnosis. The finding that the vast majority of those recently diagnosed had last been tested in clinical settings may therefore reflect re-testing patterns with follow up tests done in sexual health settings, rather than low diagnosis rates among non-clinical settings. However this is likely to have minimal impact on these findings as routine re-testing before one year after a positive test was not recommended in England until 2013.[119]

Despite the size of Natsal-3 and oversampling of younger people,[172] the number of participants aged under 25 limited statistical power to explore all associations of potential interest including local area and ethnicity. Given the relatively small absolute numbers of prevalent infections (n=62), the proportions in specific sub-groups should be interpreted with caution. These findings may be affected by who agreed to take part in the survey or provide a urine sample. Survey weights were used to minimise bias but unmeasured bias remains feasible. Comparisons between risk factors for prevalent infection and recent testing may have been affected by the estimation of outcomes among different denominators. This was explored further in a sensitivity analysis, which showed no notable difference between ORs for testing when estimated in sexually-experienced participants versus urine study participants (data not shown). A further limitation is the accuracy of self-reporting. Detailed questions were answered via self-completion, which are expected to have minimised social desirability bias.

7.5.3 Comparison to other studies/data

Recent testing was not associated with area-level deprivation in this analysis. This is contrary to an analysis of data from the South East of England, which found higher rates of chlamydia screening in more deprived areas in 2008.[265] This difference in findings may reflect the different study period, when screening coverage was lower, or regional variation in screening patterns.

National surveillance data on chlamydia tests and diagnoses among 15 to 24 year-olds are available for England for the period covered by Natsal-3. The average coverage of chlamydia testing in England in 2010-12 among 15 to 24 year-olds was 40% in women and 20% in men.[189,266] This is lower than the 57%

of women and 37% of men resident in England estimated to have been test in the last year in Natsal-3. Differences between denominators (all versus sexually-experienced only) and age ranges (surveillance data for this period use partly aggregated data and are not available for 16 to 24 year-olds) may partly explain these differences. Applying the proportion of 16 to 24 year-olds with one or more sexual partner estimated in Natsal-3 (80%[235]) to surveillance data results in an estimated coverage per year of 51% and 25% among sexually-experienced women and men respectively. This is more comparable, but still somewhat lower than the estimates presented in this chapter, especially since surveillance data may include repeat tests among from the same individual within one year.[120] This may indicate some residual bias arising from who took part in Natsal-3. The findings on location of last test among those recently diagnosed are consistent with 2011 surveillance data, where 42% of diagnoses among 15 to 24 year-olds were reported from GUM clinics, 15% from family planning services, 7% GPs, 2% from education and 33% from other/unknown settings.[189] The proportion of diagnoses from GPs was higher in Natsal-3 (27%) than in surveillance data. This may reflect the partially- aggregate nature of surveillance data as a large proportion of diagnoses made in other/unknown settings are likely to be from GPs.

7.5.4 Implications for evaluation of chlamydia control

Those reporting risk factors for chlamydia were generally more likely to report having been recently tested. This is contrary to uptake patterns often seen in public health interventions, where those in most need are often least likely to access care.[267] However, at least one quarter of women and around half of men reporting a risk factor associated with prevalent infection had not been recently

tested. This presents a clear potential for ongoing transmission of chlamydia from high risk but untested individuals. Almost all prevalent infections in men were among 20 to 24 year-olds, less than a third of whom reported recent testing. As young women tend to have slightly older male partners,[268] sexual mixing patterns by age may play a key role in transmission.

These findings also suggest that the likelihood of having an infection diagnosed and treated varies by deprivation, as although screening coverage was uniform by area-level deprivation, chlamydia prevalence was higher in those living in more deprived areas. This raises the question as to whether efforts to expand or intensify chlamydia screening should prioritise those living in more deprived areas to address this potential inequality. A high proportion of infections were found in those who had not used a condom at last sex, and around one fifth of recent diagnoses were made following a test prompted by a partner having chlamydia, which emphasises the importance of condom use and partner notification in chlamydia prevention and control.

7.5.5 Summary

Comparison of factors associated with prevalent infection and with diagnosis and testing showed that those with risk factors for chlamydia were more likely to have accessed a chlamydia test in the last year. While this alignment between need and uptake of the intervention suggests the NCSP may be reaching those at risk of infection, this analysis demonstrated substantial opportunities for ongoing transmission of infection, and incident infections were evident. Given that comparisons between chlamydia prevalence in Natsal-2 and Natsal-3 did not provide any strong evidence for chlamydia prevalence to have decreased in

the decade up to 2010-12, these opportunities for transmission present a possible explanation for an absence of a decrease in prevalence.

The findings presented up to this point in the thesis still leave us in a position of considerable uncertainty as to whether there has or has not been any change in the incidence or prevalence of chlamydia during a time of widespread screening among under 25-year-olds. In the next chapter I therefore move to investigation of a third outcome measure, that of antibody seroprevalence as a marker of age-specific cumulative incidence.

8 Trends in *C. trachomatis* antibody seroprevalence, as a marker of age-specific cumulative incidence, measured using stored sera from participants in the Health Survey for England (HSE) (1994 to 2012)

In previous chapters, my analysis of surveillance data showed that there was a decrease in percentage testing positive for chlamydia between 2008 and 2011 that remained after adjusting for known confounders, but that unmeasured confounding could not be ruled out. My comparison of data from the second and third Natsal surveys did not provide evidence to support there having been a decrease in chlamydia prevalence in the decade between the two surveys, which were conducted before and after the implementation of the NCSP. Evidence from Natsal-3 highlighted important opportunities for transmission of infection in 2010-12. In this chapter I present a study that applied a novel C. trachomatis antibody assay to stored sera from participants in a series of nationally-representative health surveys to investigate whether these data support there having been a change in age-specific cumulative incidence following the implementation of widespread screening.

8.1 Background

As well as being resource-intensive and hard to achieve, population-based estimates of chlamydia prevalence using NAATs measure only *current* infections. Such studies are therefore unable to estimate the proportion of the population who have ever been infected and who are therefore at risk of chlamydia-related sequelae. Serology has therefore been proposed as an alternative approach for evaluating the impact of chlamydia control programmes.[99] Chlamydia antibodies persist and thus provide a longer-term marker of past infection.[100,269] Using blood samples collected for a purpose

other than chlamydia testing can also avoid the bias associated with data from populations accessing chlamydia testing.

As set out in Chapter 3, chlamydia seroepidemiology has been previously hampered by the lack of a suitable assay.[99] Commercially available assays to detect *C. trachomatis* antibodies suffered from poor sensitivity and specificity with several subject to cross-reactive with other species of *Chlamydia*. Assays also lacked robust validation against panels of sera from individuals with known previous infection and negative controls. In recent years tests with better specificity - not so affected by inter-species cross-reaction - have become available.[209,269]

The analysis presented in this chapter used data and stored sera from a nationally-representative household survey, the Health Survey for England (HSE), to explore sociodemographic and behavioural factors associated with serological evidence of a previous infection and to evaluate the impact of widespread opportunistic chlamydia screening on age-specific cumulative incidence of chlamydia in England up to 2012.

8.2 Aims & objectives

The aims of this analysis were firstly, to explore the utility of chlamydia seroprevalence as an epidemiological tool for the evaluation of chlamydia control and secondly, to investigate trends in age-specific chlamydia incidence among 16 to 24 year-old women in England between before and after the implementation of the National Chlamydia Screening Programme. This aim was addressed through the following objectives:

- To describe the association between sociodemographic variables and self-reported health and sexual behaviours and the presence of chlamydia and antibodies in serum among HSE2010 and HSE2012 participants.

- To compare age-specific Pgp3 seroprevalence (defined as the prevalence of Pgp3 antibodies detected in serum) at selected years (1994 to 2012) during a period of increased chlamydia screening.

- To compare age-specific Pgp3 seroprevalence between birth cohorts exposed to differing levels of chlamydia screening.

8.3 Methods

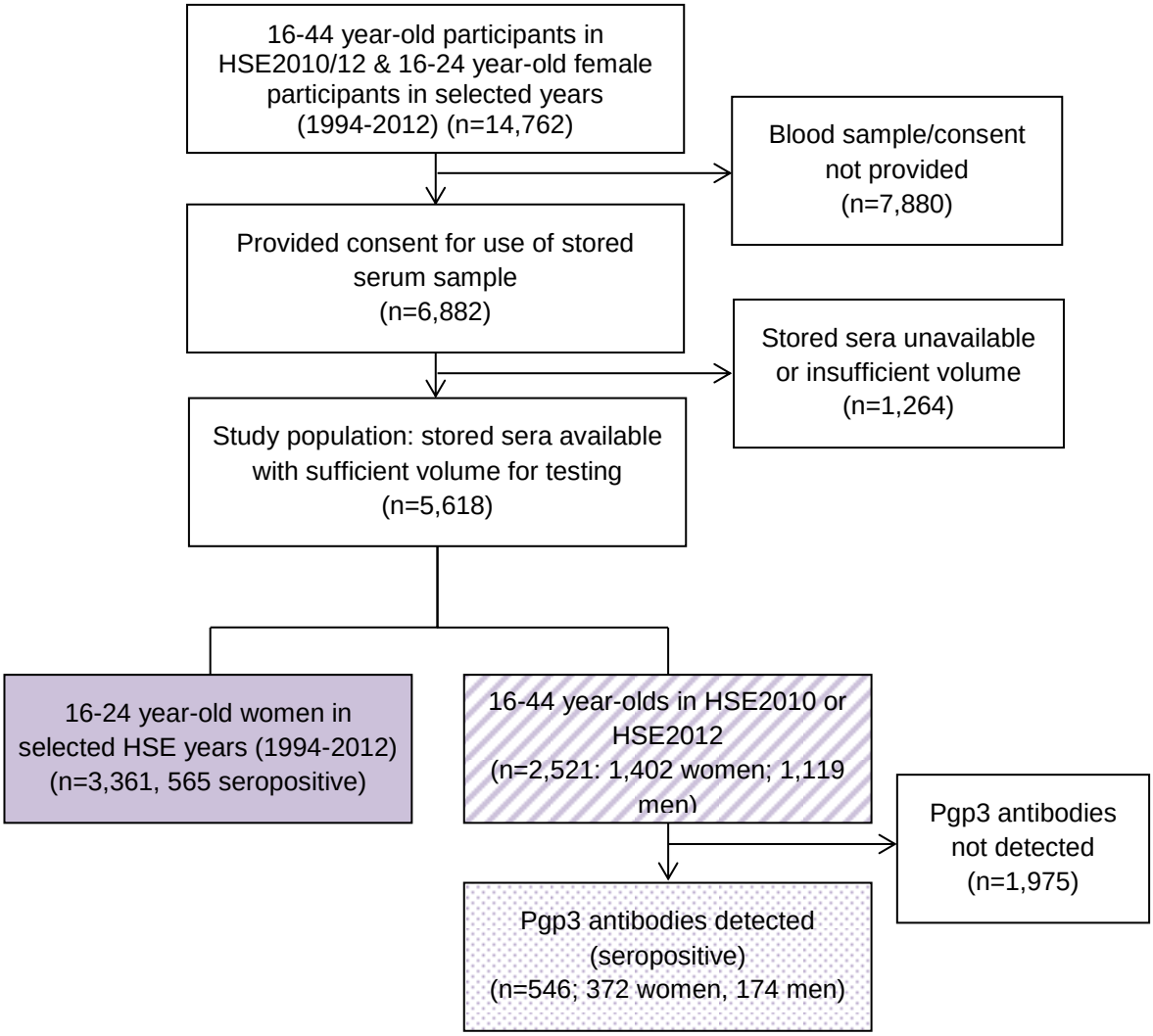
8.3.1 Participants

HSE is a series of nationally-representative surveys carried out annually since 1991. Participants are invited to provide a blood sample for laboratory analyses and storage for future research. Details of HSE methodology are reported elsewhere.[7,270] In summary, each annual survey used a multi-stage stratified probability sampling design. In each year a random sample of postcode sectors was selected from the Postcode Address File, from which a random sample of postal addresses was drawn. All adults aged 16 years and over at each selected household were selected for interview. Information on participants' health and wellbeing, along with detailed sociodemographic information, was collected using a combination of face to face interviews and self-completed questionnaire booklets and a nurse visit.[7] HSE2010 and HSE2012 also included questions on sexual behaviours and chlamydia diagnosis history, which were collected using the self-completed booklet. Other household members could be

present during interviews and questionnaire completion but did not see others' booklets.[7]

Sera were obtained from HSE participants who provided consent for their blood sample to be stored and used in future anonymous analyses (Figure 8-1). Sera were obtained from a) 16 to 44 year-old HSE2010/12 participants to explore factors associated with testing positive for anti-Pgp3 antibodies in serum (hereafter 'Pgp3 seropositive') and b) female participants aged 16 to 24 who took part in HSE years when stored sera were available (1994-1996, 2001-02 and each year from 2008-2012), to examine trends in the prevalence of anti-Pgp3 antibodies in serum (hereafter 'Pgp3 seroprevalence') in the age group targeted by the NCSP. Trends over time among men were not investigated as lower assay sensitivity[209,269] complicates interpretation of trends and as monitoring chlamydia infections in women is of greater public health value given that most chlamydia-related complications are among women.

Figure 8-1: Flow chart showing selection of stored sera from Health Survey for England (HSE) participants



Key

Included in analysis of age-specific Pgp3 seroprevalence over time

Included in analysis of factors associated with seroprevalence

Included in description of reported chlamydia diagnoses among seropositive

Note: analysis groups are not mutually exclusive, therefore sum of number in each group is greater than total number tested (n=5,618).

8.3.2 Laboratory testing

After collection, samples had been posted to the Royal Victoria Infirmary, Newcastle and stored in the HSE serum bank at -40^{o}C. Specimens were sent to PHE Colindale where they were aliquoted, relabelled with the study ID and stored at -20°C. Specimens were transported frozen to Imperial College London and stored at -20°C until testing.

8.3.2.1 Pgp3 assay

Pgp3 is a *C. trachomatis*-specific protein. Pgp3 is considered a useful immunogen for serological tests as it is highly conserved between strains and is rarely found in *C.pneumoniae* isolates.[209] In 2009, Wills *et al* developed an "in-house" indirect immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) based on the Pgp3 antigen (hereafter 'indirect Pgp3 ELISA'). Sensitivity was measured among adult patients attending GUM clinics with a known, previously diagnosed chlamydia infection and was estimated at 73.8% (95%CI 66.5%-79.9%) in women and 44.2% (95%CI 37.3%-51.3%) in men. Specificity was estimated using microimmunfluourescence (MIF)-negative paediatric sera to reduce likelihood of a previous sexually-acquired *C. trachomatis* infection, and was found to be 97.6% (95%CI 96.2%-98.6%).[209]

The sensitivity and specificity of the indirect Pgp3 ELISA has been compared to other commercially available assays, and found to be at least 14% more sensitive in women than any of the comparator tests (Table 8-1). Sensitivity of the indirect Pgp3 ELISA is equivalent to the comparator commercial tests in men. No evidence was found of cross-reactivity with *C. pneumoniae*.

Table 8-1: Comparative sensitivities and specificities (and 95%CI) of the Indirect Pgp3 ELISA, double-antigen sandwich ELISA and commercial ELISAs

Adapted from Wills et al[209] and Horner et al[269]

Assay	Sensitivity		Specificity (women & men combined)
	Women	Men	
Double-antigen Pgp3 ELISA	82.9% (76.3-88.0)	54.4% (47.1-61.5)	97.8% (96.1-98.7)
Indirect Pgp3 ELISA	73.8% (66.5-79.9)	44.2% (37.3-51.3)	97.6% (96.2-98.6)
Ani Labsystems	59.8% (52.1-67.0)	40.5% (33.8-47.6)	99.0% (97.7-99.6)
SeroCT	55.5% (47.8-62.9)	40.0% (33.3-47.1)	97.2% (95.7-98.2)
Medac	45.7% (38.3-53.4)	43.7% (36.8–50.8)	96.0% (94.3-97.2)

Since the publication of the original performance of the indirect Pgp3 ELISA, investigators at Imperial College London and University of Bristol have developed a double-antigen sandwich ELISA for the detection of anti-Pgp3 antibody (hereafter 'double-antigen Pgp3 ELISA'. This assay has demonstrated equivalent specificity (97.8%, 95%CI 96.1%–98.7%) and higher sensitivity (82.9%, 95%CI 76.3%-88.0% in women; 54.4%, 95%CI 47.1%-61.5% in men)[269].

Although the double-antigen Pgp3 ELISA has demonstrated higher sensitivity than the indirect Pgp3 ELISA to detect a previous known infection in both women and men, the double-antigen Pgp3 ELISA requires around a 25-fold higher volume of sera. A study of female participants in a cohort study in New Zealand tested sera using both the indirect and double-antigen Pgp3 ELISA.[269] Comparison of results from the two assays showed that the indirect Pgp3 ELISA has good agreement with the double-antigen Pgp3 ELISA at low (<0.1) and high (>1.0) absorbance values (Table 8-2). Imperial College London therefore recommend the use of the indirect Pgp3 ELISA for initial screening, with subsequent testing of sera with absorbance values between 0.1 and 1.0

using the double-antigen Pgp3 ELISA to resolve 'equivocal' specimens (personal communication, Myra McClure, Gillian Wills, Imperial College London).

In the study presented in this chapter, all specimens were tested for *C. trachomatis* anti-Pgp3 antibody using the indirect Pgp3 ELISA.[209] Specimens with an optical density between 0.1 and 1.0 on the indirect Pgp3 ELISA were re-tested using the double-antigen Pgp3 ELISA. Specimens which were positive on both assays (cut-off values were determined by the testing laboratory), positive on the double-antigen Pgp3 ELISA only, or which were above the cut-off value for re-testing (i.e. absorbance value over 1.0) were considered Pgp3 seropositive. Those which were negative on both assays, were positive on the Indirect Pgp3 ELISA but negative on the double-antigen Pgp3 ELISA, or were below the cut-off value for re-testing (i.e. absorbance value less than 0.1) were considered Pgp3 seronegative. This testing strategy represents a 98.0% sensitivity, and 99.8% specificity compared to the results that would have been achieved had all samples been tested on the double-antigen Pgp3 ELISA (Table 8-2).

Table 8-2: Comparison of indirect Pgp3 ELISA and double-antigen Pgp3 ELISA by absorbance values on indirect Pgp3 ELISA.

Data are from a study of female participants in a cohort study in New Zealand where all sera were tested with both the indirect Pgp3 ELISA and the double-antigen Pgp3 ELISA (n=2,641 sera).[269] (Personal communication, M McClure & G Wills, Imperial College London)

		Double-antigen Pgp3 ELISA	
		Negative	***Positive***
Indirect Pgp3 ELISA (Absorbance range)	***Negative (<0.1)***	1817	10
	Negative (0.1-0.4731)*	302	233
	Positive (0.4731-1.0)	15	96
	Positive (>1.0)	4	164

**An absorbance (450-620nm) value of 0.473 is the cut-off for the indirect assay.*

8.3.3 Statistical analyses

Data were analysed in Stata 12.1 accounting for weighting, clustering and stratification. Weights were applied in line with HSE analysis guidelines and included weights to correct for uneven probability of selection and - from HSE2003 onwards - non-response weights to ensure the sample is representative with regard to age, sex and region and to adjust for differential participation in blood specimen collection by sociodemographic and general health variables.[271]

Pgp3 seroprevalence among HSE2010/12 participants was estimated by sex, number of lifetime sexual partners and reporting of a previous chlamydia diagnosis, regardless of reported sexual activity. Associations between being Pgp3 seropositive and sociodemographic and behavioural factors among sexually-experienced HSE2010/12 participants were investigated using univariable and multivariable logistic regression. Associations with deprivation were explored using a residence-based measure, the IMD quintile of the LSOA of residence. Sexual behaviour variables reflecting exposure over the lifetime (years since first heterosexual sex, number of lifetime sexual partners) and more recent exposures (number of sexual partners in the last year, condom used at last sex) were included. Odds ratios (ORs) adjusted for number of lifetime sexual partners were calculated to reduce confounding of the association between predictors and being Pgp3 seropositive. Pgp3 seroprevalence among individuals ever diagnosed with chlamydia was estimated to explore sensitivity of serological testing to detect a previous known infection in this population. Pgp3 seroprevalence in those reporting no lifetime sexual partners was also estimated to explore test specificity and validity of

reporting of sexual activity. Analyses were conducted on those with non-missing data on the variable(s) of interest.

Pgp3 seroprevalence was estimated among 16 to 24 year-old women for each year with available sera from 1994 to 2012. The trend in Pgp3 seroprevalence was estimated from 2008 (the first year when the NCSP was nationally-available) to 2012 using a generalised linear model with year entered as a continuous variable.

Pgp3 seroprevalence by birth cohort was explored among women aged 16 to 24, with birth cohorts grouped to reflect their relative exposure to widespread chlamydia screening. The median age at first sex reported among 16 to 24 year-olds in Natsal-3 (16 years)[235] was used as a proxy age of sexual debut for the purposes of categorisation by birth cohort. Women who were ≤16 years in 2008 (the first year of national implementation of the NCSP) were defined as having high exposure. Women aged 17 to 24 in 2008 were defined as having partial exposure as they would have had some of their years post sexual debut before the NCSP was nationally-implemented but would have still been within the target age group when national implementation occurred. Women aged over 24 years in 2008 were defined as having 'limited' exposure as they would have been outside the NCSP target age group when the programme was nationally implemented. The numbers in each group by year of age are set out in Table 8-3 below.

Table 8-3: Numbers of women aged 16 to 24 contributing to seroprevalence estimates by birth cohort, by year of age

Exposure to widespread screening	Year born	Year turned 16	Number of women by year of age									
			16	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**16-24**
Limited (born 1966-1975)	1970	1986									66	66
25 or older in 2008	1971	1987								61	81	142
	1972	1988							63	76	87	226
	1973	1989						47	66	70		183
	1974	1990					52	50	69			171
	1975	1991				40	46	55				141
Total			**0**	**0**	**0**	**40**	**98**	**152**	**198**	**207**	**234**	**929**
Limited (born 1976-1983)	1976	1992				52	56					108
25 or older in 2008	1977	1993		51	41	44					45	181
	1978	1994	40	54	55					46	76	271
	1979	1995	68	61					40	87		256
	1980	1996	65					31	87			183
	1981	1997					48	82				130
	1982	1998				39	75					114
	1983	1999			37	69						106
Total			**173**	**166**	**133**	**204**	**179**	**113**	**127**	**133**	**121**	**1349**
Partial (born 1984-1991)	1984	2000		29	74						36	139
17 to 24 in 2008	1985	2001	37	107						27	9	180
	1986	2002	88						23	11	21	143
	1987	2003						21	9	17	19	66
	1988	2004					26	7	15	24	21	93
	1989	2005				16	8	15	11	20		70
	1990	2006			22	6	10	20	20			78
	1991	2007		28	14	13	12	17				84
Total			**125**	**164**	**110**	**35**	**56**	**80**	**78**	**99**	**106**	**853**
High (born 1992-1996)	1992	2008	27	5	14	15	6					67
16 or younger in 2008	1993	2009	8	17	13	18						56
	1994	2010	9	12	10							31
	1995	2011	16	11								27
	1996	2012	10									10
Total			**70**	**45**	**37**	**33**	**6***	**0**	**0**	**0**	**0**	**185**

**Not included in Figure 8-7 due to small group size.*

8.3.4 Regulatory approval

HSE is approved by an NHS research ethics committee each year. The use of stored sera from HSE participants for this study was approved by the Yorkshire and the Humber–South Yorkshire research ethics committee (ref: 13/YH/0304). All analyses were carried out anonymously and Pgp3 results were not linked to any identifiable information.

8.4 Results

A flow chart of included participants is shown in Figure 8-1. Of 14,762 eligible participants 6,882 (46.6%) provided a sample with consent for future testing. Of

these, samples for 1,264 were unavailable due to a missing sample or insufficient residual volume. Overall, 1,111/5,618 eligible participants with a valid chlamydia antibody test result were Pgp3 seropositive. Among HSE2010/12 participants, 546/2,521 were seropositive. Among 16 to 24 year-old women in selected HSE years from 1994 to 2012, 565/3,361 were seropositive. HSE2010/12 participants included in the analysis were comparable to the overall HSE population on a range of sociodemographic and behavioural variables (Table 8-4).

Table 8-4: Comparison of reported sociodemographic and behavioural variables between HSE participants and the study population by sex and age group (16-44 year-olds, HSE2010 & HSE2012)

	Women						Men					
	16-24 years			25-44 years			16-24 years			25-44 years		
	HSE participants	Study population	Difference	HSE participants	Study population	Difference	HSE participants	Study population	Difference	HSE participants	Study population	Difference
IMD quintile of LSOA area of residence*												
Least deprived	18.2%	16.6%	-1.6%	18.5%	17.8%	-0.7%	18.7%	17.8%	-0.9%	17.2%	16.1%	-1.0%
2	18.9%	19.6%	0.8%	18.9%	19.4%	0.5%	18.1%	19.2%	1.1%	19.7%	19.5%	-0.1%
3	21.0%	21.4%	0.3%	21.6%	21.4%	-0.2%	21.0%	19.9%	-1.1%	21.0%	21.8%	0.8%
4	21.2%	21.4%	0.2%	19.5%	19.3%	-0.1%	18.1%	17.6%	-0.5%	21.1%	21.5%	0.4%
Most deprived	20.6%	21.0%	0.4%	21.6%	22.1%	0.5%	24.2%	25.6%	1.5%	21.1%	21.0%	-0.1%
Ethnicity												
White	84.9%	85.5%	0.6%	84.5%	86.0%	1.5%	81.2%	82.2%	1.0%	86.2%	86.6%	0.4%
Black or Black British	4.0%	3.0%	-1.1%	3.6%	3.1%	-0.5%	2.3%	2.5%	0.2%	2.8%	2.8%	0.0%
Asian or Asian British	5.7%	5.3%	-0.4%	8.5%	7.8%	-0.7%	10.4%	9.7%	-0.6%	7.7%	7.6%	-0.1%
Mixed	1.7%	1.9%	0.2%	1.3%	1.2%	-0.1%	4.8%	4.0%	-0.8%	1.5%	1.4%	0.0%
Other ethnic groups	3.8%	4.4%	0.5%	2.0%	1.9%	-0.1%	1.3%	1.5%	0.2%	1.8%	1.6%	-0.2%
Marital status												
Single	78.5%	77.9%	-0.7%	18.5%	18.5%	-0.1%	86.7%	86.6%	-0.1%	22.7%	22.1%	-0.6%
Married	2.8%	2.5%	-0.2%	52.7%	52.0%	-0.7%	1.5%	1.7%	0.3%	48.6%	50.0%	1.4%
Separated	0.2%	0.3%	0.0%	8.2%	8.6%	0.4%	0.0%	0.0%	0.0%	5.2%	5.1%	-0.1%
Cohabiting	18.5%	19.3%	0.8%	20.6%	20.9%	0.3%	11.8%	11.7%	-0.2%	23.5%	22.8%	-0.7%
Ever had sex	80.4%	80.2%	-0.2%	98.4%	98.5%	0.0%	73.7%	76.5%	2.8%	97.3%	97.2%	-0.1%
Ever diagnosed with chlamydia	5.8%	4.2%	-1.5%	6.5%	6.7%	0.2%	2.1%	2.4%	0.4%	5.1%	5.5%	0.4%
Ever been tested for chlamydia	47.6%	47.7%	0.1%	33.5%	33.2%	-0.4%	39.1%	39.9%	0.9%	18.0%	17.7%	-0.4%

**IMD: index of multiple deprivation; LSOA: Lower super output area*

8.4.1 Pgp3 seroprevalence in HSE2010 & HSE2012

The overall Pgp3 seroprevalence among 16 to 44 year-olds in HSE2010/12 was 24.4% (95%CI 22.0%-27.1%) in women and 13.9% (95%CI 11.8%-16.2%) in

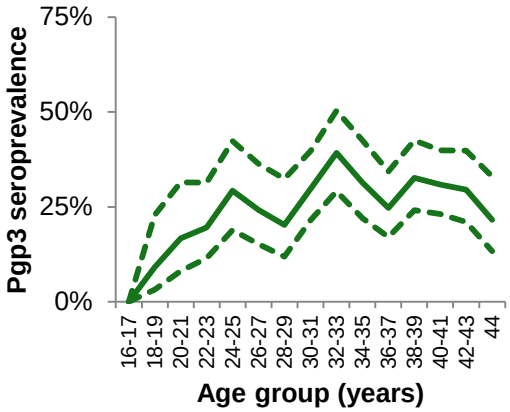
men. A further 2.1% of women and 2.6% of men aged 16 to 44 reported having been diagnosed with chlamydia but were Pgp3 seronegative. Among individuals who reported a previous chlamydia diagnosis, 64.7% (95%CI 51.9%-75.6%) of women and 43.9% (95%CI 26.5%-63.0%) of men were Pgp3 seropositive.

Among sexually-experienced participants, Pgp3 seroprevalence increased with age (Figure 8-2), years since first sex (Figure 8-3) and with increasing numbers of lifetime sexual partners (Figure 8-4). Peak Pgp3 seroprevalence was seen in women aged 30 to 34 (33.5%) and in men aged 35 to 39 (18.7%).

Figure 8-2: Pgp3 seroprevalence by age group (sexually-experienced 16 to 44 year-olds, HSE2010 & HSE2012)

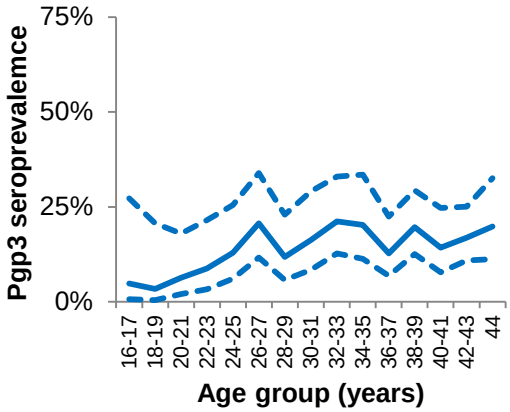
Solid lines show point estimates; dashed lines show 95% confidence intervals. N shows unweighted denominator.

Women



N=1,194

Men

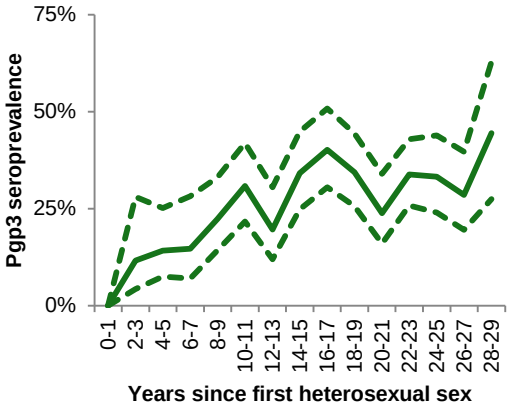


N=948

Figure 8-3: Pgp3 seroprevalence by years since first heterosexual sex, (sexually-experienced 16 to 44 year-olds, HSE2010 & HSE2012)

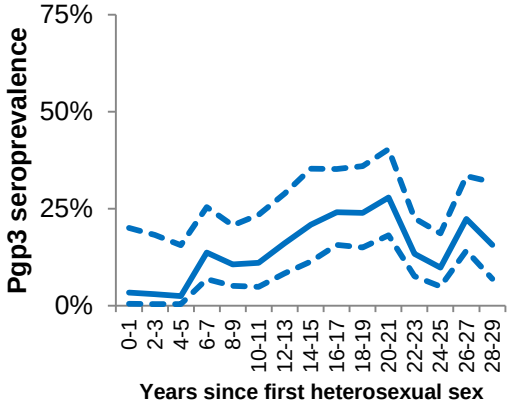
Solid lines show point estimates; dashed lines show 95% confidence intervals.

Women



N=1,188

Men



N=936

Figure 8-4: Pgp3 seroprevalence by reported numbers of lifetime sexual partners (16 to 44 year-olds, HSE2010 & HSE2012)

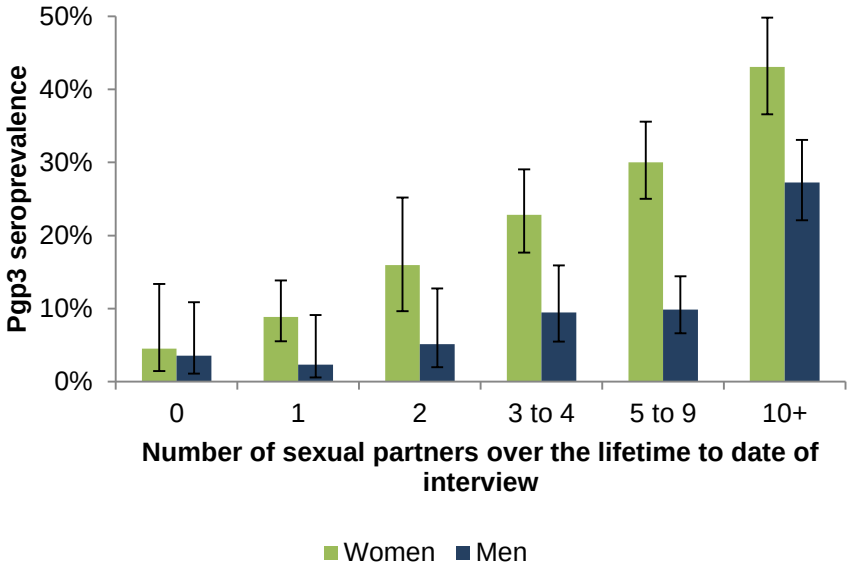


Table 8-5 presents Pgp3 seroprevalence by selected sociodemographic and behavioural factors among sexually-experienced women and men. In women, those reporting ≥10 lifetime sexual partners had almost four-fold higher odds of being Pgp3 seropositive than those with 1-4 partners (OR 3.84, 95%CI 2.68-5.51). Being Pgp3 seropositive was also significantly associated with living in more deprived areas, younger age at first sex, non-condom use in the last year and reporting a previous chlamydia diagnosis. All variables associated with being Pgp3 seropositive in univariable analyses remained statistically significant after adjusting for number of lifetime sexual partners. The lifetime sexual partner-adjusted odds ratio (AOR) of being seropositive was 1.68 (95%CI 1.18-2.39) in women aged less than 16 at first heterosexual sex versus those aged 16 or over. Women who reported non-condom use in the last 4 weeks had two-fold higher odds of being seropositive (AOR 2.17, 95%CI 1.41-3.35).

In sexually-experienced men, similar factors were associated with being seropositive as seen in women in univariable analyses although age group and

deprivation of residence were not statistically significant. After adjusting for number of lifetime sexual partners, only reporting a previous diagnosis of chlamydia remained a significant predictor of being seropositive in men (AOR 3.55, 95%CI 1.53-8.25).

Among Pgp3 seropositive individuals, 84.7% (80.3%-88.3%) of 16 to 44 year-olds did not report a previous chlamydia diagnosis. This proportion varied by age group, whereby 76.7% of 16 to 24 year-olds, 79.0% of 25 to 34 year-olds and 92.9% of 35-44 year-olds did not report a previous diagnosis. Furthermore, among 16 to 24 year-olds 36.3% of seropositive individuals reported having been tested for chlamydia, but had never been diagnosed. Among those aged 16 to 24 years who had any evidence of a previous *C. trachomatis* infection (i.e. those who were Pgp3 seropositive or who reported a previous chlamydia diagnosis), 75.5% (95%CI 70.8%-79.7%) did not report a previous diagnosis.

Table 8-5a: Percentage Pgp3 seropositive by sociodemographic and sexual behavioural variables, and unadjusted and lifetime sexual partners-adjusted odds ratios for detection of Pgp3 antibody in serum (sexually-experienced 16 to 44 year-old <u>women</u>, HSE2010 & HSE2012)

	Percent Pgp3 positive (95%CI)		Unadjusted OR (95%CI)		p(uOR)	Lifetime SP-adjusted OR (95%CI)		p (aOR)	Bases (W,UW)[a]
Overall	25.8%	(23.1-28.6)							1423, 1194
Age group									
16-19	6.3%	(2.3-16.4)	1.00	-	0.002	1.00	-	0.009	114, 55
20-24	21.4%	(15.3-29.2)	4.05	(1.29-12.78)		3.70	(1.17-11.71)		255, 139
25-29	23.3%	(17.1-30.8)	4.50	(1.44-14.07)		3.92	(1.26-12.16)		229, 166
30-34	33.5%	(27.5-40.2)	7.50	(2.50-22.54)		6.34	(2.11-19.04)		284, 224
35-39	29.5%	(24.2-35.6)	6.23	(2.08-18.65)		5.07	(1.71-15.06)		240, 278
40-44	28.5%	(23.2-34.3)	5.91	(1.99-17.60)		5.47	(1.84-16.26)		302, 332
IMD quintile of LSOA of residence[b]									
Least deprived	22.7%	(17.1-29.5)	1.00	Ref	0.033	1.00	Ref	0.037	256, 238
2	25.8%	(20.3-32.2)	1.18	(0.74-1.89)		1.08	(0.67-1.73)		292, 248
3	19.6%	(15.1-25.2)	0.83	(0.51-1.35)		0.83	(0.50-1.38)		309, 256
4	32.1%	(26.1-38.8)	1.61	(1.02-2.53)		1.61	(1.00-2.61)		290, 230
Most deprived	28.9%	(22.7-36.0)	1.38	(0.86-2.24)		1.46	(0.87-2.43)		276, 222
Age at first heterosexual sex									
16+ at first intercourse	22.5%	(19.6-25.7)	1.00	Ref	0.000	1.00	Ref	0.004	1080, 911
<16 at first intercourse	39.6%	(33.0-46.6)	2.26	(1.61-3.16)		1.68	(1.18-2.39)		304, 246
Years since first heterosexual sex									
0 to 4	8.1%	(3.8-16.7)	1.00	-	<0.001	1.00	Ref	<0.001	184, 90
5 to 9	18.5%	(13.1-25.4)	2.56	(1.01-6.49)		2.05	(0.80-5.20)		289, 174
10 to 14	25.9%	(20.1-32.8)	3.95	(1.61-9.69)		2.79	(1.14-6.79)		256, 199
15 to 19	38.2%	(32.0-44.7)	6.96	(2.98-16.26)		5.40	(2.31-12.62)		271, 264
20+	31.1%	(26.5-36.0)	5.08	(2.19-11.77)		3.61	(1.55-8.37)		415, 461
Number of partners of the opposite sex in last year									
0	19.2%	(11.7-30.0)	1.00	Ref	0.370	1.00	Ref	0.028	91, 81
1	26.8%	(23.8-30.0)	1.53	(0.84-2.79)		1.58	(0.80-3.12)		1159, 993
2+	25.7%	(17.9-35.4)	1.45	(0.69-3.06)		0.89	(0.41-1.94)		149, 103
Number of lifetime sexual partners[c]									
1 to 4	16.5%	(13.2-20.3)	1	-	<0.001				
5 to 9	30.0%	(25.0-35.6)	2.18	(1.51-3.14)					
10+	43.1%	(36.6-49.8)	3.84	(2.68-5.51)					
Condom use in last 4 weeks									
Used on every occasion	15.8%	(11.4-21.6)	1.00	Ref	0.001	1.00	Ref	0.001	262, 207
Used on some occasions	19.4%	(12.7-28.5)	1.28	(0.68-2.41)		1.09	(0.57-2.09)		133, 95
Not used in last 4 weeks	30.1%	(26.4-34.1)	2.30	(1.49-3.53)		2.17	(1.41-3.35)		735, 630
Not had vaginal or anal sex in last 4 weeks	26.8%	(20.5-34.3)	1.95	(1.15-3.31)		1.79	(1.03-3.11)		239, 209
Ever diagnosed with chlamydia?									
No	23.6%	(20.9-26.7)	1.00	-	<0.001	1.00	Ref	<0.001	1145, 960
Yes	65.5%	(52.7-76.3)	6.12	(3.57-10.51)		5.08	(2.79-9.23)		76, 68

Table 8-5b: Percentage Pgp3 seropositive by sociodemographic and sexual behavioural variables, and unadjusted and lifetime sexual partners-adjusted odds ratios for detection of Pgp3 antibody in serum (sexually-experienced 16 to 44 year-old <u>men</u>, HSE2010 & HSE2012)

	Percent Pgp3 positive (95%CI)		Unadjusted OR (95%CI)		p(uOR)	Lifetime SP-adjusted OR (95%CI)		p (aOR)	Bases (W,UW)[a]
Overall	14.6%	(12.3-17.1)							1424, 948
Age group									
16-19	4.1%	(1.0-15.0)	1.00	-	0.113	1.00	-	0.385	142, 66
20-24	10.1%	(5.8-17.0)	2.66	(0.57-12.40)		1.74	(0.35-8.61)		220, 114
25-29	14.3%	(9.2-21.5)	3.94	(0.88-17.68)		2.32	(0.48-11.20)		255, 139
30-34	18.1%	(12.6-25.3)	5.22	(1.19-23.00)		3.21	(0.70-14.76)		251, 165
35-39	18.7%	(13.4-25.6)	5.45	(1.24-23.96)		3.22	(0.70-14.76)		242, 214
40-44	16.7%	(12.4-22.1)	4.74	(1.09-20.65)		2.74	(0.60-12.62)		314, 250
IMD quintile of LSOA of residence[b]									
Least deprived	13.7%	(8.9-20.5)	1.00	Ref	0.680	1.00	Ref	0.795	241, 184
2	12.4%	(8.5-17.8)	0.90	(0.47-1.72)		0.98	(0.50-1.92)		283, 195
3	14.8%	(10.0-21.3)	1.10	(0.56-2.14)		1.31	(0.65-2.61)		304, 199
4	13.8%	(9.5-19.6)	1.01	(0.54-1.88)		0.90	(0.44-1.82)		285, 179
Most deprived	17.7%	(12.7-24.0)	1.36	(0.73-2.52)		1.22	(0.61-2.45)		310, 191
Age at first heterosexual sex									
16+ at first intercourse	12.0%	(9.6-15.0)	1.00	Ref	0.002	1.00	Ref	0.233	980, 658
<16 at first intercourse	22.6%	(17.5-28.8)	2.14	(1.41-3.24)		1.50	(0.94-02.38)		357, 231
Years since first heterosexual sex									
0 to 4	3.5%	(1.1-10.5)	1.00	Ref	0.003	1.00	-	0.077	230, 109
5 to 9	10.1%	(6.2-16.2)	3.11	(0.86-11.18)		1.78	(0.47-6.82)		283, 154
10 to 14	16.3%	(10.7-24.0)	5.36	(1.51-19.03)		3.12	(0.85-11.42)		236, 148
15 to 19	22.3%	(16.2-29.8)	7.91	(2.31-27.02)		4.10	(1.15-14.66)		249, 186
20+	18.0%	(14.1-22.6)	6.03	(1.84-19.76)		3.04	(0.90-10.33)		409, 339
Number of partners of the opposite sex in last year									
0	10.4%	(3.8-25.5)	1.00	Ref	0.741	1.00	-	0.687	100, 59
1	14.5%	(12.1-17.4)	1.46	(0.49-4.35)		1.52	(0.43-5.38)		1059, 745
2+	15.6%	(10.2-23.1)	1.59	(0.49-5.16)		1.28	(0.32-5.06)		215, 115
Total number of lifetime sexual partners[c]									
1 to 4	5.9%	(3.7-9.2)	1.00	Ref	<0.001				575, 361
5 to 9	9.9%	(6.6-14.4)	1.74	(0.90-3.33)					322, 223
10+	27.2%	(22.1-33.1)	5.95	(3.41-10.35)					446, 306
Condom use in last 4 weeks									
Used on every occasion	10.8%	(7.0-16.3)	1.00	Ref	0.046	1.00	-	0.272	285, 181
Used on some occasions	13.0%	(7.6-21.2)	1.23	(0.58-2.61)		1.24	(0.54-2.82)		173, 98
Not used in last 4 weeks	17.6%	(14.3-21.4)	1.76	(1.04-3.00)		1.51	(0.83-2.72)		657, 479
Not had vaginal or anal sex in last 4 weeks	9.7%	(5.7-15.8)	0.88	(0.43-1.81)		0.86	(0.39-1.90)		246, 151
Ever diagnosed with chlamydia?									
No	12.8%	(10.6-15.4)	1.00	Ref	<0.001	1.00	Ref	0.003	1145, 776
Yes	44.6%	(26.9-63.8)	5.47	(2.47-12.15)		3.55	(1.53-8.25)		62, 35

[a] *Denominator totals vary due to item-missingness & include individuals where the specified characteristic is unknown*
[b] *IMD: index of multiple deprivation; LSOA: Lower super output area*
[c] *Includes partners of both the opposite and of the same gender.*

8.4.2 Pgp3 seroprevalence over time among 16 to 24 year-old women

Figure 8-5 shows Pgp3 seroprevalence among 16 to 24 year-old women in each year sampled. There was no significant difference in Pgp3 seroprevalence between the first (1994 to 1996) and second (2001 to 2002) time-periods sampled. Between 2008 and 2012, there was a non-significant decline in Pgp3 seroprevalence among 16 to 24 year-old women (prevalence ratio per year: 0.94, 95%CI 0.84-1.05; p=0.26). After stratifying by age group, there was no notable trend among 16 to 19 year-olds (prevalence ratio: 0.96, 95%CI 0.74-1.24; p=0·76), and a non-significant decline in Pgp3 seroprevalence among 20 to 24 year-olds (prevalence ratio: 0.92, 95%CI: 0.83-1.04; p=0.18, (Figure 8-6).

Figure 8-5: Pgp3 seroprevalence by year (16 to 24 year-old women, HSE 1994 to 2012)

Solid lines show point estimates; dashed lines show 95% confidence intervals. Unweighted denominators: 1994-1996, n=1,555; 2001-2002, n=1097 2008-2012, n=709.

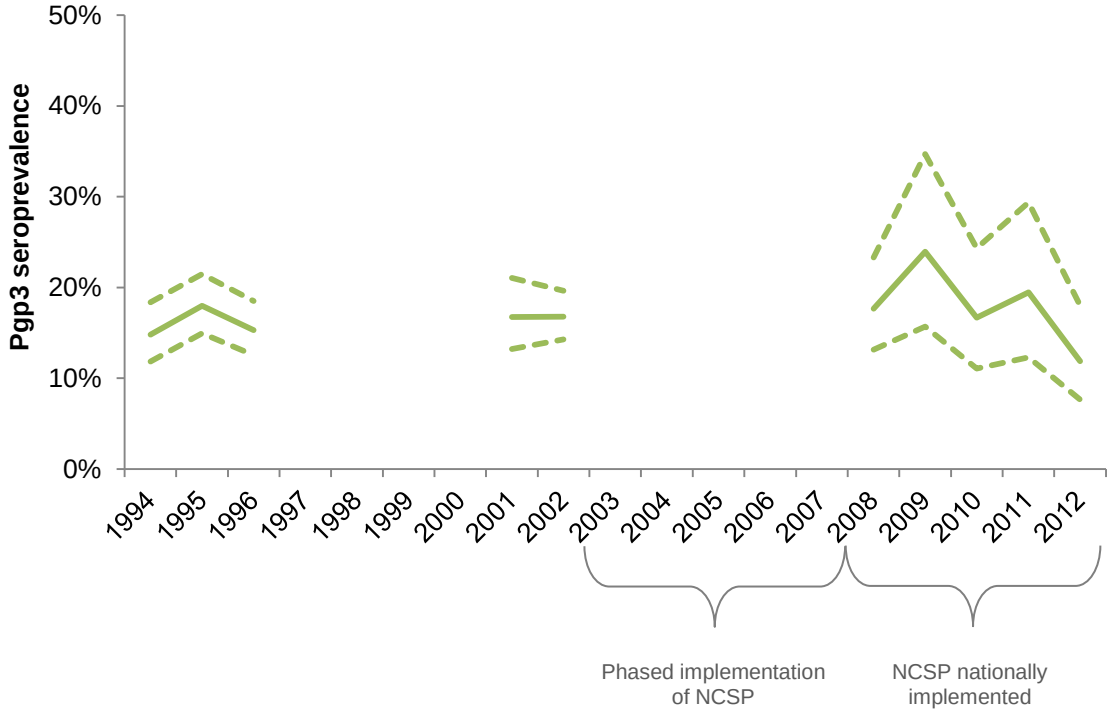


Figure 8-6: Pgp3 seroprevalence by year and age group (16 to 24 year-old women, HSE 2008 to 2012)

Solid lines show point estimates; dashed lines show 95% confidence intervals. Unweighted denominators: 16-19 year-olds, n=284; 20-24 year-olds, n=425.

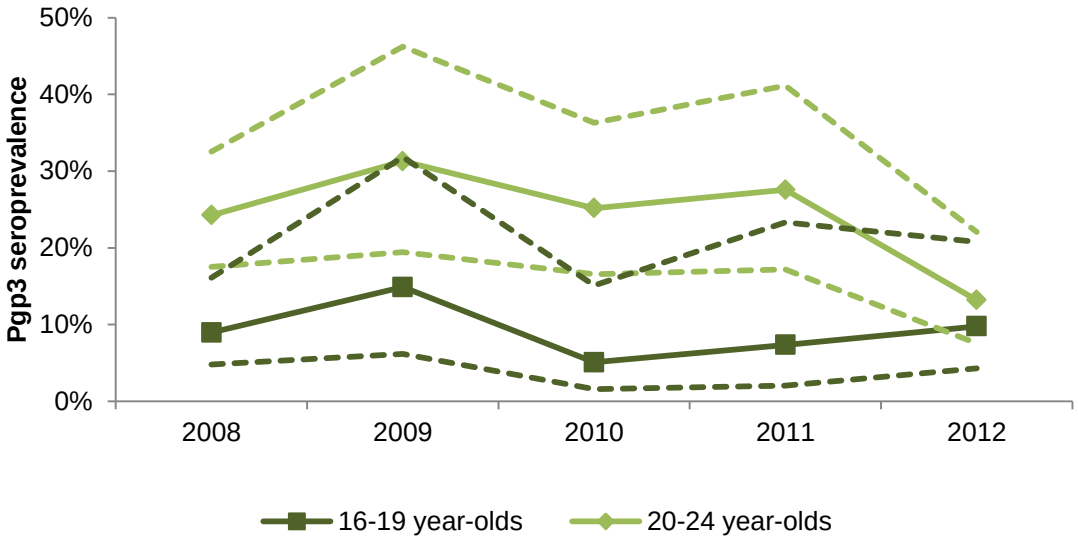
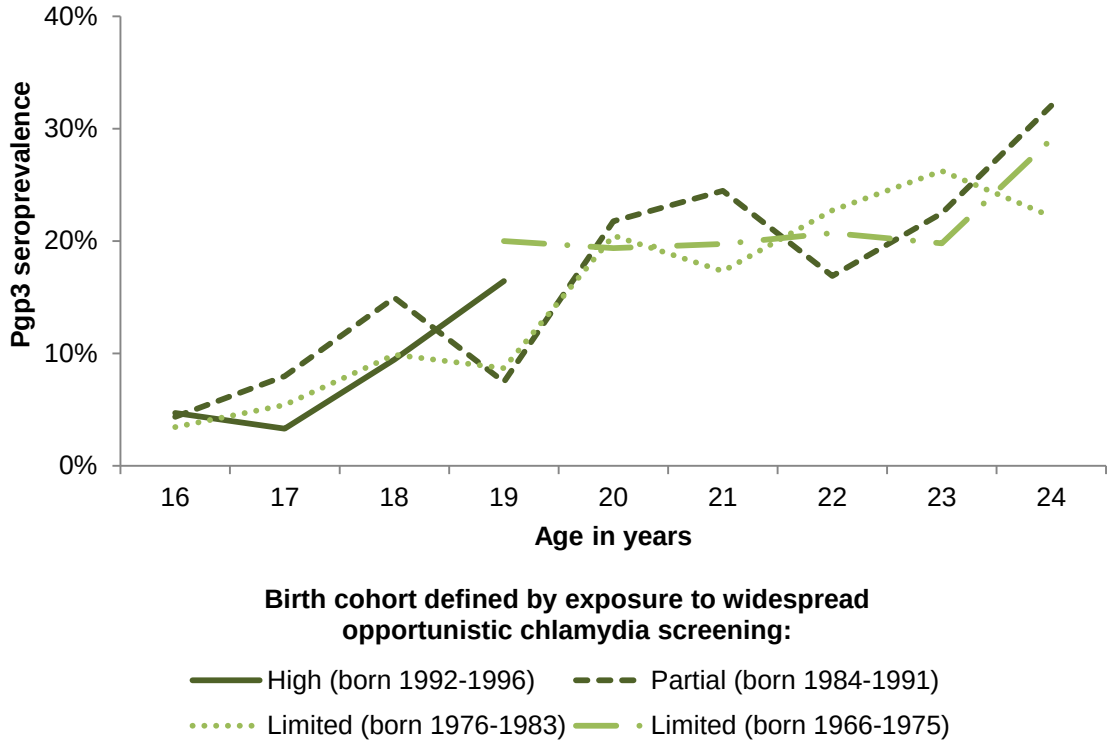


Figure 8-7 shows Pgp3 seroprevalence by year of age and birth cohort defined by exposure to widespread chlamydia screening. Although data were only available on those aged up to 19 years in the group who had high exposure to screening (due to the number of HSE survey years available since 2008), there was no indication of a difference in the age-specific seroprevalence by birth cohort, with similar age curves seen in each group.

Figure 8-7: Pgp3 seroprevalence by birth cohort and year of age (16 to 24 year-old women, HSE 1994 to 2012)*



**Unweighted denominators: High (born 1992-1996), n=185; Partial (born 1984-1991), n=853; Limited (born 1976-1983), n=1349; Limited (born 1966-1975), n=929. See Table 8-3 for details of denominators by year of age.*

8.5 Discussion

8.5.1 Key findings

In 2010/12, one quarter of 16 to 44 year-old and one in three 30 to 34 year-old women had evidence of a previous chlamydia infection as indicated by the presence of detectable Pgp3 antibodies in serum. Being Pgp3 seropositive was strongly associated with increasing age, years since first sex and numbers of lifetime sexual partners, as would be expected from a marker of previous infection with a sexually-transmitted infection. Three quarters of under-25 year-olds with evidence of previous infection did not report a previous chlamydia diagnosis, suggesting a high level of undiagnosed infections. There was no

significant trend in age-specific Pgp3 seroprevalence over time or between birth cohorts exposed to different levels of opportunistic chlamydia screening.

The proportion of the population who acquire chlamydia infection by their mid-40s is much greater than suggested by prevalence studies of *current* infection as measured by NAATs. For example in Natsal-3, which was conducted at a similar time, the prevalence of current chlamydia infection was estimated to be 1.5% in women and 1.1% in men aged 16 to 44 years.[23] Studies that focus on current infection underestimate the lifetime risk of chlamydia infection.

8.5.2 Strengths and limitations

The major strengths of this analysis are that it used data and stored sera from a series of nationally-representative samples and applied novel serological tests to investigate age-specific cumulative incidence of chlamydia. For HSE2010/12 participants Pgp3 seroprevalence could be investigated by sociodemographic and behavioural factors at an individual level. The assays used in the testing strategy have demonstrated higher sensitivity than commercially-available assays.[209,269]

There were some limitations. The findings may be affected by who agreed to take part in the survey or provide a blood sample. Non-response weights were applied to account for non-participation in the overall survey and provision of a blood sample. HSE2010/12 participants who contributed to this study were comparable to the overall HSE population on a range of sociodemographic and variables, however unmeasured bias remains feasible. A further limitation is that all behavioural data were self-reported. Sensitive items were collected using the self-completion booklet to minimise social desirability bias. However, as

questions were completed using a booklet rather than the best-practice of computer-assisted self-interview and as household members could be present during booklet completion, underreporting remains possible.[272]

Estimated sensitivity of both the indirect and the double-antigen ELISAs to detect a previous chlamydia infection is less than 100% (e.g. 74% and 83% respectively in women). The percent Pgp3 seropositive among individuals who had ever been diagnosed with chlamydia was comparable to the reported sensitivity of the indirect, but slightly lower than that of the double-antigen ELISA. Pgp3 seroprevalence will therefore be a biased estimator of age-specific cumulative incidence of *C. trachomatis* due to misclassification arising from test performance (i.e. misclassification of presence/absence of antibodies) or patterns of seroconversion and subsequent loss of antibodies (i.e. absence of antibodies does not always reflect an absence of previous infection). Evidence from a study by Horner *et al* suggests that anti-Pgp3 antibodies are more likely to be detectable in the first few weeks/months of an infection and are more likely to remain detectable in women with repeat versus those with first infections.[100] In that study, sera from women attending two GUM clinics with at least one known previous chlamydia diagnosis were tested using the indirect Pgp3 ELISA. The percentage Pgp3 seropositive declined with increasing time since last detection up to ~6 months and remained relatively stable thereafter. The percent seropositive in women with more than one known previous chlamydia diagnosis remained higher for a longer period than in women with only one previous diagnosis. Thus interpreting Pgp3 seroprevalence as a measure of age-specific cumulative incidence of *C. trachomatis* infection will be complicated by test performance, time since infection and patterns of re-infection. Nevertheless, Pgp3 seroprevalence represents a lower bound of age-

specific cumulative incidence; the proportion of the population ever infected with *C. trachomatis* would be even higher than estimated Pgp3 seroprevalence presented in this chapter. While this misclassification error is important to understand and ideally quantify, measurement of Pgp3 seroprevalence is a promising approach for surveillance and for impact evaluation of chlamydia control programmes given the ability to measure minimum age-specific cumulative incidence.

Pgp3 antibodies were detected among people who had never had sexual intercourse. This may be due to under-reporting of sexual experience or to false positives that would be expected from low prevalence populations. Interestingly, the percentage Pgp3 seropositive among those with no lifetime sexual partners when measured on the indirect ELISA only was higher than when estimated using the testing strategy of combined indirect and double-antigen Pgp3 ELISAs (5.7% versus 4.0%). This may suggest a higher specificity of the double-antigen ELISA and supports its use within the testing strategy.

Interpreting Pgp3 seroprevalence patterns among men is complicated by lower test sensitivity to detect a previous infection, which may reflect differences in immune response following infection by gender and site of infection.[209] The lower Pgp3 seroprevalence also limits the power to investigate risk factors for Pgp3 seropositivity given the smaller number of men with detectable antibodies. The more gradual increase in Pgp3 seroprevalence with age in men may partly reflect age-mixing patterns whereby women tend to have older male sexual partners. Thus as the prevalence of infection in men is higher in those aged 20 to 24 than in 16 to 19 year-olds,[23] women may be at higher risk of incident infection at sexual debut than men. However, the more gradual increase in men

might also reflect the importance of repeated exposure in developing a persistent, detectable Pgp3 antibody response.

8.5.3 Comparison to other studies

STI incidence is thought to have been low in the early 1990s following changes in sexual risk-taking behaviour after sexual health campaigns aimed at HIV prevention in the early- to mid-1980s.[273] From the mid-1990s there were increases in reports of bacterial STI[273] and sexual risk behaviours increased between 1990 and 2000,[235] suggesting a likely rise in STIs. It might therefore be expected that Pgp3 seroprevalence would have increased between the mid-1990s and early 2000s, but there was no significant difference between these periods. One possible explanation for this is that STI incidence had already started to increase by the mid-1990s. Chlamydia incidence may also have been less affected by changes in sexual behaviour over the period as it is more widely distributed in the population than STI such as gonorrhoea or syphilis[23]. It is also feasible that participation bias not reflected in the survey weights changed over this period.

More interestingly for the evaluation of chlamydia screening is that no significant change was found in age-specific seroprevalence between 2008 and 2010 and there was no difference between birth cohorts exposed to different levels of opportunistic chlamydia screening. This is perhaps surprising given the increase in chlamydia control efforts over the last decade. Possible reasons for this and comparisons with findings from other studies are discussed in detail in the following chapter.

In this analysis, women with greater numbers of sexual partners and who reported younger age at first sex were more likely to have evidence of a previous infection. This is consistent with findings from a cohort study of women in New Zealand whose sera were tested using the double-antigen ELISA, among whom lifetime sexual partners and age at first sex were both associated with being seropositive.[269] The steep increase in seroprevalence from age 16 to age 25 also suggests a particularly high rate of infection among young women soon after commencing sexual debut. Based on the observed seroprevalence at 10-11 years after first heterosexual sex (31%), the average annual incidence of chlamydia infection in women can be estimated to be at least 3% per year in the ten years following sexual debut. This will be an underestimate of the overall rate of transmission, as repeat infections are common[48-57] but cannot be quantified from seroprevalence data. This emphasises the importance of adolescence and young adulthood as periods when chlamydia prevention and screening activities are needed to prevent development of adverse consequences.

Pgp3 seroprevalence estimated among HSE participants was higher than that reported from a recent population-based study in the Netherlands reported by Van Aar et al, which used the Medac CT IgG ELISA (9.8% in women and 5.7% in men aged 15 to 39[132]). Van Aar *et al* also found a less marked relationship with age. This may be due to the difference in assay sensitivity (Medac: 46·2% versus double-antigen ELISA: 82·9%),[269] or to country differences in the epidemiology of chlamydia.

8.5.4 Implications for evaluation of chlamydia control

The clear relationship between Pgp3 seroprevalence and number of lifetime sexual partners, especially among women, further supports the use of age-specific seroprevalence as a marker of previous infection. The insight gained from these results demonstrates the strengths of this approach to outcome measurement.

The findings from this analysis do not support there having been a decrease in age-specific cumulative incidence among 16 to 24 year-old women following the implementation and national roll-out of the NCSP. As discussed in more detail in the next section, the evidence for high lifetime cumulative incidence and suggestion of high fraction of undiagnosed infections may offer a partial explanation for the absence of a decline in age-specific cumulative incidence.

8.5.5 Summary

A decrease in age-specific cumulative incidence of chlamydia following the national implementation of opportunistic chlamydia screening has not yet been demonstrated. The implications of these findings and possible reasons for an apparent absence of any decline are explored in detail in the next chapter.

9 Summary and discussion

In the previous five chapters I examined four different approaches to outcome measurement for the evaluation of chlamydia screening. In this chapter I discuss the meaning of my findings in the context of the original aims of the thesis, which were:

1. to identify and appraise outcome measures, and methods of their measurement, for the purpose of evaluating the impact of opportunistic chlamydia screening on the incidence and prevalence of infection (or related measures); and

2. using the outcome measures and methods identified in (1), to examine whether widespread opportunistic chlamydia screening, as it has been delivered in practice, has led to a reduction in the incidence or prevalence of chlamydia among young adults in England up to 2012 that would otherwise have been seen in the absence of opportunistic chlamydia screening.

I make recommendations about whether and how this range of methods should be incorporated into ongoing evaluation of chlamydia screening and discuss the implications of my findings for the future development of chlamydia control policies in England. Finally, I set out suggestions for future research given the questions raised by my research that, as yet, remain unanswered.

9.1 Critical appraisal of outcome measures for the evaluation of the impact of chlamydia screening on incidence and prevalence of infection

9.1.1 Trends in percentage testing positive for chlamydia using surveillance data

As discussed in Chapter 3, it is well established that, as a large proportion of chlamydia infections are asymptomatic[10,11,20] the number of chlamydia diagnoses reported and proportion of tests which are positive are highly dependent on the population tested. Thus reported diagnoses do not represent the true burden of incident infections and percentage testing positive does not equate to population prevalence.[201]

My analysis using surveillance data from populations accessing chlamydia testing showed that the percentage testing positive varies according to testing venue type, and that significant differences between venues in the odds of testing positive remained even after adjustment for sexual behaviour variables. This suggests that the sexual behaviour and demographic data items that were available in the NCSP dataset could not fully explain the difference in risk of having a current chlamydia infection between populations attending different services. Given that the available sexual and behavioural variables were not sufficient to capture the difference in risk of infection between people attending different venues, it is also possible that these variables would be insufficient to capture difference in risk arising from a different profile of people accessing testing over time, even in analyses stratified by testing venue type. This potential for unmeasured confounding would be especially true in the presence of changes in testing policy, for example if a venue were to move from universal to targeted testing. Thus trends in percentage testing positive from populations

accessing chlamydia testing do not provide definitive measures of change in the underlying population prevalence of infection.

As NAATs have been widely available since at least 2006 in the UK,[128] then there will have been minimal measurement error in the trends in percentage testing positive introduced by detection strategies used. However it is important to remain vigilant to changes in test technology that might affect surveillance data as changes in tests used have repeatedly been shown to affect observed trends in percentage testing positive for chlamydia.[192,200,203,204,274] Future developments in test technologies and testing pathways including point of care testing[275] and remote testing via mobile devices[276] are on the horizon and may in the future present a shift in test performance that would be reflected in cases reported and estimates of percentage testing positive. Maintaining consistency in test technologies is beneficial to permit comparisons over time, but the need to deliver the best diagnostic services means that changes will likely occur. Future analysis of longitudinal trends should therefore consider changes in test sensitivity and specificity. As with changes in testing strategies within the Natsal surveys (Chapter 6), head to head comparisons of different test technologies used in routine practice as developments occur will be useful to provide data for comparisons over time.

It was not possible to measure uptake of testing (i.e. the percentage of eligible individuals attending services who were tested) among those attending all venues. This would have been possible with data from GUM clinics as a clinic-attending denominator is available. However as the offer and uptake of a chlamydia test is less likely to vary in GUM settings this was not investigated in the analysis presented in Chapter 4. Developments in the GUMCADv2

surveillance system, whereby comparable information to that collected in GUM clinics is now collected for all commissioned 'level 2' (i.e. non-GUM) sexual health services, mean that a measure of uptake of testing within sexual and reproductive health services and some GP clinics will be available in coming years. The extent to which percentage testing positive varies with test uptake within a setting would be useful to explore in future analyses.

Some of the issues of using surveillance data may be addressed if chlamydia screening were to be delivered as a register-based screening programme, where a defined population were invited to participate. By standardising the offer of screening, this might make the resulting data less susceptible to confounding arising from differences in who is offered a test. However, even register-based screening programmes face challenges in reliable outcome measurement. As described in Chapter 3, the CSI project in the Netherlands was a register-based programme and invited all 16 to 29 year-olds resident in three areas of the Netherlands to be tested for chlamydia once a year for three years. In their write-up of findings from the CSI project, van den Broek *et al* noted that the population tested each year appeared to be at higher risk, on average, in each subsequent year.[88] Thus even in the context of a RCT of register-based screening the study's findings remain open to question due to the potential for unmeasured confounding. In another (ongoing) RCT in Australia, the Australian Chlamydia Control Effectiveness Pilot 'ACCEPt' aims to assess the feasibility, acceptability and effectiveness of chlamydia testing in GP settings.[277] The primary outcome of the trial is chlamydia 'prevalence' measured among women and men attending GP services. However, as this is based on a clinic-attending population this would be more akin to percentage testing positive according to the definitions applied throughout this thesis.

Prevalence will be compared between clinics in the intervention arm where clinics have been asked to offer chlamydia testing to all sexually active under-30 year-olds to that measured in control clinics. While the baseline prevalence survey achieved high response rate (69.7%),[278] participants were provided with their results. It is therefore feasible that follow up collections might be affected by previous offers of testing meaning that participation bias may vary between the intervention and control arms. While the results of this study are not yet available, this further illustrates the potential limitations of using percentage testing positive as an outcome measure even when utilised as part of a RCT.

In summary, trends in percentage testing positive should not be interpreted as trend in underlying burden of disease without first ruling out or addressing sources of selection bias and confounders affecting trends over time.

9.1.2 Repeat cross-sectional anonymous postal surveys of chlamydia prevalence

As described in Chapter 4, the pilot of a postal survey of young women with anonymous testing for chlamydia resulted in low participation rates. Both provision of a home sampling kit and offering a small financial incentive increased participation, and reduced the cost per sample received. Although the sample size in the pilot was not sufficient to provide strong evidence for, or to rule out selection bias, given the low participation rates achieved, future surveys using this methodology would be open to substantial and potentially varying selection bias. There was some indication that demographic characteristics varied between the groups, suggesting the very real potential for selection bias using this methodology. The piloted approach is therefore not feasible or

suitable for population-based monitoring of chlamydia prevalence among young women in England.

The maximum achieved participation rate of 14% (in the group with the voucher) was comparable with other population based approaches using postal invitation for chlamydia testing. In a pilot of a postal offer of chlamydia screening, Bracebridge *et al* achieved a participation rate of 13% among women aged 18 to 24.[158] In the Netherlands, the CSI project achieved a 21% participation rate among 15 to 29 year-old women in year one, which fell to 13% in year 3.[88] Studies such as Natsal and NHANES, which invited participants to provide a sample during a face to face interview, have achieved response rates of upwards of 50%.[141,172] This suggests that high response rates can be achieved, but that a far more resource-intensive recruitment approach would be needed. Additionally, surveys with a broader focus than chlamydia prevalence may be of more interest to the eligible participants meaning a larger and potentially more representative population could be recruited.

9.1.3 Repeat cross-sectional surveys of chlamydia prevalence embedded within sexual behaviour or general health surveys

The Natsal surveys have achieved much higher response rates than were observed in my pilot of a chlamydia-specific postal survey of chlamydia prevalence.[172] As with other probability surveys among general population samples,[7,135,141] participation in Natsal is far from universal and there therefore remains some, theoretical, potential for non-participation bias. However these surveys are far more robust than postal surveys for chlamydia with regard to representativeness of the population.

My analyses presented in chapter 6 showed that, while changing approaches to prevalence measurement pose challenges for comparisons over time, adjustments can be made to allow for differences in diagnostic tests used in each survey where the relative sensitivity and specificity of tests is known. The adjustments for detection strategy were made using data from two separate studies where the tests and specimen collection devices used in Natsal-2 had been compared to those used in Natsal-3. As estimated sensitivity and specificity are dependent on the gold standard used, such head to head comparisons are invaluable. Given ongoing technological developments it is possible that tests for chlamydia (and other infections) used in any subsequent Natsal survey may differ from those in Natsal-3. In anticipation of this, maintaining a panel of residual biological samples for the purposes of validating using any future tests will be useful to strengthen the possibility for future comparisons.

While adjustments for different detection strategies could be made, the comparisons between age- and gender-specific measures of chlamydia prevalence were ultimately limited by the sample size available in each survey. The Natsal-2 and Natsal-3 surveys were not powered to detect changes in chlamydia prevalence, so it is not perhaps surprising that these comparisons were limited by the number of participants in specific groups. Other surveys have also been limited by the sample size available. In NHANES in the US, estimates by age, gender and race/ethnicity become somewhat unstable due to the small denominators in some cases, and small numerators in groups with very low measured prevalences.[141]

Given the limitations in sample size and survey methodologies, the real strength of the Natsal surveys for understanding effectiveness of chlamydia screening was in providing a source of data where chlamydia infection, testing and diagnoses within the same population could be investigated incorporating individual-level data on both outcomes and demographic and behavioural details. The implications of these findings for chlamydia control are discussed below (section 0). In summary, the combination of data available made it possible to investigate how chlamydia screening was being implemented in relation to risk, to identify potentially unmet need and to hypothesise why chlamydia screening up to 2012 may not have had a substantial impact on chlamydia incidence or prevalence. I therefore propose that future use of prevalence surveys should continue to assess prevalence but do so in the context of screening and sexual behaviours rather than focus on direct comparisons of prevalence alone.

Natsal has been conducted decennially since 1990. HSE is conducted every year, and therefore presents an opportunity for more regular monitoring of chlamydia-related outcomes. As described in Chapter 8 HSE successfully collected data on sexual behaviour in 2010 and 2012. To date, it has not collected data on prevalent chlamydia infections. However this may be feasible, as several biological measures are taken, including an array of tests using urine specimens.[7] Prah *et al* have shown that some sexual risk behaviours and STI-related factors were less-commonly reported in HSE2010 than in Natsal-3. This is likely due to differences in the administration of the surveys (household versus personal interviews) and to differences in participation in general health versus sexual attitude and lifestyle-specific surveys.[272] However survey-derived estimates are broadly consistent, which supports the use of both sources for

future monitoring of sexual health parameters including chlamydia prevalence, history of chlamydia testing and diagnosis and uptake of chlamydia screening. Given the major limitations due to available sample size in comparisons between Natsal-2 and Natsal-3, future surveys would also benefit from a larger sample size to allow sufficient power for comparison of outcomes across repeated surveys.

9.1.4 *C. trachomatis* antibody seroprevalence as a marker of age-specific cumulative incidence

The use of *C. trachomatis* antibody seroprevalence as an outcome measure for evaluating chlamydia screening faces some of the same challenges as surveys that measure prevalence of current infection and surveillance data, in that bias may arise from the population sampled and changes in the population who contribute serum samples for testing may lead to confounding of the relationship between testing antibody seropositive and time. The analysis presented in Chapter 8 used data from a nationally-representative probability survey with standardised data collection over time in order to minimise the impact of these potential problems. However separating the effects of sexual behaviour from those of increased access to chlamydia screening remains an issue when looking at antibody seroprevalence. Sexual behaviour data were not available in all years in the Health Survey for England thus it was not possible to adjust for sexual behaviour as a potential confounder of the relationship between seroprevalence and exposure to chlamydia screening, which remains a limitation of this analysis. Future serum collections should prioritise the collection of sexual behaviour data to allow more detailed analysis of trends over time in relation to factors that may influence cumulative incidence of infection.

Another problem in common with surveys of chlamydia prevalence is that of power. Although antibody seroprevalence is several-fold higher than that of prevalence of current chlamydia infection, the analysis presented in Chapter 8was restricted to the number of serum samples that were available from previous HSE surveys and may have limited the ability of the analysis to detect a significant decline in Pgp3 seroprevalence among 16 to 24 year-olds. This is explored further in Table 9-1 below, which shows the significance of the prevalence ratio that would have been observed had the same point estimates been observed in each year, but a larger sample size had been recruited. This suggests that a sample size between two to three times larger in each year may have resulted in a conclusion of there having been a statistically significant (at $p<0.05$ level) decline in Pgp3 seroprevalence among 16 to 24 year-old women between 2008 and 2012. However, although power may be an issue, it is important to note that a larger sample would not necessarily have achieved the same point estimates and that the downward (non-significant) trend in seroprevalence measured in HSE participants was especially driven by seroprevalence among 20 to 24 year-olds in 2012 (Figure 8-6). This may be an early indication of falling seroprevalence, but additional years of data would be needed to investigate this further.

Table 9-1: Hypothetical scenario showing point estimates, 95%CI and p values for prevalence ratio of Pgp3 seroprevalence achieved with different sample sizes (16 to 24 year-old women, HSE2008 to HSE2012)

Prevalence ratios, p values and 95%CI are based on the actual sample size available (as presented in section 8.4.2) and three hypothetical scenarios based on two to four times the number of participants recruited (maintaining the balance of positive and negative results).

Point estimate (prevalence ratio per year)	Sample size		95%CI	P value
	In relation to actual	Total N		
0.94	Actual size	707	0.85-1.04	0.250
0.94	x 2	1414	0.87-1.01	0.103
0.94	x 3	2121	0.88-1.00	0.046
0.94	x 4	2828	0.89-0.99	0.021

Data from the analysis of HSE participants presented in this paper, and the two other analyses using the Pgp3 indirect ELISA among residual sera from women attending GUM clinics[214] and those submitting sera for routine investigations[213] now provide a wealth of data to indicate the seroprevalence that would be expected in future studies in different settings, which can be used to power future surveys or collections of residual sera.

Measurement error remains a major limitation for using *C. trachomatis* antibody seroprevalence as an outcome measure for evaluating chlamydia control programmes. While the double-antigen Pgp3 ELISA demonstrates higher sensitivity in women than the indirect Pgp3 ELISA and other commercial assays, estimated sensitivity to detect a previous known infection remains well under 100% at 82.9%.[269] Thus Pgp3 seroprevalence remains an imperfect measure of cumulative incidence of infection by any given age. It is unclear whether this imperfect sensitivity is due in part to some women not developing serum antibodies following genital infection with *C. trachomatis*, or only to waning of antibodies over time and/or assay performance, although a combination of these factors is likely. Waning of antibodies has been demonstrated using the indirect Pgp3 ELISA[100] and other commercial assays.[210] The ability of the double-antigen Pgp3 ELISA to detect antibodies appears to be less affected by time since infection.[269] However, further work is needed to better quantify the relationship between having detectable antibodies and time since infection, to allow future estimates using *C. trachomatis* antibody assays to adjust for this measurement error.

A further limitation with *C. trachomatis* antibody seroprevalence assays is that repeat infections cannot be distinguished from first infections. As is discussed in

more detail below, re-infection may play an important part in preventing chlamydia screening from having a substantial impact on chlamydia prevalence. Being able to measure rates of re-infection among the general population would therefore be informative. However it is not yet possible to use serological studies to measure rates of re-infection.

Among men, my analysis of HSE2010/12 participants demonstrated that the percentage Pgp3 seropositive correlated with numbers of sexual partners, as would be expected as a marker of previous infection with a STI. However, the lower sensitivity of the assay to detect a previous infection among men limits the use of Pgp3 seroprevalence as an outcome measure for the evaluation of chlamydia control. The extent to which this lower sensitivity reflects a difference in the immune response to *C. trachomatis* infection between women and men or by anatomical site of infection or differences in antibody waning by sex is unclear. However, as discussed in section 9.3 below, as men have an important part to play in the transmission of infection and in understanding the challenge of controlling the incidence and prevalence of chlamydia, a more detailed understanding of the relationship between *C. trachomatis* infection, antibody response and protective immunity in men is warranted.

Despite these limitations, the application of the Pgp3 indirect and double antigen ELISAs present a powerful tool for the evaluation of chlamydia screening programmes in England and elsewhere. As with data from Natsal-3, the analysis of Pgp3 seroprevalence among HSE2010/12 participants provided important insights into the epidemiology of chlamydia in relation to testing patterns. Specifically, my analysis showed that chlamydia is widespread through the population among women and that a high percentage of infections

had, up to 2012, gone undiagnosed. The use of *C. trachomatis* antibody tests combined with information on history of diagnoses provides a valuable and novel outcome measure, as a high level of undiagnosed infections represents both opportunities for transmission and potential development of complications arising from untreated infections. Future serum collections should incorporate data on history of chlamydia diagnoses wherever feasible.

9.2 Summary of recommendations for future evaluation of the impact of chlamydia control programmes in England

In summary, I propose the following recommendations for the ongoing and future evaluation of the impact of chlamydia screening on chlamydia incidence, prevalence and related measures:

- Repeat cross-sectional postal surveys of chlamydia prevalence in the general population are open to bias and are unlikely to provide value for money. They should not be pursued as a means to monitor chlamydia prevalence in England.
- Surveys such as Natsal, which are nationally representative, have relatively high response rates and collect data on a range of topics, will present better value for money than cross-sectional, chlamydia prevalence-specific postal surveys. Analysis of such surveys should focus on assessing prevalence in the context of reported screening and diagnoses and sexual behaviours rather than on direct comparisons of prevalence alone.
- The potential to incorporate the following measures into the HSE on a routine basis should be considered: current chlamydia infections (as measured using NAAT tests of urogenital specimens); previous infection with *C. trachomatis* (as measured using antibody tests of serum specimens); sexual behaviour and reported chlamydia testing and diagnosis history.
- Boosting the available sample size among young adults in both future rounds of the HSE and Natsal surveys would increase the power available

for comparative analyses and should be considered, using available data to determine the sample size required.

- Trends over time in percentage testing positive for chlamydia among populations accessing testing should not be interpreted as trends in the underlying burden of disease without first ruling out or addressing sources of selection bias and confounders. Future analyses should also consider any changes in test technology that may affect the sensitivity and specificity of tests used.
- Estimates of Pgp3 seroprevalence by birth cohort should be extended. In addition to continued use of sera from HSE participants, routine collections of residual sera from sentinel groups should be pursued, with appropriate consideration of the potential bias in each (e.g. sera collected for routine microbiological investigations, GUM clinic attenders, antenatal populations, blood donors).
- Future serum collections should incorporate measures of previous chlamydia diagnoses and sexual behaviour where possible to allow the measurement of the undiagnosed fraction of *C. trachomatis* infections and to reduce reduce confounding of the relationship between chlamydia control interventions and antibody seroprevalence arising from changes in sexual behaviour over time.

9.3 Has chlamydia screening effected a reduction in the incidence or prevalence of chlamydia infection?

I turn now to the second aim of the PhD, which was to address whether chlamydia screening as it has been delivered in practice in England has led to a reduction in the incidence or prevalence of chlamydia among young adults.

There is some evidence from analyses presented in this thesis and from other sources to support there having been a decrease in the transmission of chlamydia infection since the national implementation of the NCSP in 2008. Specifically, my analysis of surveillance data (Chapter 7) showed a consistent

pattern of a declining trend in percentage testing positive in most subgroups (with the exception of tests among MSM). There remained a declining trend over time even after adjusting known confounders. This is consistent with the hypothesis that chlamydia prevalence among heterosexual young adults has declined in recent years. However, as discussed above, there was the potential - and some evidence - for unmeasured confounding. It is not, therefore, possible to reach a definitive conclusion of declining prevalence using these data alone. The second piece of supporting evidence comes from the study by Horner *et al*, which estimated Pgp3 seroprevalence (using the indirect Pgp3 ELISA) among 17 to 24 year-old women in England using residual sera submitted for routine microbiological or biochemical investigations,[213] which found a significant decrease in Pgp3 seroprevalence from 20% in 2007 to 15% in 2010 ($p<0.001$).[213] This observed decline is consistent with there having been a decrease in age-specific cumulative incidence in the years following the national implementation of the NCSP.

However, other analyses from population-based probability samples presented in this thesis do not support there having been a decrease in incidence or prevalence of infection following the national implementation of the NCSP. Firstly, comparisons between population prevalence as measured in Natsal-2 and Natsal-3 (Chapter 6) did not provide evidence to support there having been a decrease in prevalence in the decade between the surveys. There was no significant difference between prevalence in Natsal-3 compared to Natsal-2, although the utility of direct comparisons of age-specific prevalence was ultimately limited by the sample size available. Adjustments to correct for differences between the surveys suggested a trend towards there having been an increase, rather than a decrease in prevalence over the last decade. My

analysis of Natsal-3 data (Chapter 7) also showed evidence of ongoing transmission in 2010-12 as incident infections were found among those recently tested.

Secondly, my analysis using stored sera from participants in the Health Survey for England (Chapter 8) showed that Pgp3 seroprevalence among 16 to 24 year-old women decreased between 2008 and 2012, but that this observed decrease was not statistically significant. Importantly, there was no notable difference in age-specific Pgp3 seroprevalence between birth cohorts exposed to high levels of opportunistic screening and those who became sexually active before widespread screening. This absence of a decline in seroprevalence is in contrast to Horner *et al*'s study mentioned above, where a significant decrease in Pgp3 seroprevalence between 2007 and 2010 was found.[213] The difference between my findings from HSE participants and those of Horner *et al* may be due to the slightly different time-periods investigated or the sources of sera. Horner *et al* used residual sera submitted to laboratories for routine investigations rather than a probability sample. While such sera are considered broadly representative of the general population with respect to relatively common infections, it is not known whether the data are representative with respect to STI.[213] It is feasible that some bias may have arisen due to possible oversampling of antenatal sera in women of childbearing age and changes in the way that samples from GUM clinics were recorded (and thus excluded) may have affected the trends that were observed, as it is possible that not all GUM samples were excluded from the earlier panels. Another possible reason for difference in results is that my analysis may have been limited by the number of residual sera available. Horner *et al* had a sample size of 2,519 between 2007 and 2011 versus the 707 available from 16 to 24 year-old female HSE

participants between 2008 and 2012. Thus a larger sample size may have resulted in the observed trend being statistically significant.

In summary, based on my analyses and the available literature there is no strong empirical evidence to support the hypothesis that chlamydia screening, as delivered in practice, has led to a reduction in either the incidence or prevalence of chlamydia infection among young adults up to 2012.

Given the increases in screening over the last decade (Chapter 2), this lack of empirical evidence is perhaps surprising. Screening has certainly led to a large number of diagnoses among young adults. Among Natsal-3 participants, around a half of 16 to 24 year-olds diagnosed in the last year were considered to be 'screen-detected' infections as defined by the given reason for test (section 7.4.1.1) Surveillance data show large increases in testing and diagnoses over the decade up to 2012 (Figure 2-5; Figure 2-6). These data also show that ~60% of diagnoses made in 2010 to 2012 among 15-24 year-olds were reported from non-specialist GUM settings,[279]showing the expansion of chlamydia screening in recent years. So long as the detected infections were adequately treated, this increase in detection of chlamydia infections should have reduced their duration (relative to the counterfactual of there having been no national screening programme). As set out in section 2.2, reducing the average duration of infection is expected to reduce the number of transmission events (given the relationship $R_0=\beta cD$) and also decrease the prevalence of infection (given prevalence=incidence x duration). The absence of evidence for any such reductions may be due to the limitations of the specific outcome measures used, as described above (section 9.1). In particular, my analyses using population-based samples may not have had sufficient power to detect

changes over time in the outcome measures of interest. However, if the opportunistic chlamydia screening efforts among young adults had really not effected a reduction in the incidence or prevalence of infection by 2012, this begs the question 'Why not?'

9.3.1 Insufficient time since implementation of screening

One possible explanation is that screening might not have been in place for long enough to have had a meaningful effect on transmission dynamics of infection in the population. As described in Chapter 2, opportunistic screening efforts increased substantially between in the first few years after the NCSP had achieved national implementation. Between 2008 and 2010 the estimated percentage of 15 to 24 year-olds tested in each year (assuming one test is equivalent to one person) increased from 26% to 44% in women and 11% to 24% in men.[189] Data up to 2012 therefore represent only three years of opportunistic screening at levels of the current programme. The mathematical model reported by Turner *et al* that explored the potential impact of chlamydia screening in England on the prevalence of infection demonstrated a reduction could be achieved over ten years after introducing screening (Figure 2-1),[81] so it is perhaps unreasonable to expect there to have been a notable impact on prevalence by 2012. However it should be noted that Turner *et al*'s model predicted the greatest declines to be in the first two to three years following screening. The implications of my findings for mathematical modelling are discussed in more detail below.

My analysis of age-specific Pgp3 seroprevalence is perhaps more limited by the available time between national implementation of screening and measurement. The presence or absence of antibodies to infection will depend on the full

history of chlamydia infection up to the time of antibody measurement. Thus exposure to chlamydia screening should be considered from the time of sexual debut. Women who have turned 16 since the national implementation of the NCSP were a maximum of age 20 in the analysis using data up to HSE2012, which limited the comparison of age-specific Pgp3 seroprevalence by birth cohort. Additional years of data are needed to extend these analyses to maintain robust monitoring of chlamydia in coming years.

9.3.2 Opportunities for transmission arising from undiagnosed infections and untested groups

An alternative hypothesis is that chlamydia screening up to 2012 was not diagnosing a high enough proportion of infections to lead to substantial interruptions in transmission. My findings from the Pgp3 seroprevalence study showed that the proportion of the population ever infected with chlamydia was much greater than suggested by studies that have measured prevalence of *current* infection. Additionally, screening patterns up to 2012 had left a high proportion of infections undiagnosed, as shown by the high proportion of women and men with evidence of a previous infection who did not report a previous diagnosis (75.5% of 16 to 24 year-old, see section 8.4.1).

Comparative analysis of factors associated with testing and with prevalent infection presented in Chapter 6 also highlighted gaps in testing coverage that present opportunities for ongoing transmission among young adults. Although testing rates were generally higher in those reporting risk factors for chlamydia, in Natsal-3 at least one quarter of women and around half of men reporting a risk factor associated with prevalent infection had not been recently tested. Testing rates were relatively low in men, especially among 20-24 year-olds who

contributed the majority of prevalent infections and diagnoses. Therefore the interpretation of existing testing strategies also leaves room for transmission, for example, from men to their (often younger)[268,280] partners and from people with multiple sexual partners who are not accessing testing.

9.3.3 Frequency and timing of screening

Testing frequency in relation to time since infection and rate of partner change may also have been insufficient to meaningfully interrupt transmission. The impact of screening on incidence will be diminished if onward transmission has already occurred before being tested, for example if someone has had one or more new sexual partners between the time of infection and testing. Given that in some cases untreated chlamydia infections persist for over a year,[18] if testing is not accessed soon in the course of infection then this presents a potentially long time for an infected individual to be at risk of passing the infection on. This would be especially relevant in those groups reporting high rates of partner change or frequency of non-condom use. This has been explored in the context of partner notification by Althaus et al, who used a mathematical model to explore the effect of notifying partners on reducing transmission, comparing current to previous sexual partners.[117] They found that the longer the look-back period, the more likely it was that infections would already have been passed on, thus models predicted testing of non-current partners to have negligible effect on transmission. This highlights that the timing of testing in relation to time since infection could substantially affect the expected benefits of screening in terms of interrupting transmission.

The NCSP recommends that young adults be screened on change of sexual partner, with the aim of reducing the period between time of infection and time

of treatment. The extent to which this recommendation is emphasised in health promotion activities is unclear, as is our understanding of whether clinicians and young adults interpret this recommendation as a need to test at the end of a relationship or to test soon after having a new sexual partner. However, data from Natsal-3 suggests there is substantial room for improvement. Among sexually-experienced 16 to 24 year-olds in Natsal-3 36% of women and 59% of men with at least one new sexual partner in the last year had not been tested for chlamydia in the last year. Again, this points towards gaps between screening activity and infection risk such that ongoing transmission would be expected.

9.3.4 Re-infection, partner notification and treatment

The precise relationship between chlamydia infection and subsequent immunity is unclear, although studies to date suggest that a previous infection with chlamydia confers, at best, only partial immunity.[47] In a modelling study using data from case rates in British Columbia, Brunham *et al* hypothesised that high levels of testing would lead to higher rates of repeat infections, if treatment prevents development of protective immune response. This notion of 'abrogated immunity' is a contested hypothesis,[47] and immunological evidence for this is yet to be provided.

However, even if treatment does not affect the development of protective immunity, repeat infections may partially account for high diagnosis rates without a corresponding reduction in prevalence. Returning to the relationship between prevalence and incidence, if the average duration of infection has been reduced (by screening and treatment of infection) but the prevalence has remained the same, then mathematically the rate of new infections must have

increased, given the relationship prevalence=incidence x duration. However, this does not necessarily mean new infections in previously uninfected individuals. Instead, re-infection of an individual may counteract any reduction in duration, which in turn would limit the impact of screening on the prevalence of infection. Given the acknowledged risk of re-infection, in 2013 the NCSP introduced a recommendation that young adults who test positive for chlamydia be re-tested around three months after treatment.[119]

My analyses and other previously published studies[48-57] demonstrate that re-infection is common. In my analysis of surveillance data presented in Chapter 4, the odds of testing positive were higher in people with a known chlamydia diagnosis in the last year compared to those without, even after adjusting for other available demographic and sexual behavioural variables (AOR 1.13/1.04; 1.27/1.15 for women and men respectively in the NCSP/GUMCAD datasets, section 4.4.2). In a complementary analysis of surveillance data from 2010, I have previously shown that 10% of chlamydia diagnoses made in GUM clinics in 15 to 24 year-olds were among individuals with at least one known previous diagnosis that calendar year.[120]

Re-infection may occur due to incomplete treatment of sexual partner(s) or re-infection due to continuing risk behaviour. Although my analysis did not incorporate trends over time in partner notification rates (Chapter 4), available data suggest that, on average, fewer than 0.5 partners per index case are tested,[281,282] leaving a high proportion of those diagnosed with chlamydia exposed to re-infection. Opportunities for re-infection from new partners are also indicated by the high rates of partner change in the age group targeted for

screening, with one fifth of sexually-experienced 16 to 24 year-old women and one quarter of men reporting two or more new sexual partners in the last year.

While these data indicate that re-infection is common and demonstrate opportunities for re-infection, they do not provide definitive evidence of there having been a change in re-infection rates over time that might counteract any reduction in the duration of infection. Thus, while re-infection is likely to be important, the relative contribution of repeat infections to overall annual incidence rates is not known.

Incomplete treatment of the index case would also reduce the expected impact of screening on incidence and prevalence. Infections that are diagnosed but not treated would not contribute to a reduction in the average duration of infection. Data on treatment rates are also limited, such that trends in treatment rates could not be incorporated into my analyses. However, data from clinical audits suggest that around 5% to 10% of diagnoses go untreated.[89,283]

While data on re-infection rates, partner notification and treatment are not sufficient to allow a quantitative analyses of their impact in the context of my findings, I hypothesise that reductions in incidence and prevalence that could be expected by high diagnosis rates will have been attenuated by re-infections due to incomplete treatment of sexual partner(s) and new sexual partners and by incomplete treatment of a proportion of those diagnosed with chlamydia.

9.3.5 Underlying changes in sexual behaviour

Another possible explanation for an absence of change in chlamydia prevalence or age-specific cumulative incidence is that the underlying risk of transmission

due to sexual behaviour may have changed over the period of expansion of chlamydia screening. My analyses of data from the Natsal-2 and Natsal-3 surveys (Chapter 6) present a mixed picture. There was no notable increase in reported numbers of sexual partners among women or men between the surveys. However, the proportion reporting sexual debut before age 16 increased with subsequent birth cohorts which may suggest increased sexual activity or opportunities for transmission over the last decade. In their comparison of sexual behaviours between Natsal surveys, Mercer *et al* reported an increase in proportion of participants reporting heterosexual oral and particularly anal sex[235] between Natsal-2 and Natsal-3. Although not necessarily a risk factor for transmission, this may indicate some increase in higher risk sexual behaviours and practices. However, if the underlying risk of STI has changed, this was not reflected in differences in the prevalence of non-vaccine HPV types, which did not differ between surveys. In summary, there is no strong evidence to support or to rule out there having been an increase in underlying transmission risk in recent years. It remains possible that in the absence of widespread chlamydia screening, incidence and prevalence may have been even higher.

In summary, there are several features of the relationship between chlamydia infection and approaches to screening that provide possible explanations as to why high rates of testing might not have resulted in a fall in transmission. It remains to be seen whether additional years will have a more dramatic and lasting effect. I now turn to consideration of my findings in relation to how chlamydia control efforts might be improved and developed in future years.

9.4 Implications for chlamydia control policies

9.4.1 Targeted versus universal screening strategies

The extent to which public health interventions are targeted among specific groups is an important question for policymakers. Different approaches have implications for costs, effectiveness and equity of potential benefit.[267,284,285]

Current chlamydia screening recommendations in England strike a balance between universal and targeted approaches. Screening is recommended to all sexually-active under 25 year-olds. However, from a cost efficiency perspective, it might be tempting to pursue a more targeted approach. Since 2012 the Health Protection Agency, and then Public Health England, have prioritised the detection of infections over testing volumes by recommending that local authorities aim to achieve a diagnosis rate of at least 2,300 diagnoses per 100,000 population.[121] This placed an implicit emphasis on testing among populations likely to be infected. Shifting screening activity to higher risk populations where infections are more likely to be detected might therefore be appealing in terms of detecting as many infections as possible for the fewest number of tests. One way to achieve this would be through the use of selective screening criteria using a combination of behavioural and demographic characteristics to determine an individual's eligibility for screening. Such criteria have been suggested and used elsewhere[88,286,287] and data from Natsal-3 could theoretically be used to develop such a scoring system for use in England.

However there are some fundamental disadvantages to such an approach for chlamydia screening. Selective screening criteria would be unlikely to reduce the eligible population by a substantial amount, as infections – at least among

women - are relatively widespread. Data from Natsal-3 show that 52% of prevalent infections and 31% of reported diagnoses in the last year were among women who reported fewer than two sexual partners in the last year (Table 7-3a). Selective screening may be more appropriate in men where infections are more concentrated (e.g. 80% of prevalent infections and 77% of reported diagnoses in the last year were in men with ten or more sexual partners by the time of the interview, Table 7-3b). Possibilities for different screening approaches by gender are discussed in the next section. However, even if a scoring system could be developed, there would likely be substantial challenges in implementing individual risk-based criteria. Risk-scores based on sexual behaviour would require accurate sexual history taking that may go beyond that usually provided, or that would be easily obtained, in normal practice. Furthermore, targeted interventions in sexual health have been shown to have adverse consequences by increasing the stigmatisation of those targeted.[91] It is also important to note that restricting screening to high risk groups would not necessarily achieve full coverage in those groups, so would not in itself improve diagnosis rates or reduce the opportunities for transmission presented by undiagnosed infections in relatively under-tested groups.

A further argument against selective screening criteria is that they would limit the proportion of all infections that could be diagnosed as infections are not restricted to high risk populations. This would restrict the potential direct benefit of screening – i.e. the potential reduction in the risk of developing complications – to the target population. In the interests of achieving an equitable approach, an alternative would be to implement screening so that the chance of having an infection diagnosed is balanced across different groups. This would support the

distribution of screening according to the risk of infection without restricting screening to high risk groups.

My analysis of Natsal-3 data showed that in 2010-12, screening distributions were broadly aligned to risk, but that more could be done to align these distributions (Chapter 6). Specifically, under the screening distributions in 2010-12 women and men with a chlamydia infection living in deprived areas would have less of a chance of having their infection diagnosed than those with an infection living in less deprived areas. Strategies that achieve higher testing in women living in more deprived areas - but not to the exclusion of those living in low risk areas - or those at higher risk due to other behavioural factors would provide a more equitable approach to diagnosing chlamydial infections and should be considered.

9.4.2 Screening in men

In contrast to many other countries with recommendations for asymptomatic chlamydia testing, the NCSP does not have separate screening recommendations for women and men. As set out in Chapter 2, in the late 1990s when screening policies were under development in England, men were not considered to be part of the target population. However when the NCSP was implemented in 2003 men were included, partly to prevent stigmatisation of women and in recognition of men's role in transmitting infection to their female sexual partners.[79] As the majority of chlamydia-related complications are thought to occur in women, the suitability of asymptomatic screening in men has been questioned.[288]

The research presented in this thesis did not aim to address the question of screening in men, but my findings raise some important issues that warrant consideration. Firstly, in Natsal-3, peak prevalence in men was among 20 to 24 year-olds, with no prevalent infections detected among <19 year-olds. However, testing rates in this age group were lower than among 16 to 19 year-old men. Low levels of testing in men may, therefore, be contributing to ongoing transmission to women. Secondly, my analysis showed that chlamydia infections in men appeared to be more focussed among those with higher numbers of sexual partners, whereas in women infections were more evenly distributed in the population. Non-condom use was an important risk factor for infection among men, but low testing rates were also seen in those who reported recent non-condom use. Therefore focussing screening and prevention efforts on 20 to 24 year-old men and those with higher numbers of sexual partners may be warranted.

The optimum means of achieving this is not clear. Achieving high rates of screening in men is notoriously challenging[79] and increased dedication of resources would not necessarily achieve higher testing.[289] As chlamydia appears to be more focussed in those with more sexual partners, risk-based screening criteria may be a way to focus resources more appropriately in men. However, these would still face the difficulties of operationalising such scoring systems as discussed above. An alternative would be to place more emphasis on the control of chlamydia at a partnership level, rather than an individual level. Turner *et al* have proposed focussing on partner notification as a more cost-efficient alternative to increasing screening in men with regard to the cost per diagnosis. This is attractive in terms of preventing re-infection and in the potential to identify partners of the partner.[290] However, Turner *et al* did not take

into account the potential benefit of identifying infections in women who may not have accessed testing themselves so there remains a question about comparative cost effectiveness of different approaches. In times of limited resources it is also difficult to argue for increased screening in men when the majority of chlamydia-related complications are thought to be among women. Determining the optimum approach to screening in men is beyond the remit for this PhD, but it is perhaps time for some of these questions to be revisited to consider screening at the partnership level.

In the previous section I described how inadequate treatment and partner notification can attenuate the potential benefit of screening in terms of transmission and that re-infection is an important feature to consider in the transmission dynamics of chlamydia. Therefore, independent of the distribution or level of chlamydia screening implemented, robust case management of individuals diagnosed with infection is needed to maximise the potential benefit afforded by each diagnosis. Timely and effective treatment, partner notification and re-testing should remain priorities for service delivery.

9.5 Future research

The research presented in this thesis raises a number of questions that warrant further consideration.

9.5.1 Validation of the relationship between chlamydia infection and the development and persistence of detectable antibodies

Given the challenges of chlamydia seroepidemiology set out in section 9.1.4, further work is needed to develop serological assays so that they can distinguish between first and repeat infections. This would in turn allow future

studies to investigate the relative contributions of first infections, re-infections and treatment to *C. trachomatis* antibody seroprevalence over time. The relationship between antibody-inducing chlamydia infection and complications also requires further elucidation to understand the meaning of serological findings for understanding the impact of chlamydia screening on long-term morbidity. Future outcome monitoring could feasibly comprise monitoring of first, repeat and complication-causing infections. A study using clinical samples characterised by previous diagnosis history is now ongoing and aims to develop the use of the indirect and double-antigen Pgp3 ELISAs in this way.[291]

9.5.2 Implications for mathematical modelling

The most recently published mathematical modelling study to have examined the potential impact of chlamydia in England is that by Turner *et al.*[80,81] The model results suggested that opportunistic chlamydia screening in GP practices of women or women and men aged <25 years could at least halve the prevalence of chlamydia within ten years (with substantial reductions seen in the first few years after screening implementation as shown in Figure 2-1), providing screening is offered to the entire eligible population when they attend a GP, that 50% of those offered screening accept the invitation and that 20% of partners are treated.[81] As Turner *et al* point out, the predictions derived from the model do not represent the truth, but instead present "the likely outcome, if our description of reality is accurate".[81] Findings from Natsal-3 showed that 62.5% of sexually-experienced women and 43.2% of sexually-experienced men reported having a chlamydia test in the last year and surveillance data suggest similar levels of testing were in place between 2009 and 2012 (Figure 2-5; Figure 2-6). However the dramatic reductions in prevalence predicted by the

model do not yet appear to have been borne out, thus raising some queries about the model predictions. There are a number of infection- and testing-related parameters in the model that are challenged by my findings.

The model was fitted to chlamydia prevalence among women estimated from a meta-analysis of studies among GP attenders or those registered with a GP[123]. The resulting baseline prevalence is substantially higher than that estimated in Natsal-2 and suggests the baseline prevalence in the model may have been high. For example in 16 to 19 year-old women, chlamydia prevalence estimated in Natsal-2 was 3.9% (Table 6-4), but the model baseline prevalence was over 6%. My analysis of Natsal-3 data also shows that the age distribution of infection and diagnoses varies by gender, and that screening patterns vary by age, gender and, sexual behaviour (Chapter 6). However, the Turner model assumed the same distribution of infection and diagnosis in both women and men and assumed that acceptance of screening was not associated with age, gender or numbers of sexual partners. Given interactions between model parameters, the full impact of these departures between the model assumptions and empirical data are unclear without further runs of an amended model.

Findings from the serological study presented in Chapter 8 provide new parameters which may be useful either for fitting or validation of mathematical models. *C. trachomatis* antibody seroprevalence by age can be used as a marker of minimum age-specific cumulative incidence and the prevalence of reporting a chlamydia diagnosis among seropositive individuals represents a proportion of those ever infected who have ever been diagnosed.

While increasing the complexity of mathematical models may not always result in an improvement in their explanatory or predictive capability,[292] the impact of varying infection and testing by age, gender and sexual behaviour simultaneously and the use of newly available parameters should be considered in future mathematical models of chlamydia screening in England and elsewhere.

9.5.3 Screening early in the course of infection.

I have hypothesised that timing of testing in relation to time since infection may have been insufficient to prevent transmission. As well as potentially reducing onward transmission, testing early in the course of infection has the potential to reduce an individual's risk of developing complications.[39] Increasing testing rates either at the end of a sexual partnership or following change of sexual partner therefore warrants attention. Specifically, future research to examine current adherence to recommendations of testing on change of sexual partner should be considered. This could include both quantitative analyses among those accessing testing and qualitative work in young adults to understand attitudes towards current recommendations. This work could contribute to developing and evaluating an intervention to increase testing soon after partner change with the aim of reducing both onward transmission and the risk of developing complications in those with chlamydia.

9.6 Concluding statement

In summary, there is some evidence from my analysis of trends in the percentage testing positive for chlamydia using surveillance data and Horner *et al*'s analysis of *C. trachomatis* antibody seroprevalence to support there having

been a decrease in chlamydia incidence and prevalence in recent years. However, findings from population–based studies using probability sampling do not support there having been such a decline. Thus, taken together there is no strong empirical evidence that chlamydia screening, as it has been delivered in practice in England, has had an effect on the incidence or prevalence of chlamydia infection among under 25 year-olds.

This absence of any such evidence may be due to insufficient power to detect changes in the outcome measures investigated due to available sample size or to insufficient time since the national implementation of the NCSP in 2008. Alternatively, a combination of high lifetime risk of infection, high proportion of infections that go undiagnosed, insufficient testing levels or frequency among high risk groups and – potentially – re-infection due to incomplete treatment of sexual partners may have limited the impact of chlamydia control efforts.

Future evaluation of the impact of chlamydia control programmes should focus on applying *C. trachomatis* antibody assays to population-based serum samples and the use of existing population-based surveys to monitor chlamydia screening in relation to the risk of infection.

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APPENDIX 1: Study paperwork used in pilot postal survey to measure the population prevalence of chlamydia among young women

Relevant to Chapter 5

The following documents are available in the printed version of the thesis:

- Patient Information leaflet (Leaflets varied by group. The leaflet for group A is provided as an example)
- Study questionnaire

APPENDIX 2: Comparison of maximal and parsimonious multivariable models of prevalent chlamydia infection, recent diagnosis and recent testing

Relevant to Chapter 7

As set out in Chapter 7, two approaches to multivariable modelling to investigate associations between sociodemographic and behavioural variables and prevalent chlamydia infection, recent diagnosis and recent testing were explored: maximal and parsimonious models were constructed for prevalent chlamydia infection, self-reported chlamydia diagnosis in the last year and self-reported chlamydia test in in the last year.

To fit parsimonious models, variables found significant at $p<0.1$ in univariable analyses were entered into a multivariable model selection process based on backwards selection whereby variables were removed from the model if the statistical significance of their association with the outcome had an associated p value of >0.05. Only those variables significantly associated with the outcome were retained in the final parsimonious models. With two exceptions, all variables included in univariable models were included in multivariable maximal models: number of sexual partners in the last year was not included due to collinearity with other sexual partnership variables; age left school was not included as data were unavailable for 16 year-olds.

Table 9-2below shows results from univariable models along with maximal (Multivariable model 1) and parsimonious (Multivariable model 2) multivariable models for women for the three outcomes of interest (prevalent infection, recent diagnosis, recent testing). Table 9-3 shows results for men.

Adjusted ORs in the maximal models tended to be closer to 1 than those in parsimonious models, reflecting some confounding of associations between predictor and outcome variables. Factors which remained statistically significant were largely comparable between models, with some exceptions. Firstly, in men the maximal model found deprivation of area of residence to be significantly associated with prevalent infection and non-condom use was not, whereas in the parsimonious model non-condom use remained a significant predictor in the model whereas deprivation did not. Age group and number of lifetime sexual partners were significant in both models. The adjusted odds ratio (OR) for prevalent infection among those reporting non-condom use was similar between the models (3.59 versus 4.43 in the maximal and parsimonious models respectively). The difference between the models likely reflects, in part, the sample size available meaning that maximal models would have reduced power to detect associations after adjusting for multiple confounders. In the maximal models, no factors were statistically significant predictors of recent diagnosis among those tested, reflecting the smaller sample size available when limiting to those recently tested and when entering several covariates into the model.

Table 9-2: Percentage with a) prevalent chlamydia infection, b) self-reported diagnosis in the last year and c) self-reported testing and unadjusted and adjusted odds ratios for prevalent chlamydia infection by sociodemographic and behavioural variables (16-24 year-old sexually-experienced <u>women</u>)

	1a) Prevalent infection detected in urine (n=992)										
	%	(95%CI)	Univariable			Multivariable model 1			Multivariable model 2			Denominator (wt, unwt)
			OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	
Age group												
16-19	3.8%	(2.2-6.3)	1.00	-	0.36	1.00	-	0.50				214, 395
20-24	2.7%	(1.7-4.3)	0.71	(0.35-1.46)		0.71	(0.27-1.87)					383, 597
Country[c]												
England	2.9%	(2.0-4.3)	1.00	-	0.53	1.00	-	0.48				504, 817
Scotland	3.1%	(1.1-8.6)	1.08	(0.35-3.33)		1.34	(0.43-4.14)					56, 103
Wales	5.3%	(1.9-13.8)	1.87	(0.63-5.60)		1.88	(0.63-5.54)					37, 72
IMD quintile of LSOA of residence[d]												
2 least deprived	1.3%	(0.5-3.4)	1.00	-	**0.01**	1.00	-	**0.01**	1.00	-	**<0.01**	213, 355
Middle quintile	1.8%	(0.8-4.2)	1.37	(0.38-4.90)		1.40	(0.39-4.98)		1.45	(0.40-5.20)		111, 174
2 most deprived	4.9%	(3.3-7.3)	3.82	(1.35-10.8)		4.23	(1.53-11.6)		4.11	(1.45-11.7)		273, 463
Age left school[e]												
17+	3.2%	(2.1-4.8)	1.00	-	0.88							445, 700
16	3.4%	(1.9-6.0)	1.06	(0.50-2.22)								120, 229
Age at first heterosexual sex												
17+	1.6%	(0.7-3.7)	1.00	-	0.15	1.00	-	0.42				188, 246
16	3.9%	(2.1-6.9)	2.52	(0.86-7.36)		2.20	(0.67-7.17)					178, 304
<16	4.0%	(2.4-6.6)	2.65	(0.95-7.36)		1.82	(0.60-5.42)					213, 415
Number of sexual partners in the last year												
0 or 1	2.5%	(1.5-4.0)	1.00	-	**0.03**							387, 600
2	3.9%	(1.8-8.5)	1.62	(0.63-4.15)								90, 161
3 to 4	1.9%	(0.7-5.1)	0.75	(0.24-2.33)								63, 127
5+	8.3%	(3.9-16.8)	3.57	(1.39-9.17)								49, 93
Number of new sexual partners in the last year												
0	2.2%	(1.3-3.7)	1.00	-	**0.03**	1.00	-	0.70				313, 495
1	2.8%	(1.2-6.3)	1.26	(0.47-3.41)		1.17	(0.38-3.52)					160, 263
2+	5.9%	(3.5-9.8)	2.73	(1.26-5.93)		1.65	(0.50-5.39)					118, 225
Number of sexual partners in the last year without a condom												
0	2.9%	(1.2-7.1)	1.00	-	**0.03**	1.00	-	0.18				120, 173
1	2.2%	(1.4-3.6)	0.76	(0.26-2.17)		0.34	(0.10-1.10)					368, 606
2+	6.3%	(3.5-11.2)	2.25	(0.73-6.93)		0.49	(0.12-1.83)					108, 212
Number of lifetime sexual partners												
1 to 4	2.4%	(1.4-4.2)	1.00	-	0.14	1.00	-	0.67				321, 482
5 to 9	2.8%	(1.4-5.2)	1.15	(0.48-2.75)		0.87	(0.32-2.32)					150, 267
10+	5.4%	(2.9-9.7)	2.29	(0.97-5.39)		1.39	(0.45-4.18)					121, 234
Condom used for most recent sex with most recent partner												
Yes	2.8%	(1.5-5.3)	1.00	-	0.53	1.00	-	0.29				202, 314
No	3.6%	(2.4-5.4)	1.28	(0.59-2.80)		1.59	(0.67-3.74)					352, 613
Concurrent partnerships in last year[f]												
No	2.7%	(1.8-4.2)	1.00	-	0.19	1.00	-	0.85				439, 706
Yes	6.3%	(2.9-13.4)	2.40	(0.94-6.15)		1.34	(0.48-3.70)					66, 134
Unknown	3.1%	(1.3-7.2)	1.14	(0.43-3.04)		1.13	(0.38-3.31)					73, 127
Frequency of binge drinking												
never / <u>≤</u>monthly	2.5%	(1.5-4.1)	1.00	-	**<0.01**	1.00	-	**0.01**	1.00	-	**<0.01**	373, 598
monthly	1.2%	(0.5-3.3)	0.49	(0.16-1.52)		0.46	(0.13-1.51)		0.54	(0.17-1.68)		130, 226
<u>≥</u>weekly	7.9%	(4.7-13.1)	3.35	(1.55-7.25)		2.51	(1.08-5.76)		3.73	(1.73-8.08)		95, 168
Ever had any same sex experience/contact												
No	3.1%	(2.1-4.4)	1.00	-	0.92	1.00	-	0.49				473, 750
Yes	3.2%	(1.4-7.1)	1.05	(0.42-2.63)		0.74	(0.30-1.76)					124, 242

Table 9-2 continued.

	1b) Diagnosed with chlamydia in the last year (among those tested in the last year) (n=471)											
	%	(95%CI)	Univariable			Multivariable model 1			Multivariable model 2			Denominator (wt, unwt)
			OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	
Age group												
16-19	6.0%	(3.8-9.2)	1.00	-	0.62	1.00	-	0.58				193, 375
20-24	5.1%	(3.4-7.6)	0.86	(0.46-1.60)		0.80	(0.35-1.78)					329, 565
Country[c]												
England												469, 832
Scotland												30, 58
Wales												24, 50
IMD quintile of LSOA of residence[d]												
2 least deprived	4.8%	(2.8-8.1)	1.00	-	0.23	1.00	-	0.36				183, 319
Middle quintile	3.5%	(1.6-7.3)	0.71	(0.27-1.86)		1.06	(0.37-3.04)					102, 176
2 most deprived	6.8%	(4.6-10.0)	1.46	(0.73-2.93)		1.70	(0.73-3.91)					236, 445
Age left school[e]												
17+	5.2%	(3.6-7.5)	1.00	-	0.58							387, 658
16	6.2%	(3.7-10.5)	1.21	(0.62-2.37)								109, 228
Age at first heterosexual sex												
17+	4.1%	(1.8-8.9)	1.00	-	0.37	1.00	-	0.93				137, 215
16	5.0%	(2.8-8.9)	1.24	(0.44-3.55)		0.80	(0.26-2.42)					154, 272
<16	6.9%	(4.8-9.9)	1.76	(0.70-4.41)		0.89	(0.35-2.25)					220, 429
Number of sexual partners in the last year												
0 or 1	3.0%	(1.7-5.4)	1.00	-	**0.01**							291, 507
2	6.6%	(3.7-11.6)	2.25	(0.98-5.18)								93, 178
3 to 4	8.8%	(5.2-14.6)	3.08	(1.34-7.05)								76, 146
5+	11.6%	(6.2-20.8)	4.19	(1.69-10.4)								58, 101
Number of new sexual partners in the last year												
0	2.8%	(1.5-5.0)	1.00	-	**<0.01**	1.00	-	0.11	1.00	-	**0.02**	226, 397
1	4.8%	(2.5-9.1)	1.76	(0.71-4.38)		1.89	(0.69-5.16)		1.82	(0.74-4.50)		156, 287
2+	10.7%	(7.3-15.6)	4.23	(2.04-8.79)		3.09	(1.07-8.86)		3.07	(1.41-6.67)		137, 249
Number of sexual partners in the last year without a condom												
0	4.2%	(1.5-11.6)	1.00	-	**<0.01**	1.00	-	0.84				76, 130
1	3.8%	(2.4-6.1)	0.90	(0.27-2.94)		0.72	(0.15-3.21)					319, 567
2+	10.3%	(7.0-15.0)	2.60	(0.80-8.46)		0.90	(0.18-4.49)					126, 241
Number of lifetime sexual partners												
1 to 4	2.1%	(1.1-4.0)	1.00	-	**<0.01**	1.00	-	0.08	1.00	-	**<0.01**	218, 391
5 to 9	6.2%	(3.7-10.3)	3.07	(1.33-7.07)		2.40	(0.90-6.37)		2.54	(1.06-6.12)		161, 289
10+	9.9%	(6.5-14.7)	5.12	(2.31-11.3)		3.76	(1.19-11.8)		3.81	(1.67-8.68)		141, 254
Condom used for most recent sex with most recent partner												
Yes	3.4%	(1.6-7.0)	1.00	-	0.14	1.00	-	0.14				170, 303
No	6.3%	(4.4-8.9)	1.90	(0.81-4.49)		1.88	(0.81-4.32)					328, 592
Concurrent partnerships in last year[f]												
No	4.3%	(2.9-6.4)	1.00	-	0.13	1.00	-	0.46				361, 639
Yes	8.1%	(4.1-15.3)	1.95	(0.84-4.54)		0.75	(0.27-2.00)					78, 146
Unknown	7.8%	(4.3-13.9)	1.88	(0.90-3.94)		1.46	(0.62-3.38)					76, 144
Frequency of binge drinking												
never / ≤monthly	3.7%	(2.4-5.7)	1.00	-	**0.03**	1.00	-	0.28				312, 561
monthly	6.6%	(3.6-11.8)	1.85	(0.85-4.01)		1.91	(0.74-4.89)					112, 200
≥weekly	9.4%	(5.2-16.3)	2.69	(1.25-5.80)		2.06	(0.75-5.61)					97, 177
Ever had any same sex experience/contact												
No	5.3%	(3.7-7.5)	1.00	-	0.72	1.00	-	0.44				388, 704
Yes	5.9%	(3.5-10.0)	1.13	(0.57-2.24)		0.71	(0.30-1.68)					134, 236

Table 9-2 continued.

1c) Tested for chlamydia in the last year (n=1,375)

	%	(95%CI)	Univariable			Multivariable model 1			Multivariable model 2			Denominator (wt, unwt)
			OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	
Age group												
16-19	56.6%	(52.5-60.6)	1.00	-	0.16	1.00	-	0.15				343, 672
20-24	52.8%	(49.2-56.4)	0.86	(0.69-1.06)		0.82	(0.62-1.07)					623, 1064
Country[c]												
England	57.1%	(54.1-60.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	823, 1452
Scotland	32.4%	(24.4-41.5)	0.36	(0.24-0.54)		0.29	(0.18-0.45)		0.31	(0.21-0.47)		91, 178
Wales	45.6%	(36.2-55.4)	0.63	(0.42-0.94)		0.53	(0.32-0.85)		0.54	(0.34-0.86)		52, 106
IMD quintile of LSOA of residence[d]												
2 least deprived	54.2%	(49.5-58.8)	1.00	-	0.99	1.00	-	0.94				338, 595
Middle quintile	54.4%	(48.0-60.7)	1.01	(0.74-1.38)		1.03	(0.71-1.48)					189, 324
2 most deprived	54.0%	(49.8-58.2)	0.99	(0.77-1.27)		0.97	(0.73-1.29)					439, 817
Age left school[e]												
17+	54.3%	(51.0-57.6)	1.00	-	0.70							715, 1217
16	55.5%	(50.1-60.8)	1.05	(0.82-1.35)								196, 405
Age at first heterosexual sex												
17+	43.9%	(38.7-49.1)	1.00	-	**<0.01**	1.00	-	0.05	1.00	-	**<0.01**	313, 489
16	56.4%	(51.6-61.1)	1.66	(1.25-2.20)		1.39	(0.99-1.92)		1.48	(1.09-2.01)		273, 503
<16	63.9%	(59.8-67.9)	2.27	(1.75-2.94)		1.44	(1.05-1.97)		1.66	(1.24-2.21)		344, 680
Number of sexual partners in the last year												
0 or 1	46.6%	(43.3-50.0)	1.00	-	**<0.01**							624, 1096
2	65.2%	(58.8-71.1)	2.15	(1.59-2.89)								143, 275
3 to 4	69.7%	(62.0-76.4)	2.63	(1.82-3.80)								111, 210
5+	74.8%	(64.4-83.0)	3.40	(2.05-5.65)								77, 135
Number of new sexual partners in the last year												
0	45.6%	(41.9-49.3)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	495, 873
1	59.2%	(54.0-64.2)	1.73	(1.34-2.23)		1.69	(1.25-2.27)		1.94	(1.48-2.54)		264, 485
2+	70.0%	(63.8-75.6)	2.79	(2.03-3.84)		1.46	(0.95-2.21)		2.03	(1.40-2.94)		197, 359
Number of sexual partners in the last year without a condom												
0	36.4%	(30.8-42.3)	1.00	-	**<0.01**			0.05	1.00	-	**<0.01**	210, 361
1	54.7%	(51.4-58.0)	2.11	(1.61-2.78)		1.52	(1.03-2.24)		1.74	(1.29-2.35)		585, 1049
2+	74.2%	(68.3-79.4)	5.04	(3.47-7.32)		1.86	(1.09-3.15)		2.19	(1.43-3.36)		169, 322
Number of lifetime sexual partners												
1 to 4	43.5%	(40.0-47.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	503, 894
5 to 9	63.8%	(58.5-68.7)	2.29	(1.76-2.96)		1.96	(1.43-2.69)		1.90	(1.43-2.54)		252, 453
10+	69.6%	(63.9-74.7)	2.97	(2.22-3.98)		2.11	(1.41-3.13)		2.00	(1.42-2.82)		202, 373
Condom used for most recent sex with most recent partner												
Yes	51.6%	(46.9-56.3)	1.00	-	**0.03**	1.00	-	0.97				330, 586
No	58.0%	(54.6-61.3)	1.30	(1.03-1.63)		1.01	(0.74-1.35)					567, 1027
Concurrent partnerships in last year[f]												
No	51.0%	(47.8-54.2)	1.00	-	**<0.01**	1.00	-	0.05				710, 1256
Yes	74.6%	(67.1-80.8)	2.81	(1.93-4.09)		1.46	(0.93-2.28)					105, 196
Unknown	64.6%	(57.5-71.2)	1.76	(1.27-2.42)		1.53	(1.02-2.28)					117, 226
Frequency of binge drinking												
never / ≤monthly	52.1%	(48.7-55.5)	1.00	-	**0.01**	1.00	-	0.08				601, 1085
monthly	52.4%	(46.6-58.2)	1.01	(0.78-1.32)		0.75	(0.54-1.02)					214, 375
≥weekly	64.4%	(57.6-70.7)	1.66	(1.22-2.27)		1.16	(0.81-1.64)					151, 274
Ever had any same sex experience/contact												
No	51.9%	(48.8-55.0)	1.00	-	**<0.01**	1.00	-	0.24				749, 1352
Yes	61.9%	(56.0-67.5)	1.51	(1.15-1.98)		1.21	(0.88-1.65)					218, 384

[a]N in column headings shows unweighted denominators. Total denominators by characteristic and in multivariable models vary due to item-missingness. [b]AOR: Adjusted odds ratios, adjusted for all variables shown. [c]Results for recent diagnosis are not reported due to small sample size in Scotland and Wales when limited to those tested. [d]IMD: Index of multiple deprivation of LSOA (lower super output area) of residence. IMD scores for England, Scotland and Wales were adjusted before being combined and assigned to quintiles, using the method described by Payne and Abel[264]. [e]Excludes 16 year-olds. [f]Among those with at least 1 sexual partner in last year.

Table 9-3: Percentage with a) prevalent chlamydia infection, b) self-reported diagnosis in the last year and c) self-reported testing and unadjusted and adjusted odds ratios for prevalent chlamydia infection by sociodemographic and behavioural variables (16-24 year-old sexually-experienced men)

	2a) Prevalent infection detected in urine (n=840)										
			Univariable			Multivariable model 1			Multivariable model 2			Denominator (wt, unwt)
	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	
Age group												
16-19	0.3%	(0.1-1.4)	1.00	-	**<0.01**	1.00	-	**0.02**	1.00	-	**0.03**	234, 343
20-24	3.4%	(2.2-5.2)	10.6	(2.40-46.3)		7.54	(1.37-41.3)		5.71	(1.23-26.6)		391, 497
Country[c]												
England	1.9%	(1.2-3.0)	1.00	-	0.12	1.00	-	0.27				532, 719
Scotland	5.7%	(2.1-14.3)	3.13	(1.04-9.45)		3.16	(0.78-12.8)					60, 72
Wales	1.7%	(0.2-12.1)	0.88	(0.11-7.02)		1.20	(0.18-7.63)					33, 49
IMD quintile of LSOA of residence[d]												
2 least deprived	1.3%	(0.4-3.6)	1.00	-	0.14	1.00	-	**0.04**				241, 315
Middle quintile	1.6%	(0.6-4.4)	1.24	(0.26-5.88)		1.01	(0.15-6.68)					114, 164
2 most deprived	3.4%	(2.1-5.6)	2.71	(0.83-8.82)		3.75	(1.11-12.5)					269, 361
Age left school[e]												
17+	1.6%	(0.9-2.7)	1.00	-	**0.01**							439, 568
16	5.0%	(2.7-9.2)	3.28	(1.38-7.82)								143, 206
Age at first heterosexual sex												
17+	1.0%	(0.3-2.8)	1.00	-	**0.03**	1.00	-	0.67				210, 245
16	1.5%	(0.5-4.6)	1.49	(0.31-7.15)		1.14	(0.27-4.74)					148, 205
<16	4.0%	(2.4-6.5)	4.18	(1.31-13.3)		1.65	(0.55-4.90)					238, 352
Number of sexual partners in the last year												
0 or 1	1.5%	(0.7-3.0)	1.00	-	**0.01**							359, 466
2	1.3%	(0.4-4.2)	0.86	(0.21-3.56)								123, 159
3 to 4	3.1%	(1.1-8.5)	2.16	(0.60-7.78)								70, 110
5+	7.5%	(3.7-14.6)	5.47	(1.89-15.9)								67, 100
Number of new sexual partners in the last year												
0	1.8%	(0.9-3.8)	1.00	-	**0.01**	1.00	-	0.49				263, 335
1	0.8%	(0.2-2.5)	0.42	(0.10-1.72)		0.33	(0.05-2.06)					203, 270
2+	5.1%	(2.9-8.8)	2.87	(1.08-7.63)		0.47	(0.09-2.45)					152, 229
Number of sexual partners in the last year without a condom												
0	0.3%	(0.1-1.3)	1.00	-	**<0.01**	1.00	-	0.09				205, 248
1	1.7%	(0.8-3.6)	5.26	(1.05-26.2)		1.23	(0.09-15.2)					287, 396
2+	6.5%	(3.9-10.9)	21.3	(4.67-97.2)		4.95	(0.42-57.9)					130, 194
Number of lifetime sexual partners												
1 to 4	0.4%	(0.1-1.5)	1.00	-	**<0.01**	1.00	-	**0.03**	1.00	-	**<0.01**	332, 412
5 to 9	1.2%	(0.3-4.0)	3.21	(0.47-21.9)		1.78	(0.20-15.5)		2.21	(0.31-15.9)		141, 200
10+	7.6%	(4.8-11.7)	22.6	(4.92-104)		8.69	(1.21-62.0)		14.2	(3.02-66.7)		148, 224
Condom used for most recent sex with most recent partner												
Yes	0.7%	(0.2-2.0)	1.00	-	**<0.01**	1.00	-	0.10	1.00	-	**<0.01**	301, 391
No	4.1%	(2.6-6.4)	6.03	(1.87-19.4)		3.59	(0.77-16.6)		4.43	(1.32-14.9)		283, 398
Concurrent partnerships in last year[f]												
No	2.6%	(1.6-4.2)	1.00	-	0.74	1.00	-	0.05				418, 557
Yes	2.0%	(0.7-5.4)	0.75	(0.24-2.37)		0.18	(0.04-0.71)					82, 121
Unknown	1.7%	(0.5-5.6)	0.64	(0.17-2.37)		0.60	(0.11-3.00)					92, 122
Frequency of binge drinking												
never / ≤monthly	1.1%	(0.4-2.7)	1.00	-	0.08	1.00	-	0.62				322, 421
monthly	3.0%	(1.4-6.2)	2.79	(0.85-9.18)		1.47	(0.33-6.48)					125, 177
≥weekly	3.8%	(2.0-7.0)	3.58	(1.17-11.0)		2.03	(0.49-8.38)					177, 241
Ever had any same sex experience/contact												
No	2.3%	(1.5-3.5)	1.00	-	0.89	1.00	-	0.37				577, 762
Yes	2.0%	(0.4-9.0)	0.90	(0.18-4.48)		0.31	(0.02-4.16)					47, 78

Table 9-3 continued

	2b) Diagnosed with chlamydia in the last year (among those tested in the last year) (n=940)											
			Univariable			Multivariable model 1			Multivariable model 2			
	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	Denominator (wt, unwt)
Age group												
16-19	4.7%	(2.4-9.0)	1.00	-	0.41	1.00	-	0.61				151, 226
20-24	6.7%	(3.9-11.1)	1.46	(0.59-3.58)		0.76	(0.26-2.15)					192, 245
Country[c]												
England												316, 440
Scotland												20, 22
Wales												7, 9
IMD quintile of LSOA of residence[d]												
2 least deprived	5.2%	(2.5-10.5)	1.00	-	0.85	1.00	-	0.85				127, 180
Middle quintile	5.0%	(1.7-13.8)	0.96	(0.26-3.58)		0.68	(0.15-2.97)					60, 86
2 most deprived	6.5%	(3.6-11.4)	1.26	(0.48-3.33)		1.06	(0.42-2.64)					155, 205
Age left school[e]												
17+	5.3%	(3.1-9.0)	1.00	-	0.49							233, 304
16	7.2%	(3.6-13.8)	1.38	(0.55-3.45)								87, 134
Age at first heterosexual sex												
17+	2.8%	(0.7-9.9)	1.00	-	0.26	1.00	-	0.74				87, 112
16	4.7%	(1.8-11.8)	1.75	(0.33-9.27)		1.14	(0.24-5.30)					84, 108
<16	7.8%	(4.7-12.6)	2.99	(0.70-12.7)		1.58	(0.37-6.62)					167, 243
Number of sexual partners in the last year												
0 or 1	3.4%	(1.5-7.8)	1.00	-	**<0.01**				1.00	-	**<0.01**	145, 196
2	0.9%	(0.2-3.9)	0.27	(0.05-1.41)					0.18	(0.03-1.17)		74, 99
3 to 4	1.5%	(0.4-6.2)	0.44	(0.08-2.30)					0.23	(0.04-1.31)		57, 83
5+	21.2%	(12.9-32.7)	7.54	(2.66-21.3)					2.67	(0.88-8.08)		63, 89
Number of new sexual partners in the last year												
0	5.5%	(2.3-12.6)	1.00	-	0.37	1.00	-	0.31				108, 136
1	4.0%	(1.7-9.0)	0.71	(0.21-2.47)		1.13	(0.09-13.9)					115, 161
2+	8.0%	(4.5-13.7)	1.48	(0.50-4.35)		2.87	(0.26-30.7)					115, 170
Number of sexual partners in the last year without a condom												
0	1.8%	(0.4-8.4)	1.00	-	**0.04**	1.00	-	0.45				88, 115
1	4.9%	(2.6-8.9)	2.75	(0.50-15.0)		0.78	(0.19-3.15)					160, 222
2+	10.9%	(6.0-19.0)	6.51	(1.19-35.6)		0.46	(0.11-1.83)					95, 134
Number of lifetime sexual partners												
1 to 4	1.0%	(0.3-3.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**0.01**	133, 176
5 to 9	3.8%	(1.3-10.8)	4.15	(0.82-21.0)		4.87	(0.58-40.2)		4.25	(0.61-29.7)		84, 123
10+	12.3%	(7.6-19.2)	14.6	(3.89-54.5)		19.80	(3.03-129.)		8.30	(1.77-38.8)		121, 167
Condom used for most recent sex with most recent partner												
Yes	4.3%	(2.0-8.9)	1.00	-	0.22	1.00	-	0.91				163, 221
No	7.4%	(4.5-12.0)	1.79	(0.70-4.59)		1.06	(0.35-3.21)					172, 237
Concurrent partnerships in last year[f]												
No	6.7%	(4.1-10.8)	1.00	-	0.10	1.00	-	0.07				219, 298
Yes	6.5%	(2.7-14.8)	0.96	(0.34-2.72)		0.60	(0.19-1.79)					67, 92
Unknown	1.3%	(0.3-5.5)	0.19	(0.04-0.88)		0.06	(0.00-0.71)					52, 75
Frequency of binge drinking												
never / ≤monthly	3.5%	(1.6-7.7)	1.00	-	0.07	1.00	-	0.46				146, 204
monthly	4.0%	(1.5-10.3)	1.15	(0.31-4.18)		0.60	(0.13-2.67)					80, 113
≥weekly	9.8%	(5.6-16.6)	2.98	(1.07-8.34)		1.23	(0.48-3.14)					117, 154
Ever had any same sex experience/contact												
No	5.8%	(3.8-8.9)	1.00	-	0.87	1.00	-	0.82				311, 427
Yes	5.1%	(1.0-22.0)	0.87	(0.17-4.54)		0.79	(0.10-6.09)					31, 44

Table 9-3 continued

	2c) Tested for chlamydia in the last year (n=1,736)											
			Univariable			Multivariable model 1			Multivariable model 2			
	%	(95%CI)	OR	(95%CI)	p	AOR[b]	(95%CI)	p	AOR[b]	(95%CI)	p	Denominator (wt, unwt)
Age group												
16-19	40.4%	(35.9-45.1)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	374, 582
20-24	31.1%	(27.8-34.7)	0.67	(0.52-0.86)		0.53	(0.37-0.73)		0.55	(0.40-0.77)		629, 793
Country[c]												
England	37.3%	(34.3-40.3)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	859, 1181
Scotland	22.2%	(14.0-33.5)	0.48	(0.27-0.85)		0.33	(0.16-0.64)		0.37	(0.19-0.73)		89, 111
Wales	12.8%	(6.9-22.3)	0.25	(0.13-0.48)		0.19	(0.08-0.40)		0.22	(0.09-0.50)		55, 83
IMD quintile of LSOA of residence[d]												
2 least deprived	34.5%	(30.0-39.2)	1.00	-	0.89	1.00	-	0.75				369, 509
Middle quintile	33.3%	(27.4-39.9)	0.95	(0.67-1.35)		1.04	(0.70-1.52)					183, 263
2 most deprived	35.2%	(31.1-39.5)	1.03	(0.78-1.36)		1.13	(0.82-1.53)					450, 603
Age left school[e]												
17+	33.6%	(30.4-37.1)	1.00	-	0.21							703, 927
16	37.8%	(32.3-43.5)	1.20	(0.91-1.58)								230, 334
Age at first heterosexual sex												
17+	25.6%	(21.4-30.3)	1.00	-	**<0.01**	1.00	-	0.05	1.00	-	**0.045**	340, 431
16	33.4%	(27.9-39.4)	1.46	(1.03-2.06)		1.13	(0.75-1.67)		1.10	(0.75-1.62)		253, 351
<16	45.3%	(40.7-49.9)	2.40	(1.78-3.23)		1.53	(1.07-2.19)		1.52	(1.06-2.16)		376, 539
Number of sexual partners in the last year												
0 or 1	26.0%	(22.6-29.7)	1.00	-	**<0.01**				1.00	-	**<0.01**	568, 768
2	40.3%	(33.2-47.7)	1.92	(1.34-2.75)					1.63	(1.11-2.39)		185, 251
3 to 4	43.0%	(35.5-50.9)	2.15	(1.49-3.10)					1.44	(0.93-2.22)		134, 194
5+	60.9%	(51.8-69.3)	4.42	(2.93-6.67)					2.43	(1.49-3.98)		103, 146
Number of new sexual partners in the last year												
0	26.0%	(22.0-30.5)	1.00	-	**<0.01**	1.00	-	0.37				416, 540
1	36.7%	(31.8-41.8)	1.64	(1.21-2.24)		1.28	(0.88-1.85)					323, 452
2+	46.3%	(40.7-52.0)	2.45	(1.78-3.37)		1.06	(0.67-1.68)					251, 366
Number of sexual partners in the last year without a condom												
0	27.0%	(22.4-32.1)	1.00	-	**<0.01**	1.00	-	0.49				331, 450
1	34.3%	(30.2-38.7)	1.41	(1.02-1.96)		1.12	(0.72-1.71)					475, 640
2+	48.8%	(42.3-55.4)	2.59	(1.81-3.70)		1.37	(0.80-2.34)					194, 281
Number of lifetime sexual partners												
1 to 4	25.3%	(21.8-29.2)	1.00	-	**<0.01**	1.00	-	**<0.01**	1.00	-	**<0.01**	524, 706
5 to 9	39.6%	(33.6-45.9)	1.93	(1.39-2.69)		1.50	(1.01-2.21)		1.49	(1.01-2.20)		222, 314
10+	49.2%	(43.2-55.2)	2.86	(2.09-3.92)		2.23	(1.45-3.42)		2.03	(1.31-3.13)		247, 342
Condom used for most recent sex with most recent partner												
Yes	33.5%	(29.7-37.6)	1.00	-	0.13	1.00	-	0.87				491, 671
No	38.0%	(33.9-42.4)	1.22	(0.95-1.56)		0.97	(0.70-1.34)					458, 621
Concurrent partnerships in last year[f]												
No	32.9%	(29.6-36.3)	1.00	-	**<0.01**	1.00	-	0.24				676, 916
Yes	49.7%	(41.0-58.4)	2.02	(1.37-2.96)		1.52	(0.92-2.50)					136, 188
Unknown	38.5%	(30.9-46.7)	1.28	(0.88-1.86)		1.18	(0.77-1.80)					137, 193
Frequency of binge drinking												
never / ≤monthly	28.1%	(24.6-32.0)	1.00	-	**<0.01**	1.00	-	**0.04**	1.00	-	**0.04**	527, 715
monthly	39.9%	(33.4-46.7)	1.69	(1.21-2.37)		1.48	(1.01-2.16)		1.51	(1.05-2.19)		202, 289
≥weekly	43.2%	(37.5-49.1)	1.94	(1.44-2.62)		1.50	(1.04-2.15)		1.42	(1.00-2.00)		273, 370
Ever had any same sex experience/contact												
No	33.9%	(31.1-36.8)	1.00	-	0.11	1.00	-	**0.02**				922, 1260
Yes	42.4%	(32.2-53.4)	1.44	(0.92-2.26)		2.08	(1.12-3.84)					80, 115

[a]N in column headings shows unweighted denominators. Total denominators by characteristic and in multivariable models vary due to item-missingness..[b]AOR: Adjusted odds ratios, adjusted for all variables shown. [c]Results for recent diagnosis are not reported due to small sample size in Scotland and Wales when limited to those tested. [d]IMD: Index of multiple deprivation of LSOA (lower super output area) of residence. IMD scores for England, Scotland and Wales were adjusted before being combined and assigned to quintiles, using the method described by Payne and Abel[264]. [e]Excludes 16 year-olds. [f]Among those with ≥1 sexual partner in last year.

Appendix 3: Factors associated with prevalent infection, recent diagnosis or recent testing among 16 to 24 year-olds resident in England (Natsal-3)

Relevant to Chapter 7

Table 9-4a and Table 9-4b overleaf present equivalent tables to those presented in Table 7-2a and Table 7-2b with the population restricted to participants resident in England as opposed to the population resident in Britain.

Table 9-4a: Percentage, unadjusted and adjusted odds (OR/AOR) ratios for prevalent chlamydia infection, self-reported diagnosis in the last year and self-reported testing by sociodemographic and behavioural factors (16-24 year-old sexually-experienced <u>women</u> resident in <u>England</u> Natsal-3)

	Prevalent chlamydia infection detected in urine (n=992)							Diagnosed with chlamydia in the last year (among those tested in the last year) (n=940)							Tested for chlamydia in the last year (n=1,736)							Denominator (weighted, unweighted) [a]		
	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	Infection	Diagnosis	Tested
Age group																								
16-19	3.6%	(2.0-6.5)	1.00	-			0.35	5.8%	(3.6-9.2)	1.00	-	1.00	-	0.62	61.2%	(56.7-65.5)	1.00	-	1.00	-	0.07	181, 332	177, 341	291, 566
20-24	2.5%	(1.5-4.2)	0.68	(0.30-1.53)	0.61	(0.21-1.74)		5.5%	(3.6-8.2)	0.94	(0.49-1.81)	0.80	(0.34-1.89)		54.9%	(50.9-58.8)	0.77	(0.61-0.98)	0.76	(0.56-1.02)		323, 485	292, 491	532, 886
IMD quintile of LSOA of residence																								
2 least deprived	1.2%	(0.4-3.6)	1.00	-	1.00	-	0.01	4.7%	(2.6-8.2)	1.00	-	1.00	-	0.23	56.9%	(51.9-61.8)	1.00	-	1.00	-	0.660	179, 296	166, 289	292, 510
Middle quintile	1.3%	(0.5-3.4)	1.02	(0.23-4.44)	0.95	(0.21-4.13)		3.2%	(1.3-7.5)	0.66	(0.22-1.96)	0.92	(0.28-3.00)		58.0%	(50.9-64.7)	1.04	(0.74-1.48)	1.20	(0.80-1.79)		92, 140	92, 154	159, 267
2 most deprived	4.9%	(3.1-7.5)	4.08	(1.26-13.3)	4.40	(1.32-14.6)		7.4%	(4.9-10.9)	1.61	(0.77-3.36)	1.83	(0.77-4.31)		56.9%	(52.2-61.5)	1.00	(0.76-1.32)	1.03	(0.75-1.39)		233, 381	210, 389	371, 675
Age at first heterosexual sex																								
17+	1.3%	(0.4-3.8)	1.00	-	1.00	-	0.51	4.4%	(1.9-9.6)	1.00	-	1.00	-	0.94	47.8%	(42.1-53.6)	1.00	-	1.00	-	0.13	156, 198	127, 195	267, 406
16	3.7%	(1.9-7.1)	3.00	(0.82-11.0)	2.38	(0.54-10.3)		5.8%	(3.2-10.2)	1.34	(0.47-3.83)	0.93	(0.30-2.79)		57.7%	(52.4-62.8)	1.49	(1.09-2.04)	1.21	(0.85-1.71)		152, 245	133, 230	231, 413
<16	3.9%	(2.2-6.8)	3.11	(0.89-10.9)	1.79	(0.48-6.66)		6.5%	(4.4-9.7)	1.53	(0.60-3.89)	0.85	(0.32-2.24)		67.4%	(63.0-71.5)	2.26	(1.70-3.01)	1.42	(1.01-2.00)		181, 351	198, 385	295, 579
Number of sexual partners in the last year without a condom																								
0	2.3%	(0.7-7.7)	1.00	-	1.00	-	0.26	4.5%	(1.6-12.1)	1.00	-	1.00	-	0.79	40.3%	(34.1-46.8)	1.00	-	1.00	-	0.160	101, 143	72, 121	181, 306
1	2.0%	(1.1-3.5)	0.85	(0.22-3.33)	0.41	(0.09-1.78)		3.8%	(2.2-6.3)	0.83	(0.25-2.79)	0.79	(0.17-3.60)		57.2%	(53.5-60.7)	1.98	(1.48-2.65)	1.41	(0.92-2.14)		309, 492	282, 494	495, 869
2+	6.6%	(3.5-12.0)	2.93	(0.72-11.9)	0.81	(0.18-3.63)		10.9%	(7.3-16.1)	2.62	(0.80-8.65)	1.12	(0.22-5.63)		77.7%	(71.5-83.0)	5.18	(3.42-7.85)	1.73	(0.96-3.10)		94, 181	113, 215	146, 274
Number of new sexual partners in the last year																								
0	2.2%	(1.2-3.9)	1.00	-	1.00	-	0.99	2.9%	(1.6-5.4)	1.00	-	1.00	-	0.22	47.8%	(43.8-51.9)	1.00	-	1.00	-	0.003	263, 400	201, 348	421, 727
1	2.6%	(1.0-6.7)	1.22	(0.39-3.81)	1.06	(0.28-3.89)		5.2%	(2.7-9.9)	1.83	(0.72-4.62)	2.04	(0.71-5.80)		62.5%	(56.9-67.8)	1.82	(1.38-2.41)	1.71	(1.23-2.36)		140, 225	143, 257	229, 411
2+	5.4%	(3.0-9.7)	2.60	(1.08-6.27)	1.06	(0.28-3.98)		10.5%	(6.9-15.7)	3.91	(1.82-8.42)	2.76	(0.86-8.82)		74.1%	(67.2-80.0)	3.12	(2.16-4.51)	1.74	(1.09-2.79)		97, 186	122, 222	166, 301
Number of lifetime sexual partners																								
1 to 4	2.1%	(1.1-4.1)	1.00	-	1.00	-	0.48	2.3%	(1.2-4.3)	1.00	-	1.00	-	0.08	47.3%	(43.4-51.3)	1.00	-	1.00	-	0.0009	274, 401	203, 357	430, 751
5 to 9	2.2%	(1.0-4.7)	1.03	(0.36-2.92)	0.87	(0.28-2.72)		6.8%	(4.0-11.4)	3.16	(1.36-7.34)	2.60	(0.96-6.98)		66.3%	(60.6-71.7)	2.19	(1.64-2.93)	1.81	(1.28-2.55)		126, 217	142, 251	214, 376
10+	6.1%	(3.2-11.3)	3.02	(1.17-7.81)	1.71	(0.54-5.39)		9.8%	(6.2-15.1)	4.70	(2.07-10.7)	3.71	(1.12-12.2)		71.5%	(65.2-77.1)	2.80	(2.01-3.89)	1.92	(1.24-2.95)		100, 191	122, 219	170, 310
Condom used for most recent sex with most recent partner																								
Yes	2.3%	(1.0-5.1)	1.00	-	1.00	-	0.36	3.7%	(1.8-7.6)	1.00	-	1.00	-	0.24	55.1%	(49.9-60.2)	1.00	-	1.00	-	0.920	173, 262	156, 273	284, 494
No	3.6%	(2.3-5.5)	1.54	(0.60-3.93)	1.49	(0.63-3.50)		6.5%	(4.4-9.3)	1.80	(0.76-4.31)	1.67	(0.70-3.94)		60.9%	(57.2-64.5)	1.27	(0.99-1.63)	1.02	(0.73-1.40)		298, 505	293, 521	482, 858

Table 9-4a continued.

Concurrent partnerships in last year[†]																			
No	2.6%	(1.6-4.2)	1.00	-	1.00	-	0.46	4.5%	(2.9-6.8)	1.00	-	1.00 -	0.56	54.0%	(50.5-57.5)	1.00	-	1.00 -	0.12	369, 574	325, 564	603, 1045
Yes	7.2%	(3.3-15.1)	2.92	(1.10-7.75)	1.60	(0.55-4.64)		8.6%	(4.2-16.6)	2.00	(0.83-4.86)	0.72	(0.25-2.02)	77.5%	(69.6-83.7)	2.92	(1.92-4.44)	1.47	(0.90-2.39)	58, 117	70, 131	90, 169
Unknown	1.6%	(0.5-5.2)	0.63	(0.18-2.24)	0.66	(0.15-2.75)		7.4%	(3.8-14.0)	1.72	(0.78-3.81)	1.34	(0.55-3.25)	67.3%	(59.5-74.3)	1.75	(1.23-2.51)	1.46	(0.93-2.29)	60, 105	67, 126	99, 190
Frequency of binge drinking																			
Never / <monthly	2.3%	(1.3-4.1)	1.00	-	1.00	-	0.02	3.9%	(2.5-6.0)	1.00	-	1.00 -	0.27	55.1%	(51.4-58.7)	1.00	-	1.00 -	0.01	321, 502	289, 512	527, 934
Monthly	1.1%	(0.3-3.3)	0.46	(0.12-1.70)	0.43	(0.11-1.67)		6.8%	(3.5-12.8)	1.80	(0.78-4.12)	2.08	(0.75-5.72)	53.4%	(46.8-59.8)	0.93	(0.70-1.25)	0.66	(0.47-0.93)	108, 181	95, 165	178, 302
>weekly	8.2%	(4.6-14.1)	3.80	(1.60-9.04)	2.39	(0.97-5.89)		9.7%	(5.2-17.6)	2.66	(1.18-5.99)	2.15	(0.74-6.22)	71.7%	(64.0-78.3)	2.06	(1.42-2.99)	1.35	(0.89-2.04)	76, 134	84, 153	117, 214
Ever had any same sex experience/contact																			
No	2.7%	(1.7-4.2)	1.00	-	1.00	-	0.64	5.5%	(3.7-7.9)	1.00	-	1.00 -	0.36	54.9%	(51.4-58.3)	1.00	-	1.00 -	0.33	397, 609	346, 618	633, 1120
Yes	3.7%	(1.6-8.2)	1.39	(0.53-3.60)	0.80	(0.31-2.04)		6.0%	(3.4-10.4)	1.10	(0.54-2.27)	0.65		64.6%	(58.2-70.6)	1.50	(1.11-2.03)	1.19	(0.83-1.68)	107, 208	122, 214	190, 332

Table 9-4b: Proportion, unadjusted and adjusted odds ratios for prevalent chlamydia infection, self-reported diagnosis in the last year and self-reported testing by sociodemographic and behavioural factors (16-24 year-old sexually-experienced men resident in England, Natsal-3)

	Prevalent chlamydia infection detected in urine (n=992)							Diagnosed with chlamydia in the last year (among those tested in the last year) (n=940)							Tested for chlamydia in the last year (n=1,736)							Denominator (weighted, unweighted) [a]		
	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	%	(95%CI)	OR	(95%CI)	AOR[b]	(95%CI)	p	Infection	Diagnosis	Tested
Age group																								
16-19	0.2%	(0.0-1.5)	1.00	-	1.00	-	0.06	3.7%	(1.8-7.8)	1.00	-	1.00	-	0.91	44.3%	(39.6-49.2)	1.00	-	1.00	-	0.0001	202, 303	141, 218	319, 511
20-24	2.9%	(1.8-4.8)	13.85	(1.80-106)	9.72	(0.92-102)		5.9%	(3.3-10.6)	1.63	(0.60-4.44)	0.93	(0.27-3.12)		33.1%	(29.4-37.1)	0.62	(0.48-0.81)	0.50	(0.35-0.70)		330, 416	175, 222	540, 670
IMD quintile of LSOA of residence																								
2 least deprived	0.9%	(0.3-3.1)	1.00	-	1.00	-	0.04	4.7%	(2.1-10.3)	1.00	-	1.00	-	0.54	37.1%	(32.3-42.1)	1.00	-	1.00	-	0.64	214, 284	121, 171	327, 457
Middle quintile	0.8%	(0.2-3.5)	0.92	(0.14-6.04)	0.78	(0.06-9.66)		3.4%	(1.0-10.4)	0.70	(0.17-2.96)	0.47	(0.11-1.94)		35.3%	(28.6-42.6)	0.92	(0.63-1.34)	0.97	(0.64-1.45)		95, 137	53, 77	151, 217
2 most deprived	3.3%	(1.9-5.7)	3.69	(0.96-14.2)	4.13	(0.91-18.5)		5.7%	(3.0-10.7)	1.22	(0.41-3.58)	0.97	(0.35-2.67)		38.2%	(33.8-42.8)	1.05	(0.79-1.39)	1.13	(0.81-1.56)		222, 298	142, 192	381, 507
Age at first heterosexual sex																								
17+	0.9%	(0.3-2.9)	1.00	-	1.00	-	0.64	3.1%	(0.8-11.0)	1.00	-	1.00	-	0.86	26.9%	(22.5-31.9)	1.00	-	1.00	-	0.02	173, 207	78, 105	291, 371
16	1.7%	(0.5-5.3)	1.93	(0.35-10.5)	2.13	(0.43-10.5)		4.5%	(1.6-12.2)	1.48	(0.27-8.27)	1.01	(0.18-5.60)		36.2%	(30.2-42.6)	1.54	(1.07-2.20)	1.17	(0.78-1.74)		129, 179	80, 103	221, 308
<16	3.0%	(1.7-5.3)	3.47	(0.89-13.5)	1.21	(0.32-4.50)		6.3%	(3.6-10.8)	2.11	(0.48-9.22)	1.38	(0.28-6.66)		49.4%	(44.3-54.4)	2.64	(1.94-3.60)	1.64	(1.14-2.35)		205, 301	154, 225	318, 458
Number of sexual partners in the last year without a condom																								
0	0.4%	(0.1-1.6)	1.00	-	1.00	-	0.12	0.0%	-						28.3%	(23.4-33.7)	1.00	-	1.00	-	0.08	167, 207	77, 107	276, 382
1	1.3%	(0.5-3.1)	3.20	(0.59-17.2)	0.41	(0.03-4.64)		3.8%	(1.9-7.4)	0.31	(0.11-0.83)				36.4%	(31.9-41.1)	1.45	(1.03-2.04)	1.25	(0.79-1.97)		259, 356	152, 209	424, 568
2+	5.9%	(3.3-10.5)	15.56	(3.32-73.0)	1.82	(0.12-26.4)		11.3%	(6.1-20.0)	1.00	-				56.2%	(48.8-63.3)	3.26	(2.20-4.81)	1.86	(1.06-3.25)		104, 154	88, 124	156, 227
Number of new sexual partners in the last year																								
0	1.2%	(0.5-3.1)	1.00	-	1.00	-	0.99	4.5%	(1.7-11.3)	1.00	-	1.00	-	0.99	28.3%	(24.0-33.1)	1.00	-	1.00	-	0.77	234, 298	105, 132	371, 477
1	0.9%	(0.3-3.0)	0.75	(0.16-3.49)	0.94	(0.15-5.80)		3.0%	(1.2-7.8)	0.67	(0.16-2.71)	1.12	(0.24-5.21)		38.2%	(32.8-43.8)	1.56	(1.13-2.16)	1.14	(0.77-1.66)		167, 226	99, 145	269, 381
2+	4.5%	(2.4-8.2)	3.74	(1.18-11.9)	0.92	(0.16-5.18)		7.3%	(3.9-13.4)	1.67	(0.50-5.51)	1.11	(0.29-4.12)		52.1%	(46.0-58.1)	2.75	(1.97-3.84)	1.17	(0.72-1.87)		127, 190	108, 159	208, 309
Number of lifetime sexual partners																								
1 to 4	0.4%	(0.1-1.8)	1.00	-	1.00	-	0.03	0.7%	(0.2-3.1)	1.00	-	1.00	-	0.00	27.1%	(23.4-31.2)	1.00	-	1.00	-	0.004	281, 357	122, 167	451, 616
5 to 9	0.3%	(0.0-2.2)	0.72	(0.06-8.26)	0.30	(0.02-3.45)		2.0%	(0.5-8.3)	2.86	(0.35-23.2)	2.31	(0.22-23.3)		43.2%	(36.6-50.1)	2.04	(1.44-2.89)	1.52	(1.01-2.26)		125, 173	80, 118	193, 270
10+	6.9%	(4.1-11.3)	17.25	(3.68-80.8)	6.27	(0.88-44.2)		12.0%	(7.2-19.3)	19.23	(3.87-95.5)	14.44	(2.19-94.9)		53.4%	(46.8-59.9)	3.08	(2.21-4.31)	2.15	(1.36-3.38)		124, 186	110, 151	206, 284
Condom used for most recent sex with most recent partner																								
Yes	0.3%	(0.1-1.4)	1.00	-			0.04	2.8%	(1.1-7.0)	1.00	-	1.00	-	0.14	36.1%	(32.1-40.4)	1.00	-	1.00	-	0.59	252, 330	149, 209	417, 576
No	3.6%	(2.2-6.0)	10.99	(2.45-49.3)	9.41	(1.06-82.9)		7.2%	(4.2-12.1)	2.73	(0.88-8.50)	2.47	(0.75-8.12)		40.8%	(36.3-45.6)	1.22	(0.94-1.59)	0.91	(0.64-1.28)		245, 343	160, 218	395, 532

Table 9-4b continued.

Concurrent partnerships in last year[f]															
No	2.0% (1.1-3.6)	1.00 -	1.00 -	0.09	6.1%(3.6-10.2)	1.00 -		0.05	36.0%(32.4-39.8)	1.00 -	1.00 -	0.72	357, 475	207, 281	582, 789
Yes	2.6% (0.9-7.0)	1.27 (0.39-4.21)	0.18 (0.03-0.84)		5.0%(1.8-13.5)	0.81(0.24-2.71)	1.00 -		51.5%(42.4-60.5)	1.89(1.26-2.82)	1.11(0.69-1.78)		62, 97	55, 80	106, 152
Unknown	1.4% (0.3-6.0)	0.70 (0.15-3.37)	0.62 (0.09-4.05)		0.6%(0.1-4.2)	0.09(0.01-0.73)	0.07(0.00-0.70)		41.6%(33.4-50.3)	1.26(0.86-1.87)	1.20(0.76-1.86)		83, 111	50, 73	123, 173
Frequency of binge drinking															
Never / <monthly	0.8% (0.3-2.5)	1.00 -	1.00 -	0.49	2.8%(1.2-6.5)	1.00 -	1.00 -	0.18	30.3%(26.4-34.5)	1.00 -	1.00 -	0.06	279, 363	138, 194	463, 624
Monthly	2.9% (1.3-6.2)	3.56 (0.88-14.5)	1.89 (0.31-11.4)		2.1%(0.7-6.7)	0.76(0.17-3.27)	0.48(0.09-2.36)		44.0%(36.8-51.5)	1.81(1.27-2.59)	1.52(1.01-2.28)		108, 154	75, 106	171, 246
>weekly	3.3% (1.6-6.6)	4.13 (1.07-16.1)	2.73 (0.51-14.3)		9.8%(5.3-17.5)	3.78(1.25-11.4)	1.78(0.61-5.16)		46.6%(40.5-52.8)	2.01(1.46-2.75)	1.41(0.97-2.04)		143, 201	103, 140	224, 310
Ever had any same sex experience/contact															
No	2.0% (1.2-3.2)	1.00 -			5.4%(3.4-8.5)				36.4%(33.4-39.6)	1.00 -	1.00 -	0.02	499, 661	289, 401	799, 1093
Yes	0.9% (0.1-6.5)	0.44 (0.06-3.44)			0.0%-				48.4%(36.7-60.3)	1.64(1.01-2.68)	2.22(1.11-4.42)		33, 58	27, 39	60, 88

[a]N in column headings shows unweighted denominators. Total denominators by characteristic and in multivariable models vary due to item-missingness. [b]AOR: Adjusted odds ratios, adjusted for all variables shown. [c]Results for recent diagnosis are not reported due to small sample size in Scotland and Wales when limited to those tested. [d]IMD: Index of multiple deprivation of LSOA (lower super output area) of residence. IMD scores for England, Scotland and Wales were adjusted before being combined and assigned to quintiles, using the method described by Payne and Abel[264]. [e]Excludes 16 year-olds. [f]Among those with ≥1 sexual partner in last year. Shaded areas indicate variables that were not entered into univariable or multivariable logistic regression due to small sample sizes.

Appendix 4: Thesis outputs

Peer-reviewed publications

Woodhall SC, Soldan K, Sonnenberg P, Mercer CH, Clifton S, Saunders P, da Silva F, Alexander S, Wellings K, Tanton C, Field N, Copas AJ, Ison CA, Johnson AM. Is chlamydia screening and testing in Britain reaching young adults at risk of infection? Findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Sex Transm Infect. 2015 [Epub ahead of print]

Woodhall SC, Nichols T, Alexander S, da Silva FC, Mercer CH, Ison C, Gill ON, Soldan K. Can we use postal surveys with anonymous testing tomonitor chlamydia prevalence in young women in England? Pilot study incorporating randomised controlled trial of recruitment methods. Sex Transm Infect. 2015;91(6):412-4. doi: 10.1136/sextrans-2015-052067

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