Rationale, public health approaches, and policy implications of implementing community-level screening programmes for *Chlamydia trachomatis* infection.

D. Scott LaMontagne, MPH, FRIPH, CS
HIV and Sexually Transmitted Infections Department
Health Protection Agency
London, United Kingdom

Submitted in partial fulfilment of PhD requirements,
Middlesex University, School of Health and Social Sciences,
London, United Kingdom
27 May 2005

Acknowledgments

I would like to thank all of the co-authors who were involved in the research presented in this context statement. I have been fortunate to have had the privilege of working with two leaders in the field of sexual health, Drs. Jeanne M. Marrazzo (US) and Kevin A. Fenton (UK). Jeanne set my grounding and provided insight and inspiration as I began to specialise in chlamydia epidemiology. Kevin sheltered me and gave me a place to grow professionally, to expand my knowledge and skills, and to utilise my experience in the US screening programme for my work in the UK. Heartfelt thanks to both Jeanne and Kevin for their mentorship and friendship.

I would also like to thank Drs. Lesley Vernon and Hemda Garelick for guiding me through the context statement process, for helping me focus my writing, and for getting me to contextualise my body of research into a coherent whole.

Mostly, I would like to thank my partner, Raleigh Watts, for supporting my academic and professional goals, for providing me an isolated space to work like a maniac, and for tolerating my, sometimes gruff and oft times emotionally distant, behaviour through the stress of it all.

Table of contents

Abstract

This context statement outlines my published research in three themes, adapted from the ten criteria for screening established by Wilson and Jungner (1968): *Chlamydia trachomatis* as a public health problem; implementation of large-scale chlamydia screening programmes; and monitoring and evaluation of chlamydia screening programmes. These themes are supported by seven published papers quantifying the epidemiology of chlamydial infection in several populations; describing the development, implementation and first year results of a national chlamydia screening programme; and demonstrating four methods of evaluation— assessment of screening criteria, use of positivity to measure disease changes in the population, clinical audits of provider adherence to screening guidelines, and fiscal analysis of costs through economic modelling.

My research utilised a diverse set of study designs and methodological approaches: a) confirmatory studies of previously published research; b) cross-sectional studies with differing levels of statistical sophistication; c) clinical policy review using questionnaires to health care providers; d) economic modelling of budget expenditures, and decision-tree and sensitivity analyses; and e) an evaluation of a chlamydia screening programme combining retrospective cross-sectional analysis and multivariate logistic regression with sensitivity and efficiency analyses.

My research has revealed significant levels of chlamydia morbidity in a variety of populations and settings in the United States and United Kingdom and has demonstrated consistently increasing trends in rates of diagnosed chlamydial infections among genitourinary medicine (GUM) clinic attenders in the UK. These data suggest that chlamydial infection is a prevalent disease in both countries and contributes to a significant global public health problem. I have examined the genesis of a new national chlamydia

screening programme in the UK, and have shown the continued feasibility and acceptability of chlamydia screening, affirmed that screening in high prevalence populations is a successful strategy for disease detection, and improved our understanding of the sexual behaviours that continue to drive this epidemic. My evaluation of the longest running chlamydia screening programme in the US has illustrated the value of periodic assessments in screening protocols and lead to the revision in selection criteria for women screened in the north western US. I have found utility in a variety of methods to monitor and evaluate chlamydia screening programmes. The application of sensitivity and efficiency thresholds to sets of screening criteria proved useful in evaluating criteria performance and increasing criteria efficiency. Using chlamydia test positivity as a surrogate measure for prevalence could adequately measure programme impact for the National Chlamydia Screening Programme in England. Clinical audits of service providers regarding published guidelines for chlamydia screening in termination of pregnancy services demonstrated practice variation for chlamydia screening in these settings and suggested harmonisation of guidelines to increase adherence. Finally, my research of screening programme costs using economic models proved a useful tool to explore the average costs of screening and variations in estimates as local programmes revise their implementation and operational structure for chlamydia screening, and recommends this method be used to inform resource allocation for future phases of the National Chlamydia Screening Programme in England.

Chapter 1
Introduction

This context statement summarises my research in defining the epidemiology and public health significance of *Chlamydia trachomatis* infection, developing and implementing new screening initiatives, and monitoring and evaluating existing chlamydia screening programmes. Large-scale chlamydia screening programmes began in Sweden and the US in the 1980's. At that time, the evidence for the magnitude and the consequences of chlamydial infection was building. Multiple studies of infertility (Cates 1984; Mabey, Ogbaselassie, Robertson, Heckels and Ward 1985; Tjiam *et al.* 1985; Robertson, Ward, Conway and Caul 1987; Miettienen, Heinonen, Teisala, Hakkarainen and Punnonen 1990), ectopic pregnancy (Chow *et al.* 1990) and pelvic inflammatory disease (PID) (Mardh, Ripa, Svensson and Westrom 1977; Moller, Mardh, Ahrons, and Nussler 1981; DeMuylder *et al.* 1990; Westrom, Joesoef, Rynolds, Hagud and Thompson 1992) were concluding that this bacteria was a prime suspect in the aetiology of these conditions. Given the potential devastating consequences to women, research began to focus on how to intervene. The initial detection method for *C. trachomatis* was cell culture, difficult to perform accurately and requiring a high level of skill in the laboratory (Stamm 1999). The populations infected seemed to be diverse, at least from the small epidemiologic studies thus concluded (McCormack *et al.* 1979), but focusing on those at high risk of other sexually transmitted diseases seemed most logical.

Sweden was the first country to organize at the national level to use targeted chlamydia screening for those at high risk as a disease control strategy, as well as an approach to reduce the occurrences of PID. In Sweden, the programme targeted routine chlamydia testing in conjunction with genital examinations already performed at sexual health clinics. This approach was nationally implemented across the network of health care settings

providing these examinations (Herrmann and Egger 1995). In the US, the programme targeted women attending sexually transmitted disease (STD) clinics (given the high risk sexual behaviours within this group) and women attending family planning clinics (focusing on "infertility prevention") through the use of selection criteria (Handsfield *et al.* 1986). Criteria that were found to be predictive of infection were aged 24 years or less, new sex partner in the last two months, mucopurulent cervicitis, easily induced endocervical bleeding, and use of no contraception or a non-barrier method (Handsfield *et al.* 1986). The US public health care system is divided into ten regions (numbered I, II, III, etc. to IX, and X), and established a demonstration project for chlamydia screening in Region X (north western US) to test the utility of selective screening as an approach for targeting women at high risk for chlamydial infection. Even though the two strategies were organized and implemented in different ways, both the US and the Swedish programmes experienced appreciable decreases in chlamydia morbidity after three years of screening (Lossick *et al.* 1990; Herrmann and Egger 1995). Sweden continued in this vein through the 1990's and the US expanded its programme across the other regions over the same time. Both programmes began to be viewed as 'models of success' and several European cities started to explore or implement chlamydia screening based on selecting "at risk" women, including Aarhus in Denmark and Amsterdam in the Netherlands (Moeller, Andersen, Olesen, and Ostergaard 2003; Westh and Kolmos 2003). In the United Kingdom in 1998, a government-sponsored investigation of whether a national screening programme for chlamydia should be established concluded genital chlamydial infection met the Wilson-Jungner criteria (Wilson and Jungner 1968) for a screening programme focusing on women (Chief Medical Officer 1998).

However, given the depth of evidence, screening for chlamydia is still controversial. Many unresolved questions remain, namely:

- Do we really know how much chlamydia is in the population?

- Who are the right populations to screen: women, men, both or only young adults?
- Are the complications of infection as severe as we think?
- Does screening really decrease a woman's chances of becoming infertile?
- Are our selection procedures for determining who is infected and our laboratory tests for detecting the organism sufficiently accurate to not miss infections but also to not classify someone as infected when they aren't?
- Can we develop better diagnostics to improve the detection of infection?
- Does treatment really work and can it reverse the damage already done?
- Is there a correct way to offer screening: either during a gynaecological examination, by invitation to attend a clinic, or through testing kits posted in the mail?
- Do we really know that screening saves money and can reduce the prevalence of this infection in the population?

The findings of my research presented here examine the epidemiology of chlamydial infection in several populations (LaMontagne, Fine and Marrazzo 2003; Brown *et al.* 2004), summarise the development, implementation and first year results of a national chlamydia screening programme (LaMontagne, Fenton, Randall, Anderson and Carter 2004b), and demonstrate approaches for monitoring and evaluating chlamydia screening programmes (LaMontagne, Patrick, Fine and Marrazzo 2004a; Adams *et al.* 2004b; LaMontagne, Pimenta, Fenton, Mallinson and Hopwood 2004c; LaMontagne *et al.* 2005;). My research has shown high levels of disease in male and female populations in two countries. In the United States, we found prevalence among women from 4-7% and among men 5-18%, depending upon the presence of symptoms. In England, chlamydia positivity in the first year of the national screening programme was 10.1% and reported rates of diagnosed infections from genitourinary medicine (GUM) clinics were 66 per 100,000 for men and 167 per 100,000 for women. I demonstrated how to implement a national chlamydia screening programme and quantified the results of the first year, confirming previous

research on the risk factors for infection and ideal populations for screening. My research presented in this context statement also examines several methods for monitoring and evaluation chlamydia screening programmes, including assessment of selection criteria, measurement of sensitivity and efficiency of screening criteria, analysis of programme costs for fiscal jurisprudence, use of chlamydia positivity as an accurate measure to monitor reductions in disease in the screened population, as well as clinical audits of service providers to ensure adherence to established guidelines.

Even though each of my seven published manuscripts included in this context statement has a team of authors,[a] my personal contribution requires explanation. I conceptualised and designed four of the studies, including collection and collation of data, all statistical analyses, data interpretation and principal authorship of the manuscripts: LaMontagne *et al.* 2003; LaMontagne *et al.* 2004a; LaMontagne *et al.* 2004b; and LaMontagne *et al.* 2005. I collated, analysed, and interpreted existing data that was originally collected by the study's co-authors, and I was the principal author of the published manuscript for LaMontagne *et al.* 2004c. I assisted in conceptualising the methods, collated data, assisted with data analysis, and production and interpretation of results, and I also contributed to writing the manuscript and revisions for Adams *et al.* 2004b. For Brown *et al.* 2004, I collated, analysed and interpreted retrospective data, and provided substantive written comments on the sexually transmitted infection (STI) trend data presented in the manuscript.

Professional ethics were considered prior to each study. The infringement of patient confidentiality and confirmation of patient consent is paramount in any clinical research. Five of my studies consisted of previous collected surveillance data, where patient consent was already received for the clinical service provided and information was disseminated to patients regarding the reporting of de-identified (pseudo-anonymised) STI data to local or

---

[a] Co-author statements of my individual contribution to the research are on file at Middlesex University.

national health bodies with the mandate for the surveillance of STIs (LaMontagne *et al.* 2003, 2004a, 2004b, 2005; and Brown *et al.* 2004). Because de-identified data were used in accordance to the US or UK legal mandates, as appropriate, for handling routine STI surveillance data, formal ethical approval for each study was not required. LaMontagne *et al.* (2004c) was a policy review, surveying clinic managers; thus, no patient data were used and ethical approval was not required. The cost analysis of chlamydia screening (Adams *et al.* 2004b) also did not require an ethics review, as the study utilised previously consented patient data in aggregate only, combined with publicly available health care cost data.

The research included in this context statement employed a diverse set of study designs and methodological approaches. LaMontagne *et al.* (2005), was specifically designed to confirm a previously published statistical method of adjusting test positivity estimates for the measurement of prevalence to establish its accuracy and usefulness as a programme monitoring tool for the National Chlamydia Screening Programme (NCSP) in England. Cross-sectional techniques with differing levels of statistical sophistication were used for the descriptive epidemiological studies of the trends in sexually transmitted infections (STIs) in the United Kingdom (Brown *et al.* 2004), asymptomatic chlamydial infection in men (LaMontagne *et al.* 2003), and results from the first year of the NCSP (LaMontagne *et al.* 2004b). To assess chlamydia screening and treatment practice patterns among termination of pregnancy providers, clinical policy review techniques using questionnaires was employed (LaMontagne *et al.* 2004c). In the study of the costs of operating an opportunistic screening programme among 16-24 year old women, economic modelling of budget expenditures matched with patient flow quantification in decision-tree and sensitivity analyses was used to estimate the costs of screening tests and the components that provided the greatest variability in those costs (Adams *et al.* 2004b). Lastly, I developed a unique design for the evaluation of the screening programme in the north western U.S. (Region X) that combined retrospective cross-sectional analysis and multivariate logistic

regression with sensitivity and efficiency analyses which resulted in a more robust evaluation of selective screening criteria (LaMontagne *et al.* 2004a).

Taken in concert, these seven papers robustly contribute to the evidence that chlamydia screening fulfils the criteria for public health intervention (Wilson and Jungner 1968). I have further refined the epidemiology of chlamydia— the magnitude of the problem and the factors most associated with infection. The most significant contribution being made to the understanding of chlamydial infection in men. I have taken the best scientific evidence available, as well as the best practice lessons learned from other programmes, to develop and implement the first nationally coordinated chlamydia screening programme in England. Finally, I have provided research evidence for monitoring and evaluating chlamydia screening programmes.

Chapter 2
Theoretical framework

I have used the criteria developed in the 1960's by Wilson and Jungner (1968) as the theoretical framework of my research. The principles described in their manuscript established the current model by which public health determines whether, when and how to screen for disease. Over time, these criteria have been used in infectious disease control, as well, to justify a screening response to a perceived threat to the population's health. Several examples are cited, including tuberculosis and cervical cancer (Wilson and Jungner 1968).

The criteria cover ten general concepts that seek to qualify and quantify the clinical intervention of early detection from both the patient's and the provider's perspective. Firstly, the condition should be an important health problem. Importance can be relative, but suggested evidence includes scope and magnitude of the disease, types of populations affected, and the impact on both the individual with the disease, as well as the population at large.

Secondly, the natural history of the condition, including development from latent to declared disease, should be adequately understood. For certain conditions, natural history studies have been possible, either in humans or appropriate animal models, especially if the condition is new, *e.g.*, severe acute respiratory syndrome (SARS), or rare, *e.g.*, sickle cell anaemia, or untreatable, *e.g.*, certain cancers prior to adequate therapeutic regimens. Given modern medicine's climate of studies involving human subjects, the focus on meeting these criteria has been on the "adequacy" of our knowledge of the disease, rather than a complete understanding of the entire natural history.

Along with understanding the natural history, Wilson and Jungner (1968) argue that a recognisable latent or early symptomatic stage of the disease is required for preventive public health action— the third criteria. The goal of screening otherwise healthy populations is to determine those who are infected and could develop disease complications in the future (Friis and Sellers 2004). Basically, there is a need to halt the (potentially) less harmful infection before it becomes a more significant disease.

The fourth and fifth criteria build of this concept of early detection. There needs to be a suitable test for detecting who is infected and who is not. This relates to the ability of the diagnostic test (or examination) to be sufficiently sensitive enough to detect the people who really are infected (true positives) from those who are truly uninfected (true negatives); thus the diagnostics need to have high sensitivity and high specificity. Fifth, this diagnostic test/examination needs to be acceptable to the population. Because screening targets "apparently" healthy people, the potential harm (physical or psychological) of the diagnostic test needs to be minimized for population acceptance.

There is potential to do more harm than good with a screening test if there are no facilities for diagnosis and treatment, if the treatment is unacceptable (causes more harm than no treatment) by either the population or the medical care providers, or if there is no acceptable and agreed definition of who is a patient. In the sixth, seventh and eighth criteria, Wilson and Jungner (1968) focus on the health care aspects of the screening intervention. There must be an adequate service delivery infrastructure, either through physical clinics/hospitals or networked outreach of health care personnel that can reach the target population. Treatment that is costly, has severe side-effects, or is not efficacious might be a deterrent to a population being screened. This might also make it difficult for a coherent and clinically-sound treatment policy to be developed by health care providers. Lastly, if there is no clear definition of who is patient, either in the selection procedure for

screening or the interpretation of laboratory diagnostics, there is a potential that a person who should have been treated will be missed and those who are not considered to be infected will be treated unnecessarily.

The costs of finding infections, 'case-finding,' in an otherwise healthy population must be balanced with the expenditure for medical care. Costs include supplies, personnel, establishing the screening programme, and on-going maintenance of the intervention within the health care system. Additionally, there could be societal costs or long-term costs in terms of loss of productivity by those undergoing diagnosis and treatment or medical costs incurred from not detecting infection before disease or sequelae from disease are experienced by the population. The total cost must balance the financial outlays required for the screening intervention versus the potential expenditures required in the absence of screening.

Lastly, Wilson and Jungner (1968) advocate for screening to be a continual process, as single-occasion interventions may only hit a small proportion of the affected population or only detects persons infected now, but not those who subsequently become infected.

RATIONALE FOR THEORETICAL FRAMEWORK

The concepts described in the Wilson-Jungner monograph are not original; they have origins in chronic disease prevention, shaped by earlier works in the 1950's reported in the Commission on Chronis Illness (1956-9) and by Chapman (1949), Moutin (1950), and Smillie (1952). However, Wilson and Jungner were able to synthesise these earlier works into a more digestible and comprehensive format, which has enabled the concepts to find a broader application in the field of infectious disease. Additionally, the work of Wilson and Jungner has influenced epidemiologic methods (Mausner and Kramer 1985; Hennekens

and Buring 1987; Friis and Sellers 2004) through an approach that can be applied regardless of the "agent" causing disease, whether that is a bacteria, such as *Chlamydia trachomatis* causing pelvic inflammatory disease and infertility, a virus, such as hepatitis causing chronic liver failure, or a condition, such as diet contributing to heart disease. Indeed, with the *gravitas* of the World Health Organisation's seal of approval, these criteria have been widely used in programmes as diverse as diabetic retinopathy (Wilson and Jungner 1968), cervical cancer (Hanselaar 2002), skin cancer/melanoma (Rampen, Neumann and Kiemeney 1992), and newborn screening (Seymour *et al.* 1997).

Even though widely used, some have expressed concern that the criteria are subjective (Pollitt 1999) or conflict with evidence-based views (Seymour *et al.* 1997). Pollitt (1999) has noted that qualitative descriptors in the criteria are difficult to define and measure. For example, what is 'important' in determining the importance of the public health problem—the very first criteria to be met according to Wilson and Junger. Importance could be based on the magnitude of the disease or the magnitude of the consequences of the disease. However, who determines the thresholds for these? Other words, such as 'adequate', 'suitable', 'unacceptable', and the like, are used throughout the criteria and could be biased in measurement or interpretation (Pollitt 1999). These limitations suggest a more judicious and cautious use of the Wilson and Jungner criteria.

Despite these critiques, the criteria developed in the 1960's by Wilson and Junger find application today. They provide a tool for scientists and public health practitioners in developing programmes and policies for a wide-range of conditions affecting the health of the population, including the review of evidence for newborn screening of in-born metabolic disorders which criticised these very criteria (Seymour *et al.* 1997). For example, the Chief Medical Officer's Expert Advisory Group (1998) structured their comprehensive review of the evidence for chlamydia screening based on these criteria. These ten criteria

encompass broad themes within the field of chlamydia screening to facilitate review and understanding of the current research evidence, as well as to explore gaps in our knowledge that require further work. They can be used to provide a logical progression from quantifying the problem to summarising approaches for resolution to evaluating the course of action taken— these are the three themes of the research studies included in this statement.

Chapter 3
Literature review

The principles of screening outlined in Wilson and Jungner's sentinel work have implicitly or explicitly guided the development of widespread chlamydia screening as a method of secondary prevention for the control of this prevalent sexually transmitted infection. Because of this, it is useful to review the literature following the logic and flow of the Wilson and Jungner criteria.

PUBLIC HEALTH IMPORTANCE

Chlamydia trachomatis is a prevalent and potentially devastating infection (Stamm 1999). The scope and magnitude of this infection is adequately understood and quantified (Cates and Wasserheit 1991). Groundbreaking research on the aetiology of tubal factor infertility illustrated the critical role of chlamydial infection plays in this devastating sequelae. Cates (1984) cites early research from Sweden that first suggested the link between chlamydial infection and infertility, via pelvic inflammatory disease (PID), and encapsulates the evidence to date to assert the causal pathway of infertility. Women with salpingitis and/or PID have a 3-7 fold risk of involuntary infertility (Cates 1984; Mardh *et al.* 1977). Subsequent studies from 1985-1987 confirmed these early findings (Mabey *et al.* 1985; Tjiam *et al.* 1985; Robertson *et al.* 1987). However, the exact mechanisms of the causal pathway were yet to be elucidated. The intervening step of PID was found to be the immediate consequence of untreated chlamydial infection. In a retrospective study of 166 women with acute PID, Moller (1981) found that 21% of cases had chlamydial organisms cultured from the cervix, and at least 25% of additional acute PID was directly attributable to infection with *Mycoplasma hominis* (another bacterium). Further research has confirmed chlamydia as one cause of PID (DeMuylder *et al.* 1990; Marks, Tideman, Estcourt, Berry,

and Mindel 2000). Additionally, the etiologic role of chlamydial infection with ectopic pregnancy has also been documented in several studies (Miettinen *et al.* 1990; Chow *et al.* 1990; Egger, Low, Smith, Lindblom, and Herrmann 1998; Cates 1999). Lastly, recent evidence has come to light to suggest that *Chlamydia trachomatis* infection is related to ovarian cancer, cervical cancer, and male infertility (Ness, Goodman, Shen and Brunham 2003; Paavonen *et al.* 2003; Idahl, Boman, Kumlin and Olofsson 2004). This empirical evidence confirms the severity of the consequences of untreated chlamydial infection on personal and public health.

The risk of developing these sequelae can be assessed through measuring the burden of the infection in various populations. Prevalence studies have been undertaken to estimate the magnitude of infection and project proportions that may suffer sequelae. In an early study, McCormack *et al.* (1979) found nearly 5% of female college students in the US were infected. A review of the literature on the prevalence of infection among European women by Wilson *et al.* (2002) showed levels of infection from 1% (2,494 Spanish women ages 15-35) to 17% (306 French women ages 15-55), depending upon the population under study. A meta-analysis of prevalence studies from the United Kingdom by Adams and colleagues (2004a) found a consistent 9% prevalence among women attending family planning clinics.

Prevalence estimates have varied considerably depending upon the sampling frame, which is not surprising because various sampling methods select different populations. For example, population-based household probability samples drawn from the general adult aged population have tended to find a lower prevalence of infection than clinic-based samples, e.g., in China female prevalence was 2.6% (Parish *et al.* 2003), in the US prevalence among women ranged from 2.3% in white non-Hispanics to 7.5% among non-Hispanic black women (Mertz *et al.* 1998), in Slovenia 4.1% in women 18-24 years old (Klavs, Rodrigues, Wellings, Kese and Hayes 2004), in the United Kingdom the National Survey of

Attitudes and Sexual Lifestyle found 3% among adult women (Fenton *et al.* 2001), and in Nadu, India a prevalence of 3.3% among 15-45 year old women was reported (Joyee *et al.* 2004). Clinic-based estimates of prevalence in England have found 1 in 10 young women infected (Pimenta *et al.* 2003b). Other researchers have confirmed similar levels of infection in various female populations, depending upon setting, laboratory test methods, and age of the population sampled (Gerbase, Rowley, Heymann, Berkeley and Piot 1998; Skjeldestad, Nordbo and Hadgu 1997; Simms *et al.* 1997; Hiltunen-Back, Haikala, Kautiainen, Paavonen and Reunala 2001; Richardson E *et al.* 2003).

Among men, the estimates of the burden of chlamydial infection have also varied; these are also dependent upon the population sampled, age of the men, presence of symptoms, type of specimen tested, and laboratory test method (Hart 1993; Sutton, Martinko, Hale and Fairchok 2003; Ku *et al.* 2002; Aronson and Phillips 1993; Gunn *et al.* 1998; Oh *et al.* 1994; Johnson, Neas, Parker, Fortenberry and Cowan 1993; Ciemins *et al.* 2000; LaMontagne *et al.* 2003; LaMontagne *et al.* 2004b). Among male military populations in three different countries, prevalence was 4.6% in Denmark (van den Brule *et al.* 2002), 5.3% in the US (Cecil *et al.* 2001), and 9.8% in Scotland (McKay, Clery, Carrick-Anderson, Hollis and Scott 2003). Marrazzo *et al.* (2001) found a similar level of infection, 5.5%, among asymptomatic men attending sexually transmitted disease clinics in Seattle (US) tested via urine samples. High prevalence of infection in both male and female populations coupled with significant reproductive health consequences of untreated infection demonstrate that genital chlamydial infection is an important public health problem.

Natural history

Animal models and quasi-natural history studies of infertility have facilitated our understanding of the natural history of genital chlamydial infection (Patton, Wolner-

Hanssen, Cosgrove and Holmes 1990; Cates 1984; Miettinen *et al.* 1990; Westrom *et al.* 1992). DeMuylder *et al.* (1990) showed that untreated lower genital tract infection in women leads to upper genital tract infection, which manifests itself as PID. It is estimated that PID causes up to 47% of all ectopic pregnancies and 20% of cases of tubal factor infertility (Stamm 1999). In men, the consequences of infection seem to be less severe, but can include urethritis, epididymitis, and Reiter's syndrome (Cates and Wasserheit 1991); and recently, infection has been implicated in male infertility through damage to viable semen (Idahl *et al.* 2004). The precise understanding of the exact pathogensis of genital chlamydial infection in both men and women is not fully known; however, the knowledge base is sufficient enough for our adequate understanding of the natural history (Stamm 1999).

Asymptomatic stage

There is a recognizable latent or asymptomatic stage of the infection prior to disease (or sequelae) manifestation, which would lend itself to early detection prior to adverse consequences. Seventy percent of infected women are estimated to experience no or very mild symptoms (Cates and Wasserheit 1991). In men, chlamydial infection seems to be more symptomatic, about 50% of men will develop symptoms if infected (Stamm 1999). Symptoms suggestive of infection include dysuria (pain in urination), abnormal penile or vaginal discharge, abdominal pain (in women), and irregular or intermenstrual bleeding (in women), and can present three to fourteen days after exposure (Stamm 1999). Stamm (1999) suggested that people infected at younger ages are more likely to experience mild symptoms. Because symptoms generally encourage people to seek medical attention, a disease with high frequency of symptom development among infected persons is not considered a good candidate for screening. The goal of screening is to detect unrecognised disease in a population of apparently healthy people and sort those with disease from those

without (Mausner and Kramer 1985). Thus, for chlamydia, especially among infected women, 70% of the infected population seemingly "apparently well," i.e., asymptomatic, provides a good case for screening.

DIAGNOSTIC TESTS

As previously stated, the chlamydia bacteria has been difficult to grow in cell culture (Black 1997; CDC 2002). However, since its recognition as a potentially debilitating infection for women, advances in laboratory detection of the organism in clinical samples, such as cervical or urethral swabs, have intensified to make laboratory diagnosis easier and more sensitive. In the 1970's direct fluorescence assays were the standard (CDC 2002). In the 1980's more sensitive enzyme immunoassays (EIA or ELISA) became commonly used (CDC 2002; Watson *et al.* 2002). However, those tests had sensitivities of 80% at best. Currently, the best tests available utilize techniques that amplify DNA. Called nucleic acid amplification tests (NAATs), these new diagnostics have shown sensitivities as high as 95% and specificities approaching 100% (Newhall *et al.* 1999; Johnson *et al.* 2000; Cheng, Macaluso, Vermund, and Hook 2001; Battle *et al.* 2001; Verkooyen, Peeter, van Rijsoort-Vos, van der Meijden and Mouton 2002; Ostergaard 2002; Chernesky 2002; Stary 2002; Semeniuk, Zentnerr, Read and Church 2002; Verkooyen *et al.* 2003; Koumans *et al.* 2003). Even though ranges of sensitivity from 49-100% have been reported by Ostergaard (2002), a meta-analysis by Watson *et al.* (2002) demonstrated a mean sensitivity for two NAA tests of 87-94% (depending upon sample type). When implemented in non-research laboratory environments, estimates of 90% sensitivity and 99.5% specificity are considered more realistic (Schachter 1999; Schachter 2001).

Another significant development in diagnostics, which has not only enhanced the justification for screening for chlamydia but has also made it easier, is the use of non-

invasive specimens (Knox *et al.* 2002; Sylvan *et al.* 2002; Zenilman, Miller, Gaydos, Rogers and Turner 2003). In the early years, detection was only available from a urethral or cervical specimen; the latter requiring women to undergo a full pelvic examination with visualisation of the cervix. The current laboratory methods can be deployed on urine samples (for both men and women) or self-collected vulva-vaginal swabs, without sacrificing the sensitivity or specificity of the laboratory test (Stary, Najim, and Lee 1997; Rompalo *et al.* 2001; Hseih *et al.* 2003; Shafer *et al.* 2003; Schachter *et al.* 2003). Studies have also demonstrated that pooling non-invasive samples can reduce costs without reducing the sensitivity or specificity of the test method (Clark *et al.* 2001).

Acceptability of tests

The newer diagnostic methods have been welcomed by populations being screened (Serlin *et al.* 2002; Hsieh *et al.* 2003; Lane *et al.* 2003; Gotz *et al.* 2003). Lane *et al.* (2003) found that 76% of women preferred to collect their own sample via a vulva-vaginal swab, and Gotz *et al.* (2003) showed that home-testing for chlamydia was acceptable— 84% of responders to a survey of home-testing agreed to send a urine sample from home. In health care settings, especially genitourinary medicine (GUM) or sexually transmitted disease (STD) clinics, internal examinations for both men and women are standard, as a battery of tests are performed, requiring multiple clinical samples to be collected (Clinical Effectiveness Workgroup 2002). Thus, in the context of a routine diagnostic work-up, the acquisition of a cervical or urethral specimen has not been controversial. However, that does not make them any less comfortable. As screening needs to reach to those who are apparently well, i.e., those not experiencing genital symptoms that would prompt them to seek a GUM or STD clinic, the acceptability of the test becomes more important (CDC 2002). The advent of more sensitive laboratory test methods (NAATs) has increased the range of clinical specimens that can be used for testing, including non-invasive specimens such as urine and

self-taken vaginal swabs. This development has allowed screening to expand beyond the confines of health care facilities (Garrow, Smith, and Harnett 2002). Studies investigating the potential psychological or emotional 'harm' from chlamydia screening have not demonstrated severe consequences of providing a urine or vaginal specimen (Lane *et al.* 2003; Gotz *et al.* 2003). Indeed, screening studies have largely utilized non-invasive samples for the very reason that they are more acceptable to the target population (Serlin *et al.* 2002; Hsieh *et al.* 2003).

Facilities for diagnosis and treatment

Health care systems in industrialised nations are fortunate enough to have sophisticated networks of hospitals and clinics to provide facilities for the provision of diagnostic tests to populations screened and necessary treatment to those infected. Large networks of specialist clinics, GUM in Europe and STD in the US, are available specifically for the diagnosis and treatment of sexually transmitted infections (STIs). Increasingly, other health care delivery networks focused on women's health services, such as family planning and contraception clinics, have expanded services to include the provision of screening for STIs. These systems are financed through public funds in European countries but through private insurance in the United States. Even though the financing of health care is different between the two systems, Levine, Dicker, Devine and Mosure (2004) found that the chlamydia screening programme in the U.S. has been able to achieve higher screening coverage of the at-risk population (60%), than the 50% coverage recently achieved in a pilot of opportunistic screening in England (Pimenta *et al.* 2003a) or nearly 30% uptake in the Danish pilot of postal screening through population registries (van Bergen *et al.* 2005). This suggests that, despite differing funding schemes, uptake of chlamydia screening can achieve similar levels.

Treatment Efficacy and Acceptance

Wilson and Jungner (1968, p27-8) argue that this is the most important criterion to be met prior to initiating screening. "[I]t is clearly vital to determine... whether a better prognosis is given by treating conditions found at an earlier stage... Unless this is so, there can be no advantage to the patient." Studies exploring the pathogenesis and sequelae of chlamydial infection in women have shown that the earlier an infection is treated the less likely that infection is to ascend or cause further complications (Honey and Templeton 2002). Other studies have additionally found that a woman's chance of developing PID increase exponentially with repeated untreated infections, providing additional evidence that the earlier the treatment, the better (Hillis, Owens, Marchbanks, Amsterdam and Mac Kenzie 1997). However, the treatment should not cause harm. Therefore, toxicity of therapeutic regimens for chlamydial infection needs to be minimal. Studies of doxycycline and azithromycin, the two most commonly prescribed antibiotics for chlamydial infection (CDC 2002; Clinical Effectiveness Workgroup 2002) have shown high tolerance among infected persons (Lau and Qureshi 2002). Safe, effective and easy therapy has facilitated treatment compliance and acceptability by patients (Martin *et al.* 1992).

Defining the population

Screening targets healthy individuals to detect persons who might be infected. Critical to sorting out potentially diseased persons (true positives) from those without disease (true negatives) is the selection procedure for categorizing the healthy population for whom the screening intervention is designed (Hennekens and Buring 1987; Friis and Sellers 2004). This selection process operates on two levels: the population and the screening test. At the population level, the selection process must be sensitive enough to capture persons most likely to be infected, while not over-screening those who are not. And once the screening

population is selected, then the screening test must also do the same procedure, this time through the laboratory methods employed. In both cases, the ideal is to have a high positive predictive value with both the selection of the population to be screened, and the determination of the infected population within those screened (Mausner and Kramer 1985).

A vast array of research on chlamydia has focused on determining the appropriate population for screening, as the infection is highly asymptomatic. The most notable being the studies by Orr *et al.* 1994; Mosure, Berman, Kleinbaum and Halloran 1996; Mosure *et al.* 1997; Burstein *et al.* 1998; Richey, MacAluso, and Hook 1999; the Unites States Preventive Services Task Force 2001; Mardh 2002; Sipkin, Gillam, and Bisset Grady 2003; and Williams, Tabrizi, Lee, Kovnes and Garland 2003. Various locations for screening have also been advocated, including family planning clinics (Handsfield *et al.* 1986) and primary care and general practices (Simms, Hopwood, Mallinson, Rogers, and Webb 2000; Verhoeven *et al.* 2003). Ford, Viadro and Miller (2004) provide a summary of screening practices in non-clinical locations in the US and Europe and conclude that schools and home testing are viable places for screening and ease is facilitated by the use of non-invasive specimen collection.

Specific at-risk populations have been selected using screening criteria to ensure the maximum likelihood of finding asymptomatic cases for early treatment. Handsfield *et al.* (1986) were one of the first to research this aspect of chlamydia screening and concluded that using age, clinical symptoms and signs, and sexual risk behaviour for women undergoing pelvic examinations in family planning clinics was a sensitive method to detect infections. Other studies, notably by Marrazzo, Fine, Celum, DeLisle and Handsfield (1997a), Howell, Quinn, Brathwaite and Gaydos (1998a), Miller *et al.* (2000), and Paukku *et*

al. (2003), have demonstrated the consistent performance of selection criteria in screening programmes targeting women.

The microbiological aspects of determining chlamydia-infected persons from non-infected persons has undergone the most remarkable transformation over the last decade with the development of highly sensitive and specific laboratory methods using new techniques targeting chlamydial antigen DNA (CDC 2002). These new methods also allow for non-invasive specimens, such as urine, to be used, thus improving the possibility of test acceptance to the population targeted for chlamydia screening (Stephenson *et al.* 2000; Andersen, Ostergaard, Moller and Olesen 2001; Andersen, Olesen, Moller and Ostergaard 2002). In a unique study by Novak, Edman, Jonsson and Karlsson (2003), the internet was utilized for notification of results after an invitation of home-based urine testing was accepted. Novak *et al.* (2003) found that 38.5% of young men aged 22 years accepted testing. In both selecting the appropriate population for screening and having the ability to detect the infection within that screened population, the goal is to maximize finding those who need treatment while minimizing missing infections (not screening those who should be) and over-treating persons not infected. Striking this balance has been one of the most challenging of the Wilson-Jungner criteria to meet.

Costs of screening

Estimating the economic benefits of chlamydia screening has been particularly difficult, principally because if a programme is not in operation, acquiring exact figures of how much the programme costs will be imprecise. Initially, programmes in the US were not established based on their cost-effectiveness. Only after several years of screening was a rigorous cost-effectiveness study performed; Marrazzo *et al.* (1997b) confirmed that indeed

the costs of the sequelae were greater than the costs of the screening intervention, given the prevalence of infection and population selected for screening.

There have been additional cost-effectiveness and cost-benefit analyses of chlamydia screening performed and have concluded that the benefits outweigh the costs and cost-effectiveness can be reached in a few years (Kretzschmar, van Duynhoven, and Severijnen 1996; Paavonen, Puolakkainen, Paukku and Sintonen 1998; Howell, Quinn and Gaydos 1998; Welte *et al.* 2000; Kretzschmar, Welte, van den Hoek and Postma 2001; Honey *et al.* 2002). In assessing the cost-effectiveness of an opportunistic screening programme in England, targeting annual screening for women 16-20 years of age and biennial screening for women 21-24 years of age, Townsend and Turner (2000) concluded that cost-effectiveness would be achieved after four years of high volume screening.

The conditions for which screening becomes cost-effective have recently been put to scrutiny and include such things as: baseline prevalence of the target population, definition of the target population, uptake and coverage of screening by the target population, estimates of the preventable sequelae of chlamydial infection such as PID, ectopic pregnancy and infertility, economic costs of immediate and future sequelae, and the social costs (psychological and emotional impact) of this public health intervention. Many of these conditions are either ill-defined or difficult to measure (Washington, Arno, and Brooks 1986; van Valkengoed *et al.* 2004), thus complicating the accuracy of the cost-effectiveness evaluation and the mathematical methods employed in such an evaluation.

Sustainability

The transmission dynamics of sexually transmitted infections are such that their continued maintenance in the population is a result of three factors: the biological aspects of the

organism and host (virulence, infectiousness, inherent susceptibility and immune response); the behaviours of the host (rapidity and/or frequency of changing sex partners and types of sex partners); and the duration of infectiousness (asymptomatic infections, health care seeking behaviours of the host, clinical infrastructure for diagnosis and treatment). If any one of the components in this cycle breaks down, previously treated persons can rejoin the pool of susceptible persons in the population, continuing the transmission cycle (Garnett and Anderson 1996).

Wilson and Jungner (1968) advocate that, if started, screening should be continuous. However, the challenge for chlamydia screening has been that in order to build the evidence that screening is beneficial (reduction in morbidity and sequelae) and cost-effective (saves more than spent), the programme must be in operation for a number of years. In the United Kingdom it has been difficult to garner the funds necessary to invest in such a programme, given the scope required to make an impact in the transmission dynamic for this sexually transmitted infection, in part because there is constant movement of the population coming into the risk pool (beginning sexual activity or changing sex partners or recently treated patients returning to sexual relations with an untreated partner).

Programmes in Sweden and the US did not see appreciable reductions in the prevalence of infection until several years of aggressive screening (Lossick *et al.* 1990; Herrmann and Egger 1995; Mertz, Levine, Mosure, Berman and Dorian 1997), and in an assessment of routine testing activities for chlamydia over five years in Copenhagen by Westh and Kolmos (2003), chlamydia prevalence ranged from 3.6% in 1995 to 4.3% in 1999 with an estimate of nearly 20% of the 15-49 year old female population screened at least once in the period. However, there are now two randomised controlled trials of chlamydia screening that demonstrate a 50% reduction in incidence PID cases after one year (Scholes *et al.* 1996; Ostergaard, Andersen, Moeller and Olesen 2000). A systematic review of the

evidence by Honey and Templeton (2002) also concluded that PID can be prevented through controlling chlamydial infections in women.

Chapter 4
Contribution to knowledge

My contribution to the knowledge base for chlamydia screening is reviewed in this chapter. I follow three basic themes: 1) defining the epidemiology and public health significance of *Chlamydia trachomatis* infection, 2) developing and implementing new screening initiatives, and 3) monitoring and evaluating existing chlamydia screening programmes. As will be demonstrated, my research has increased our understanding of the public health importance of chlamydial infection, the nature of asymptomatic infection, and definitions of appropriate populations for screening— three key criteria for intervention; all of which combine to further refine the epidemiology of this infection. My research demonstrates the establishment of the new National Chlamydia Screening Programme in England, which is built upon the entire body of evidence and has been shown to meet the Wilson and Jungner criteria (CMO 1998). I will conclude with how my other body of research can be used to facilitate monitoring and evaluation of already established chlamydia screening programmes.

The manuscripts discussed in this section are grouped accordingly (see Appendix 2 for the published manuscripts).

- **_Chlamydia trachomatis_ as an important public health problem**

1. Brown, A.E., Sadler, K.E., Tomkins, S.E., McGarrigle, C.A., LaMontagne, D.S., Goldberg, D., Tookey, P., Smyth, B., Thomas, D., Murphy, G., Parry, J.V., Evans, B., Gill, O.N., Ncube, F. & Fenton, K.A. (2004). 'Recent trends in HIV and other STIs in the United Kingdom: data to the end of 2002'. Sexually Transmitted Infections. 80, (3), p.159-166.
2. LaMontagne, D.S., Fine, D.N. & Marrazzo, J.M. (2003). '*Chlamydia trachomatis* infection in asymptomatic men'. American Journal of Preventive Medicine. 24, (1), p.36-42.

- **Implementing large-scale chlamydia screening programmes**

3. LaMontagne, D.S., Fenton, K.A., Randall, S., Anderson, S. & Carter, P. (2004b). 'Establishing the national chlamydia screening programme in England: results from the first full year of screening'. Sexually Transmitted Infections. 80, (5), p.335-341.

- **Monitoring and evaluating chlamydia screening programmes**

4. LaMontagne, D.S., Patrick, L.E., Fine, D.N. & Marrazzo, J.M. (2004a). 'Re-evaluating selective screening criteria for chlamydial infection among women in the U.S. Pacific Northwest'. Sexually Transmitted Diseases. 31, (5), p.283-289.

5. LaMontagne, D.S., Fenton, K.A., Pimenta, J.M., Catchpole, M., Rogers, P.A., Randall, S., Hewitt, W.G., Mallinson, H., Underhill, G.S., McLean, L., Gleave, T., Harindra, V., Ghosh, A.K. & and Tobin, J.M. (2005). 'Using chlamydia positivity to estimate prevalence: evidence from the chlamydia screening pilot in England'. International Journal of STD and AIDS. 16, (4), p.323-327.

6. Adams, E.J., LaMontagne, D.S., Johnston, A.R., Pimenta, J.M., Fenton, K.A. & Edmunds, W.J. (2004b). 'Modelling the health care costs of an opportunistic chlamydia screening programme'. Sexually Transmitted Infections. 80, (5), p.363-370.

7. LaMontagne, D.S., Pimenta, J.M., Fenton, K.A., Mallinson, H. & Hopwood, J. (2004c). 'Management of genital chlamydial infections at termination of pregnancy services in England and Wales – where are we now?'. BJOG: an International Journal of Obstetrics and Gynaecology. 111, (12), p.1408-1412.

CHLAMYDIA TRACHOMATIS AS AN IMPORTANT PUBLIC HEALTH PROBLEM

Chlamydial trachomatis infection and other STIs in the UK

Contextualising the parallel epidemics of sexually transmitted infections and HIV in the United Kingdom has become critically important in recent years as the government has made specific action plans towards improving the sexual health of the population (Department of Health 2001). To that end, it is important to inform the policy makers, health care community and general population of the recent trends in diseases contributing to sexual ill-health. A detailed understanding of the epidemiology of various STIs, particularly chlamydial infection, can also provide baseline data for comparisons of programme impact, as the government increases its prevention activities through the phased implementation of the National Chlamydia Screening Programme.

In a cross-sectional descriptive study, I collaboratively investigated STI and HIV trend data from 2002 as reported in the major surveillance systems at national communicable disease

surveillance centres in the UK (Brown *et al.* 2004). Specifically for STI trend data, diagnosed cases of chlamydia, gonorrhoea, genital warts, herpes, and infectious syphilis among GUM clinic attenders reported on the aggregate KC60 statutory return in the UK were analysed. I also utilized enhanced surveillance data from two new initiatives, enhanced syphilis surveillance and the Gonorrhoea Resistance to Antimicrobials Surveillance Project (GRASP), to further characterise populations infected with infectious syphilis or *Neisseria gonorrhoeae*.

Continuing rises in most STIs, except gonorrhoea, and HIV were found across key populations. Genital chlamydial infection rose by 103% from 1997 to 2002, and continued to be the most commonly reported sexually transmitted infection in the UK. Chlamydial infection is particularly high among young women with rates of diagnosis among 16-24 year olds as high as 1,135 per 100,000 population. The highest rate of diagnosis among men, 842 per 100,000, was observed in those 20-24 years of age. The importance of these preventable infections to populations at highest risk, especially young people, gay men, and black and ethnic minorities was highlighted in this summary of the STI trends in the UK. These populations continue to be the most affected. Estimates of rates of disease among gay men showed increasing diagnoses since 1999, with appreciable increases in the last two years. Young people accounted for over half of all STIs and 10% of new HIV diagnoses in 2002; women aged 16-24 accounted for 72% of all female chlamydia diagnoses from GUM clinics; and black ethnic minorities, mainly black Caribbeans, accounted for a staggering 55% of heterosexual male and 44% of heterosexual female gonorrhoea cases reported in 2002.

This study of the trends in STIs and HIV in the UK has strengthened our understanding of the burden of disease in the population and has been important in quantifying the scope of these epidemics. This work was particularly important in light of the government's strategy

to address this significant health problem. The Department of Health's *National Strategy for Sexual Health and HIV* (2001) outlines key targets for the prevention and control of sexually transmitted infections and HIV, and has included recently funded initiatives, such as the modernisation of GUM services and laboratory networks and the implementation of a national chlamydia screening programme. Periodic assessment of the surveillance data for STIs and HIV will be critical in measuring whether the increase in funding has had an impact on the government targets for sexual health as well as improvements in the control of these infections in the population.

Chlamydial infection in men

Characterisation of chlamydial infection as a public health issue can only be done through studies quantifying the magnitude of the problem within the population and the ramifications if left untreated. There has been an enormous amount of research on chlamydia in female populations, principally because the greatest burden for sequelae of infection falls within this group. PID, ectopic pregnancy, salpingitis, and tubal factor infertility are severe consequences of infection in women. However, the epidemiology of chlamydial infection in men was less well characterised.

Stamm (1999) has summarised the knowledge to date concluding that urethritis and dysuria are common among infected men and a small proportion of untreated infections can advance to Reiter's syndrome, but on the whole, the severity of disease among men is less significant. A strong argument can be made for understanding the burden of infection among men as they are the primary transmitters of infection to women (Garnett and Anderson 1996). Failure to identify asymptomatic infections in men might allow for the

maintenance of a reservoir of untreated infection that might hinder efforts to decrease the incidence among women.

Previous studies of chlamydia, especially in asymptomatic male populations, had been hampered by relatively small sample sizes (Braverman, Biro, Brunner, Gilchrist and Rauh 1990; Domenika, Bassiri and Mardh 1994; Moncada *et al.* 1994). In the north western region of the US (Region X), chlamydia screening of women has been routine since 1988. The universal testing of men attending STD clinics within this region was standard clinical practice and utilised the same data collection instrument employed in the chlamydia screening programme for women. This data source provided an opportunity to design a study that could help characterise the epidemiology of chlamydial infection in men. My research questions were three-fold: 1) how much chlamydial infection is in the male population?; 2) what is the level of asymptomatic infection in men?; and 3) can this evidence be used to develop screening initiatives to target men?

I designed a retrospective cross-sectional epidemiologic study of men attending STD clinics who were tested for chlamydia (LaMontagne *et al.* 2003). I analysed data from 43,094 men universally tested from 1997-1999 at 103 STD clinics and assessed age-specific prevalence of chlamydial infection, controlling for signs of infection and report of contact to a person with an STD.

Overall prevalence of chlamydial infection in men was 10.3% and varied by age: 16.2% in men under 18 years old, 18.3% in men aged 18-19 years, 14.5% among 20-24 year olds, 10.1% among 25-29 year old men, and 4.8% in men over the age of 29 years. This is similar

to the 11.0% prevalence found by Ciemins *et al.* (2000) at the STD clinic in San Francisco. Marrazzo *et al.* (2001) found men under 25 years of age were three times more likely to test positive than those 25 years and older, and the prevalence among 19-20 year old asymptomatic men was 10.4%. In this study, peak prevalence among asymptomatic men, 7.3%, was at 18-19 years of age, and these men were nearly five times as likely as men aged over 29 to test positive for chlamydia. For asymptomatic male populations, no other demographic or behavioural risk factor was more strongly associated with infection than age.

In addition to age, prevalence was correlated with the presence of clinical signs suggestive of infection, principally urethritis, and exposure to infection from known sexual contact with an infected partner. Over 75% of all men tested had no signs of infection upon examination, however, over 70% of men who tested positive for chlamydia had clinical signs of infection. Men without either signs of infection or a history of contact with an infected partner had a prevalence of 3.4%, but contributed to over two-thirds of all men tested for chlamydia at STD clinics.

In focusing on clinician assessed signs in conjunction with sexual exposure to someone known to be infected, I found gradients of prevalence among all age groups of men. In each age strata, men with signs of infection who had contact with someone infected had the highest prevalence. For example, among 18-19 year old men, 62% of those with signs and contact to someone infected tested positive for chlamydia, compared to only 7.3% of men without these factors. Among men over 29 years of age, prevalence was 31.1% in the signs/contact group and 1.6% in those without. Clinician-assessed signs and exposure to persons known to be infected were highly correlated with infection. Efforts to detect those

men most likely to be infected could be enhanced through utilising signs and exposure, combined with age, regardless of seeking care at an STD clinic. These data raise the question of whether certain groups of men without signs should be tested routinely by virtue of their attendance in the STD clinic. The 3rd US Preventive Services Task Force (2001) concluded that there was no strong evidence for selective screening strategies among asymptomatic males. These findings question the standard approach of testing all male STD attenders for chlamydial infection, especially when resources in publicly funded clinics in the US are scarce.

While this study did not specifically address the cost-effectiveness of such approaches, the data do suggest that testing men with no signs in an STD clinic could certainly be made more efficient by reducing testing in subgroups unlikely to be infected. For example, if only the men in this study with signs, contact to infected partner, or those under 25 years of age had been tested over the study period, 58% of our subjects would have been tested and 91% of all positives would have been detected. Miller *et al.* (2000) suggested that this approach would be both sensitive and efficient, and similar selective screening approaches are currently employed among female populations (Marrazzo *et al.* 1997b). This results from this study suggest that screening criteria could be developed for use in STD clinics to select men to test for chlamydial infection.

This study used a robust data set on a large population of men tested over three years, which was a significant improvement in sample size over previous studies of the epidemiology of infection among men. Additionally, I uniquely quantified the role of clinical signs, rather than symptoms, and exposure to disease in the epidemiology of chlamydia among men. This was important in the STD setting, as clinical protocol dictated

full genital examinations as the standard of care for all attenders. The results from this study suggest that in the context of an existing clinical examination, signs could be highly predictive of infection in men. Other published studies at the time of my study had not been able to tease out the different contributions of signs in relation to sexual contact with a known infected partner, client age and sexual behaviour to predict infection among men.

A result from this study of asymptomatic chlamydial infection in men was the lower prevalence of chlamydia found among men who reported sex with men (MSM), 7.3%, versus men who reported sex with women (MSW), 10.8%. At that time, studies of STIs among MSM focused on STD clinic populations and were reporting increasing STI rates among MSM attending those STD clinics (Ciemins *et al.* 2000). Although not published in a peer-review journal, I did a follow-up study of chlamydial infection in asymptomatic men that focused on men who have sex with men (LaMontagne, Patrick and Marrazzo 2001). A brief description of this study, its results and implications is provided to illustrate how I have continued to investigate questions raised by my own previous research.

In this study, I used the same methods and data source as the previous study of chlamydia in men (LaMontagne *et al.* 2003) for consistency and comparability, and explored three key unanswered questions: 1) what is the epidemiology of chlamydial infection among MSM within and outside of STD clinic settings?; 2) are rates of chlamydial infection among MSM increasing?; and 3) are asymptomatic MSM different than asymptomatic MSW in terms of risk factors for chlamydia? I analysed records for 8,981 men who have sex with men, which was 8% of the total male population tested from 1996-2000.

I found an overall prevalence of 7.7% among all MSM, and this was correlated with three factors: the presence of clinical signs suggestive of infection, the exposure to infection from known sexual contact with an infected partner; and young age. Prevalence was higher

in MSM tested outside of STD clinics (9.0%). There was a statistically significant temporal trend for increasing prevalence of chlamydia among MSM from 5.4% in 1996 to 8.5% in 2000. Risk factors for infection among asymptomatic MSM and asymptomatic MSW were similar, but asymptomatic MSM tended to be slightly older. The highest prevalence among asymptomatic MSM was 7.3% in those ages 18-19 years old; the same peak prevalence, 7.3%, was found among MSW who were 18-19 years of age.

This study of chlamydial infection in MSM confirmed some of our findings from our previous study of infection in asymptomatic men. I again found utility in use of clinical signs and exposure to divide the male population into risk groups, and quantified appreciable increases in likelihood of infection as one progresses from the 'no clinical signs and no exposure' group to the population of men 'who had signs of chlamydial infection (urethritis) and reported recent sexual activity with an infected partner.' Once again, this can be an important aid during a clinical consultation in discussing need for testing a person with low probability of infection. Seventy percent of the MSM population in this study was asymptomatic and not recently exposed to an STD and had a prevalence of only 4.2%.

A trend of increasing prevalence of chlamydia among all MSM and among just the asymptomatic MSM population was statistically significant; prevalence among asymptomatic men increased from 2.2% in 1996 to 5.4% in 2000, even after adjusting for signs of infection or recent exposure. These results have broad implications for the control of this infection in a population already impacted by the AIDS epidemic. It also raises the question of co-factors for acquisition of HIV: will an increase in chlamydia facilitate a concomitant increase in HIV infection?

Additionally, I found that asymptomatic MSM tested outside STD clinics had a higher prevalence, 5.8%, than those attending urban STD clinics (2.7%), raising the question of whether MSM who do not seek services at an STD clinic warrant a different intervention to decrease their risk, or conversely, whether these men feel less stigmatised based on their sexual orientation and are comfortable attending more general health settings. This follow-up study of chlamydial infection among men confirmed that asymptomatic MSM have the same risk factors for chlamydial infection as asymptomatic men who have sex with women, suggesting that prevention campaigns targeting heterosexual men may be applicable to MSM populations or should emphasise that the risks are the same for both groups of men.

IMPLEMENTING LARGE-SCALE CHLAMYDIA SCREENING PROGRAMMES

The National Chlamydia Screening Programme in England

The establishment of a national chlamydia screening programme in England has its genesis in discussions by the government dating to the mid-1990's. The Chief Medical Officer (1998) gathered a panel of experts to review the evidence for chlamydia screening and concluded that evidence exists for the effectiveness of chlamydia screening. This was followed by a call for the government to take action towards establishing a national screening programme (CMO 1998). As a first step, the Department of Health (England), funded a study of opportunistic screening among women in England to determine the feasibility and acceptability of such a programme. Pimenta *et al.* (2003a, 2003b) illustrated that screening was both feasible and acceptable and that high prevalence of disease, approximately 10%, existed among sexually active 16-24 year old women.

Subsequent to this successful pilot of opportunistic screening, the Department of Health (DoH) began a phased implementation of the National Chlamydia Screening Programme

(NCSP) in late 2002 with selection of 10 programme areas for the first phase (Department of Health 2004a). This effort was also combined with the *National Strategy for Sexual Health and HIV* (Department of Health 2001) to provide a unified platform for addressing the rise in rates of STIs in England (Brown *et al.* 2004). Given the high public profile of this effort and the intense interest in the implementation stage of the programme, a description of the programme and an analysis of the epidemiological data from the first year of screening in phase 1 programme areas was performed (LaMontagne *et al.* 2004b). This paper had three main goals: a) to examine the development and evolution of the National Chlamydia Screening Programme in England; b) to comprehensively detail the components required to implement a nationally-directed chlamydia screening programme on a large-scale; and c) to quantitatively analyse the results of screening in the first year to characterise the population tested, their risk factors, and the burden of disease across England.

A descriptive study of the NCSP with retrospective analysis of opportunistic screening data for young men (n = 1,172) and women (n = 15,241) under 25 years of age attending over 300 clinical and non-clinical settings across England was designed. In this, the programme's components are elaborated. Using univariate and multivariate statistical techniques, I measured chlamydia test positivity and explored factors associated with testing positive. The statistical analysis excluded tests performed for diagnostic reasons or on contacts to known cases, those persons 25 years or older, or those that were missing or had unknown data for test result, sex, age, type of test, or inconsistent sample type (for example, male tests with self-collected vulva-vaginal swabs). Separate analyses were performed for men and women screened opportunistically.

In the first year of the NCSP, opportunistic screening occurred in a staged approach with the number of programme areas and screening venues within programme areas offering chlamydia screening increasing from April 2003 to March 2004. Over 16,400 opportunistic

screens for genital chlamydial infection were performed, with nearly 50% occurring from January-March 2004. Positivity among women was 10.1% (1,538 / 15,241) and 13.3% (156 / 1,172) among men under 25 years of age opportunistically screened at 302 venues across England, excluding GUM clinics. Women 16-19 years of age were almost twice as likely to be positive than those under 16 and 43% more likely to be positive than women 20-24. Other risk factors for women included Black Caribbean, Black British, or mixed ethnicity, a new sex partner in the last three months, or two or more sex partners in the last 12 months. Among men, only age 20-24 years old and Black ethnicity were associated with infection, even after adjusting for covariates; sexual risk behaviours had elevated odds ratios, but were not statistically significant. For both men and women, those tested via the Becton-Dickinson strand displacement assay (SDA) were more likely to test positive than persons tested with another nucleic acid amplification test.

This manuscript also provided the first detail of the components of the English programme in the peer-reviewed literature. To review, the goal of the NCSP is to control genital chlamydial infection through the early detection and treatment of asymptomatic infections and prevention of sequelae and onward transmission. This is consistent with the general approach to selective screening employed in other countries (CDC 2003). Screening protocols for the national programme area contained in a core requirements document (Department of Health 2004a), and are disseminated to local programmes to standardise local screening activity. Local programmes consist of consortia of primary care trusts (PCTs), which are the geographic and service boundaries of the National Health Service (NHS). A regionally organised chlamydia screening programme operates in the US and has acted as a model for the geographic organisation of services.

The target population for screening is young men and women under the age of 25 years who are attending health care facilities not traditionally associated with providing specialist

sexual health services. These include contraceptive clinics, general practices, young people's services, antenatal services, colposcopy and infertility units, and termination of pregnancy clinics. Screening is also encouraged to those within the target age group through innovative outreach strategies, such as "pee in a pot" days at military bases, university campuses or health fairs, mobile vans or buses for contact with young people, prisons, and other non-traditional settings. The target population for the NCSP is different than that of the US screening programme (CDC 2002), in that persons out of the age range, those attending GUM clinics, and persons presenting with symptoms are excluded from opportunistic screening. These persons are usually diagnostically or routinely tested for chlamydia as a part of standardised clinical protocols, and as such are not the primary target for the "opportunistic" nature of this national programme.

All screening is performed using non-invasive samples, urine for men and urine or self-collected vulva-vaginal swabs for women, and tested via nucleic acid amplification, the most sensitive testing method available (Black 1997). All positive patients are treated following established clinical guidelines (Clinical Effectiveness Workgroup 2002), and partners of positive patients are contacted for prophylaxis and/or chlamydia screening. Standardised information about the demographic and behavioural characteristics of the population screened, location of screening, laboratory test method used, and test result is collected uniformly across all programme areas by the use of a test request form and is reported in disaggregate nationally to the Health Protection Agency (Department of Health 2004a).

The first year of the NCSP has also detected similar levels of infection as was observed in the original screening pilot in England (Pimenta *et al.* 2003b). Screening programmes in other countries reported chlamydia prevalences ranging from 6% in Sweden (Herrmann and Egger 1995) to 12% in the north western US (Britton, DeLisle and Fine 1992). The

similar levels of infection at the start affirm that the opportunistic approach is a successful strategy for disease detection and justify our continued focus on young women and men attending a variety of health care settings. Encouragingly, the second highest volumes of screening came from general practices and young people's services, both of which do not traditionally provide sexual health services. Oakeshott, Hay and Pakianathan (2004) recently suggested that GPs would not participate in screening without remuneration. The findings from the first year of the NCSP question that assertion. Over 10% of all screening tests were done within general practice (without payment), and increased over the course of the first year. This was due in part to the create ways in which the service was delivered locally, such as patients self-selecting screening whilst waiting in practice reception areas, invitations to screening made by practice nurses rather than GPs, and shifting responsibility for notification of results and follow-up to a local chlamydia screening office (LaMontagne *et al.* 2004b). However, the devolved nature of general practice provision in England means that efforts to encourage local involvement of primary care in chlamydia screening need to be strengthened and robustly supported to maximise participation.

My analysis of the population screened in the first year of the NCSP confirmed that the epidemiological profile of both men and women screened is nearly identical to that found in other studies of UK populations (Adams *et al.* 2004a) and those in Europe (Wilson *et al.* 2002), with highest chlamydia positivity among women 16-19 years of age and men 20-24 years old. Additionally, I found that women who had acquired a new sex partner in the last three months or who had two or more sex partners over the past 12 months were about 50% more likely to test positive. The NCSP is the first large scale sexual health programme to include behavioural surveillance, and allows for monitoring changes in sexual behaviours that contribute to the acquisition and spread of chlamydia.

Because the NCSP is in the early stages of implementation, it is important to place in context the screening volume and its impact on coverage. Economic models have shown that one of the most critical aspects to ensure the success of a widespread screening programme is uptake (Paavonen *et al.* 1998; Welte *et al.* 2000; Kretzschmar *et al.* 2001; Honey *et al.* 2002). Recent estimates from the US by Levine *et al.* (2004) suggest that screening coverage was highest in areas that experienced reductions in prevalence after several years of aggressive screening. Data from the first few years of routine chlamydia testing in Sweden also reflect the impact of high screening volumes (Herrmann and Egger 1995). It will be imperative for the NCSP to continue to rapidly increase the offer and uptake of screening throughout all participating local programme areas to maximize the impact of the intervention.

This manuscript and the analysis of the population screened in the NCSP fills an important gap in the existing literature because it comprehensively explains the genesis of a national screening programme, illustrates the individual programme components necessary for actual implementation in local communities, assesses what can be expected in the first year, outlines some of the pitfalls in embarking on such an immense effort, and most importantly, reaffirms the importance and necessity of this public health problem by quantifying the magnitude of infection among young people in England.

MONITORING AND EVALUATING CHLAMYDIA SCREENING PROGRAMMES

Chlamydia screening seeks to reduce the prevalence of infection in the population and the severe sequelae of untreated infection. There is strong evidence from two randomised controlled trials that incident PID can be reduced from screening (Scholes *et al.* 1996; Ostergaard *et al.* 2000). As previously mentioned, several programmes implemented in the United States and Sweden observed decreases in prevalence after several years of screening

(Lossick *et al.* 1990; Addiss, Vaughn, Ludka, Pfister and Davis 1993; Herrmann and Egger 1995; Mertz *et al.* 1997). Prior to observing these long term outcomes, screening programmes require close monitoring to ensure the service is appropriately administered, the target population is screened, the outcome is measured correctly, there is sound value for money, and the clinical providers are adhering to the guidelines. There is a general dearth in the literature on programme monitoring and evaluation for chlamydia screening. The majority of published studies cover aspects of selecting or ensuring the target population is correctly identified and screened (Paukku *et al.* 2003; Marrazzo *et al.* 1997a; Miller *et al.* 2000), and the cost-effectiveness of such approaches (Marrazzo *et al.* 1997b; Howell *et al.* 1998; Welte *et al.* 2000; Kretzschmar *et al.* 2001). It is within this context that my programme-related research is discussed below.

Evaluating selective screening criteria

Since 1988, annual systematic chlamydia screening of women under 25 years of age and of older women based on behavioural risks has been in operation in the north western region of the US (Region X). This was the first large-scale chlamydia screening programme in that country. Screening, based on these selection criteria, occurs in conjunction with a pelvic examination during attendance at family planning clinics (Center for Health Training 2003). From 1988 to 1993 the selective screening criteria remained unchanged. These criteria were evaluated in 1995 with few changes resulting from that evaluation (Marrazzo *et al.* 1997a). It is not unusual to periodically evaluate the selective screening criteria. Assessments of such criteria had been made by other researchers (Miller *et al.* 2000). Using selection criteria to determine how to direct scarce screening resources had been a cornerstone of the US effort to control genital chlamydial infection (CDC 2003). All public health regions in the country (numbered I, II, etc.) have a selection procedure in their programme.

Several developments in the field that could impact the performance of existing selective screening criteria suggested the criteria required a re-evaluation, specifically declines in prevalence observed in the first eight years of screening were not sustained after 1997; the introduction of more sensitive laboratory detection methods in the mid-1990's (Gudgel and LaMontagne 1999; Dicker, Mosure, Levine, Black and Berman 2000); and assurance of programme credibility and efficiency in the face of increasing budgetary pressures was needed. I set out to re-evaluate the programme with three goals: assess the performance of the existing screening criteria in Region X, explore whether the risk factors for infection had changed since 1995, and evaluate whether the criteria could be optimised to improve sensitivity or efficiency (LaMontagne *et al.* 2004a).

Using cross-sectional screening data of tests performed on women from 1998-2000, a programme evaluation was designed. Data analysis included multivariate logistic regression to quantify risk factors for infection, and sensitivity and efficiency analyses to measure the performance of the existing criteria and assess optimisation strategies. The dataset comprised 409,882 chlamydia test records for women attending 252 family planning, 123 STD and 251 other clinics, including community/migrant, college health, public health nursing, and adolescent clinics, in Region X from 1998-2000. To define the performance of the current selective screening criteria in Region X, all tests were analysed for the sensitivity and efficiency of the criteria. Sensitivity was defined as the percentage of positives detected, and efficiency was the percentage of tests that met the criteria (Miller *et al.* 2000). Thresholds of 60% efficiency and 90% sensitivity were used as performance benchmarks to identify the most positives (high sensitivity) while testing the fewest number of women (low percentage for efficiency). To define risk factors associated with infection, data from women universally screened at STD clinics were used. Odds ratios for independent associations were calculated with chlamydia positivity as the dependent variable, and adjusted in multivariate logistic regression models. Using the results of the risk factor

analysis, five different sets of selective screening criteria were developed to evaluate for sensitivity and efficiency to determine whether the current criteria in Region X could be simplified. These five sets of criteria were also compared with recent recommendations from the US Preventive Services Task Force (2001).

The positivity among women attending STD clinics was 7.0%; 4.1% among FP attenders and 3.8% among women attending a variety of community clinics. The strongest predictor of infection was young age, especially those under 25 years old, regardless of clinical signs or exposure to an STD. The selective screening criteria used in Region X were very sensitive, detecting 95.6% of all infections in the female population, but were less efficient than the target benchmark, requiring testing 85.6% of women. The sensitivity of the criteria remained high and exhibited little variation (range, 94.5-97.5%). Even after stratifying by test type within clinical settings, the sensitivity remained above 90% (range, 90.8-98.7%). The five sets of selective screening criteria developed from multivariate modelling showed marked differences in sensitivity and efficiency. On average, age-only based criteria required testing the fewest number of women, but were just over 80% sensitive. Conversely, the recently recommended criteria from the Task Force resulted in over 98% sensitivity, but would have required testing over 93% of the women in our study, clearly less efficient than our benchmark. These findings suggested that the selective screening criteria in Region X could be optimised by focusing on those populations found to be at highest risk, mainly all women under 25 years of age and women 25 and older with clinical signs of infection or exposure to a sex partner with chlamydia.

There are several significant aspects of this study with implications for existing and newly established chlamydia screening programmes. First, this study was timely, since it had been over five years since publication of the last evaluation of the Region X screening programme (Marrazzo *et al.* 1997a), and that evaluation had used data from the early days

of the programme when less sensitive laboratory tests were employed and the baseline prevalence of infection in the population was high. As the first comprehensive chlamydia screening programme in the US, Region X has a unique position of leading the field, but also setting the example of good practice. Furthermore, it is recommended that periodic evaluations be a part of any population-based intervention (Mosure, Berman, Dicker and Levine 1998), as new developments occur or programme impact begins to plateau. This is critical for the credibility of the programme and can influence the operations of other screening efforts.

Secondly, this evaluation re-affirmed that the risk factors for chlamydial infection for women have remained stable in recent years, even after adjusting for the use of more sensitive testing methods. The strength of age as the number one predictor of chlamydial infection in women, although known from other studies (Handsfield *et al.* 1986; Simms *et al.* 1997; Mertz *et al.* 1998; Wilson *et al.* 2002; Adams *et al.* 2004a), was a surprising finding, principally because of the very high odds ratios for younger women, even after adjusting for all other major factors. Women 17 years and younger were nearly 8 times more likely to be infected than those over 29; but even 20-24 year old women were almost 5 times more likely to be infected. Additionally, the finding that recent exposure was more predictive of infection than clinical signs reinforced the asymptomatic nature of this infection in women (Stamm 1999). Age, clinical signs and recent exposure were the same factors elucidated in my two previous studies of chlamydia infection in men and MSM (LaMontagne *et al.* 2001; LaMontagne *et al.* 2003).

Thirdly, this study confirmed that the selection criteria used in Region X to determine which women should be screened were sensitive— the criteria accurately detected positives. However, the criteria in use were not particularly efficient, requiring testing a high percentage of women attending clinical settings. Other studies (Miller *et al.* 2000) have used

a similar approach in measuring criteria performance, but used lower thresholds for sensitivity (80%) which allowed for up to 20% of positives to go undetected. The programme managers in Region X thought that threshold was too low for adequate disease control, and looked to build criteria that could detect 90% of positives while screening about 50% of the target population. Although we could not find criteria that would result in that level of efficiency, we did conclude that the criteria currently in use could be optimised by focusing on the populations most likely to be infected: young women, those with clinical signs, women recently exposed either through sex with a symptomatic partner or report of sexual contact to a partner with an STD, and women with a positive chlamydia test in the last year.

Most importantly, this research had immediate practical application in policy decisions by the programme. The Region X screening programme initiated this evaluation study, and agreed to incorporate the study findings, regardless of the outcome. This willingness to directly apply research findings for policy and programme change illustrates the leadership role this programme sets for the other regions in the US. Based on the findings of this study, the Region X screening programme changed their selective screening criteria for women attending the clinical venues participating in the programme (Center for Health Training 2003).

Using chlamydia test positivity for programme monitoring

Another aspect of monitoring gains made through chlamydia screening is assessing the impact on prevalence (Addiss *et al.* 1993; Herrmann and Egger 1995; Marrazzo *et al.* 1997a). Prevalence of genital chlamydial infection in women in the United Kingdom varies widely depending upon the study population selected, methodology employed, clinical setting and laboratory test method (Adams *et al.* 2004a). Pimenta *et al.* (2003b) have noted the difficulty

in measuring prevalence in large cohorts of women, principally due to the need to track individuals and their testing behaviour over time and geographic and clinic locations. Individuals may have more than one test and may attend a variety of clinical settings over the testing period. In the implementation of larger screening programmes based on an opportunistic approach, as is currently the design of the National Chlamydia Screening Programme (NCSP) in England, the ability to measure prevalence becomes increasingly difficult due to the lack of a national unique identifier. The Department of Health in England (2004a) has proposed to use positivity as a surrogate measure for prevalence.

Chlamydia test positivity has been used in the US screening programme and has shown to be a useful tool in programme monitoring (CDC 2003). This approach has been validated in only one published study (Dicker, Mosure and Levine 1998). However, in that study data were collected from limited health settings and women were screened with less sensitive enzyme immunoassays, so questions regarding the ability to generalise results using this method remain. I sought to re-examine the original chlamydia screening pilot data to cross-validate whether positivity could be used as a proxy measure for prevalence and to assess the appropriateness and utility of using positivity to monitor the NCSP (LaMontagne *et al.* 2005).

Using the testing episode data from the cohort of women enrolled in the original chlamydia screening pilot (Pimenta *et al.* 2003a), positivity within the populations for which prevalence had already been measured (Pimenta *et al.* 2003b) was recalculated. Data analysis included 16,595 tests from 16-24 year old women attending family planning, GUM, general practice, and youth clinics from September 1999 – August 2000. Positivity, defined as the number of positive tests divided by the total number of tests, was calculated with accompanying 95% confidence intervals. Positivity estimates were compared to prevalence. Prevalence for each health care setting and by symptoms within health care setting had

been previously published (Pimenta *et al.* 2003b) and was used as the comparison estimate; however, prevalence by single years of age within the study locations was recalculated because the published age-specific prevalence included a wider selection of testing locations. Two-sided binomial probability tests were conducted to confirm no difference between the estimated positivity and measured prevalence.

Overall positivity was 9.4% (95% CI: 8.9-9.9) in Portsmouth and 11.0% (95% CI: 10.1-11.9) in the Wirral. This was marginally lower than the published prevalence but not statistically different. Additionally, slight and non-statistically significant differences were found between positivity and prevalence by health care setting, age and reason for test. Absolute differences between positivity and prevalence within health care settings ranged from -1.43 to 0.04 and the percentage difference between the two ranged from -8.58% to 0.47%, neither of which were statistically significant. In general, positivity underestimated prevalence, possibly due to the frequency of testing within the population. However, even in spite of this limitation, the estimates of positivity among a population tested using very sensitive laboratory methods varied little from prevalence and did not change the interpretation of the outcome data. This study demonstrated that measuring positivity, in lieu of prevalence, would not sacrifice the accurate measurement or the interpretation of disease trends and would be easier to implement within a large-scale national screening programme.

This re-examination of the data from the original screening pilot to assess positivity was significant in two ways. First, it validates a measurement technique that has only been through one scientifically rigorous review process (Dicker *et al.* 1998). Confirmatory studies have a critical role to play in research, as isolated findings from one study may not apply more generally. Particularly if a methodology is advocated, the assumption that the methods apply across study settings requires validation. I confirmed the method proposed

by Dicker *et al.* (1998), even though the setting of this study was radically different than theirs: the screened population was from outside the US, tested in a wider variety of clinical venues, provided only urine samples, and utilized more sensitive laboratory techniques.

Second, there has been some criticism that the National Chlamydia Screening Programme was not going to be able to measure its effectiveness because it could not directly measure prevalence (Low, Macleod, Salisbury and Egger 2003). This study demonstrates that this is not necessary for large-scale programmes, as positivity is a robust surrogate. Therefore, changes in positivity are reflective of changes in prevalence in the population.

The implications of my study for programme monitoring are two-fold: 1) the programme monitoring method proposed for the NCSP is backed by sound scientific evidence; and 2) this method reduces the reporting burden for clinical providers participating in the NCSP. The collection of data in a large national programme can be politically sensitive, as the balance needs to be struck between gathering the data required to make robust evaluations of the programme's impact whilst not overburdening the clinical staff in communities who are implementing the programme locally. It is a delicate balance as the former requires strict and accurate data collection standards and the later might not participate in a programme with such stringent data collection needs. By proposing to use positivity as the outcome measurement for programme monitoring, the NCSP has been able to find a middle ground whereby the scientific rigour is maintained and the local burden of data collection is minimised.

<u>Estimating the costs of opportunistic screening for chlamydia</u>

In the CMO's (1998) review of the evidence for chlamydia screening, the cost-effectiveness of such programmes came under particular scrutiny. The key concerns expressed were that

previous cost-effectiveness studies over-estimated the sequelae of untreated infection and under-estimated the unit costs of the screening programme. These studies also used approximated prevalence levels were not verified in population-based studies in England, and utilised testing modalities, principally opportunistic or postal-invitation, that may not be feasible in this country. Further, the published cost-effectiveness studies failed to adequately account for the dynamism involved in the transmission cycle of this sexually transmitted infection. Specific calls for more research into the cost-effectiveness of chlamydia screening have also come from others in the field (Roberts *et al.* 2004).

However, without knowing specific unit costs of items used in an organised opportunistic screening programme, it is difficult to estimate these parameters for a more detailed cost-effectiveness study. Because the National Chlamydia Screening Programme is currently being phased in throughout the country, it is also timely to assess the cost of screening and examine in detail the relative contribution of cost elements, such as personnel, supplies and overheads. A study of the costs of chlamydia screening was performed (Adams *et al.* 2004b). The goals of this cost study were: 1) to estimate the average cost per test offer, cost per testing episode, and cost per chlamydia positive episode, based on the costs incurred by the health care system; and 2) to run a series of 'what if' scenarios to illustrate cost changes vis-à-vis practice changes and screening implementation strategies (Adams *et al.* 2004b).

The study design utilised a decision-tree model to mirror the patient flow of the original chlamydia screening pilot and to reflect the current clinical flow of patients screened in the NCSP. Empirical data on women screened in the chlamydia pilot were analysed for parameter estimates in the model. Patient flow was based on urine samples tested with nucleic acid amplification tests and follow-up of positive patients and their partners by nurse health advisers. Separate decision-trees were constructed for patients and partners, as

partner notification focused on prophylaxis rather than the 'test then treat' approach used with screened patients. The overall health care costs were estimated from direct expenditures recorded in the original screening pilot for test kits, reagent, personnel, materials, supplies, equipment, office space, treatment and contact tracing. Additionally, costs borne by the health care system for clinical staff involvement and administration in the programme were included to reflect activities not receiving direct remuneration from the NCSP funding. Planning and set-up costs and overheads were also fixed and incorporated into the model. Variable costs were added at each step in the decision-tree model and summed to acquire total cost. Sensitivity analyses were performed to assess which costs and patient flow values were most important to the outcomes, and to explore the range of possible outcomes for this screening programme. This facilitated running the model through several 'what if' scenarios that reflected practice variations reported in phase 1 of the implementation of the NCSP (Department of Health 2004a; LaMontagne *et al.* 2004b).

The estimated overall annual cost of opportunistic screening for over 33,000 women ages 16-24 was over £493,000. Eighty percent of the costs were variable patient costs, 5% were associated with partner notification activities, and 15% were overhead costs for running the programme. Each screening episode cost was estimated to be £21.83, inclusive of all downstream healthcare costs associated with testing. The cost per offer was under £15 and cost of a positive episode was less than £40. In sensitivity analyses, three key parameters had the greatest impact on the cost per screening offer: 1) the proportion of the population accepting screening— as test acceptance increased, so did costs; 2) the involvement of the GP versus the practice nurse in patient recruitment— costs decreased with less GP involvement; and 3) the amount of time spent by either receptionists or clinicians in the screening episode— cost decreased as clinicians spent less time explaining screening.

These findings illustrate that the proportion of the population accepting screening has the largest impact on costs. While a high test acceptance rate accounts for higher costs, it may help identify the greatest number of infections if the correct population is tested; indeed, this is the goal of the NCSP. The laboratory test cost was important to the total cost of screening, which suggests that stabilisation of the cost through contractual arrangements of bulk-purchasing test kits and reagents, combined with efficient use of laboratory staff to process specimens, could facilitate reductions in overall costs.

Partner notification activities contributed to only 5% of the overall programme costs. This was expected given the results of the screening pilot which showed that partners only comprised about 5% of all persons tested (Pimenta *et al.*, unpublished data). Although partner contacting is critical to the spread and control of chlamydial infection (Garnett and Anderson 1996), it was less resource intensive in this study, providing convincing evidence that this component of a chlamydia screening programme may not be financially burdensome.

This study also highlights areas of uncertainty in the data that influence the costs of screening. For example, the time spent by clinicians in explaining screening had a large impact on the costs because of its high variability and impact on all screening offers. Reduction in the time for the screening offer, such as through a patient self-selection process, could also reduce the overall costs of the programme.

This research provided significant contribution to the body of evidence in four ways. Firstly, this study is the only recently published analysis to explicitly estimate the time and costs at each step of a chlamydia screening programme. Previous studies have estimated the time and involvement of health care workers for different outcomes, such as PID,

ectopic pregnancy, and infertility (Welte *et al.* 2000), but without the precision of costs at each step in the process as afforded by this study.

Secondly, this study quantified the health care-associated costs of opportunistic chlamydia screening in England, directly responding to a key component of the Wilson and Junger criteria (1968). They advocate the need to know the costs of a screening intervention in order to assess the economic effectiveness of the programme (1968). Thirdly, the use of empirical patient flow data and exact cost data from the original chlamydia screening pilot strengthened the interpretation of our model.

Additionally, utilising decision analysis was novel in assessing the uncertainty of various parameters and how those parameters impacted costs at each stage of the screening episode. This allowed the model to reflect actual screening practice and provided flexibility to simulate other screening scenarios as they arise. This can be a powerful tool to explore the average costs of screening and variations in estimates as local programmes revise their implementation and operational structure for chlamydia screening. This also provides an opportunity to estimate costs based upon locally-derived figures for time and staff mix involved in the programme as well as the actual costs incurred for equipment, supplies, personnel and overheads.

Lastly, this study demonstrated the utility of employing the lessons learned from this model to advise on the appropriate cost of screening for the National Chlamydia Screening Programme, and potentially similar programmes being explored in other countries. Indeed, the NCSP has used the results of this study to develop "cost templates" that suggest a standardised budget for local programmes based on projected testing volume for new areas applying to be a part of the next phase of the programme.

Clinical audits for assessing adherence to screening guidelines

Monitoring and evaluating chlamydia screening programmes can occur at many levels. Assessing adherence to screening criteria (LaMontagne *et al.* 2004a), measuring changes in the disease burden (LaMontagne *et al.* 2005), and ensuring fiscal prudence (Adams *et al.* 2004b) are three approaches I have previously researched. For most programmes addressing sexual health, clinical standards and guidelines exist. In England, the British Association for Sexual Health and HIV (BASHH) published care and treatment guidelines for genital chlamydial infection (Clinical Effectiveness Workgroup 2002). For the NCSP, the Department of Health (2004a) has published core requirements as guidelines for screening implementation. Assessing adherence to these published guidelines will provide an additional programme monitoring tool for nationally-organised chlamydia screening efforts.

For women seeking termination of pregnancy, the Royal College of Obstetricians and Gynaecologists (RCOG) (2002) have published guidelines for appropriate chlamydia screening and treatment, which allow for either prophylactic treatment of all attenders or a 'screen then treat' approach for women testing positive. Women undergoing termination procedures are an ideal population for chlamydia screening because studies have found higher prevalence levels than other populations of women screened (Skjeldestad *et al.* 1997). Moller *et al.* (1981) have found women who have surgical terminations were at increased risk of ascending upper genital tract infection and demonstrated a high incidence of PID in chlamydia-positive women following termination. In England, over 180,000 medical or surgical terminations are performed each year (Office of National Statistics 2000) and may place this population of women at increased risk of ascending upper genital tract infection. Because of this risk, clear guidelines for the detection and management of infection among women seeking termination are necessary.

In addition to the RCOG guidelines, the Chief Medical Officer (1998) has advocated all women seeking terminations should be screened for chlamydia. Investigating the adherence to either of these guidelines by clinical providers of pregnancy termination services through clinical audits can be beneficial in understanding practice patterns to address any non-compliance or deviations in practice that may be harmful. This study sought to explore the policy and practice for chlamydia testing and treatment at termination of pregnancy providers in England and Wales, and examined variations by region and service size as well as the degree to which practices and policies followed either of the recommended guidelines.

A survey questionnaire was distributed to all providers reporting terminations to the Department of Health in 1999. The questionnaire queried current policies for screening and treating genital chlamydial infection, assessed testing and treatment behaviour to client populations, gathered information on patient treatment and follow-up, and recorded perceived barriers to implementing chlamydia screening. Assessment of practice was collected separately for surgical and medical terminations, as medical terminations usually do not employ an invasive procedure. I analysed survey responses in themes: policy, practice for screening, and practice for treatment. Variations in policy and practice by size of service, geographic region, and NHS and non-NHS providers were explored in statistical analyses.

All 284 identified termination of pregnancy providers were invited to participate, of which 48% (138/284) responded. All NHS regions except the West Midlands were evenly represented in services of different sizes. Most services (87%) were NHS funded. Ninety-six services (70%) reported a written policy for screening and/or treatment of chlamydia. No practice differences between surgical and medical terminations were found.

Slight regional differences in practice were uncovered. For example, surgical terminations in Yorkshire and Humberside and the North East were more likely to provide prophylaxis without testing ($p < 0.05$). Practice differences were found between NHS and non-NHS providers and between small and medium-large services. Over 50% of termination providers collected cervical swabs as the specimen of choice for chlamydia testing. The use of less sensitive non-amplified laboratory tests was noted by 50% of providers surveyed. In general, clinical practice for screening and treating of chlamydial infection followed three patterns: providers screening prior to termination and treating if warranted (over 70% of services); providers administered antibiotic prophylaxis without screening (about 25% of services); or providers did neither screen or treat for chlamydial infection (less than 5% of services). These practice variations might be due to the diverging recommendations from the RCOG and CMO.

Among the nearly 70% of providers that engaged in chlamydia screening before termination, over 90% tested everyone. The RCOG and CMO guidelines are most similar on this point but the RCOG guidelines do not explicitly recommend testing **all** patients. Most providers who did screen, did so prior to termination, as recommended; however, less than half used the current NAAT diagnostic standard (Department of Health 2004a). For all services, differences in the treatment regimen administered were apparent. Inconsistency in the recommended treatment regimens between the RCOG and CMO guidelines may be influencing these providers' practices. Lastly, the most divergent point between the CMO and RCOG is the practice of prophylaxis without screening, which occurred among 25% of providers surveyed but is not advised by the CMO (1998).

This study found that over 95% of responding termination of pregnancy providers reported practice consistent with either the RCOG or CMO guidelines for chlamydia, although there were discrepancies. Specifically, this study recommended guideline

clarification and harmonisation on three points: (1) whether antibiotic prophylaxis should be offered to all termination of pregnancy attenders without screening for chlamydia; (2) the appropriate treatment regimen for both prophylactic and curative regimens; and (3) the laboratory test standard for both the sample and the test platform.

This study has provided two direct and relevant insights for consultation within the programme implementation of the NCSP. Firstly, this study was beneficial in quantifying the behaviour of clinical providers regarding chlamydial screening to a high-risk population. The uncovering of discrepancies between policy and practice, as well as between the guidelines from two national bodies, highlights the importance of understanding how services are delivered in the field and can act as a monitoring technique for adherence to guidelines. Because the risk of sequelae from infection is increased by the invasive nature of the termination procedure, sound clinical practice that ensures the health of the patient is paramount. Women attending for termination of pregnancy are more likely to have chlamydia, even after considering age and sexual behaviour risk factors. Therefore, the clinical management of women undergoing pregnancy termination requires a clear and consistent policy followed-up with sound clinical practice.

Secondly, by surveying the practice patterns of screening for chlamydia within this high risk population, this study has illustrated service delivery areas that might need strengthening by the NCSP. For example, invasive samples tested using tests with lower sensitivity were common. The NCSP funds screening based on non-invasive urine or self-collected vulva-vaginal swab samples using the highly sensitive tests (Department of Health 2004a). As termination providers join the programme, they will be able to access these more acceptable testing methods. This may increase the termination providers' adherence to national guidelines for screening and acceptance of screening by this population.

Chapter 5
Discussion

My research into various aspects of chlamydia screening has covered three broad themes across two countries. Individually, these studies have strengthened the evidence base for determining whether chlamydia screening meets the criteria for public health intervention, as outlined by Wilson and Jungner (1968), by enriching our current knowledge of the epidemiology of genital chlamydial infection and demonstrating several approaches for monitoring and evaluating existing screening programmes. As diverse as these studies are, there is a thread that brings them together, and that is the National Chlamydia Screening Programme (NCSP). My early work for the Region X screening programme in the US (LaMontagne *et al.* 2004a) and my research on chlamydia infection in men (LaMontagne *et al.* 2003) has provided me the academic foundation and critical experience for my role as the lead scientist in the NCSP in the UK. Additionally, the research I have performed since arriving to the UK has been done to provide critical input on several facets of the NCSP (Brown *et al.* 2004; LaMontagne *et al.* 2004b; Adams *et al.* 2004b; LaMontagne *et al.* 2004c; LaMontagne *et al.* 2005). How these diverse research studies in two different countries have influenced the field, in general, and the development of the NCSP in the UK, specifically, is the focus of the discussion below.

LaMontagne *et al.* (2003) has provided the field with a more robust understanding of the epidemiology of chlamydial infection in men. This study has raised again the question of whether men should be screened. The high prevalence of infection found in asymptomatic men suggests they should. Two recently published papers have argued for the inclusion of men in screening efforts and have cited this study as evidence (Peipert 2003; Stamm 2004). Additionally, this research questioned the utility of testing all men attending STD clinics, especially since over two-thirds of male attenders had no signs of infection and were not

contacts of known cases. The study explored screening strategies for men and suggested that age, clinical signs of infection (principally urethritis), and recent contact to a known case would be sensitive in detecting infections and greatly reduce the number of men requiring testing. The challenge for the field is to test this hypothesis. The logical outcome from this work would be for Region X, where the study was done, to trial different selection criteria in various STD and non-STD locations and critically evaluate their efficiency and sensitivity, as has been done for screening criteria for women (LaMontagne *et al.* 2004a). Unfortunately, I left my post shortly after this study was completed, and was not able to see through this next step; however, as a peer-reviewer for the journal *Sexually Transmitted Infections*, I have assessed a study from Australia that has tested screening criteria in men, reflecting that with time, the influence of my research will be observed.

LaMontagne *et al.* (2004a) has provided the field with the second evaluation of the long-standing chlamydia screening programme in Region X. As noted in Chapter 4, this programme has set the tenor and pace for chlamydia screening in the US. My evaluation of the programme's selective screening criteria resulted in a direct change in programme policy and structure. This study found that the criteria previously in use could be optimised for efficiency without a significant loss to criteria sensitivity. This result was taken forward to the programme's advisory committee after the study's end, and the new criteria were put into programme use beginning January 2003 (Center for Health Training 2003).

Four of my studies from the UK have helped shape the establishment and structure of the National Chlamydia Screening Programme. My first task when joining the programme in early 2003 was to develop the data collection system and programme monitoring and evaluation components. Using experience with the Region X programme and existing research that suggested positivity could be a surrogate measure for prevalence, I proposed to collect data for all tests, rather than data on all women (Department of Health 2004).

This study (LaMontagne *et al.* 2005) has already been reviewed in Chapter 4. The important influence of this work was two-fold. Firstly, I demonstrated that the suggested plan to monitor test trends for positivity was appropriate and could act as a surrogate measure for prevalence. This helped advance the data collection system for the programme, and greatly eased local implementation of data collection instruments as well as reporting requirements for local screening programmes. Secondly, this research provided a significant contribution to the knowledge base by confirming a method, that although was widely used, had only been verified in one peer-reviewed published study. As is often the case with research, it is important that the findings from one study are replicated in others, enhancing the validity of the study and confirming the study's conclusions.

LaMontagne *et al.* (2004c) has shaped the discussions at the national level of what clinics to include in the NCSP. Even though studies of chlamydia prevalence in women attending for termination of pregnancy have shown levels of infection as high as 14% (Pimenta *et al.* 2003b), the inclusion of providers of pregnancy terminations into the screening programme was not automatic. Conflicts with existing policies and practices and the potential for additional training for these providers were areas of concern. My work examining the current policies and practices of termination providers illustrated what baseline practices were being employed and what training would be needed for providers that were not already adhering to a screening guideline. This study also showed the divergent policies between the CMO (1998) and the Royal College of Obstetricians and Gynaecologists (2000), and suggested harmonising the two guidelines. Since the publication of this study, questions of how to take the issue forward have been discussed by those involved in the NCSP as well as external agencies, such as the Health Protection Agency and the National Institute for Clinical Effectiveness. How to continue to take this issue forward is one of many current topics on the agenda of the NCSP.

The Adams *et al.* study (2004b) of the cost of chlamydia screening has provided the first published analysis of the actual costs of screening at each step in an organised programme, from screening offer to treating the partners of positives. Previous cost studies were only focused on 'health care costs' more generally, and have not detailed the costs for each component. This has enhanced our knowledge base significantly. Additionally, the sensitivity analysis performed in this study has helped define the most variable costs. This is important to the NCSP because it has provided a tool for financial audits, has illustrated where money might be saved, *e.g.*, through the reduction of physician involvement, and has informed the NCSP on specific costs in the programme that are not terribly expensive, *e.g.*, partner notification and treatment. The NCSP has already used the results from this study in two important ways. Firstly, the programme has used the average costs of screening from this paper to analyse budget proposals by the local programmes included in phase 2 of implementation, which will also form the basis of yearly financial audits. Secondly, the average cost of screening from this study was used in conjunction with the estimated number of sexually active young people in England to determine the funding required for full national coverage of the NCSP.

Brown *et al.* (2004) reconfirmed how prevalent STIs are in the UK, examined observed trends in increased diagnoses, and was in the top ten frequently downloaded articles from the journal's website in 2004 (http://sti.bmjjournals.com/misc/topten04.shtml). The presentation of annual epidemiological statistics for STIs has provided more evidence of the burden of these diseases in the population, especially among persons aged under 25. This study provided additional confirmation that the NCSP is targeting the appropriate age group for chlamydia screening. Often reports of this magnitude can act as a catalyst for greater attention by the public and by government. The English government has recently announced its current health priorities and have earmarked £300 million to tackle the rising trends in all sexually transmitted diseases, including chlamydia (Department of Health

2004b). Certainly, this study is not the only evidence used to influence the government's recent decision, rather the research literature taken in total, of which this paper has made a significant contribution, has provided the evidence base.

Ultimately, these six research papers have lead to the most recently completed study— the description of the establishment of the National Chlamydia Screening Programme in England and analysis of results from the first year of screening outside GUM clinics (LaMontagne *et al.* 2004b). My work in establishing this programme has utilised all of my prior research, in addition to the existing body of evidence. The NCSP has benefited from the lessons learned by other programmes and from the enriched body of knowledge that was not available at the time programmes were established in the US. The programme has been able to robustly build its structure and components from the best available evidence, as well as from the additional research that I have performed whilst the NCSP has evolved. The programme has confirmed that opportunistic screening for genital chlamydial infection is feasible and acceptable and can occur in a wide variety of settings, without loss to quality care for persons testing positive and their partners. Most importantly, the first year of the NCSP has shown that chlamydial infection is highly prevalent among young people in England.

The evidence for the magnitude of this disease can no longer be in dispute. Action towards reducing the burden of disease and the potential devastating consequences of infection can no longer be delayed. The establishment of the NCSP has received significant attention recently, in the press— popular and academic, and by the government. Popular press has included lengthy articles in broadsheets and interviews with the BBC, Reuters and others by myself and NCSP staff. The academic press has shown its interest in the NCSP by fast-tracking the paper describing the first year's results (Ward H and Miller R 2004). I believe that the work of the NCSP to date has had direct influence on the recent decisions by the

government to make sexual health a priority and to specifically allocate £80 million to fully fund the National Chlamydia Screening Programme for national coverage by March 2007 (Department of Health 2004b).

Chapter 6
Conclusion

This context statement considered the structure and context of chlamydia screening in two different countries, the United States and United Kingdom. I have critically examined the epidemiology of chlamydial infection in several populations across both countries, detailed the development, implementation and first year results for the newly established National Chlamydia Screening Programme in England, and have demonstrated four methods for monitoring and evaluation of chlamydia screening— assessment of screening criteria, use of positivity to measure disease changes in the population, fiscal analysis of costs through economic modelling, and clinical audits of provider adherence to screening guidelines. My research was developed within the framework of the Wilson and Jungner (1968) criteria, which are used to examine the case for screening as a public health intervention.

My research has been chronological with increasing sophistication over the years. The lessons learned from each study have been taken to the next, as illustrated by my investigation of the epidemiology of chlamydial infection among men and MSM. The combination of all seven papers has provided additional support for the Wilson and Jungner (1968) criteria and has had direct influence on policies and screening programmes in the US and the UK. The studies from the US have shown significant disease burden in men, and suggested selective screening criteria might be beneficial. Additionally, my evaluation of the Region X screening programme lead to direct programme change for screening criteria used to test women. The lessons learned from this evaluation have been incorporated in the programme monitoring structure of the NCSP in the UK, particularly through the use of positivity as a surrogate measure to monitor prevalence changes as screening becomes increasingly wide-spread. This is just one example of how I have been

able to bring my experience in the US and expertise in chlamydia screening to bear on components of the NCSP; others have been highlighted throughout this context statement.

Even though the scientific evidence presented, both my own and that of the published literature, covered many aspects of chlamydia screening, there is still more work to be done. I continue to be intimately involved in contributing to gaps in our knowledge of chlamydia screening programmes.

For example, there are two questions that are still inadequately studied and consume a portion of the debate about chlamydia screening in England today. First, do we know how frequently women should be screened for chlamydia to reduce prevalence? One published study (Burstein *et al.* 1998) of adolescents in Baltimore (US) suggests young women with negative results on their first chlamydia test should be screened every six months. To date, three prospective cohort studies of chlamydia re-infection from the US have suggested women with positive results on their first chlamydia test should be re-screened every three-to-six months (Oh *et al.* 1996; Fortenberry *et al.* 1999; Whittington *et al.* 2001).

Because these studies were unable to assess the long-term impact on chlamydia prevalence of their recommended screening intervals for women testing negative and those testing positive and are limited in their inference outside the US, I am studying chlamydia incidence and re-infection in women aged 16-24 years in England. My prospective cohort study has recently concluded and showed an incidence rate of 5.8 per 100 woman-years and a re-infection rate of 24.0 per 100 woman-years (LaMontagne, Emmett, Baster and the Chlamydia Recall Study Advisory Group 2004d). Women with multiple partner changes over the preceding six months were at highest risk of both infection and re-infection. Most infections occurred within 14.4 months of follow-up for initially negative tests; most re-infections occurred within six months of follow-up for initially positive tests (LaMontagne

et al. 2004d). We are currently modelling these data to calculate the optimal screening interval for initially negative and initially positive women to reduce chlamydia prevalence in the population.

The second question under debate is whether screening women for chlamydia is cost-effective. Even though several cost-effectiveness analyses have been published in the US (Marrazzo *et al.* 1997b), Europe (Welte *et al.* 2000; Krtzschmar *et al.* 2001), and England (Townsend and Turner 2000), some have suggested methodological shortcomings of these studies (Roberts *et al.* 2004), principally the lack of empirical data to verify the mathematical models developed and the inability of previously published models to account for the unique dynamics of chlamydia transmission in the population. My colleagues and I are performing economic analyses based on a recently developed transmission dynamic model of chlamydia (Turner, Garnett, Ghani, Sterne and Low 2004) using data from our incidence and re-infection study to more accurately estimate the scenarios of chlamydia screening that are most cost-effective. Various strategies of screening are being explored including those operating on an invitation-to-screen or 'call/recall' basis, those arising from opportunistic screening in clinical settings, and those that include a variety of age cut-offs for both men and women.

The results of the chlamydia incidence and re-infection study and the subsequent modelling of screening intervals and cost-effectiveness will be a great addition to our understanding of how to improve upon current approaches to chlamydia screening. The results from these studies will also be used by the National Chlamydia Screening Programme in developing scientifically robust screening frequency recommendations to enhance the programme's impact on the morbidity and sequelae of this preventable public health epidemic.

Appendix 1. References

Adams, E.J., Charlett, A., Edmunds, W.J. & Hughes, G. (2004a). '*Chlamydia trachomatis* in the United Kingdom: a systematic review and analysis of prevalence studies'. Sexually Transmitted Infections. 80, (5), p.354-362.

Adams, E.J., LaMontagne, D.S., Johnston, A.R., Pimenta, J.M., Fenton, K.A. & Edmunds, W.J. (2004b). 'Modelling the health care costs of an opportunistic chlamydia screening programme'. Sexually Transmitted Infections. 80, (5), p.363-370.

Addiss, D.G., Vaughn, M.L., Ludka, D., Pfister, J. & Davis, J.P. (1993). 'Decreased prevalence in *Chlamydia trachomatis* infection associated with a selective screening program of family planning clinics in Wisconsin'. Sexually Transmitted Diseases. 20, (1), p.28-35.

Andersen, B., Ostergaard, L., Moller, J.K. & Olesen, F. (2001). 'Effectiveness of a mass media campaign to recruit young adults for testing of *Chlamydia trachomatis* by use of home obtained and mailed samples'. Sexually Transmitted Infections. 77, (6), p.416-418.

Andersen, B., Olesen, F., Moller, J.K. & Ostergaard, L. (2002). 'Population-based strategies for outreach screening of urogenital *Chlamydia trachomatis* infections: a randomized, controlled trial'. Journal of Infectious Diseases. 185, (2), p.252-258.

Aronson, M.D. & Phillips, R.S. (1993). 'Screening young men for chlamydial infection'. Journal of the American Medical Association. 270, (17), p.2097-2098.

Battle, T.J., Golden, M.R., Suchland, K.L., Counts, J.M., Hughes, J.P., Stamm, W.E. & Holmes, K.K. (2001). 'Evaluation of laboratory testing methods for *Chlamydia trachomatis* infection in the era of nucleic acid amplification'. Journal of Clinical Microbiology. 39, (8), p.2924-2927.

Black, C.M. (1997). 'Current methods of laboratory diagnosis of *Chlamydia trachomatis* infections'. Clinical Microbiology Review. 10, (1), p.160-184.

Braverman, P.K., Biro, F.M., Brunner, R.L., Gilchrist, M.J. & Rauh, J.L. (1990). 'Screening asymptomatic adolescent males for chlamydia'. Journal of Adolescent Health Care. 11, (2), p.141-144.

Britton, T.F., DeLisle, S. and Fine, D. (1992). 'STDs and family planning clinics: a regional program for chlamydia control that works.' American Journal of Gynecologic Health. 6, (3), p.80-87.

Brown, A.E., Sadler, K.E., Tomkins, S.E., McGarrigle, C.A., LaMontagne, D.S., Goldberg, D., Tookey, P., Smyth, B., Thomas, D., Murphy, G., Parry, J.V., Evans, B., Gill, O.N., Ncube, F. & Fenton, K.A. (2004). 'Recent trends in HIV and other STIs in the United Kingdom: data to the end of 2002'. Sexually Transmitted Infections. 80, (3), p.159-166.

Burstein, G.R., Gaydos, C.A., Diener-West, M., Howell, M.R., Zenilman, J.M. & Quinn, T.C. (1998). 'Incident *Chlamydia trachomatis* infections among inner-city adolescent females'. Journal of the American Medical Association. 280, (6), p.521-526.

Cates, W. Jr. & Wasserheit, J.N. (1991). 'Genital chlamydial infections: epidemiology and reproductive sequelae'. American Journal of Obstetrics and Gynecology. 164, (6), p.1771-1781.

Cates, W. Jr. (1999). 'Chlamydial infections and the risk of ectopic pregnancy'. Journal of the American Medical Association. 281, (2), p.117-118.

Cates, W. Jr. (1984). 'Sexually transmitted organisms and infertility: the proof of the pudding'. Sexually Transmitted Diseases. 11, (2), p.113-116.

Cecil, J.A., Howell, M.R., Tawes, J.J., Gaydos, J.C., McKee, K.T., Quinn, T.C. & Gaydos, C.A. (2001). 'Features of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection in male army recruits'. Journal of Infectious Diseases. 184, (9), p.1216-1219.

Center for Health Training. (2003). Region X Infertility Prevention Project – project manual. Seattle: Center for Health Training.

Centers for Disease Control and Prevention. (2002). 'Sexually transmitted diseases treatment guidelines 2002'. Morbidity and Mortality Weekly Report. 51, (RR-6), p.1-78.

Centers for Disease Control and Prevention. (2002). 'Screening tests to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections— 2002'. Morbidity and Mortality Weekly Report. 51, (RR-15), p.1-38.

Centers for Disease Control and Prevention. (2003). Sexually Transmitted Disease Surveillance 2002 Supplement: Chlamydia Prevalence Monitoring Project Annual Report 2002. Atlanta: CDC, Division of STD Prevention.

Chapman, A.L. (1949). 'The concept of multiphasic screening'. Public Health Reports. 64, p.1311.

Cheng, H., Macaluso, M., Vermund, S.H. & Hook, E.W. 3rd. (2001). 'Relative accuracy of nucleic acid amplification tests and culture in detecting chlamydia in asymptomatic men'. Journal of Clinical Microbiology. 39, (11), p.3927-3937.

Chernesky, M.A. (2002). '*Chlamydia trachomatis* diagnostics'. Sexually Transmitted Infections. 78, (4), p.232-234.

Chief Medical Officer's Expert Advisory Group. (1998). Main report of the CMO's Expert Advisory Group on *Chlamydia trachomatis*. London: Department of Health.

Chow, J.M., Yonekura, M.L., Richwald, G.A., Greenland, S., Sweet, R.L. & Schachter, J. (1990). 'The association between *Chlamydia trachomatis* and ectopic pregnancy: a matched-pair, case-control study'. Journal of the American Medical Association. 263, (23), p.3164-3167.

Clemins, E.L., Flood, J., Kent, C.K., Shaw, H., Rowniak, S., Moncada, J., Klausner, J.D., Schachter, J. (2000). 'Reexamining the prevalence of *Chlamydia trachomatis* infection among gay men with urethritis'. Sexually Transmitted Diseases. 27, (5), p.249-251.

Clark, A.M., Steece, R., Crouse, K., Campbell, J., Zanto, S., Kartchner, D., Mottice, S. & Pettit, D. (2001). 'Multisite pooling study using ligase chain reaction in screening for genital *Chlamydia trachomatis* infections'. Sexually Transmitted Diseases. 28, (10), p.565-568.

Clinical Effectiveness Workgroup (MSSVD and AGUM). (2002). Management of *Chlamydia trachomatis* genital tract infection. London: British Association for Sexual Health and HIV.

Commission on Chronic Illness. (1959). Chronic illness in the United States: volumes I-IV. Cambridge, MA: Harvard University Press.

DeMuylder, X., Laga, M., Tennstedt, C., Van Dyck, E., Aelbers, G.N. & Piot, P. (1990). 'The role of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in pelvic inflammatory disease and its sequelae in Zimbabwe'. Journal of Infectious Diseases. 162, (2), p.501-505.

Department of Health. (2001). The National Strategy for Sexual Health and HIV. London: Department of Health.

Department of Health. (2004a). The national chlamydia screening programme in England: programme overview, core requirements, and data collection. (2nd ed). London: Department of Health.

Department of Health. (2004b). Choosing health: making healthier choices easier. London: Department of Health.

Dicker, L.W., Mosure, D.J. & Levine, W.C. (1998). 'Chlamydia positivity versus prevalence. What's the difference?'. Sexually Transmitted Diseases. 25, (5), p.251-253.

Dicker, L.W., Mosure, D.J., Levine, W.C., Black, C.M. & Berman, S.M. (2000). 'Impact of switching laboratory tests on reported trends in *Chlamydia trachomatis* infections'. American Journal of Epidemiology. 151, (4), p.430-435.

Domenika, M., Bassiri, M. & Mardh, P-A.(1994). 'Diagnosis of genital *Chlamydia trachomatis* infections in asymptomatic males by testing urine by PCR'. Journal of Clinical Microbiology. 32, (10), p.2350-2352.

Egger, M., Low, N., Smith, G., Lindblom, B. & Hermann, B. (1998). 'Screening for chlamydia infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis'. British Medical Journal. 316, (7147), p.1776-1780.

Fenton, K.A., Korovessis, C., Johnson, A.M., McCadden, A., McManus, S., Wellings, K., Mercer, C.H., Carde, C., Copas, A.J., Nanchahal, K., Macdowall, W., Ridgway, G., Field, J. & Erens, B. (2001). 'Sexual behaviour in Britain: reported sexually transmitted infections and prevalence genital *Chlamydia trachomatis* infection'. Lancet. 358, (9296), p.1851-1854.

Ford, C.A., Viadro, C.I. & Miller, W.C. (2004). 'Testing for chlamydial and gonorrheal infections outside of clinic settings – a summary of the literature'. Sexually Transmitted Diseases. 31, (1), p.38-51.

Fortenberry, J.D., Brizendine, E.J., Katz, B.P., Wools, K.K., Blythe, M.J. & Orr, D.P. (1999). 'Subsequent sexually transmitted infections among adolescent women with genital infection due to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Trichomonas vaginalis*'. Sexually Transmitted Diseases. 26, (1), p.26-32.

Friis, R.H. & Sellers, T.A. (2004). 'Screening for disease in the community'. in R.H. Friis & t.A. Sellers (eds). Epidemiology for Public Health Practice. (3rd ed). Sudbury, MA: Jones and Bartlett Publishers.

Garnett, G.P. & Anderson, R.M. (1996). 'Sexually transmitted diseases and sexual behaviour: insights from mathematical models'. Journal of Infectious Diseases. 174, (Suppl 2), p.S150-S161.

Garrow, S.C., Smith, D.W. & Harnett, G.B. (2002). 'The diagnosis of chlamydia, gonorrhoea, and trichomonas infections by self obtained low vaginal swabs, in remote northern Australian clinical practice'. Sexually Transmitted Infections. 78, (4), p.278-281.

Gerbase, A., Rowley, J., Heymann, D., Berkeley, S. & Piot, P. (1998). 'Global prevalence and incidence estimates of selected curable STDs'. Sexually Transmitted Infections. 74, (Suppl 1), p.S12-S16.

Gotz, H., Veldhuijzen, I., de Zwart, O., Broer, J., de Groot, F., Hoebe, C., Verhooren, M., van Schnaik, D., Coenen, T., van Bergen, J. & Richardus, J. (2003). 'Acceptability of screening for *Chlamydia trachomatis* by home based urine testing'. [poster]. Ottawa, Canada: 15th Biennial Congress of the International Society of Sexually Transmitted Disease Research, 27-30 July.

Gudgel, K.L. & LaMontagne, D.S. (1999). 'Enhanced detection of *Chlamydia trachomatis* (CT) infection in women through ligase chain reaction (LCR) testing'. [poster]. Denver, CO: 13th Meeting of the International Society of Sexually Transmitted Diseases Research, 11-14 July.

Gunn, R.A., Podschun, G.D., Fitzgerald, S., Hovell, M.F., Farshy, C.E., Black, C.M. & Greenspan, J.R. (1998). 'Screening high-risk adolescent males for *Chlamydia trachomatis* infection'. Sexually Transmitted Diseases. 25, (1), p.49-52.

Handsfield, H.H., Jasman, L.L., Roberts, P.L., Hanson, V.W., Kothenbeutel, R.L. & Stamm, W.E. (1986). 'Criteria for selective screening for *Chlamydia trachomatis* infection in women attending family planning clinics'. Journal of the American Medical Association. 255, (13), p.1730-1734.

Hanselaar, A.G. (2002). 'Criteria for organized cervical screening programs. Special emphasis on The Netherlands program'. Acta Cytologica. 46, (4), p.619-629.

Hart, G. (1993). 'Factors associated with genital chlamydial and gonococcal infection in males'. Genitourinary Medicine. 69, (5), p.392-396.

Hennekens, C.H. & Buring, J.E. (1987). 'Screening'. in S.L. Mayrent (ed). Epidemiology in Medicine. Philadelphia, PA: Lippincott, Williams and Wilkins.

Herrmann, B. & Egger, M. (1995). 'Genital *Chlamydia trachomatis* infections in Uppsala County, Sweden, 1985-1993: declining rates for how much longer?'. Sexually Transmitted Diseases. 22, (4), p.253-260.

Hillis, S.D., Owens, L.M., Marchbanks, P.A., Amsterdam, L.F. & Mac Kenzie, W.R. (1997). 'Recurrent chlamydial infections increase the risks of hospitalization for ectopic pregnancy and pelvic inflammatory disease'. American Journal of Obstetrics and Gynecology. 176, (1 Pt 1), p.103-107.

Hiltunen-Back, E., Haikala, O., Kautiainen, H., Paavonen, J. & Reunala, T. (2001). 'A nationwide sentinel clinic survey of *Chlamydia trachomatis* infection in Finland'. Sexually Transmitted Diseases. 28, (5), p.252-258.

Honey, E. & Templeton, A. (2002). 'Prevention of pelvic inflammatory disease by the control of *C. trachomatis* infection'. International Journal of Gynecology and Obstetrics. 78, (3), p.257-261.

Honey, E., Augood, C., Templeton, A., Russell, I., Paavonen, J., Mardh, P-A., Stary, A. & Stray-Pedersen, B. (2002). 'Cost effectiveness of screening for *Chlamydia trachomatis*: a review of published studies'. Sexually Transmitted Infections. 78, (6), p.406-412.

Howell, M.R., Quinn, T.C., Brathwaite, W. & Gaydos, C.A. (1998a). 'Screening women for *Chlamydia trachomatis* in family planning clinics— the cost-effectiveness of DNA amplification assays'. Sexually Transmitted Diseases. 25, (2), p.108-117.

Howell, M.R., Quinn, T.C. & Gaydos, C. (1998b). 'Screening for *Chlamydia trachomatis* in asymptomatic women attending family planning clinics: a cost-effectiveness analysis of three strategies'. Annals of Internal Medicine. 128, (4), p.277-284.

Hsieh, Y.H., Howell, M.R., Gaydos, J.C., McKee, K.T. Jr., Quinn, T.C. & Gaydos, C.A. (2003). 'Preference among female Army recruits for use of self-administrated vaginal swabs or urine to screen for *Chlamydia trachomatis* genital infections'. Sexually Transmitted Diseases. 30, (10), p.769-773.

Idahl, A., Boman, J., Kumlin, U. & Olofsson, J.I. (2004). 'Demonstration of *Chlamydia trachomatis* IgG antibodies in the male partner of the infertile couple is correlated with a reduced likelihood of achieving pregnancy'. Human Reproduction. 19, (5), p.1121-1126.

Johnson, J., Neas, B., Parker, D.E., Fortenberry, J.D. & Cowan, L.D. (1993). 'Screening for urethral infection in adolescent and young adult males'. Journal of Adolescent Health. 14, (5), p.356-361.

Johnson, R.E., Green, T.A., Schachter, J., Jones, R.B., Hook, E.W. 3rd., Black, C.M., Martin, D.H., St Louis, M.E. & Stamm, W.E. (2000). 'Evaluation of nucleic acid amplification tests as reference tests for *Chlamydia trachomatis* infections in asymptomatic men'. Journal of Clinical Microbiology. 38, (12), p.4382-4386.

Joyee, A.G., Thyagarajan, S.P., Rajendran, P., Hari, R., Balakrishnan, P., Jeyaseelan, L. & Kurien, T. (2004). '*Chlamydia trachomatis* genital infection in apparently health adult population of Tamil Nadu, India: a population-based study'. International Journal of STD & AIDS. 15, (1), p.51-55.

Klavs, I., Rodrigues, L.C., Wellings, K., Kese, D. & Hayes, D. (2004). 'Prevalence of genital *Chlamydia trachomatis* infection in the general population of Slovenia: serious gaps in control'. Sexually Transmitted Infections. 80, (2), p.121-123.

Knox, J., Tabrizi, S.N., Miller, P., Petoumenos, K., Law, M., Chen, S. & Garland, S.M. (2002). 'Evaluation of self-collected samples in contrast to practitioner-collected samples for detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* by polymerase chain reaction among women living in remote areas'. Sexually Transmitted Diseases. 29, (11), p.647-654.

Koumans, E.H., Black, C.M., Markowitz, L.E., Unger, E., Pierce, A., Sawyer, M.K. & Papp, J.R. (2003). 'Comparison of methods for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using commercially available nucleic acid amplification tests and a liquid pap smear medium'. Journal of Clinical Microbiology. 41, (4), p.1507-1511.

Kretzschmar, M., van Duynhoven, Y.T.H.P. & Severijnen, A.J. (1996). 'Modeling prevention strategies for gonorrhea and chlamydia using stochastic network simulations'. American Journal of Epidemiology. 144, (3), p.306-317.

Kretzschmar, M., Welte, R., van den Hoek, A. & Postma, M.J. (2001). 'Comparative model-based analysis of screening programs for *Chlamydia trachomatis* infections'. American Journal of Epidemiology. 153, (1), p.90-101.

Ku, L., St Louis, M., Farshy, C., Aral, S., Turner, C.F., Lindberg, L.D. & Sonenstein, F. (2002). 'Risk behaviors, medical care, and chlamydial infection among young men in the United States'. American Journal of Public Health. 92, (7), p.1140-1143.

LaMontagne, D.S., Patrick, L.E. & Marrazzo, J.M. (2001). 'Risk factors for *Chlamydia trachomatis* among men who have sex with men: results from a population-based screening programme, Region X, 1996-2000'. [oral presentation]. New Orleans, LA: 19th Annual Conference of the Gay and Lesbian Medical Association, 28 September-1 October.

LaMontagne, D.S., Fine, D.N. & Marrazzo, J.M. (2003). '*Chlamydia trachomatis* infection in asymptomatic men'. American Journal of Preventive Medicine. 24, (1), p.36-42.

LaMontagne, D.S., Patrick, L.E., Fine, D.N. & Marrazzo, J.M. (2004a). 'Re-evaluating selective screening criteria for chlamydial infection among women in the U.S. Pacific Northwest'. Sexually Transmitted Diseases. 31, (5), p.283-289.

LaMontagne, D.S., Fenton, K.A., Randall, S., Anderson, S. & Carter, P. (2004b). 'Establishing the national chlamydia screening programme in England: results from the first full year of screening'. Sexually Transmitted Infections. 80, (5), p.335-341.

LaMontagne, D.S., Pimenta, J.M., Fenton, K.A., Mallinson, H. & Hopwood, J. (2004c). 'Management of genital chlamydial infections at termination of pregnancy services in England and Wales – where are we now?'. BJOG: an International Journal of Obstetrics and Gynaecology. 111, (12), p.1408-1412.

LaMontagne, D.S., Emmett, L., & Baster, K., on behalf of the Chlamydia Recall Study Advisory Group. (2004d). 'Incidence and re-infection rates of genital chlamydial infection in young women in England: results from the Chlamydia Recall Study'. [oral presentation]. Mykonos, Greece: Conference on Sexually Transmitted Infections, European branch of the International Union Against Sexually Transmitted Infections, 7-9 October.

LaMontagne, D.S., Fenton, K.A., Pimenta, J.M., Catchpole, M., Rogers, P.A., Randall, S., Hewitt, W.G., Mallinson, H., Underhill, G.S., McLean, L., Gleave, T., Harindra, V., Ghosh, A.K. & and Tobin, J.M. (2005). 'Using chlamydia positivity to estimate prevalence: evidence from the Chlamydia Screening Pilot in England'. International Journal of STD & AIDS. 16, (4), p.323-327.

Lane, J.R., Chernesky, M., Martin, D.H., Jordan, J., Fuller, D., Willis, D., Fine, P., Janda, W. & Hook, E.W. (2003). 'Women prefer collection of their own vaginal swabs to cervical swabs or urine to investigate sexually transmitted infections'. [poster]. Ottawa, Canada: 15th Biennial Congress of the International Society for Sexually Transmitted Disease Research, 27-30 July.

Lau, C.Y. & Qureshi, A.K. (2002). 'Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials'. Sexually Transmitted Diseases. 29, (9), p.497-502.

Levine, W.C., Dicker, L.W., Devine, O. & Mosure, D.J. (2004). 'Indirect estimate of chlamydia screening coverage using public health surveillance data'. American Journal of Epidemiology. 160, (1), p.91-96.

Lossick, J., DeLisle, S., Fine, D., Mosure, D., Lee, V. & Smith, V. (1990). 'Regional program for widespread screening for *Chlamydia trachomatis* in family planning clinics'. in W.R. Bowie, H.D. Caldwell, R.P. Jones, P.A. Mardh, G.L. Ridgway, J Schachter, *et al.* (eds). Cambridge: Cambridge University Press, p.575-579.

Low, N., Macleod, J., Salisbury, C. & Egger, M. (2003). 'Bias in chlamydia prevalence surveys'. Lancet. 362, (9390), p.1157-1158.

Mabey, D.C.W., Ogbaselassie, G., Robertson, J.N., Heckels, J.E. & Ward, M.E. (1985). 'Tubal infertility in the Gambia: chlamydial and gonococcal serology in women with tubal occlusion compared with pregnant controls'. Bulletin of the World Health Organization. 63, (6), p.1107-1113.

Mardh, P-A., Ripa, T., Svensson, L. & Westrom, L. (1977). '*Chlamydia trachomatis* infection in patients with acute salpingitis'. New England Journal of Medicine. 296, (24), p.1377-1379.

Mardh, P-A. (2002). 'Is the prevention of genital chlamydial infections by community involvement possible?'. Best Practice Research in Clinical Obstetrics and Gynaecology. 16, (6), p.829-846.

Marks, C., Tideman, R.L., Estcourt, C.S., Berry, G. & Mindel, A. (2000). 'Assessment of risk for pelvic inflammatory disease in an urban sexual health population'. Sexually Transmitted Infections. 76, (6), p.470-473.

Marrazzo, J.M., Fine, D., Celum, C.L., DeLisle, S. & Handsfield, H.H. (1997a). 'Selective screening for chlamydial infection in women: a comparison of three sets of criteria'. Family Planning Perspectives. 29, (4), p.158-162.

Marrazzo, J.M., Celum, C.L., Hillis, S.D., Fine, D., DeLisle, S. & Handsfield, H. (1997b). 'Performance and cost-effectiveness of selective screening criteria for *Chlamydia trachomatis* infection in women: implications for a national chlamydia control strategy'. Sexually Transmitted Diseases. 24, (3), p.131-141.

Marrazzo, J.M., Whittington, W.L.H., Celum, C.L., Handsfield, H.H., Clark, A., Cles, L., Krekler, B. & Stamm, W.E. (2001). 'Urine-based screening for *Chlamydia trachomatis* in men attending sexually transmitted disease clinics'. Sexually Transmitted Diseases. 28, (4), p.219-225.

Martin, D.H., Mroczkowski, T.F., Dalu, Z.A., McCarthy, J., Jones, R.B., Hopkins, S.J. & Johnson, R.B. (1992). 'A controlled trial of a single dose of azithromycin for the treatment of chlamydial urethritis and cervicitis'. New England Journal of Medicine. 327, (13), p.921-925.

Mausner, J.S. & Kramer, S. (1985). Epidemiology – an introductory text. (2nd ed). Philadelphia, PA: W.B. Saunders Company.

McCormack, W.M., Alpert, S., McComb, D.E., Nichols, R.L., Semine, D.Z. & Zinner, S.H. (1979). 'Fifteen-month follow-up study of women infected with *Chlamydia trachomatis*'. New England Journal of Medicine. 300, (3), p.123-125.

McKay, L., Clery, H., Carrick-Anderson, K., Hollis, S. & Scott, G. (2003). 'Genital *Chlamydia trachomatis* infection in a subgroup of young men in the UK'. Lancet. 361, (9371), p.1972.

Mertz, K.J., Levine, W.C., Mosure, D.J., Berman, S.M. & Dorian, K.J. (1997). 'Trends in the prevalence of chlamydial infections – the impact of community-wide testing'. Sexually Transmitted Diseases. 24, (3), p.169-175.

Mertz, K.J., McQuillan, G.M., Levine, W.C., Candal, D., Bullard, J.C., Johnson, R.E., St Louis, M.E. & Black, C.M. (1998). 'A pilot study of the prevalence of chlamydial infection in a national household survey'. Sexually Transmitted Diseases. 25, (5), p.225-228.

Miettinen, A., Heinonen, P.K., Teisala, K., Hakkarainen, K. & Punnonen, R. (1990). 'Serologic evidence for the role of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in the etiology of tubal factor infertility and ectopic pregnancy'. Sexually Transmitted Diseases. 17, (1), p.10-14.

Miller, W.C., Hoffman, I.F., Owen-O'Dowd, J., McPherson, J.T., Privette, A., Schmitz, J.L., Woodlief, G. & Leone, P.A. (2000). 'Selective screening for chlamydial infection: which criteria to use?'. American Journal of Preventive Medicine. 18, (2), p.115-122.

Moller, B.R., Mardh, P-A., Ahrons, S. & Nussler, E. (1981). 'Infection with *Chlamydia trachomatis*, *Mycoplasma hominis* and *Neisseria gonorrhoeae* in patients with acute pelvic inflammatory disease'. Sexually Transmitted Diseases. 8, (3), p.198-202.

Moller, J.K., Andersen, B., Olesen, F. & Ostergaard, L. (2003). 'Reasons for *Chlamydia trachomatis* testing and the associated age-specific prevalences'. Scandinavian Journal of Clinical Laboratory Investigations. 63, (5), p.339-345.

Moncada, J., Schachter, J., Shafer, M.A., Williams, E., Gourlay, L., Lavin, B & Bolan, G. (1994). 'Detection of *Chlamydia trachomatis* in first catch urine samples from symptomatic and asymptomatic males'. Sexually Transmitted Diseases. 21, (1), p.8-12.

Mosure, D.J., Berman, S., Kleinbaum, D. & Halloran, M.E. (1996). 'Predictors of *Chlamydia trachomatis* infection among female adolescents: a longitudinal analysis'. American Journal of Epidemiology. 144, (10), p.997-1003.

Mosure, D.J., Berman, S., Fine, D., DeLisle, S, Cates, W. Jr. & Boring, J.R. 3rd. (1997). 'Genital chlamydia infections in sexually active female adolescents: do we really need to screen everyone?'. Journal of Adolescent Health. 20, (1), p.6-13.

Mosure, D.J., Berman, S., Dicker, L.W., Levine W. & the Region VIII and Region X Infertility Prevention Projects. (1998). 'A re-evaluation of selective screening criteria for women attending family planning clinics in the US'. in R.S. Stephens, G.I. Byrne, G. Christiansen, I.N. Clarke, J.T. Grayston, R.G. Rank, *et al.* (eds). Proceedings of the Ninth International Symposium on Human Chlamydial Infection. San Francisco: International Chlamydia Symposium, p.333-336.

Mountin, J.W. (1950). 'Multiple screening and specialized programmes'. Public Health Reports. 65, (42), p.1359-1368.

Ness, R.B., Goodman, M.T., Shen, C. & Brunham, R.C. (2003). 'Serologic evidence of past infection with *Chlamydia trachomatis*, in relation to ovarian cancer'. Journal of Infectious Diseases. 187, (7), p.1147-1152.

Newhall, W.J., Johnson, R.E., DeLisle, S., Fine, D., Hadgu, A., Matsuda, B., Osmond, D., Campbell, J. & Stamm, W.E. (1999). 'Head-to-head evaluation of five chlamydia tests relative to a quality-assured culture standard'. Journal of Clinical Microbiology. 37, (3), p.681-685.

Novak, D.P., Edman, A-C., Jonsson, M. & Karlsson, R.B. (2003). 'The internet, a simple and convenient tool in *Chlamydia trachomatis* screening of young people'. European Surveillance. 8, (9), p.171-176.

Oakeshott, P., Hay, P. & Pakianathan, M. (2004). 'Chlamydia screening in primary care'. British Journal of General Practice. 54, (504), p.491-493.

Office of National Statistics. (2000). Population trends. National Statistics 101 [Autumn 2000]. London: Her Majesty's Stationery Office.

Oh, M.K., Cloud, G.A., Wallace, L.S., Reynolds, J., Sturdevant, M. & Feinstein, R.A. (1994). 'Sexual behavior and sexually transmitted diseases among male adolescents in detention'. Sexually Transmitted Diseases. 21, (3), p.127-132.

Oh, M.K., Cloud, G.A., Fleenor, M., Sturdevant, M.S., Nesmith, J.D. & Feinstein, R.A. (1996). 'Risk for gonococcal and chlamydial cervicitis in adolescent females: incidence and recurrence in a prospective cohort study'. Journal of Adolescent Health. 18, (4), p.270-275.

Orr, P., Sherman, E., Blanchard, J., Fast, M., Hammond, G. & Brunham, R. (1994). 'Epidemiology of infection due to *Chlamydia trachomatis* in Manitoba, Canada'. Clinical Infectious Diseases. 19, (5), p.876-883.

Ostergaard, L., Andersen, B., Moeller, J.K. & Olesen, F. (2000). 'Home sampling versus conventional swab samples for screening of *Chlamydia trachomatis* in women: a cluster-randomized 1-year follow-up study'. Clinical Infectious Diseases. 31, (4), p.951-957.

Ostergaarad, L. (2002). 'Microbiological aspects of the diagnosis of *Chlamydia trachomatis*'. Best Practices Research in Clinical Obstetrics and Gynaecology. 16, (6), p.789-799.

Paavonen, J., Puolakkainen, M., Paukku, M. & Sintonen, H. (1998). 'Cost-benefit analysis of first-void urine *Chlamydia trachomatis* screening program'. Obstetrics and Gynecology. 92, (2), p.292-298.

Paavonen, J., Karunakaran, K.P., Noguchi, Y., Antilla, T., Bloigu, A., Dillner, J., Hallmans, G., Hakulinen, T., Jellum, E., Koskela, P., Lehtinen, M., Thoresen, S., Lam, H., Shen, C. & Brunham, R.C. (2003). 'Serum antibody resopnse to the heat shock protein 60 of *Chlamydia trachomatis* in women in with developing cervical cancer'. American Journal of Obstetrics and Gynecology. 189, (5), p.1287-1292.

Parish, W.L., Laumann, E.O., Cohen, M.S., Pan, S., Zheng, H., Hoffman, I., Wang, T. & Hang Ng, K. (2003). 'Population-based study of chlamydial infection in China'. Journal of the American Medical Association. 289, (10), p.1265-1273.

Patton, D.L., Wolner-Hanssen, P., Cosgrove, S.J. & Holmes, K.K. (1990). 'The effects of *Chlamydia trachomatis* on the female reproductive tract of the Macaca nemestrina after a single tubal challenge following repeated cervical inoculations'. Obstetrics and Gynecology. 76, (4), p.643-650.

Paukku, M., Kilpikari, R., Puolakkainen, M., Okansen, H., Apter, D. & Paavonen, J. (2003). 'Criteria for selective screening for *Chlamydia trachomatis*'. Sexually Transmitted Diseases. 30, (2), p.120-123.

Peipert, J.F. (2003). 'Genital chlamydial infections'. New England Journal of Medicine. 349, (25), p.2424-2430.

Pimenta, J.M., Catchpole, M., Rogers, P.A., Perkins, E., Jackson, N., Carlisle, C., Randall, S., Hopwood, J., Hweitt, G., Underhill, G., Mallinson, H., McLean, L., Gleave, T., Tobin, J., Harindra, V. & Ghosh, A. (2003a). 'Opportunistic screening for genital chlamydial infection I: acceptability of urine testing in primary and secondary healthcare settings'. Sexually Transmitted Infections. 79, (1), p.16-21.

Pimenta, J.M., Catchpole, M., Rogers, P.A., Hopwood, J., Randall, S., Mallinson, H., Perkins, E., Jakcson, N., Carlisle, C., Hewitt, G., Underhill, G., Gleave, T., McLean, L., Ghosh, A., Tobin, J. & Harindra, V. (2003b). 'Opportunistic screening for genital chlamydial infection II: prevalence among healthcare attenders, outcome, and evaluation of positive cases'. Sexually Transmitted Infections. 79, (1), p.22-27.

Pollitt, R.J. (1999). 'Principles and performance: assessing the evidence'. Acta Paediatrics Supplement. 88, (432), p.110-114.

Rampen, F.H., Neumann, H.A. & Kiemeney, L.A. (1992). 'Fundamentals of skin cancer/melanoma screening campaigns'. Clinical Experimental Dermatology. 17, (5), p.307-312.

Richardson, E., Sellors, J.W., MacKinnon, S., Woodcox, V., Howard, H., Jang, D., Karwalajtys, T. & Chernesky, M.A. (2003). 'Prevalence of *Chlamydia trachomatis* infections and specimen collection preference among women, using self-collected vaginal swabs in community settings'. Sexually Transmitted Diseases. 30, (12), p.880-885.

Richey, C.M., MacAluso, M. & Hook, E.W. (1999). 'Determinants of reinfection with *Chlamydia trachomatis*'. Sexually Transmitted Diseases. 26, (1), p.4-11.

Roberts, T., Robinson, S., Barton, P., Bryan, S., McCarthy, A., Macleod, J., Egger, M. & Low, N. (2004). 'The correct approach to modelling and evaluating chlamydia screening'. Sexually Transmitted Infections. 80, (4), p.324-325.

Robertson, J.N., Ward, M.E., Conway, D. & Caul, E.O. (1987). 'Chlamydial and gonococcal antibodies in sera of infertile women with tubal obstruction'. Journal of Clinical Pathology. 40, (4), p.377-383.

Rompalo, A.M., Gaydos, C.A., Shah, N., Tennant, M., Crotchfelt, K.A., Madico, G., Quinn, T.C., Daniel, R., Shah, K.V., Gaydos, J.C. & McKee, K.T. Jr. (2001). 'Evaluation of use of a single intravaginal swab to detect multiple sexually transmitted infections in active-duty military women'. Clinical Infectious Diseases. 33, (9), 1455-1461.

Royal College of Obstetricians and Gynaecologists. (2000). The care of women requesting induced abortion. London: RCOG Press.

Schachter, J. (1999). 'We must be realistic in evaluating rapid diagnostic tests'. Sexually Transmitted Diseases. 26, (4), p.241-242.

Schachter, J. (2001). 'NAATs to diagnose *Chlamydia trachomatis* genital infection: a promise still unfulfilled'. Expert Reviews in Molecular Diagnostics. 1, (2), p.137-144.

Schachter, J., McCormack, W.M., Chernesky, M.A., Martin, D.H., Van Der Pol, B., Rice, P.A., Hook, E.W. 3rd., Stamm, W.E., Quinn, T.C. & Chow, J.M. (2003). 'Vaginal swabs are appropriate specimens for diagnosis of genital tract infection with *Chlamydia trachomatis*'. Journal of Clinical Microbiology. 41, (8), p.3784-3789.

Scholes, D., Stergachis, A., Heidrich, F.E., Andrilla, H., Holmes, K.K. & Stamm, W. (1996). 'Prevention of pelvic inflammatory disease by screening for cervical chlamydial infections'. New England Journal of Medicine. 334, (21), p.1362-1366.

Semeniuk, H., Zentner, A., Read, R. & Church, D. (2002). 'Evaluation of sequential testing strategies using non-amplified and amplified methods for detection of *Chlamydia trachomatis* in endocervical and urine specimens from women'. Diagnostic Microbiology of Infectious Disease. 42, (1), p.43-51.

Serlin, M., Shafer, M.A., Tebb, K., Gyamfi, A.A., Moncada, J., Schachter, J. & Wibbelsman, C. (2002). 'What sexually transmitted disease screening method does the adolescent prefer? Adolescents' attitudes toward first-void urine, self-collected vaginal swab, and pelvic examination'. Archives of Pediatric Adolescent Medicine. 156, (6), p.588-591.

Seymour, C.A., Thomason, M.J., Chalmers, R.A., Addison, G.M., Bain, M.D., Cockburn, F., Littlejohns, P., Lord, J. & Wilcox, A.H. (1997). 'Newborn screening for inborn errors of metabolism: a systematic review'. Health Technology Assessments. 1, (11), p.i-iv,1-95.

Shafer, M.A., Moncada, J., Boyer, C.B., Betsinger, K., Flinn, S.D. & Schachter, J. (2003). 'Comparing first-void urine specimens, self-collected vaginal swabs, and endocervical specimens to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by a nucleic acid amplification test'. Journal of Clinical Microbiology. 41, (9), p. 4395-4399.

Simms, I., Catchpole, M., Brugha, R., Rogers, P., Mallinson, H. & Nicoll, A. (1997). 'Epidemiology of genital *Chlamydia trachomatis* in England and Wales'. Genitourinary Medicine. 73, (2), p.122-126.

Simms, I., Hopwood, J., Mallinson, H., Rogers, P. & Webb, A. (2000). 'Changing screening strategies for genital chlamydia in family planning services: a good public health strategy?'. European Journal of Contraception and Reproductive Health Care. 5, (1), p.91-95.

Sipkin, D.L., Gillam, A. & Bisset Grady, L. (2003). 'Risk factors for *Chlamydia trachomatis* infection in a California collegiate population'. Journal of American Collegiate Health. 52, (2), p.65-71.

Skjeldestad, F.E., Nordbo, S.A. & Hadgu, A. (1997). 'Sentinel surveillance of *Chlamydia trachomatis* infection in women terminating pregnancy'. Genitourinary Medicine. 73, (1), p.29-32.

Smillie, W.G. (1952). 'Multiple screening'. American Journal of Public Health. 42, (3), p.255-258.

Stamm, W.E. (1999). '*Chlamydia trachomatis* infections of the adult'. in K.K. Holmes, P.F. Sparling, P.A. Mardh, S.M. Lemon, W.E. Stamm, P. Piot, *et al.* (eds). New York, NY: McGraw-Hill Health Professions Division, p.407-422.

Stamm, W.E. (2004). 'Chlamydia screening: expanding the scope'. Annals of Internal Medicine. 141, (7), p.570-572.

Stary, A., Najim, B. & Lee, H.H. (1997). 'Vulval swabs as alternative specimens for ligase chain reaction detection of genital chlamydial infection in women'. Journal of Clinical Microbiology. 35, (4), p.836-838.

Stary, A. (2002). '*Chlamydia trachomatis*: screening programmes and the nucleic acid amplification assays'. Clinical Dermatology. 20, (2), p.164-169.

Stephenson, J., Carder, C., Copas, A., Robinson, A., Ridgway, G. & Haines, A. (2000). 'Home screening for chlamydial infection: is it acceptable to young men and women?'. Sexually Transmitted Infections. 76, (1), p.25-27.

Sutton, T.L., Martinko, T., Hale, S. & Fairchok, M.P. (2003). 'Prevalence and high rate of asymptomatic infection of *Chlamydia trachomatis* in male college reserve officer training corps cadets'. Sexually Transmitted Diseases. 30, (12), p.901-904.

Sylvan, S.P.E., von Krogh, G., Tiveljung, A., Siwerth, B-M, Henriksson, L., Noren, L., Asp, A-K. & Grillner, L. (2002). 'Screening and genotyping of genital *Chlamydia trachomatis* in urine specimens from male and female clients of youth-health centers in Stockholm county'. Sexually Transmitted Diseases. 29, (7), p.379-386.

Tjiam, K.H., Zeilmaker, G.H., Alberda, A.T., van Heijst, B.Y., de Roo, J.C., Polak-Vogelzang, A.A., van Joost, T., Stolz, E. & Michel, M.F. (1985). 'Prevalence of antibodies to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in infertile women'. Genitourinary Medicine. 61, (3), p.175-178.

Townsend, J.R.P. & Turner, H.S. (2000). 'Analysing the effectiveness of chlamydia screening'. Journal of the Operational Research Society. 51, (7), p.812-824.

Turner, K.M., Garnett, G.P., Ghani, A.C., Sterne, J.A. & Low, N. (2004). 'Investigating ethnic inequalities in the incidence of sexually transmitted infections: mathematical modelling study'. Sexually Transmitted Infections. 80, (5), p.379-385.

United States Preventive Services Task Force. (2001). 'Screening for chlamydial infection: recommendations and rationale'. American Journal of Preventive Medicine. 20, (3 Suppl), p.90-94.

van Bergen, J., Gotz, H.H., Richardus, J.H., Hoebe, C.J., Broer, J. & Coenen, A.J. (2005). 'Prevalence of urogenital Chlamydia trachomatis increases significantly with level of urbaninsation and suggests targeted screening approaches: results from the first national population based study in the Netherlands.' Sexually Transmitted Infections. 81, (1), p.17-23.

van den Brule, A.J.C., Munk, C., Winther, J.F., Kruger Kjaer, S., Jorgensen, H.O., Meijer, C.J.L.M. & Morre, S.A. (2002). 'Prevalence and persistence of asymptomatic *Chlamydia trachomatis* infections in urine specimens from Danish male military recruits'. International Journal of STD & AIDS. 13, (Suppl 2), p.19-22.

van Valkengoed, I.G., Morre, S.A., van den Brule, A.J., Meijer, C.J., Bouter, L.M.& Boeke, A.J. (2004). 'Overestimation of complication rates in evaluations of *Chlamydia trachomatis* screening programmes – implications for cost-effectiveness analyses'. International Journal of Epidemiology. 33, (2), p.416-425.

Verhoeven, V., Avonts, D., Meheus, A., Gossens, H., Ieven, M., Chapelle, S., Lammens, C. & van Royen, P. (2003). 'Chlamydial infection: an accurate model for opportunistic screening in general practice'. Sexually Transmitted Infections. 79, (5), p.313-317.

Verkooyen, R.P., Peeters, M.F., van Rijsoort-Vos, J.H., van der Meijden, W.I. & Mouton, J.W. (2002). 'Sensitivity and specificity of three new commercially available *Chlamydia trachomatis* tests'. International Journal of STD & AIDS. 13, (Suppl 2), p.23-25.

Verkooyen, R.P., Noordhoek, G.T., Klapper, P.E., Reid, J., Schirm, J., Cleator, G.M., Ieven, M. & Hoddevik, G. (2003). 'Reliability of nucleic acid amplification methods for detection of *Chlamydia trachomatis* in urine: results of the first international collaborative quality control study among 96 laboratories'. Journal of Clinical Microbiology. 41, (7), p.3013-3016.

Ward, H. & Miller, R. (2004). 'Brief encounters'. Sexually Transmitted Infections. 80, (5), p.329.

Washington, A.E., Arno, P.S. & Brooks, M.A. (1986). 'The economic cost of pelvic inflammatory disease'. Journal of the American Medical Association. 255, (13), p.1735-1738.

Watson, E.J., Templeton, A., Russell, I., Paavonen, J., Mardh, P-A., Stary, A. & Stray-Pedersen, B. (2002). 'The accuracy and efficacy of screening tests for *Chlamydia trachomatis*: a systematic review'. Journal of Medical Microbiology. 51, (12), p.1021-1031.

Welte, R., Kretzschmar, M., Leidl, R., van den Hoek, A., Jager, J.C. & Postma, M.J. (2000). 'Cost-effectiveness of screening programs for *Chlamydia trachomatis*— a population-based dynamic approach'. Sexually Transmitted Diseases. 27, (9), p.518-529.

Westh, H. & Kolmos, H.J. (2003). 'Large-scale testing of women in Copenhagen has not reduced the prevalence of *Chlamydia trachomatis* infections'. Clinical Microbiology Infections. 9, (7), p.619-624.

Westrom, L., Joesoef, R., Reynolds, G., Hagdu, A. & Thompson, S.E. (1992). 'Pelvic inflammatory disease and fertility: a cohort study of 1844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results'. Sexually Transmitted Diseases. 19, (4), p.185-192.

Whittington, W.L.H., Kent, C., Kissinger, P., Oh, K.M., Fortenberry, J.D., Hillis, S.E., Litchfield, B., Bolan, G.A., St Louis, M.E., Farley, T.A. & Handsfield, H.H. (2001). 'Determinants of persistent and recurrent *Chlamydia trachomatis* infection in young women'. Sexually Transmitted Diseases. 28, (2), p.117-123.

Williams, H., Tabrizi, S.N., Lee, W., Kovnes, G.T. & Garland, S. (2003). 'Adolescence and other risk factors for *Chlamydia trachomatis* genitourinary infection in women in Melbourne, Australia'. Sexually Transmitted Infections. 79, (1), p.31-34.

Wilson, J.M.G. & Jungner, G. (1968). Principals and practice of screening for disease. Geneva: World Health Organization.

Wilson, J.S., Honey, E., Templeton, A., Paavonen, J., Mardh, P-A., Stary, A. & Stray-Pedersen, B. (2002). 'A systematic review of the prevalence of *Chlamydia trachomatis* among European women'. Human Reproduction Update. 8, (4), p.385-394.

Zenilman, J.M., Miller, W.C., Gaydos, C., Rogers, S.M. & Turner, C.F. (2003). 'LCR testing for gonorrhoea and chlamydia in population surveys and other screenings of low prevalence populations: coping with decreased positive predictive value'. Sexually Transmitted Infections. 79, (2), p.94-97.

Appendix 2. Full publications of work included in the context statement

Brown, A.E., Sadler, K.E., Tomkins, S.E., McGarrigle, C.A., LaMontagne, D.S., Goldberg, D., Tookey, P., Smyth, B., Thomas, D., Murphy, G., Parry, J.V., Evans, B., Gill, O.N., Ncube, F. & Fenton, K.A. (2004). 'Recent trends in HIV and other STIs in the United Kingdom: data to the end of 2002'. Sexually Transmitted Infections. 80, (3), p.159-166.

LaMontagne, D.S., Fine, D.N. & Marrazzo, J.M. (2003). '*Chlamydia trachomatis* infection in asymptomatic men'. American Journal of Preventive Medicine. 24, (1), p.36-42.

LaMontagne, D.S., Fenton, K.A., Randall, S., Anderson, S. & Carter, P. (2004b). 'Establishing the national chlamydia screening programme in England: results from the first full year of screening'. Sexually Transmitted Infections. 80, (5), p.335-341.

LaMontagne, D.S., Patrick, L.E., Fine, D.N. & Marrazzo, J.M. (2004a). 'Re-evaluating selective screening criteria for chlamydial infection among women in the U.S. Pacific Northwest'. Sexually Transmitted Diseases. 31, (5), p.283-289.

LaMontagne, D.S., Fenton, K.A., Pimenta, J.M., Catchpole, M., Rogers, P.A., Randall, S., Hewitt, W.G., Mallinson, H., Underhill, G.S., McLean, L., Gleave, T., Harindra, V., Ghosh, A.K. & and Tobin, J.M. (2005). 'Using chlamydia positivity to estimate prevalence: evidence from the chlamydia screening pilot in England'. International Journal of STD and AIDS. 16, (4), p.323-327.

Adams, E.J., LaMontagne, D.S., Johnston, A.R., Pimenta, J.M., Fenton, K.A. & Edmunds, W.J. (2004b). 'Modelling the health care costs of an opportunistic chlamydia screening programme'. Sexually Transmitted Infections. 80, (5), p.363-370.

LaMontagne, D.S., Pimenta, J.M., Fenton, K.A., Mallinson, H. & Hopwood, J. (2004c). 'Management of genital chlamydial infections at termination of pregnancy services in England and Wales – where are we now?'. BJOG: an International Journal of Obstetrics and Gynaecology. 111, (12), p.1408-1412.

EPIDEMIOLOGICAL REVIEW

Recent trends in HIV and other STIs in the United Kingdom: data to the end of 2002

A E Brown, K E Sadler, S E Tomkins, C A McGarrigle, D S LaMontagne, D Goldberg, P A Tookey, B Smyth, D Thomas, G Murphy, J V Parry, B G Evans, O N Gill, F Ncube, K A Fenton

Sex Transm Infect 2004;**80**:159–166. doi: 10.1136/sti.2004.009571

Sexual health in the United Kingdom has deteriorated in recent years with further increases in HIV and other sexually transmitted infections (STIs) reported in 2002. This paper describes results from the available surveillance data in the United Kingdom from the Health Protection Agency and its national collaborators. The data sources range from voluntary reports of HIV/AIDS from clinicians, CD4 cell count monitoring, a national census of individuals living with HIV, and the Unlinked Anonymous Programme, to statutory reports of STIs from genitourinary medicine (GUM) clinics and enhanced STI surveillance systems. In 2002, an estimated 49 500 adults aged over 15 years were living with HIV in the United Kingdom, of whom 31% were unaware of their infection. Diagnoses of new HIV infections have doubled from 1997 to 2002, mainly driven by heterosexuals who acquired their infection abroad. HIV transmission also continues within the United Kingdom, particularly among homo/bisexual men who, in 2002, accounted for 80% of all newly diagnosed HIV infections acquired in the United Kingdom. New diagnoses of syphilis have increased eightfold, and diagnoses of chlamydia and gonorrhoea have doubled from 1997 to 2002 overall; STI rates disproportionately affect homo/bisexual men and young people. Effective surveillance is essential in the provision of timely information on the changing epidemiology of HIV and other STIs; this information is necessary for the targeting of prevention efforts and through providing baseline information against which progress towards targets can be monitored.

Sexual health in the United Kingdom has deteriorated in recent years.[1 2] Increases in HIV and other sexually transmitted infections (STIs) have placed enormous pressure on existing sexual health services.[3] Consequent delays in accessing diagnosis and care may in turn be facilitating infection transmission. Since 2001, a range of new initiatives aimed at improving sexual health have been established in the United Kingdom. In England, the implementation of the 10 year National Strategy for Sexual Health and HIV [4] has seen the appointment of local sexual health leads in primary care trusts (PCTs) and the Independent Advisory Group on Sexual Health[5]; greater investment in genitourinary medicine (GUM) clinics, and phased implementation of prevention interventions, such as the National Chlamydia Screening Programme, aimed at specific population risk groups. There have been similar strategies in other UK countries (Wales,[6] Scotland,[7] and Northern Ireland).[8] The Health Select Committee report on Sexual Health,[9] the All Party Parliamentary Group on AIDS report on Migration and HIV,[10] and most recently the government's response to the Health Select Committee's report on sexual health[11] have all drawn attention to the need for greater political will and investment in tackling HIV and STIs in the United Kingdom and globally.

Surveillance data have a key role in such strategies. The collection and analysis of data, in conjunction with the monitoring of trends with timely feedback provides information for the implementation and evaluation of these initiatives. Specifically, by highlighting where prevention efforts should be targeted and through providing baseline information against which progress towards targets can be monitored.

The immediate public health challenges facing sexual health in the United Kingdom include increasing incidence and prevalence of HIV and STIs; rising costs of HIV related care; variation in disease determinants and distribution; and the associated long term morbidity and mortality of these conditions. This paper summarises recent trends in the UK surveillance data for HIV and other STIs up until the end of 2002.[12]

DATA SOURCES

In the United Kingdom, the majority of STIs, including HIV, are diagnosed and treated in GUM clinics which form part of the National Health Service. Although diagnoses of many STIs (particularly chlamydia) occur in primary care and other community settings,[13] only GUM clinics have statutory reporting of STIs to the Health Protection Agency and its collaborators by clinicians. The detailed methods of the HIV and STI surveillance systems in the United Kingdom have been described elsewhere[12] and are briefly summarised here.

HIV/AIDS reporting

New diagnoses of HIV infections, AIDS cases, and deaths[14] (HIV/AIDS reporting) are reported by laboratories and clinicians through voluntary reporting systems. The annual Survey of Prevalent HIV Infections Diagnosed (SOPHID)[15] provides a census of the number of individuals

See end of article for authors' affiliations

Correspondence to: Alison Brown, HIV and STI Department, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK; alison.brown@hpa.org.uk

Accepted for publication 2 April 2004

living with diagnosed HIV infection and receiving care in England, Wales, and Northern Ireland. Longitudinal data on CD4 T lymphocytes[16] (CD4 surveillance) are reported from laboratories in England, Wales and Scotland and are used to *monitor trends in immunosuppression associated with HIV* infection. In Scotland, these data are used to gauge the number of people in specialist HIV care.

Unlinked anonymous HIV surveys

The unlinked anonymous (UA) HIV surveys[17] measure the prevalence of HIV, including undiagnosed HIV infections, in selected subgroups of the population. The unlinked anonymous survey of GUM clinic attendees (UA GUM survey) measures HIV prevalence in a high risk population (attendees of sentinel GUM clinics in the United Kingdom).[18] In *England, Wales, and Northern Ireland the incidence of HIV* infection in homo/bisexual men included in the UA GUM survey has been determined by application of the Serological Testing Algorithm for Recent HIV Seroconversion (STARHS).[19]

Prevalence in the general population is measured by surveys of pregnant women (*UA* pregnant women surveys—pregnant women attending antenatal care and women giving birth in England and Scotland). Live births to diagnosed HIV infected women in the United Kingdom are reported to the National Study of HIV in Pregnancy and Childhood.[20] These reports are aligned with the overall prevalence estimates for HIV in pregnant women by geographical area, to produce estimates of the proportion of women giving birth who were diagnosed before antenatal attendances, diagnosed through antenatal testing, and who remained undiagnosed at delivery.[21]

STI surveillance

Statutory KC60 returns from all GUM clinics[12] in England, Wales, and Northern Ireland provide aggregate data on the total episodes of diagnosed STIs by sex and age group (and sexual orientation for selected conditions). The ISD(D)5 returns system provides disaggregate data on all STI diagnoses in GUM clinics in Scotland.[12] NHS laboratories throughout the United Kingdom provide voluntary electronic disaggregate reporting on laboratory diagnoses of selected STIs with age and sex information. Enhanced Syphilis Surveillance (ESS) collects further demographic and risk factor data in the United Kingdom, and is designed to improve interpretation of the incidence and distribution of infectious syphilis.[22] The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) is a sentinel surveillance system for monitoring gonococcal antimicrobial resistance and collects detailed behavioural information on diagnoses of gonorrhoea in England.[23]

Related surveillance techniques

Estimates of the total number of HIV infected people in the United Kingdom[24] were calculated by combining data from SOPHID (for diagnosed HIV infections) and the unlinked anonymous surveys (for undiagnosed HIV infections), with estimates of the size of the population in various exposure categories derived from the National Survey of Sexual Attitudes and Lifestyles (Natsal 2000),[25] and census 2001 *population estimates (Office for National Statistics).*

Annual rates (cases/population) of diagnoses of STIs were calculated per 100 000 people. The 2002 rates for all regions and countries in the United Kingdom were calculated by dividing the number of cases reported from GUM clinics in each area in 2002 by the mid-2002 population estimates from the *Office for National Statistics (for homo/bisexual men* population estimates were derived from Natsal 2000[25]). Descriptive epidemiology is the focus of the paper, but hypothesis tests have been used to supplement the data where appropriate using Stata 7 (StataCorp, 2001).

Previously undiagnosed HIV infection

This includes both HIV infected individuals who were *diagnosed with HIV at the episode of clinical care, and* individuals who left clinical care remaining unaware of their infection, but excludes individuals whose HIV infection was diagnosed before the episode of clinical care

OVERALL HIV/STI SURVEILLANCE TRENDS

Estimates of the total prevalent infections indicate that at the *end of 2002, 49 500 adults aged over 15 were living with HIV*

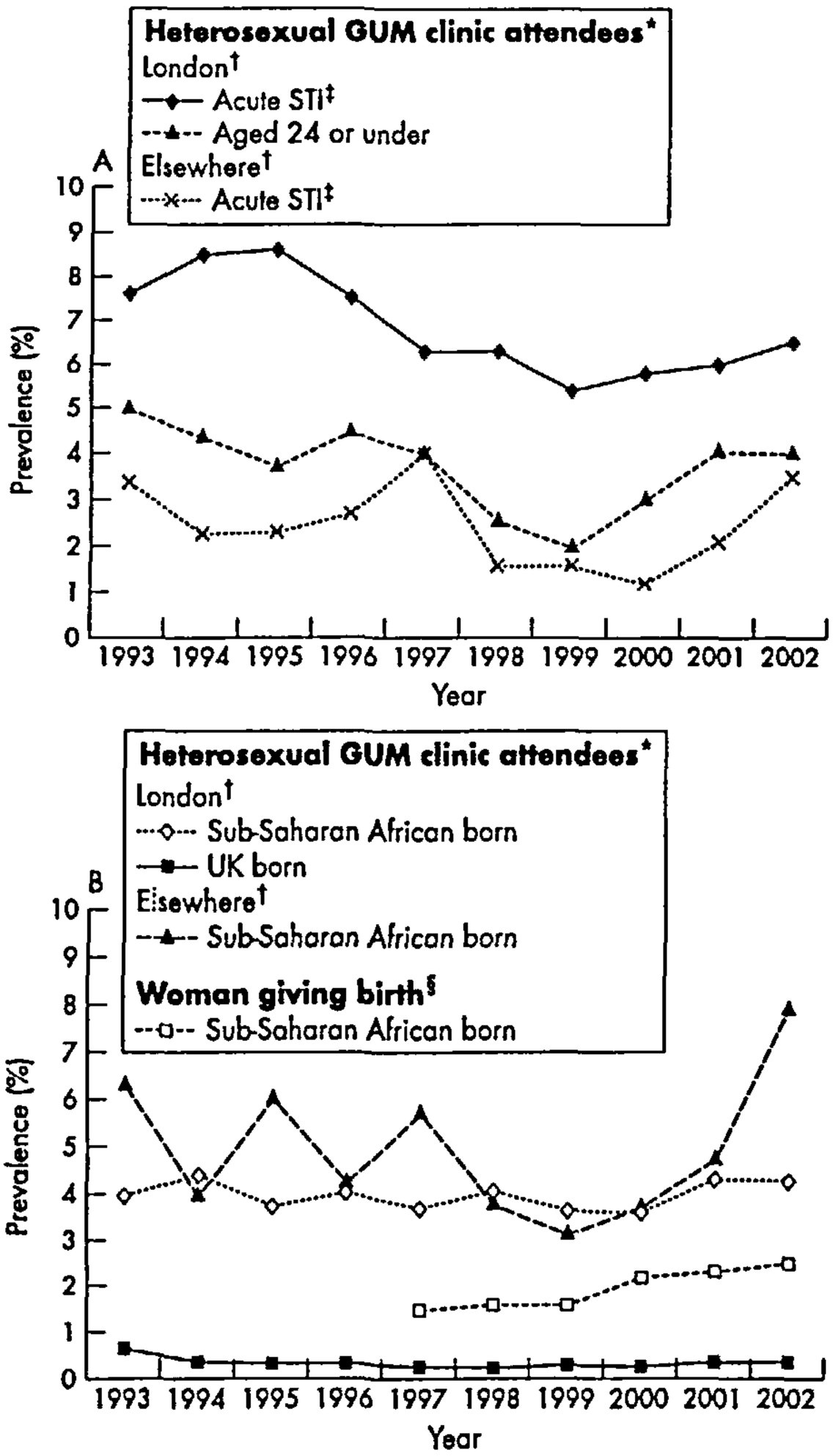

Figure 1 Prevalence of previously undiagnosed HIV infection in England, Wales, and Northern Ireland, 1993–2002. (A) Previously undiagnosed* HIV infection in homo/bisexual men† by clinical presentation and age group. (B) Previously undiagnosed* HIV infection in heterosexuals† and overall HIV prevalence in women giving birth. (*Excludes HIV infected attendees who were previously diagnosed.†Attendees at 15 GUM clinics in England, Wales, and Northern Ireland (seven in London, eight elsewhere). ‡Acute STI is defined as presenting with one of the following diagnoses: infectious syphilis, gonorrhoea, chancroid/donovanosis/LGV, chlamydia, NSU, trichomoniasis, scabies/pediculosis, HSV/HPV first attack or molluscum contagiosum. §Through unlinked anonymous testing of neonatal dried blood spots.) Data source: Unlinked Anonymous Programme.

Table 1 Subcategory of HIV infections diagnosed in the United Kingdom that were probably acquired heterosexually, 1992–2002

Heterosexual subcategory	1992 or earlier	1993	1994	1995	1996	1997	1998	1999	2000	2001*	2002*
Exposure to "high risk" partner(s) infected through:											
Male homosexual intercourse	109	24	21	12	11	10	11	12	13	23	17
Injecting drug use	199	37	31	41	33	49	48	23	22	36	16
Blood/blood products	75	5	2	4	9	6	4	5	2	4	3
Exposure to presumed heterosexually infected partner(s):											
Exposure abroad											
in Africa	1938	506	534	559	549	642	745	994	1478	2151	2338
in Latin America/Caribbean	62	24	27	14	25	28	32	62	67	82	108
in Asia	66	28	18	39	44	53	78	76	110	97	95
in North America	56	16	9	8	8	10	15	7	6	9	4
in Europe	127	38	36	42	42	50	42	49	46	46	41
in Australasia	6	2	0	2	1	2	4	6	2	5	2
in country(ies) not known	24	0	0	2	7	3	17	0	2	1	1
Exposure in the UK to partner(s) presumed infected											
outside Europe	91	17	38	48	42	71	81	90	127	155	153
within Europe	108	42	44	38	29	39	41	48	47	51	35
in country(ies) not known	152	28	30	32	28	31	25	30	27	56	87
Partner(s) exposure category undetermined:											
Investigation continuing/closed	24	2	6	10	7	11	17	25	32	113	252
Total	3037	769	796	851	835	1005	1160	1427	1981	2829	3152

*Numbers for recent years will rise as further reports are received. The table will include some records of (a) the same individuals, which are unmatchable because of differences in the information supplied and (b) individuals who left the United Kingdom at some date after diagnosis.
Data source: HIV/AIDS Reports. Reports received by the end of June 2003.

in the United Kingdom, of whom 15 200 (31%) were unaware of their infection. There were 5542 new HIV diagnoses reported for 2002: double the 2735 diagnoses in 1997.

At the end of 2002, overall HIV prevalence among homo/bisexual men in the United Kingdom was estimated at 7%, with estimates of total prevalent infections indicating that 22 600 homo/bisexual men were infected with HIV, of whom 5500 (24%) were unaware of their infection. Of the newly diagnosed HIV infections that were acquired in the United Kingdom, 80% (1500/1850) were among homo/bisexual men. The UA GUM survey found 4% (27/672) of homo/bisexual men aged under 25 in London had a previously undiagnosed HIV infection in 2002, indicating continuing transmission in this population (fig 1A). Annual incidence in GUM attendees, measured using STARHS, rose to approximately 3.5% in 2002.[26]

However, the recent increases in reports of new HIV diagnoses have largely been driven by heterosexually acquired infections, which accounted for 57% (3152/5542) of all those reported in 2002. Of these infections, three quarters (2338/3152) were probably acquired in Africa (table 1). Estimates of the total prevalent infections indicate that by the end of 2002, 15 400 African heterosexuals aged over 15 were living with HIV in the United Kingdom, of whom 4800 (31%) were undiagnosed.

In 2002, one third (1850/5542) of new HIV diagnoses were probably acquired in the United Kingdom. Although 80% (1500) of these infections were diagnosed in homo/bisexual men, since 1997 there has been a steady increase in the number of diagnoses of heterosexually acquired HIV infection in the United Kingdom. In 2002, 275 such HIV infections were diagnosed compared to 141 in 1997 (table 1); 56% (153/275) of these diagnoses were acquired through partners who were probably infected outside Europe. In England, Wales, and Northern Ireland, although remaining low, the prevalence of previously undiagnosed HIV infection rose significantly among UK born heterosexual males from 0.12% (30/24 465) to 0.3% (72/24 040) between 1997 and 2002 ($p<0.0001$); prevalence in UK born women was unchanged.

Major acute STI diagnoses reported through KC60 returns have continued their rising trend since the mid-1990s. From 1997 to 2002, there was a 103% increase to 82 206 chlamydia diagnoses (rates were 138/100 000 in males and 167/100 000 in females); a 97% increase to 24 958 gonorrhoea diagnoses (males: 66/100 000, females: 167/100 000); a 716% increase to 1232 syphilis diagnoses (males: 4/100 000, females: 0.5/100 000); a 9% increase to 69 449 genital warts diagnoses (males: 141/100 000, females: 118/100 000); and a 17% increase to 18 379 genital herpes diagnoses (males: 26/100 000, females: 42/100 000) in England, Wales, and Northern Ireland. Laboratory reports of STIs have also increased recently in Scotland; 12 392 chlamydia positive isolates were reported in 2002, a 16% increase on 2001 (10 636).

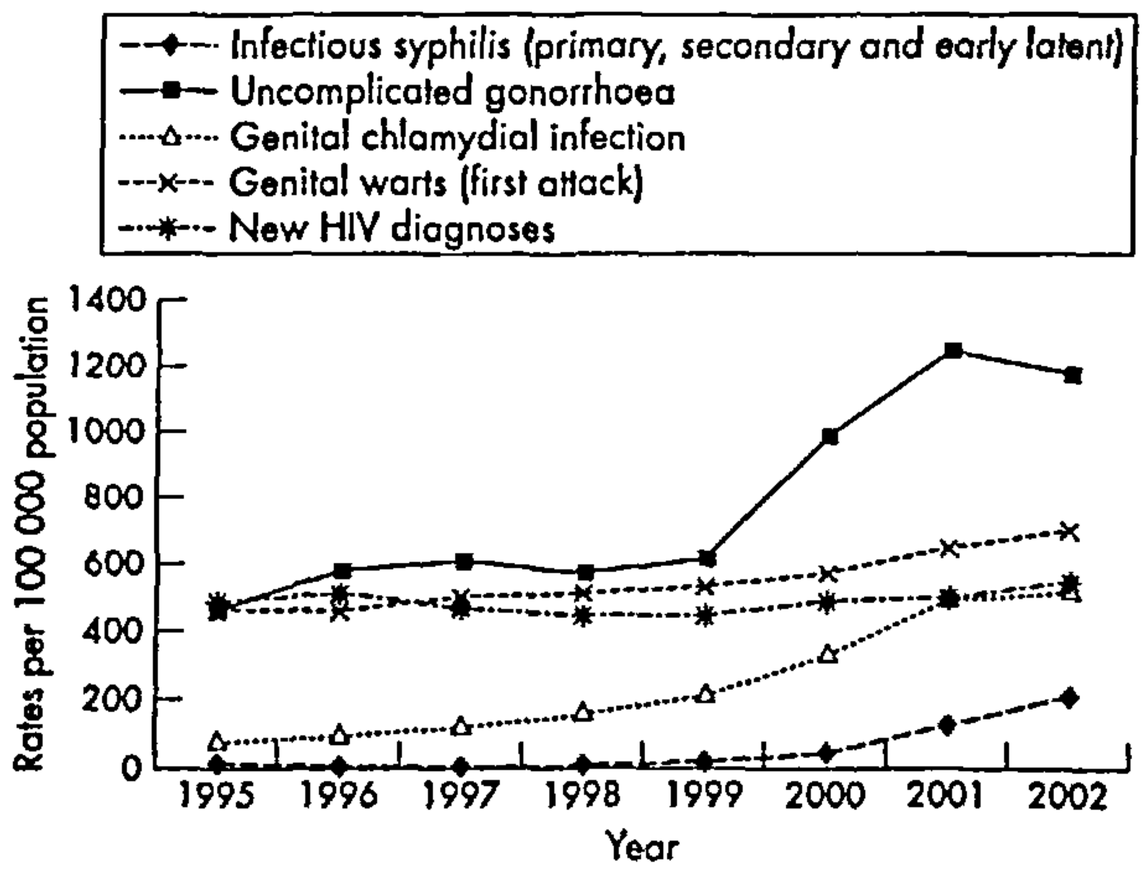

Figure 2 Trends in rates of major acute STIs in homo/bisexual men*, United Kingdom†, 1995–2002. (*Rates are based on an estimated population of 310 000 homo/bisexual men resident in England, Wales, and Scotland.[25] †2001 and 2002 data not available for Scotland for KC60 and ISD(D)5 data.) Data sources: KC60 statutory returns and ISD(D)5 data, and HIV/AIDS Reports, reports received by the end of June 2003.

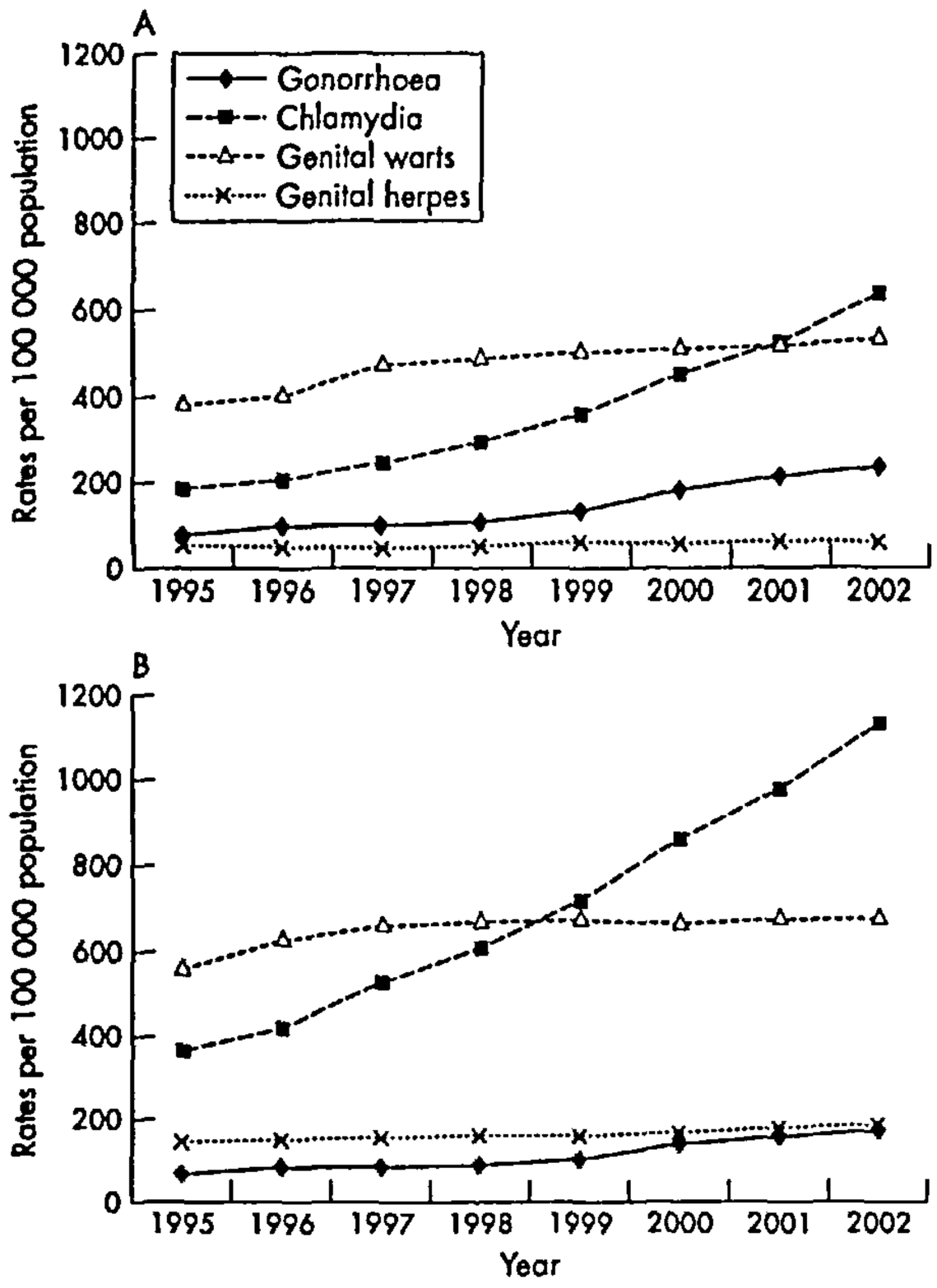

Figure 3 Trends in the rates of selected acute STIs in young females and males aged 16–24 in the United Kingdom*, 1995–2002. (A) Males. (B) Females. (*2001 and 2002 data not available for Scotland.) Data source: KC60 Statutory returns and ISD(D)5 data.

STIs have risen markedly among homo/bisexual men (fig 2). In this population, cases of gonorrhoea have almost doubled from 1842 in 1999 to 3363 in 2002, and cases of syphilis have increased from 52 to 607 over the same period; this latter rise is as a result of ongoing outbreaks in urban centres in the United Kingdom.[22]

Among heterosexuals, young people and black minority communities continue to be disproportionately represented in STI statistics. Rates of diagnoses of chlamydia in GUM clinics have increased by 215% in women aged 16–24, from 529/100 000 in 1997 to 1135/100 000 in 2002 in England, Wales, and Northern Ireland (fig 3). In the 2002 GRASP data collection, black ethnic groups, mainly black Caribbeans, accounted for 55% (516/936) and 44% (249/563) of gonococcal isolates collected from heterosexual males and females respectively (fig 4).

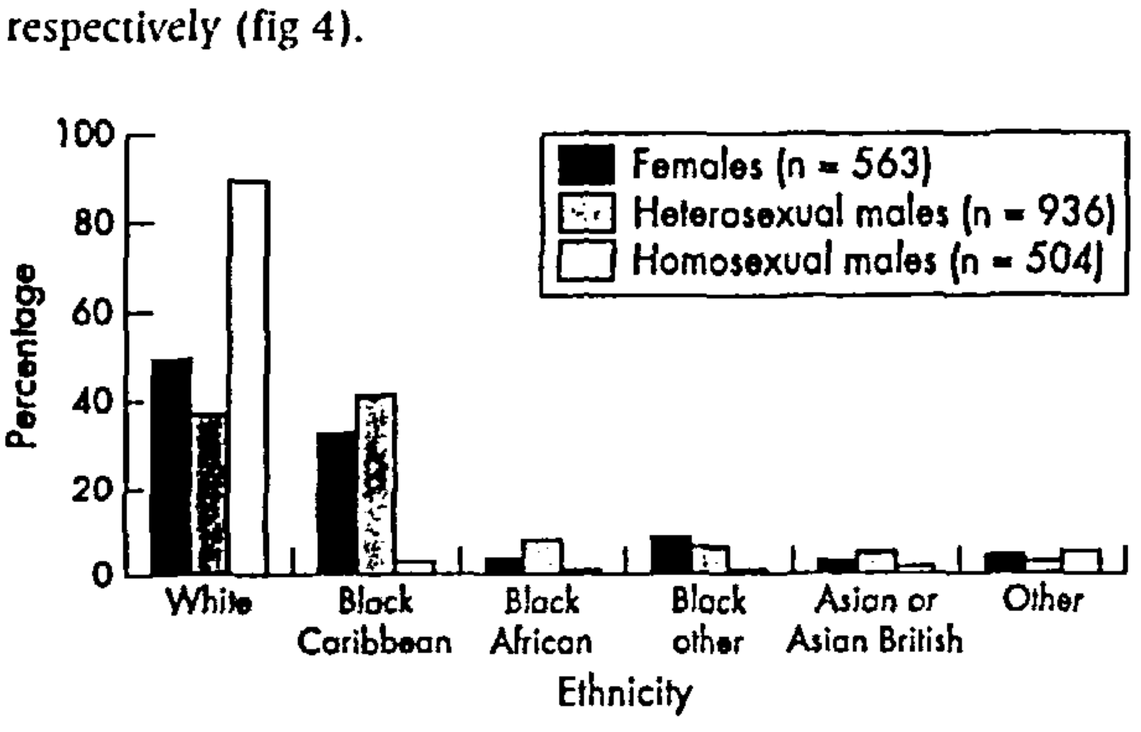

Figure 4 Proportion of new diagnoses of uncomplicated gonorrhoea by ethnicity, England and Wales, 2002. Data source: Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP).

POPULATION SUBGROUPS

Homo/bisexual men

Since HIV/AIDS reporting began in the United Kingdom in the early 1980s there have been 29 890 HIV diagnoses reported in homo/bisexual men, 12 284 of whom have progressed to AIDS, and 8761 of whom have died. HIV was the third most commonly diagnosed major STI in homo/bisexual men in 2002 (fig 2).

In 2002, the UA GUM survey found that 6.5% (97/1495) of previously undiagnosed HIV infected homo/bisexual men were co-infected with an acute STI; the equivalent figure in Scotland was 2.9% (12/416) and elsewhere in England, Wales, and Northern Ireland, 3.5% (25/719). Such individuals are of particular concern since they may be at higher risk of passing on their HIV infection to others. In London, 4% (27/672) of homo/bisexual men under 25 years attending GUM clinics had a previously undiagnosed HIV infection a clear indication of continuing HIV transmission at relatively high levels. Application of STARHS found that annual HIV incidence among homo/bisexual men rose to approximately 3.5% in 2002,[26] compared to 2–3% from 1995–2001,[27] although this difference is not statistically significant. The highest incidence was seen in those aged 35–44 (5.9%, 95% confidence intervals 3.7 to 8.8). This increasing trend occurred in a period when there were intensive health promotion campaigns and when 60–70% of diagnosed HIV infected homo/bisexual men were on antiretroviral therapy (ARV).

Since 1999, considerable increases in the rate of acute STI diagnoses in homo/bisexual men attending GUM clinics have been observed (fig 2). Rates of gonorrhoea diagnoses doubled between 1999 and 2001, from 612/100 000 to 1242/100 000. A slight decrease was observed overall in 2002, but there was no decrease in men aged 16–24 where rates increased from 648/100 000 in 1999 to 1194/100 000 in 2002. In 2002, rates of homosexually acquired infectious syphilis have shown a marked rise since 1999 (616%). This has been associated with a series of large localised outbreaks in Brighton, Manchester, Newcastle upon Tyne, London,[22] central Scotland,[28] and Northern Ireland.[29] Data collected between April 2001 and September 2003 from the ESS programme indicate that 46% of homo/bisexual men diagnosed with infectious syphilis in London were co-infected with HIV. Increases in genital chlamydia infections in homo/bisexual men were also observed in 2002, up 144% since 1999.

Factors influencing transmission

Behavioural surveillance data among homo/bisexual men in the United Kingdom have demonstrated increases in rates of unprotected anal intercourse (UAI), and specifically, UAI involving HIV discordant or unknown status partners.[30] Data from Natsal 2000[25] suggest that there have been increases in the prevalence of male homosexual behaviour in the general population, and increases in some high risk behaviours among homosexually active men.[31] The reasons for this rising risk are unclear. However, continued liberalisation of attitudes towards homosexuality,[32] and "safer sex" fatigue in the era of ARV,[33] coupled with expansions in opportunities which facilitate partner acquisition (for example, the internet, saunas)[34] may be contributing factors.

Young people

People aged 16–24 accounted for just over 10% (588/5542) of all reports of new HIV diagnoses in 2002; a proportion that has remained constant over time. Their risk exposure distribution was similar to that of people aged over 24. Heterosexual HIV acquisition accounted for 63% (370/588) of new HIV diagnoses in 2002 in those aged 16–24, with the

majority of individuals (65%, 242/370) probably infected in Africa.

Rates of STIs have risen markedly among young people (fig 3) and this population subgroup bear a disproportionate burden of STI diagnoses. In 2002, women aged 16–24 accounted for 72% (33 205/46 140) of all female chlamydia diagnoses, 66% (5031/7569) of gonorrhoea, 62% (50/137) of syphilis and 61% (19 792/32 544) of genital warts reported from GUM clinics in England, Wales, and Northern Ireland.

Rates of diagnoses from GUM clinics for chlamydia, gonorrhoea, and genital warts were highest among females aged 16–19 and males aged 20–24. The highest rates of chlamydial diagnoses were seen in women aged 16–19 and men aged 20–24 at 1209 and 842/100 000 respectively. These figures are likely to underestimate the total number of infections because most infections in women are asymptomatic, and thus care and treatment are not sought. Chlamydial infections diagnosed in primary care and other community settings[13] are not reported in the KC60 returns and also contribute to this underestimation. Of women diagnosed with gonorrhoea, 40% were under 20. In men, rates of gonorrhoea were highest in those aged 20–24 in 2002 (296/100 000), an increase of 231% since 1997. Similarly, rates of genital herpes simplex infection remain highest among males and females aged 20–24 (93/100 000 and 296/100 000 respectively). Unlike other bacterial STIs, rates of syphilis among young people remain low.

Factors influencing transmission

Young people are behaviourally more vulnerable to STI acquisition as they generally have higher numbers of sexual partners, more concurrent partnerships, and change partners more often than older age groups.[35] Although consistent and proper use of condoms reduces the risk of STI transmission and unintended pregnancy, many young people may not have developed the skills and confidence to implement this successfully.[36]

STI re-infection is a particular concern in this population. In a study of three GUM clinics,[37] young age was a key determinant of STI re-infection within a year of initial diagnosis. Studies in the United States have also found that re-infection rates are high among adolescents and young adults, particularly women,[38] including those aged under 15.[39]

Black and ethnic minority populations

The number of HIV infected black African adults born in the United Kingdom is increasing but currently remains low. It is estimated that in 2002, black African adults accounted for 63% (15 400) of the total of prevalent HIV infections in heterosexuals, and 51% (4800) of heterosexuals who are unaware of their HIV infection. In 2002, of the 12 203 HIV infected heterosexuals reported to SOPHID, 68% (8262) of those for whom ethnicity was reported were black African (a 330% increase since 1997), 4% (501) black Caribbean, and 21% (2580) white. The UA pregnant women surveys found an HIV prevalence of 2.5% (239/47 075) in women born in sub-Saharan Africa who gave birth in 2002. This compares with a prevalence of 0.03% (42/121 833) in their UK born counterparts (fig 1B). These data reflect the focus of the HIV pandemic in sub-Saharan African countries and the impact of population movement on the UK statistics.

Undiagnosed HIV infection continues to be a feature of the treatment histories of black heterosexuals. Among sub-Saharan born heterosexuals included in the UA GUM survey, the prevalence of previously undiagnosed HIV infection rose to 4.2% (159/3752) in London and 7.9% (60/757) outside London (fig 1B). The latter figure may be due to the recent dispersal to areas outside London of migrant populations originating from high HIV prevalence countries. In Scotland, the prevalence of previously undiagnosed HIV infection was 5.7% (9/157) in heterosexuals of African nationality, compared to 0.1% (13/133 314) in heterosexuals of British nationality.

STI diagnoses disproportionately fall on the United Kingdom's black minority populations.[40 41] In the 2002 GRASP[23] data collection (fig 4), black ethnic groups, mainly black Caribbean, accounted for 55% (516/936) and 44% (249/563) of gonococcal isolates in heterosexual males and females respectively. The ESS programme in London revealed that 48% (187/393) of heterosexual syphilis diagnoses were among black or black British ethnic groups.

Factors influencing transmission

Black and ethnic minority populations in the United Kingdom continue to have poor sexual health. However, few behavioural surveys give insight into sexual health among ethnic minority groups. Variations in the burden of STIs among these populations are known to be influenced by a number of behavioural and social factors.[42] Qualitative community based studies highlight variations in sexual socialisation, attitudes and community norms related to sexual behaviour; sex, religious beliefs, and degree of acculturation are all influential factors.[43] Although qualitative studies suggest that variations in high risk behaviour do exist across ethnic groups,[44 45] these alone cannot explain the observed disparities. Factors such as patterns of sexual mixing, differential access to curative services, and background disease prevalence in the communities concerned may also be contributing.[42 46] Data from population based surveys and mathematical modelling will be needed to further elucidate these associations.

HIV SCREENING AND TREATMENT

There has been some success in interventions aimed at reducing HIV transmission in the United Kingdom. Diagnosis at an earlier stage of HIV infection presents the opportunity for treatment to postpone further illness and to reduce viral load which, along with changes in sexual behaviour, may reduce the risk of onward HIV transmission.

The number of GUM clinic attendees accepting a voluntary confidential HIV test (VCT) can be measured through the UA GUM survey, which collects KC60 data in addition to limited demographic information. Voluntary confidential HIV testing (VCT) has increased in homo/bisexual men and heterosexuals respectively, from 45% (2724/6019) and 25% (16 886/66 880) in 1997, to 62% (4604/7372) and 54% (40 746/74 935) in 2002 in England, Wales, and Northern Ireland. From 2003, modified KC60 data will allow better monitoring of VCT uptake. In Scotland, data indicate that uptake of VCT has increased in homo/bisexual men and heterosexuals respectively, from 47% (454/959) and 23% (2624/11 223) in 1997, to 59% (761/1290) and 36% (5142/14 281) in 2002.

Similarly, over recent years, CD4 surveillance data show a recent trend towards earlier diagnosis for homo/bisexual men. Only 24% of homo/bisexual men had a CD4 cell count less than 200 cells $\times 10^6$/l at HIV diagnosis (an indicator of a "late diagnosis") in 2002 compared to 28% in 1997. In contrast, 43% of newly diagnosed heterosexuals had a "late diagnosis" in 2002. This may be because a high proportion of heterosexuals were infected, and previously lived abroad. Additionally, heterosexuals may perceive themselves to be at lower risk from HIV and may present for testing only when they become symptomatic.[47 48]

In England, the proportion of HIV infected pregnant women remaining undiagnosed by the time of delivery has declined since the introduction of the universal offer and recommendation of an HIV test as a routine part of antenatal care in 1999[49 50]; this policy has now been introduced elsewhere in the United Kingdom.

In 2002 there were an estimated 686 births to HIV positive women in England, Wales and Scotland, of whom at least 79% (539/686) were reported as diagnosed before delivery. Overall, HIV detection rates in 2002 are currently estimated at 75% (318/422) for London, 85% (199/234) elsewhere in England and Wales and 73% (22/30) in Scotland (fig 5). These minimum estimates are subject to reporting delay and are likely to rise as more diagnosed infections in pregnancies are reported.

These improved maternal HIV detection rates have reduced the proportion of exposed children who go on to acquire the infection vertically. In London, in 2002 (based on the current estimated detection rates), the estimated proportion of children exposed to HIV vertically who were themselves infected was 8% (35/422) compared with 19% (37/200) in 1997. In the rest of the United Kingdom this proportion decreased from 22% (25/113) in 1997 to 6% (16/264) in 2002.

A high proportion of HIV infected people who were eligible for ARV were on medication in 2002 in the United Kingdom. Of the 1708 homo/bisexual men with CD4 counts of 200 cells $\times 10^6$/l or less, 78% were on therapy; of the 2433 heterosexuals, 78% were on therapy; and of the 211 IDUs, 73% were on therapy (measured through SOPHID). Equivalent figures were higher for Scotland: 92% (72, p = 0.006), 94% (84, p = 0.0004), and 92% (98, p = 0.0002). However, in Scotland ARV therapy is measured through CD4 monitoring which is largely undertaken to assess a patients eligibility for ARV. These data confirm that exposure group does not affect the level of therapy uptake.

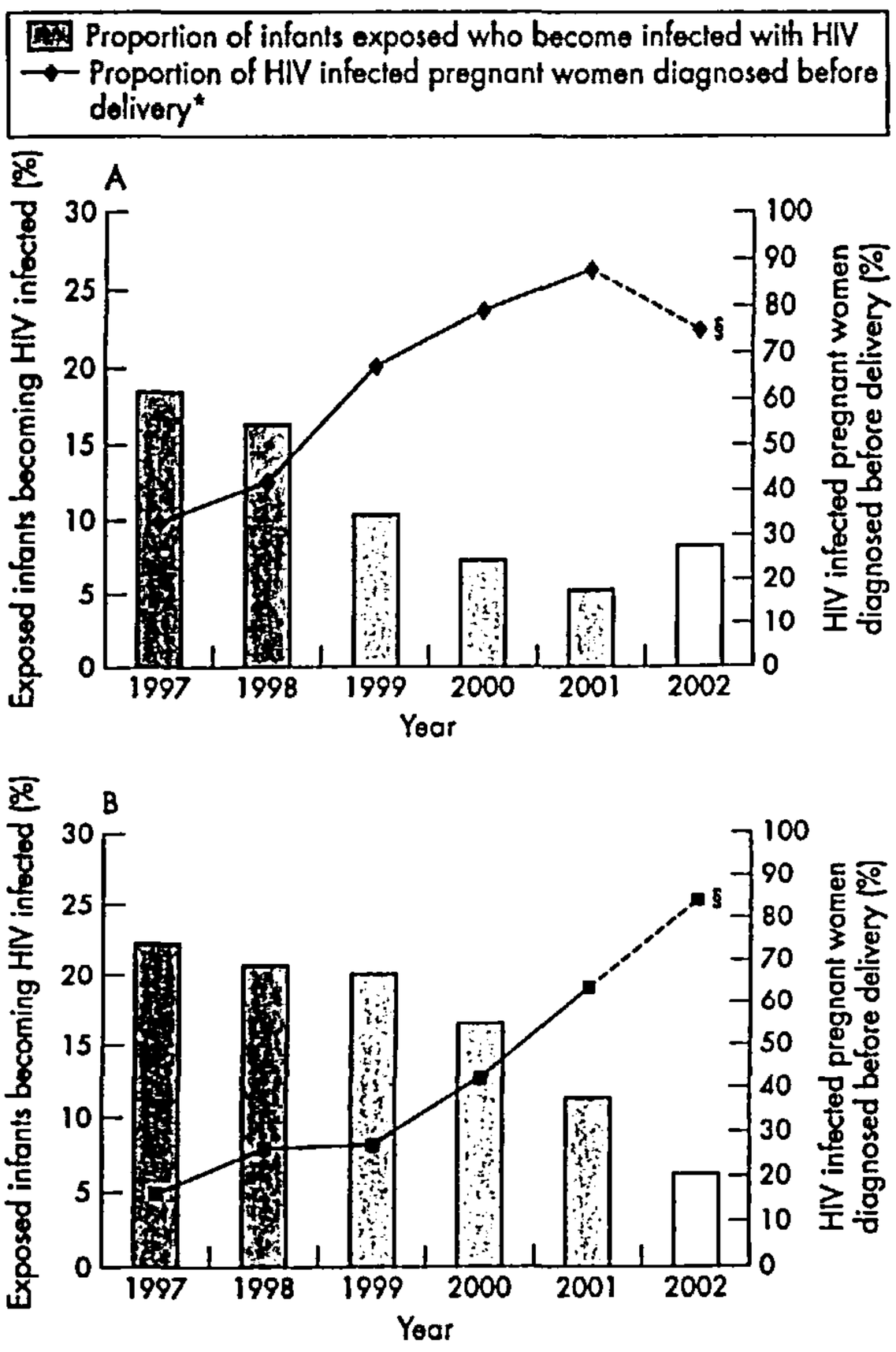

Figure 5 Estimated proportion of HIV infected women diagnosed before delivery* and of exposed children becoming infected with HIV†‡, 1997–2002. (A) London. (B) Outside London—England, Wales, and Scotland. (*Includes those previously diagnosed and those diagnosed through antenatal testing. †Assumes a vertical transmission rate of 26.5% in undiagnosed women and 2.2% in diagnosed women.[53] ‡These data contain reports received by the end of September 2003. §Data for 2002 should be considered preliminary minimum estimates, and as the number of reports rise, estimates of infants becoming HIV infected will fall.) Data source: Unlinked Anonymous Programme and the National Study of HIV in Pregnancy and Childhood (NSHPC).

DISCUSSION

The surveillance data confirm that HIV and other STIs have increased within the UK population. Population subgroups that have high rates of sexual partner change continue to have higher infection rates, in particular HIV and STIs among homo/bisexual men and STIs among young people. Black and ethnic minority populations (including subgroups born in high prevalence countries) are disproportionately affected by poor sexual health. There is some evidence of onward HIV transmission rising within the United Kingdom though as yet this is limited.

Health promotion campaigns, targeted HIV and chlamydia screening initiatives, and increased sensitivity of diagnostic tests may all have played a part in the rising number of HIV and STI diagnoses reported in 2002. The well documented pressure mounting upon GUM clinics[3] through increased numbers of high risk patients attending has undoubtedly contributed to the observed trends. Since KC60 returns data are aggregate, it is not possible to determine what proportion of attendees are re-attending for follow up and/or are becoming re-infected. A disaggregate STI surveillance system is currently under development and will help interpretation of future trends.

STI diagnoses are mainly reported through GUM clinics and voluntarily from NHS laboratories. The former misses cases diagnosed in other settings and the latter reports are incomplete. This combined with the requirement for data accuracy over data quantity may have led to a general underestimate of HIV and STI diagnoses in the United Kingdom.

Indications from Natsal 2000[25] of increasing high risk behaviour (including concurrent partnerships and higher rates of partner acquisition), the continuing immigration of heterosexuals from countries of high HIV prevalence, and the suggested rising of HIV incidence, undiagnosed HIV infection, and STI diagnoses in homo/bisexual men all indicate that sexual health is deteriorating and the documented increases are real.

Through national collaboration, high levels of data reporting, analysis and feedback performed in conjunction within a complementary set of UK surveillance systems, allow the data to be used as a powerful tool in providing information for action. The role of surveillance has been instrumental in the creation and monitoring of successful initiatives such as the introduction of the universal offer and recommendation of an HIV test in pregnant women.[49 50]

Our data confirm the need for national and local prioritisation of sexual health and HIV prevention activities. Interventions such as those outlined in the English Sexual Health and HIV Strategy[4] need to be implemented urgently. For homo/bisexual men this includes HIV/STI education, promotion of safer sex and HIV testing, and increasing the uptake of hepatitis B vaccination in GUM clinics. The strategy has also specifically identified young people as a priority group for action and the Department of Health is currently implementing a range of interventions including the National Chlamydia Screening Programme. The persistent ethnic disparities in sexual health outcomes deserve even greater attention, particularly with emerging evidence of increasing HIV transmission within the United Kingdom among black communities. The disaggregate STI surveillance system currently under development[51] will allow ethnic disparities

Key messages

- Prevalence of HIV infection in the United Kingdom is increasing; an estimated 49 500 adults aged over 15 were living with HIV in the United Kingdom in 2002, of whom 31% were unaware of their infection
- While many newly diagnosed heterosexual cases are thought to have acquired their infection overseas, there is evidence of continuing transmission of HIV in the United Kingdom, particularly among homo/bisexual men
- New diagnoses of major acute STIs have risen in the past 5 years, with rates highest in homo/bisexual men and young people
- Effective surveillance is essential to provide timely information on the changing epidemiology of HIV and other STIs in the United Kingdom

in sexual health to be monitored in the future and will facilitate the determination of where preventive efforts need to be targeted. In the meantime, key interventions for prioritisation include improving access to treatment and care services in hyperendemic areas; raising community HIV/STI awareness; and enhancing secondary prevention actives including partner notification.[42]

Elsewhere in the United Kingdom, health promotion campaigns aimed at high risk subgroups are being implemented and will undoubtedly require scaling up in the near future. In Wales, for example, the "Come Clean" multimedia campaign has been run by BBC Wales and the Welsh Assembly and is targeted at young people.[52] Effective secondary prevention activities are also needed to tackle the growing problem of STI re-infection and epidemiological synergy between STIs and HIV infection. Such initiatives need to be fully supported and sustained if further deterioration in the United Kingdom's sexual health is to be prevented. Finally, although the impact of these initiatives can only be recognised over many years it is important that medium and long term targets are set and progress monitored to ensure the most appropriate, cost effective, and efficient use of scarce resources.

Further information on HIV/STI surveillance trends can be found in a report published by the Health Protection Agency and others: Health Protection Agency, SCIEH, ISD, National Public Health Service for Wales, CDSC Northern Ireland and the UASSG. Renewing the focus. HIV and other Sexually Transmitted Infections in the United Kingdom in 2002. London: Health Protection Agency November 2003[12] (www.hpa.org.uk/infections/topics_az/hiv_and_sti/publications/annual2003/annual2003.pdf).

ACKNOWLEDGEMENTS

We extend our thanks to everybody who contributed to the writing of the annual report: *Renewing the Focus*: Tim Chadborn, Glenn Codere, Leah de Souza, Sarah Dougan, Gillian Elam, Josh Forde, John Harris, Vivian Hope, Alisha Johnston, Louise Logan, Catherine Lowndes, Neil MacDonald, Helen Munro, Bela Patel, Lara Payne, Brian Rice, Elizabeth Rudd, Ian Simms, and Katy Sinka.

We gratefully acknowledge the continuing collaboration of the Sexually Transmitted and Blood Borne Viruses Laboratory, Specialist and Reference Microbiology Division, Health Protection Agency, and of clinicians, microbiologists, immunologists, public health practitioners, occupational health doctors and nurses, and other colleagues who contribute to the surveillance of HIV and STIs in the United Kingdom.

We would like to thank our collaborating centres for HIV and AIDS surveillance in the UK: The Scottish Centre for Infection and Environmental Health; The Institute of Child Health (London); The UK Haemophilia Centres Doctors Organisation; members of the Scottish ISD(D)5 Collaborative Group; Collaborators on the Unlinked Anonymous Programme (a full list of collaborators available at www.hpa.org.uk/infections/topics_az/hiv_and_sti/hiv/epidemiology/ua.htm).

Finally, we thank Philip Mortimer for commenting on this paper and we are also grateful to colleagues at the UK Departments of Health both for funding specific surveys and for helpful comments on this paper at draft stage.

CONTRIBUTORS

AB, ST with KS, CM, SLM, and GM, analysed the data from the Unlinked Anonymous Surveys, HIV/AIDS reports, prevalence estimates and behavioural surveillance, STI surveillance, and STARHS respectively with support from BG, NG, FN, and KF; DG, DT, and BS analysed and are responsible for data from the Scottish Centre Infection and Environmental Health, the National Public Health Service for Wales, CDSC, and the Health Protection Agency, CDSC, Northern Ireland respectively; PT coordinates the National Study of HIV in Pregnancy and Childhood and collaborated with the analysis of the Unlinked Anonymous Pregnant Women Surveys; NG is the programme manager and is responsible for data from the Unlinked Anonymous Programme; BG is responsible for data from HIV/AIDS reports; and FN is responsible for data from the unlinked anonymous surveys of Pregnant Women. JP is responsible for laboratory aspects for the Unlinked Anonymous Surveys and assisted with the interpretation of data; all authors were involved in interpretation of the results and drafting the paper; AB undertook the main writing of the paper.

Authors' affiliations

A E Brown, K E Sadler, S E Tomkins, C A McGarrigle, D S LaMontagne, B G Evans, O N Gill, F Ncube, K A Fenton, *HIV and STI Department,* Health Protection Agency, Communicable Disease Surveillance Centre, UK
D Goldberg, The Scottish Centre for Infection and Environmental Health, UK
P A Tookey, Institute of Child Health (ICH), University College London, UK
B Smyth, Health Protection Agency, Communicable Disease Surveillance Centre (Northern Ireland), UK
D Thomas, National Public Health Service for Wales, Communicable Disease Surveillance Centre, UK
G Murphy, J V Parry, The Sexually Transmitted and Blood Borne Viruses Laboratory, Specialist and Reference Microbiology Division, Health Protection Agency, UK
K A Fenton, The Centre for Sexual Health and HIV Research, Department of Primary Care and Population Sciences, Royal Free and University College Medical School, London, UK

REFERENCES

1 **Nicoll A,** Hamers FF. Are trends in HIV, gonorrhoea and syphilis worsening in Western Europe? *BMJ* 2002;324:1324–7.
2 **Adler MW.** A survey of STI policies and progress in Europe. *Sex Transm Infect* 2003;79:171.
3 **Djuretic T,** Catchpole M, Bingham JS, *et al. Genitourinary medicine services in* the United Kingdom are failing to meet current demand. *Int J STD AIDS* 2001;12:571–2.
4 **Department of Health.** *The national strategy for sexual health and HIV implementation action plan.* London: Department of Health, 2002.
5 **Department of Health.** Press Release. Health minister announces group to *advise on sexual health. London: DoH, 6 March 2003. Available at* www.doh.gov.uk/sexualhealthandhiv/pdfs/press_release_6march2003.pdf
6 **The National Assembly for Wales.** *A strategic framework for promoting sexual health in Wales. Cardiff: National Assembly for Wales, The Health* Promotion Division, 2000.
7 **Scottish Executive.** *Enhancing sexual wellbeing in Scotland. A sexual health and relationship strategy. Edinburgh: Scottish Executive, 2003 October.*
8 **Department of Health, Social Services and Public Safety (DHSSPS).** *Sexual health promotion strategy and action plan consultation document, Northern Ireland. DHSSPS, 2003 December.*
9 **House of Commons Health Committee.** *Sexual health. Third report of session 2002–03.* London: Stationary Office, 11 June 2003.
10 **All-Party Parliamentary Group on AIDS Migration and HIV.** *Improving lives in Britain.* London: APPG-AIDS, 2003 July. Available at www.appgaids.org.uk/Publications/Migration%20and%20HIV%20Improving%20Lives.pdf

11 **Government response** to the Health Select Committee's Third Report of the Session 2002/03 on Sexual Health. London: HMSO, 2003. Available at www.doh.gov.uk/sexualhealthandhiv/pdfs/response_to_health_select_comm_three.pdf
12 **Health Protection Agency**, SCIEH, ISD, National Public Health Service for Wales, CDSC Northern Ireland and the UASSG. *Renewing the focus. HIV and other sexually transmitted infections in the United Kingdom in 2002.* London: Health Protection Agency, November, 2003.
13 **Fenton KA**, Korovessis C, Johnson AM, *et al.* Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet* 2001;358:1851–4.
14 **PHLS Communicable Disease Surveillance Centre**, ICH (London), SCIEH, HIV and AIDS in the UK. *An epidemiological review: 2000.* London: PHLS Communicable Disease Surveillance Centre, 2001.
15 **McHenry A**, Macdonald N, Sinka K, *et al.* National assessment of prevalence diagnosed HIV infections *Commun Dis Public Health* 2000;3:77–81.
16 **Gupta SB**, Dingley SD, Lamagni TL, *et al.* The national CD4 surveillance scheme for England and Wales. *Commun Dis Public Health* 2001;4:27–32.
17 **Nicoll A**, Gill ON, Peckham CS, *et al.* The public health applications of the unlinked anonymous seroprevalence monitoring programme for HIV in the United Kingdom. *Int J Epidemiol* 2000;29:1–10.
18 **Catchpole MA**, McGarrigle CA, Rogers PA, *et al.* Serosurveillance of prevalence of HIV infection in homosexual men with acute sexually transmitted infection. *BMJ* 2001;321:1318–20.
19 **Janssen RS**, Satten GA, Rawal BD, *et al.* New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA* 1998;280:42–8.
20 **Ades AF**, Davison CF, Holland FJ, *et al.* Vertically transmitted HIV infection in the British Isles. *BMJ* 1993;306:1296–99.
21 **Cliffe S**, Tookey PA, Nicoll A. Antenatal detection of HIV: national surveillance and unlinked anonymous survey. *BMJ* 2001;323:376–7.
22 **Doherty L**, Fenton KA, Jones J, *et al.* Syphilis: old problem, new strategy. *BMJ* 2002;325:153–6.
23 **Fenton KA**, Ison C, Johnson AP, *et al.* GRASP Collection. Ciprofloxacin resistence in Neisseria gonorrhoeae in England and Wales in 2002. *Lancet* 2003;362:495.
24 **Petruckevitch A**, Nicoll A, Johnson AM, *et al.* Direct estimates of prevalence HIV infection in adults in England and Wales for 1991 and 1993: an improved method. *Genitourin Med* 1997;73:348–54.
25 **Johnson AM**, Mercer CH, Erens B, *et al.* Sexual behaviour in Britain: partnerships, practices and HIV risk behaviours. *Lancet* 2001;358:1835–42.
26 **Murphy G**, Charlett A, Brown AE, *et al.* Is HIV incidence increasing in homo/bisexual men attending GUM clinics in England, Wales and Northern Ireland. *Commun Dis Public Health 2004;7:*11–14.
27 **Murphy G**, Charlett A, Jordan LF, *et al.* HIV incidence appears constant in men who have sex with men despite the widespread use of effective antiretroviral therapy *AIDS* 2004;18:265–72.
28 **Redman C.** Sharp increase in reports of infectious syphilis in Scotland in 2002 *Eurosurveillance* 2003;7:(5).
29 **Lynch A**, Smyth B. Syphilis outbreak in Northern Ireland. *Eurosurveillance* 2003;7:(24).
30 **Dodds J**, Mercey D. *Sexual health survey of gay men—London 2002: summary of results.* London: Royal Free and University College Medical School, 2003.
31 **Johnson AM**, Dodds J, Mercer CH, *et al.* HIV changing patterns of male homosexual behaviour in Britain: comparative analysis of independent community and national probability samples (Natsal) 1990–2001. Oral presentation at IUSTI-Europe 2002 18th Congress on Sexually Transmitted Infections. Vienna, 12–14 September 2002.
32 **Copas AJ**, Wellings K, Erens B, *et al.* The accuracy of reported sensitive sexual behaviour in Britain: exploring the extent of change 1990–2000. *Sex Transm Infect* 2002;78:26–30.
33 **Ostrow DE**, Fox KJ, Chmiel JS, *et al.* Attitudes towards highly active antiretroviral therapy are associated with sexual risk taking among HIV-infected and uninfected homosexual men. *AIDS* 2002;16:775–80.
34 **McFarlane M**, Bull SS, Rietmeijer CA. The Internet as a newly emerging risk environment for sexually transmitted diseases. *JAMA* 2000;284:443–6.
35 **Wellings K**, Nanchahal K, Macdowall W, *et al.* Sexual behaviour in Britain: early heterosexual experience. *Lancet* 2001;358:1843–50.
36 **Burack R.** Teenage sexual behaviour: attitudes towards and declared sexual activity. *Br J Fam Plan* 1999;24:145–8.
37 **Hughes G**, Brady AR, Catchpole MA, *et al.* Characteristics of those who repeatedly acquire sexually transmitted infections: a retrospective cohort study of attendees at three urban sexually transmitted disease clinics in England. *Sex Transm Dis* 2001;28:379–86.
38 **Orr PO**, Johnston K, Brezendine E, *et al.* Subsequent sexually transmitted infection in urban adolescents and young adults. *Arch Pediatr Adolesc Med* 2001;155:947–53.
39 **Hillis SD**, Nakashima A, Marchbanks PA, *et al.* Risk factors for recurrent Chlamydia trachomatis infections in women. *Am J Obstet Gynecol* 1994;170:801–6.
40 **Shahmanesh M**, Gayed S, Ashcroft M, *et al.* Geomapping of chlamydia and gonorrhoea in Birmingham. *Sex Transm Infect* 2000;76:268–72.
41 **Low N**, Sterne JA, Barlow D. Inequalities in rates of gonorrhoea and chlamydia between black ethnic groups in south east London: cross sectional study. *Sex Transm Infect* 2001;77:15–20.
42 **Fenton KA.** Strategies for improving sexual health in ethnic minorities. *Curr Opin Infect Dis* 2001;14:63–9.
43 **Elam G**, Fenton KA, Johnson AM, *et al. Exploring ethnicity and sexual health.* SCPR Publications, 1999.
44 **Evans BA**, Bond RA, Macrae KD. Sexual behaviour in women attending a genitourinary medicine clinic. 1988. *Sex Transm Infect* 2000;76(Suppl 1): S41.
45 **Evans BA**, Bond RA, MacRae KD. Sexual behaviour and sexually transmitted infection among African and Caribbean men in London. *Int J STD AIDS* 1999;10:744–8.
46 **Low N**, Connell P, McKevitt C, *et al.* "You can't tell by looking": pilot study of a community-based intervention to detect asymptomatic infections. *Int J STD AIDS* 2003;14:830–4.
47 **Burns FM**, Fakoya AO, Copas AJ, *et al.* Africans in London continue to present with advanced HIV disease in the era of highly active antiretroviral therapy. *AIDS* 2001;15:2453–5.
48 **Del Amo J**, Petruckevitch A, Phillips AN, *et al.* Disease progression and survival in HIV-1 infected Africans in London. *AIDS* 1998;12:1203–9.
49 **Department of Health.** Targets aimed at reducing the number of children born with HIV: report from an expert group. London: DoH, 1999.
50 **NHS Executive.** *Reducing mother to baby transmission of HIV. Health Service Circular 1999/183.* London: Department of Health, 1999.
51 **PHLS, DHSS&PS and the Scottish ISD(D)5 Collaborative Group.** *Sexually transmitted infections in the UK: new episodes seen at genitourinary medicine clinics, 1991–2001.* London: Public Health Laboratory Service, 2002.
52 **BBC Wales and the Welsh Assembly.** www.bbc.co.uk/wales/comeclean/
53 **Duong T**, Ades A, Gibb DM, *et al.* Vertical transmission rates for HIV in the British Isles: estimates based on surveillance data. *BMJ* 1999;319:1227–9.

Chlamydia trachomatis Infection in Asymptomatic Men

D. Scott LaMontagne, MPH, David N. Fine, PhD, Jeanne M. Marrazzo, MD, MPH

Background: The epidemiology of *Chlamydia trachomatis* infection in men is not well defined, especially among those who are asymptomatic or show no signs of infection. Established *C. trachomatis* screening programs for women have demonstrated the benefit of routine screening in reducing prevalence over time, but the yield and benefit of screening asymptomatic men are unclear.

Methods: Cross-sectional study of *C. trachomatis* prevalence and associated risk factors among men tested at sexually transmitted disease (STD) clinics in Alaska, Idaho, Oregon, and Washington. We analyzed data from 43,094 men universally tested from 1997 to 1999 at 103 STD clinics, and assessed age-specific prevalence of infection, controlling for signs of infection (urethritis diagnosed by clinician) and report of sexual contact to a person with an STD (defined as "contact").

Results: Overall prevalence of *C. trachomatis* was 10.3%. Age-specific prevalence was highest among men aged 18 to 19 years and lowest among those aged >29 years, regardless of signs of infection upon examination or contact to a person with an STD. If these factors and age <25 years had been used to direct *C. trachomatis* testing at STD clinics, 59% of men would have been tested and 91% of positives would have been detected.

Conclusions: Using *either* the presence of clinical signs or report of a sex partner with an STD in combination with selective screening of all men aged <25 years detects the majority of infections and, in our population, would have considerably reduced the number of negative tests performed. (Am J Prev Med 2003;24(1):36–42) © 2003 American Journal of Preventive Medicine

Background

The epidemiology of *Chlamydia trachomatis* infection in men is not well defined, especially among asymptomatic men who are not evaluated in the context of contact with a sex partner with a sexually transmitted disease (STD). However, established screening programs have described the epidemiology of chlamydial infection in women and demonstrated that routine screening of women aged <25 years is effective in reducing the prevalence of chlamydia over time.[1] Screening is critical to the control of chlamydial infection because most infections in both women (≥70%) and men (≥60%) are asymptomatic.[2] Efforts to screen asymptomatic men have evaluated small numbers of subjects; thus, our understanding of the epidemiology of chlamydial infections in this group is limited.[3–7] Failure to identify asymptomatic infections in men might allow for maintenance of a reservoir of untreated chlamydial infection, consequently hindering efforts to further decrease the incidence of chlamydial infections in women.[2]

Previous studies of chlamydial infection among men have shown moderately high prevalence, ranging from 2.8% among asymptomatic 19- to 21-year-olds in Oslo, Norway, in 1994,[7] to 18.5% among asymptomatic men in Sweden in 1990.[4] In the United States, prevalence of chlamydial infection in asymptomatic men has ranged from 4.0% in a 1997 study of male STD clinic attendees in San Francisco[8] to 6% among young men in Seattle.[9] These and other studies have compared asymptomatic and symptomatic populations.[2,4,8–10] However, patient-reported symptoms may not be reliable in predicting infection. Clinical findings of signs of infection may be more reliable in ascertaining which men are most likely infected. To date, no study of chlamydial infection among men has assessed adequately the relationship between clinician-assessed signs and sexual contact with a person with a known STD.

In STD clinics in U.S. Public Health Service Region X (Alaska, Idaho, Oregon, and Washington), universal screening of male clinic attendees for chlamydia is

From the Center for Health Training (LaMontagne, Fine), and Department of Medicine, University of Washington (Marrazzo), Seattle, Washington

Address correspondence and reprint requests to: D. Scott LaMontagne, MPH, Research Associate, Center for Health Training, 1809 Seventh Avenue, Suite 400, Seattle WA 98144. E-mail: slamontagne@jba-cht.com.

0749-3797/03/$–see front matter

PII S0749-3797(02)00573-1

standard practice. Chlamydia testing data from these STD clinics have been systematically collected using the same data collection form used in the Region X Infertility Prevention Project, a screening program for women.[11] To better understand the age-specific prevalence of chlamydial infection in men using a clinician assessment of signs of infection, and controlling for the effect of sexual contact to a partner with an STD, we used this database to retrospectively assess patterns of chlamydial infection in a large multi-year sample of men.

Methods

We analyzed 43,094 test records from men who attended 103 STD clinics throughout Region X from 1997 through 1999. Region X is a federally defined geographic area of the U.S. Department of Health and Human Services that includes the states of Alaska, Idaho, Oregon, and Washington. The number of categorical public STD clinics included in this study varied by state: 1 in Alaska, 36 in Idaho, 53 in Oregon, and 13 in Washington. All men who attended these clinics were tested for chlamydial infection, regardless of reason for visit (universal testing). Data were entered on a standardized form by clinicians and included demographics; chlamydia diagnostic test type and result; site of specimen (urethra, urine, or rectum); report of sexual contact (timing not specified) to a partner with an STD, specifically chlamydia, *Neisseria gonorrhoeae*, mucopurulent cervicitis, or non-gonococcal urethritis (NGU); and clinical findings on physical examination. Sexual behavior data were assessed by patient report and included new sex partner, two or more sex partners, or sex with a symptomatic partner in the past 60 days; condom use at last intercourse; and a positive chlamydia test in the last year. Records were excluded from analysis if data were missing for both clinical examination findings and reported sexual contact to a partner with an STD (n =5169 or 12%). Because only one study site reported *N. gonorrhoeae* test data and comparable gonorrhea data were not available from all study sites, records with a positive gonorrhea test result were excluded (n =1071 or 2.5%). A small number of records (n =686 or 1.6%) indicated "other" for both clinical examination findings and reported sexual contact to a partner with an STD. Because "other" could not be more specifically defined, these records were excluded from analysis. The final study population analyzed included 84% of all men tested for chlamydial infection (N=36,168).

To explore the role of reported sexual contact to a person with an STD in men with or without clinical signs of infection, the study population was categorized into four screening groups. These group categories were based on clinician-assessed signs and patient report of sexual contact to a partner with an STD: (1) signs, contact; (2) signs, noncontact; (3) no signs, contact; and (4) no signs, noncontact. Men were classified as "signs" if urethritis or epididymitis was present on clinical examination and as "no signs" if neither of these findings was recorded. Urethritis was defined by the presence of visible urethral discharge or ≥5 PMNs per field (×1000) on Gram stain of urethral secretions (n =8437). Epididymitis was defined as unilateral scrotal pain and swelling (n =174). Data on specific symptoms reported by subjects, such as dysuria, were not available. Classification as "contact" is a common term used by public health practitioners in the field of STDs and was defined as patient self-report of sexual contact with a partner who has an STD, as defined above (n = 4733). If no sexual contact with these conditions was reported, the record was categorized as noncontact.

Age-specific chlamydia prevalence, univariate Mantel–Haenszel odds ratios, 95% confidence intervals, and multivariate logistic regression models (forward stepwise procedure) were calculated using SPSS 8.0 (SPSS, Chicago, IL, 1998). All measures of significance were two-sided and used a statistical significance level of p <0.05.

Results

Characteristics of All Subjects

The mean age of men tested was 29 years, and over half of the population was aged ≥25 years. The racial distribution was predominately white (73%) and included 18% African Americans and 15% Latino men. Most men reported having had sex with women; 9% reported sex with other men. The principal lab test employed was enzyme immunoassay (SyvaTrak EIA, 55%); followed by cell culture (19%); nucleic acid amplification test (NAAT) (Abbot LCR, 17%); and non-amplified DNA probe (GenProbe Pace, 9%). Behavior consistent with an increased risk of STD was common; for example, 77% of all men tested did not use condoms at last intercourse. The majority of men tested were no signs, noncontact (67%); 20% were signs, noncontacts; 9% were no signs, contacts; and 4% were signs, contact.

Overall prevalence of chlamydia was 10.3% and increased from 1997 to 1999 (chi-square test for trend, p <0.001), not controlling for test type. Variations in prevalence across states ranged from 7.8% in Alaska to 12.1% in Idaho; Washington and Oregon had prevalences of 9.1% and 11.5%, respectively. Men tested at STD clinics in rural locations—cities with <25,000 people—had a higher prevalence than those tested at urban STD clinics (data not shown). The highest age-specific prevalence, 18.3%, was found among 18- to 19-year-olds. Men who had signs and who reported sexual contact to a partner with an STD (signs, contacts) were most likely to be infected, with 51% positive for chlamydia. Prevalence otherwise varied from 20.4% among signs men with no reported contact, to 22.0% among no-signs, contact men, and 3.4% among no-signs, noncontact men (Table 1).

Univariate analysis showed the risk of chlamydial infection to be associated with several demographic and behavioral factors (Table 1). Men aged <20 years were four times as likely to have a positive chlamydia test than were men aged >29 years. Asian/Pacific Islander and African-American men had a two-fold increase in risk for chlamydial infection compared to white men. Behavioral factors—including new sex partner in the past 60 days, two or more sex partners in the

Table 1. Prevalence of *Chlamydia trachomatis* by population characteristics, all men, STD clinics, Region X, 1997–1999

Population characteristic	Number tested (column %)	Number positive (row %)	Univariate OR (95% CI)[a]
Total	36,168 (100%)	3,727 (10.3%)	—
Screening group[b]			
Signs/contact	1,395 (3.9)	709 (50.8)	29.1 (25.6–33.1)
Signs/noncontact	7,098 (19.6)	1,448 (20.4)	7.2 (6.6–7.9)
No signs/contact	3,338 (9.2)	736 (22.0)	8.0 (7.2–8.9)
No signs/noncontact	24,337 (67.3)	834 (3.4)	Referent
Age (years)			
<18	1,664 (4.6)	270 (16.2)	3.8 (3.3–4.5)
18–19	3,245 (9.0)	594 (18.3)	4.4 (3.9–5.0)
20–24	9,893 (27.4)	1,439 (14.5)	3.4 (3.1–3.7)
25–29	7,486 (20.7)	753 (10.1)	2.2 (2.0–2.5)
>29	13,833 (38.3)	667 (4.8)	Referent
Race/ethnicity (*n*=35,446)[c]			
White	21,851 (61.6)	1,663 (7.6)	Referent
Black or African American	6,227 (17.6)	907 (14.6)	2.1 (1.9–2.3)
American Indian/Alaska Native	434 (1.2)	39 (9.0)	1.2 (0.8–1.7)
Asian/Pacific Islander	835 (2.4)	136 (16.3)	2.4 (1.9–2.9)
Hispanic	5,468 (15.4)	844 (15.4)	2.2 (2.0–2.4)
Other	631 (1.8)	65 (10.3)	1.4 (1.1–1.8)
Risk behaviors (yes)			
New sex partner, past 60 days (*n*=34,712)	17,447 (50.3)	1,928 (11.1)	1.2 (1.1–1.2)
Two or more sex partners, past 60 days (*n*=35,069)	11,705 (33.4)	1,411 (12.1)	1.3 (1.2–1.4)
Sex with symptomatic partner, past 60 days (*n*=28,097)	5,826 (20.7)	1,239 (21.3)	3.4 (3.1–3.7)
Positive chlamydial test last 12 months (*n*=35,359)	1,509 (4.3)	235 (15.6)	1.7 (1.4–1.9)
Condom used at last sex (*n*=33,973)	7,785 (23.2)	640 (8.1)	0.7 (0.6–0.8)
Sex partner (*n*=35,489)			
Sex with women	31,496 (88.7)	3,401 (10.8)	Referent
Sex with men	3,182 (9.0)	232 (7.3)	0.7 (0.6–0.7)
Sex with men and women	811 (2.3)	26 (3.2)	0.3 (0.2–0.4)

[a]For all ORs, p=0.05.
[b]See text for definitions of screening groups.
[c]Numbers in parentheses represent number of men for whom data on individual characteristics were available.
CI, confidence interval; OR, odds ratio; STD, sexually transmitted disease.

past 60 days, and positive chlamydia test in the last year—were also associated with an increased risk of infection. Reports of condom use at last sex and of sex with other men were significantly associated with a reduced likelihood of chlamydial infection (Table 1).

The age distribution of chlamydia prevalence was consistent across the four screening groups (Figure 1). In all groups, the highest age-specific prevalence occurred among 18- to 19-year-old men. Chlamydia prevalence declined with increasing age, regardless of screening group. The lowest prevalence (1.6%) was found among no-signs, noncontact men aged >29 years.

Chlamydia Prevalence Among Men with No Signs and No Reported Contact with STD

Most tests (67%) were performed among the no-signs, noncontact group. The demographic and behavioral characteristics of this group were generally similar to the overall study population (Table 2). However, fewer of these men were African American (p <0.001) and fewer reported recent sex with a symptomatic partner (p <0.001).

Univariate associations for chlamydial infection among no-signs, noncontact men were similar to those found among all men tested (Table 2). Age was the strongest risk factor for chlamydial infection; men aged 18- to 19 years were almost five times more likely to have a positive test than were men aged >29 years. Other associations of infection included African-American or Hispanic race/ethnicity, sex with a symptomatic partner, report of a positive chlamydia test in the last year, and two or more sex partners in the past 60 days. Reports of condom use at last sex and of sex with other men were associated with a reduced likelihood of infection. Prevalence did not increase significantly from 1997 to 1999 (data not shown), but did vary by clinic location. Rural clinics and clinics located in mixed urban/rural cities had a slightly higher prevalence of chlamydial infection, at 5.4% and 4.1%, respectively, than urban clinics at 3.1% (p <0.05).

In multivariate analysis, among no-signs, noncontact men, young age had the strongest association with chlamydial infection (Table 2). Men aged <20 years were over four times more likely to be infected than those aged >29 years. Some racial/ethnic groups had

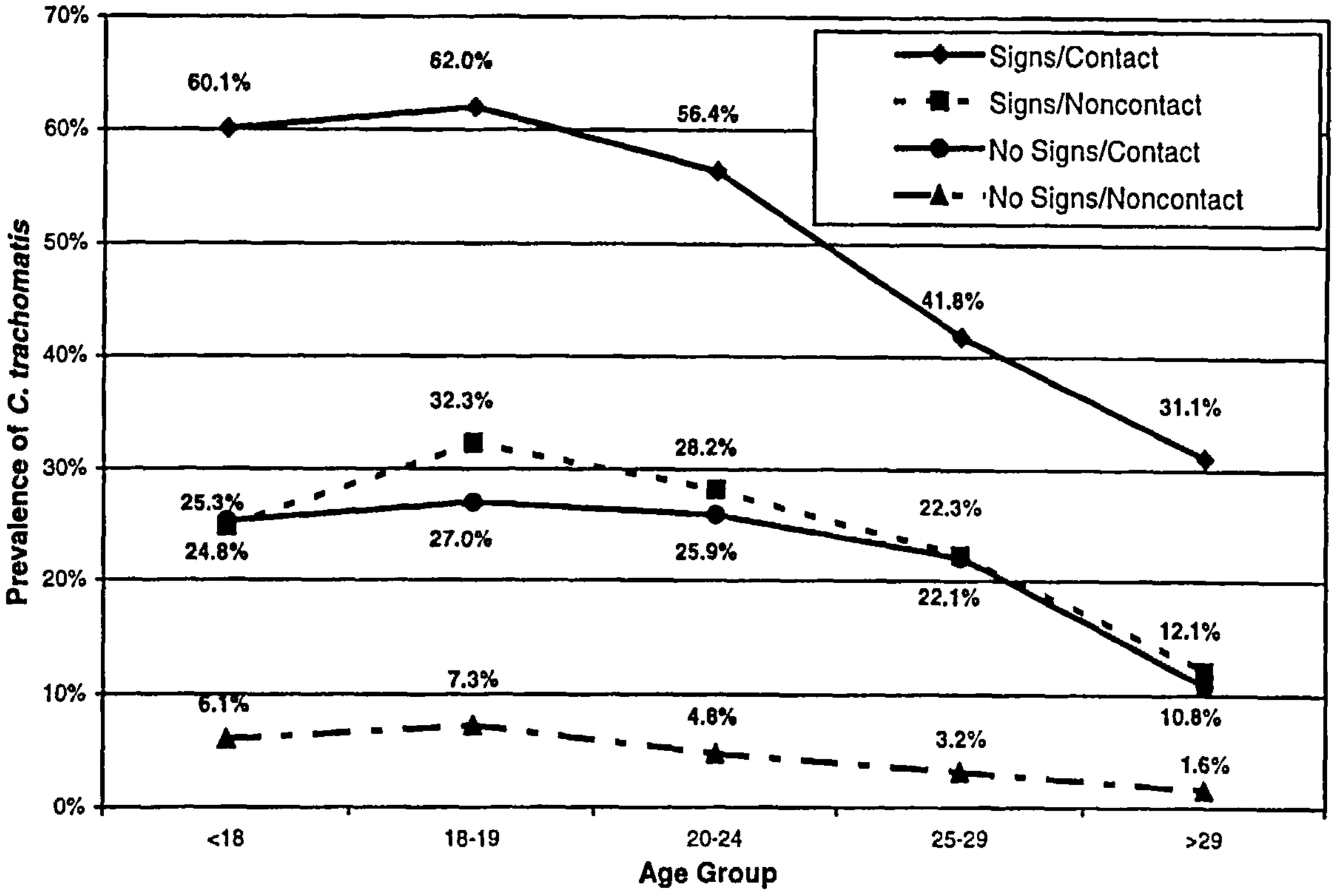

Figure 1. Age-specific prevalence of *Chlamydia trachomatis* by screening group, all men, STD clinics, Region X, 1997–1999.

an increased risk of infection in the model. African-American and Hispanic men were nearly twice as likely as white men to be positive for chlamydia. Behavioral risks of two or more sex partners or sex with a symptomatic partner remained associated with an increased risk of chlamydial infection, and condom use at last sex remained associated with a reduced risk of chlamydial infection. When considered with other factors, new sex partner, history of chlamydia in the last year, and sex with men were not statistically significant in the multivariate model.

Patterns of Testing in Population Subgroups

Men with signs of infection and/or reported contact with an STD accounted for 33% of all tests performed and 78% of all chlamydia detected at STD clinics (Figure 2). The remaining 67% of tests were performed among no-signs, noncontact men. Of these men, the largest percentage tested was aged ≥25 years (62%) and had the lowest prevalence at 2.1% (Figure 2). Over 40% of all testing was performed in the group least likely to be infected with chlamydia—no-signs, noncontact men aged >24 years.

Discussion

Our study found a relatively high prevalence of chlamydial infection, 10.3%, among men attending STD clinics in the U.S. Northwest. Clinical findings consistent with infection, report of sexual contact with a partner with an STD, and young age were strongly associated with infection. These findings are consistent with those of other studies of chlamydia among men attending STD clinics.[8,10] In a recent study at an STD clinic in San Francisco, Ciemins et al.[8] found an overall chlamydia prevalence of 11.0% among men. In our study population, prevalence varied by behavioral risk factors, race/ethnicity, gender of sex partner, type of lab test, and clinic location.

Previous studies of chlamydial infection in men have been limited by small numbers of asymptomatic men and were focused on patient-reported symptoms. Our analysis included a very large, universally tested male population and focused on clinician assessment of signs, an approach that might be more accurate in predicting infection. We examined men with and without signs in the context of their contact to sex partners with an STD. As expected, the likelihood of chlamydial infection was highest among men who had *both* clinical signs of urethral infection and report of contact to a sex partner with an STD. Men with *either* clinical findings or reported sexual contact to a partner with an STD had similar prevalence of chlamydial infection (20% to 22%), suggesting that both indicators are important tools for clinicians in assessing the likelihood of infection. Men who had no apparent signs of infection and who did not report a recent sexual contact to a partner with an STD (defined as no signs, noncontacts) were

Table 2. Univariate and multivariate associations of *Chlamydia trachomatis*, no signs/non-contact men,[a] STD clinics, Region X, 1997–1999

Population characteristic	Number tested	Number positive	Row %	Univariate OR (95% CI)[b]	Multivariate[b,c] OR (95% CI)
Total	24,337	834	3.4%	—	—
Age (years)					
<18	1,031	63	6.1%	3.9 (2.9–5.3)	4.1 (2.8–6.1)
18–19	1,973	145	7.3%	4.8 (3.8–6.1)	4.5 (3.4–6.1)
20–24	6,320	305	4.8%	3.1 (2.5–3.7)	3.1 (2.4–3.9)
25–29	5,046	159	3.2%	1.9 (1.6–2.5)	2.1 (1.6–2.8)
>29	9,937	162	1.6%	Referent	Referent
Race/ethnicity (n=23,852)[d]					
White	15,977	414	2.6%	Referent	Referent
Black or African American	3,108	136	4.4%	1.7 (1.4–2.1)	1.9 (1.5–2.5)
American Indian/Alaska Native	298	7	2.3%	0.9 (0.4–2.0)	0.3 (0.1–1.4)
Asian/Pacific Islander	535	17	3.2%	1.2 (0.7–2.1)	1.2 (0.6–2.2)
Hispanic	3,513	221	6.3%	2.5 (2.1–3.0)	1.9 (1.5–2.3)
Other	422	14	3.3%	1.3 (0.7–2.3)	1.9 (1.0–3.4)
Risk behaviors (yes)					
New sex partner, past 60 days (n=23,237)	11,231	421	3.7%	1.2 (1.0–1.4)	p=0.51
Two+ sex partners, past 60 days (n=23,523)	7,356	308	4.2%	1.4 (1.2–1.6)	1.5 (1.3–1.8)
Sex with symptomatic partner (n=19,071)	2,088	140	6.7%	2.5 (2.0–3.0)	1.9 (1.5–2.4)
Positive chlamydial test last 12 months (n=23,797)	775	48	6.2%	1.9 (1.4–2.6)	p=0.10
Condom used last sex (n=22,691)	5,679	146	2.6%	0.7 (0.6–0.8)	0.6 (0.5–0.8)
Sex partner (n=23,819)					
Sex with women	20,909	733	3.5%	Referent	p=0.18
Sex with men	2,265	71	3.1%	0.9 (0.7–1.1)	
Sex with men and women	645	7	1.1%	0.3 (0.1–0.7)	

[a]See text for definitions of screening groups.
[b]For all ORs, p=0.05, except as noted.
[c]Variables in the multivariate analysis include items listed in table plus test type, year, and clinic location (data not shown).
[d]Numbers in parentheses represent number of men for whom data on individual characteristics were available.
CI, confidence interval; OR, odds ratio; STD, sexually transmitted disease.

the largest group screened, but had the lowest prevalence of chlamydial infection.

Age was also a significant factor in our study. Chlamydia was most common among older adolescent men (aged 18 to 19), as others have noted.[9,10] As has been noted in numerous studies of chlamydial infection among women, young age is the strongest predictor of infection.[12–14] Because men aged <25 were three to four times more likely to be infected with chlamydia than those aged >29 years, even after adjusting for clinical signs and sexual contact with a person with an STD, age should factor significantly in determining the most likely population of men to be infected with chlamydia. The largest number of men tested were aged >29 years (about 40%), even among the no-signs, noncontact group, and had the lowest prevalence. It remains unclear why a large and significant number of very low-risk men sought STD testing services at a public STD clinic. Perhaps the healthcare-seeking behaviors of men, in general, and the accessibility of healthcare venues for men, in particular, redirects concerned men away from primary care facilities and into public STD clinics.[15] Further study is needed to better elucidate this phenomenon.

Our study suggests that combining age with clinician-assessed signs of infection and patient self-report of sexual contact with a person with a known STD could greatly enhance efforts to detect those men most likely to be infected, regardless of seeking care at an STD clinic. In clinical practice, men with signs of infection or history of recent sex with someone with an STD should receive diagnostic testing for chlamydia. Our data raise the question of whether certain groups of men without signs should be tested routinely by virtue of their attendance in the STD clinic. Currently, there are no guidelines on how best to address men who are asymptomatic, much less for men with no clinical signs of infection and who also have no history of sexual contact with an infected person.

Recently, the third U.S. Preventive Services Task Force concluded that there was no strong evidence for selective screening strategies among asymptomatic males.[16] While our study does not specifically address the cost-effectiveness of such approaches, our data do suggest that testing men with no signs in an STD clinic setting could certainly be made more efficient by reducing testing in subgroups unlikely to have a high prevalence, such as men aged >25 years with no signs and no contact with a sex partner with an STD. Research on chlamydial infection among women suggests that screening in settings with prevalence of <3.1% is not cost-effective[17]; the cost–benefit ratio of

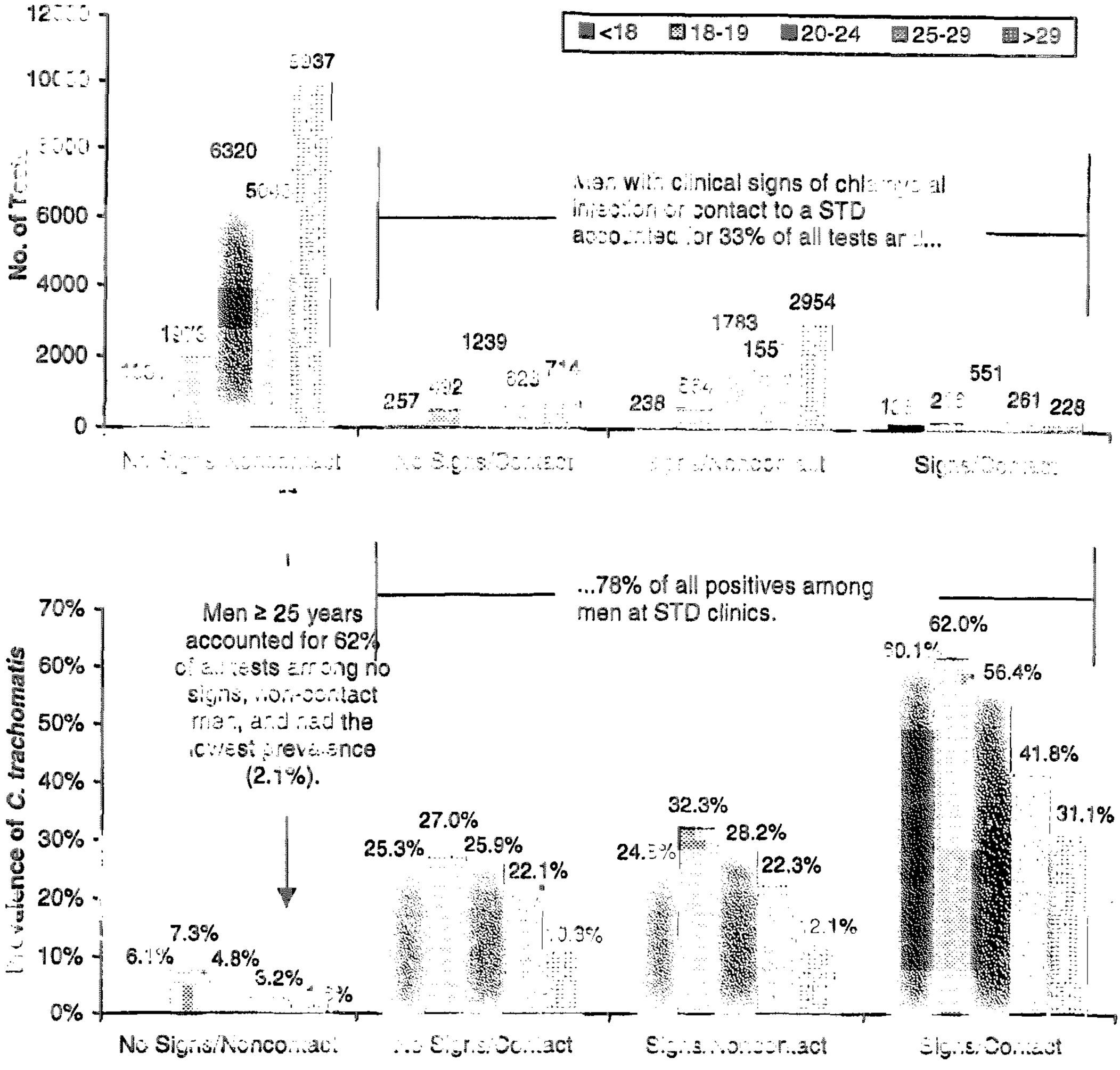

Figure 2. Comparison of age-specific testing volumes and *Chlamydia trachomatis* prevalence among men by screening group, sexually transmitted disease (STD) clinics, Region X, 1997–1999.

testing men at similarly low prevalence levels might also be questionable.

There are several potential limitations to our study. First, our population consisted of self-referred STD clinic attendees, who may not be a representative sample of men seeking care related to STD; their prevalence may not accurately approximate that of the general community, and our findings may not apply to other clinical settings. Second, we did not have data on specific patient-reported symptoms and could not compare the relative contribution of symptoms with clinical signs for predicting infection in our population. Third, our data are based on chlamydia tests; multiple visits by the same individual cannot be assessed. Fourth, clinics participating in our project may be heterogeneous; we could not assess possible differences among programs operating under different administrative or organizational structures. Further, excluding 16% of male test records, of which 15% were co-infected with *N. gonorrhoeae*, may have introduced selection bias into our study. Finally, while other studies have confirmed the role of test type in increased detection of chlamydia,[4,6,18] we cannot confirm to what extent increasing use of NAAT increased chlamydia positivity among men over time in this study.

Our analysis supports routine testing of all men with signs of infection and men who report sexual contact with a person with an STD, regardless of age. While the cost-effectiveness of such an approach requires further study, our data also support consideration of routine screening among men aged <25 years who have no signs of infection and who report no sexual contact with a person with an STD. If these factors and age <25 years had been used to direct chlamydia testing in our study population, 58% of our subjects would have been tested and 91% of all positives would have been detected. Currently, selective screening strategies based on similar indicators are used to test women in family planning clinics and have affected reductions in the

prevalence of chlamydia.[1,17] Use of a selective screening approach among men attending STD clinics might be able to achieve a similar level of success, and identifying and treating infections in men without signs may assist in efforts to further decrease the incidence of chlamydial infections in women.

Funding for this study was made possible through the Centers for Disease Control and Prevention (CDC), National Center for HIV, STD, and TB Prevention, Division of STD Prevention, Infertility Prevention Project. We would like to thank Debra J. Mosure of the CDC in Atlanta, Georgia, for her thoughtful review of this manuscript.

References

1. Mertz KJ, Levine WC, Mosure DJ, Berman SM, Dorian KJ. Trends in the prevalence of chlamydial infections—the impact of community-wide testing. Sex Transm Dis 1997;24:169–75.
2. Marrazzo JM, Stamm WE. New approaches to the diagnosis, treatment, and prevention of chlamydial infection. In: Remington JS, Swartz MN, eds. Current clinical topics in infectious diseases. 18th ed. Boston: Blackwell Science, 1998;37–59.
3. Braverman PK, Biro FM, Brunner RL, Gilchrist MJR, Rauh JL. Screening asymptomatic adolescent males for chlamydia. J Adolesc Health Care 1990;11:141–4.
4. Domeika M, Bassiri M, Mardh P-A. Diagnosis of genital Chlamydia trachomatis infections in asymptomatic males by testing urine by PCR. J Clin Microbiol 1994;32:2350–2.
5. Moncada J, Schachter J, Shafer MA, et al. Detection of Chlamydia trachomatis in first catch urine samples from symptomatic and asymptomatic males. Sex Transm Dis 1994;21:8–12.
6. Chernesky MA, Jang D, Lee H, et al. Diagnosis of Chlamydia trachomatis infections in men and women by testing first-void urine by ligase chain reaction. J Clin Microbiol 1994;32:2682–5.
7. Anestad G, Berdal BP, Scheel O, et al. Screening urine samples by leukocyte esterase test and ligase chain reaction for chlamydial infections among asymptomatic men. J Clin Microbiol 1995;33:2483–4.
8. Ciemins EL, Kent CK, Flood J, Klausner JD. Evaluation of chlamydia and gonorrhea screening criteria—San Francisco sexually transmitted disease clinic: 1997 to 1998. Sex Transm Dis 2000;27:165–7.
9. Marrazzo JM, White CL, Krekeler B, et al. Community-based urine screening for Chlamydia trachomatis with a ligase chain reaction assay. Ann Intern Med 1997;127:796–803.
10. Marrazzo JM, Whittington WL, Celum CL, et al. Urine-based screening for Chlamydia trachomatis in men attending sexually transmitted disease clinics. Sex Transm Dis 2001;28:219–25.
11. Center for Health Training. Infertility prevention project: program guidelines and data collection. Seattle, WA: Center for Health Training, 2000.
12. U.S. Department of Health and Human Services. Sexually transmitted disease surveillance 2000. Atlanta, GA: Division of STD Prevention, Center for Disease Control and Prevention, 2001.
13. Gershman KA, Barrow JC. A tale of two sexually transmitted diseases: prevalences and predictors of chlamydia and gonorrhea in women attending Colorado family planning clinics. Sex Transm Dis 1996;23:481–8.
14. Mosure DJ, Berman S, Kleinbaum D, Halloran ME. Predictors of Chlamydia trachomatis infection among female adolescents: a longitudinal analysis. Am J Epidemiol 1996;144:997–1003.
15. Alan Guttmacher Institute. New York: The Alan Guttmacher Institute, 2002.
16. U.S. Preventive Services Task Force. Screening for chlamydial infection: recommendations and rationale. Am J Prev Med 2001;20(suppl 3):90–4.
17. Marrazzo JM, Celum CL, Hillis SD, Fine D, DeLisle S, Hansfield HH. Performance and cost-effectiveness of selective screening criteria for Chlamydia trachomatis infection in women: implications for a national chlamydia control strategy. Sex Transm Dis 1997;24:131–41.
18. Dicker LW, Mosure DJ, Levine WC, Black CM, Berman SM. Impact of switching laboratory tests on reported trends in Chlamydia trachomatis infections. Am J Epidemiol 2000;151:430–5.

REVIEW

Establishing the National Chlamydia Screening Programme in England: results from the first full year of screening

D S LaMontagne, K A Fenton, S Randall, S Anderson, P Carter, on behalf of the National Chlamydia Screening Steering Group

Sex Transm Infect 2004;80:335–341. doi: 10.1136/sti.2004.012856

Background: The phased implementation of the National Chlamydia Screening Programme (NCSP) began in September 2002. The NCSP offers opportunistic screening for chlamydia to women and men under 25 years of age attending clinical and non-clinical screening venues using non-invasive urine or vulvo-vaginal swab samples tested via nucleic acid amplification. This review describes the implementation of the NCSP, reports positivity rates for the first year, and explores risk factors for genital chlamydial infection.

Methods: Cross sectional study of the first year's screening data from the NCSP. A standardised core dataset for each screening test was collected from 302 screening venues, excluding genitourinary medicine (GUM) clinics, across 10 phase 1 programme areas. We estimated chlamydia positivity by demographic and behavioural characteristics, and investigated factors associated with infection through univariate and multivariate analyses.

Results: Chlamydia positivity among people under 25 years of age screened in non-GUM settings was 10.1% (1538/15 241) in women and 13.3% (156/1172) in men. Risk factors varied by sex: for women—age 16–19, non-white ethnicity, and sexual behaviours were associated with infection; for men—only age 20–24 and non-white ethnicity were associated with infection.

Discussion: In the first phase of the NCSP, 16 413 opportunistic screens among young adults under 25 years of age were performed at non-GUM settings and testing volume increased over time. Rates of disease were similar to those found during the English screening pilot and were comparable to the first year of widespread screening in Sweden and the United States. The screening programme in England will continue to expand as further phases are included, with national coverage anticipated by 2008.

See end of article for authors' affiliations

Correspondence to: D Scott LaMontagne, MPH, FRIPH, CS, Health Protection Agency, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK; scott.lamontagne@hpa.org.uk

Accepted for publication 13 August 2004

The most commonly reported bacterial sexually transmitted infection (STI) in the England is *Chlamydia trachomatis*,[1] with serious sequelae in untreated infected women—for example, chronic pelvic pain, pelvic inflammatory disease (PID), ectopic pregnancy, and infertility.[2] Complications among men with untreated infection include urethritis, epididymitis, and Reiter's syndrome.[2] Recent evidence has also suggested that infection can cause male infertility.[3] Since a high proportion of chlamydial infections are asymptomatic,[2] screening programmes have evolved to detect and treat individuals with prevalent undiagnosed infections and their partners.[4–7] These programmes have reported reductions in prevalence[8 9 10] and incident PID[11 12] after implementation. Other studies have demonstrated that screening for genital chlamydial infection is both cost beneficial and cost effective.[13–15]

In England, a comprehensive review of the evidence justifying screening for genital chlamydial infection against the Wilson-Jungner criteria[16] was published by the chief medical officer's (CMO) expert advisory group on *Chlamydia trachomatis*.[17] The principal conclusion from this review was a call to establish a national chlamydia screening programme, focusing on young women attending clinical settings who were at risk of infection.[17] This call was strengthened through the inclusion of chlamydia screening in the action plan of the *National Strategy for Sexual Health and HIV*, which aims to reduce the transmission and prevalence of STIs.[18]

In 1998, the Department of Health (DoH) in England funded a pilot of an opportunistic screening programme to explore how best to implement chlamydia screening. The investigators of the chlamydia pilot concluded it was feasible and acceptable to opportunistically screen asymptomatic women 16–24 years of age attending different healthcare settings, including general practices, contraceptive clinics, young people's services, women's services (for example, termination, gynaecology, and antenatal), and genitourinary medicine (GUM) clinics.[19] The screening pilot also reported high rates of disease, on average 10% prevalence among young women attending general practice and other healthcare settings.[20] Based on this evidence and with the guidance from the lessons learned in the screening pilot, the DoH agreed funding for a phased implementation of the National Chlamydia Screening Programme (NCSP) for England. This paper overviews the structure and process of the NCSP, reports positivity rates by demographic and behavioural characteristics, and explores risk factors for chlamydia from the first reporting year (1 April 2003–31 March 2004) of opportunistic screening for phase 1 programmes.

METHODS

Programme overview

The goal of the NCSP in England is to control genital chlamydial infection through the early detection and treatment of asymptomatic infections and prevention of sequelae and onward transmission. Funding and national leadership

Abbreviations: CDSC, Communicable Disease Surveillance Centre; GUM, genitourinary medicine; LCR, ligase chain reaction; NAATs, nucleic acid amplification tests; NCSP, National Chlamydia Screening Programme; PCR, polymerase chain reaction; PCTs, primary care trusts; PIAG, patient information advisory group; PID, pelvic inflammatory disease; SDA, strand displacement amplification; TMA, transcription mediated amplification

are provided by the DoH, with scientific support from the Health Protection Agency Communicable Disease Surveillance Centre (CDSC). The programme is guided by a national chlamydia screening steering group (NCSSG), comprising multidisciplinary representation from relevant clinical and public health bodies engaged in sexual health, including GUM, contraception and family planning, obstetrics and gynaecology, nursing, health advising, general practice, and microbiology. This body advises the DoH on clinical and laboratory protocols and procedures for implementing opportunistic screening in primary health care settings—for example, contraception clinics, young people's services, general practices, etc. Screening protocols for the national programme are contained in a core requirements document, and are disseminated to local programme areas to standardise local screening activity.[21] Phased implementation of the NCSP began with 10 programme areas selected in September 2002 for phase 1.[21,22] Programme areas are composed of consortia of primary care trusts (PCTs), which are the geographic and service boundaries of the National Health Service (NHS). In January 2004, the second phase of the NCSP began with an additional 16 programme areas encompassing a further 54 PCTs. This brings current population coverage of the NCSP to an estimated 30% of all sexually active young people aged 15–24 years in England.

Local programme areas implement screening activities guided by the national core requirements. Administrative structures vary locally but usually include a local multidisciplinary steering group, chlamydia screening office and coordinator, programme lead, and clinical staffing, in partnership with PCTs, local laboratories, and healthcare providers.

All local screening activity is coordinated by a local chlamydia screening coordinator, working out of a designated chlamydia screening office. A multidisciplinary local CSSG oversees the local programme implementation and is responsible for ensuring that data are reported to the DoH. Mandatory guidelines on the structure, process, and outcome monitoring for local programmes have been produced by the national CSSG and are contained in a core requirements document (available at www.dh.gov.uk). Also contained within the core requirements document are the Patient Information Advisory Group (PIAG) approved standard screening dataset to be collected by all screening sites. The core data items are transferred electronically to the Health Protection Agency, Colindale, on a quarterly basis for national programme monitoring. Local programmes have some flexibility to adapt their screening activities to reflect local need. All programmes areas are developing locally relevant materials to complement nationally available screening resources; some areas are examining the feasibility of screening chlamydia positive patients for gonorrhoea; and other areas plan to include additional screening venues—for example, local prisons, in their activities. All such enhancements are funded locally. As the programme is still in its infancy, locally driven research and evaluation will needed to inform unresolved operational issues—for example, screening intervals and engaging men.[23]

The target population for screening is young men and women under the age of 25 years who are attending healthcare facilities not traditionally associated with providing specialist sexual health services. This approach expands the number of locations (that is, screening venues) that young people can attend which are offering chlamydia screening as part of their services. These include contraceptive clinics, general practices, young people's services, antenatal services, colposcopy and infertility units, and termination of pregnancy clinics. Screening is also encouraged to those within the target age group through innovative outreach strategies, such as "pee in a pot" days at military bases, university campuses or health fairs, mobile vans or buses for contact with young people, prisons, and other non-traditional settings. People routinely attending GUM clinics are already tested for *Chlamydia trachomatis* as a part of standardised clinical protocols, and as such are not the primary target for the "opportunistic" nature of this national programme. People falling within the screening guidelines are offered a chlamydia test when attending a venue participating in the programme, regardless of the reason for their attendance. The attendance, itself, is the "opportunity" created to educate and encourage the uptake of screening for chlamydia. People under 16 years of age are offered screening if they are determined by the test initiator to be "Frazer competent."[24] Every person offered screening receives a detailed patient information leaflet which summarises screening procedures and management outcomes. Implied consent is acquired by client self completion of a test request form and provision of a clinical specimen for testing.

Non-invasive samples, principally urine and self collected vulvo-vaginal swabs, are submitted to centralised local laboratories and tested using one of three common nucleic acid amplification tests (NAATs)*—polymerase chain reaction (PCR) Amplicor or Cobas Amplicor (Roche Diagnostics, Basel, Switzerland), strand displacement amplification (SDA) BDProbeTec (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), or transcription mediated amplification (TMA) Aptima Combo 2 Assay (Gen-Probe Incorporated, San Diego, CA, USA), per the manufacturer's instructions. All positive and equivocal samples are confirmed, either through testing using a different NAAT or re-run of the sample using the same platform.[21]

All clients are notified of test results, based on their preferred method, such as letter, telephone call, or text message. People testing positive are contacted up to three times for treatment and partner notification. Treatment is provided in accordance with published guidelines,[25] although directly observed azithromycin (1 g oral tablets) is the preferred option. Alternative regimens are prescribed, as clinically necessary.[25] Clients receive treatment at no charge, which may be dispensed at the original testing venue, by the local chlamydia screening coordinator, via referral to a GUM clinic, or other method as negotiated by the client. All people testing positive, and especially those who exhibit symptoms suggestive of chlamydial infection, are offered the opportunity to attend a GUM clinic for further STI testing. Routine tests of cure are not performed, unless the patient has been treated with erythromycin or there are serious concerns about treatment compliance.

Patients are offered the choice of notifying their own partners (patient referral), or supplying information for the health adviser or local chlamydia coordinator to notify the partner, without the patient's name being given (provider referral). Partner notification activities are also undertaken by various trained personnel—for example, the health adviser, chlamydia coordinator, staff based at a GUM clinic, programme lead, and/or test initiator; according to national standards.[26] Prophylactic treatment to partners is provided free of charge. All documentation relating to treatment of index patient and follow up of partner notification activities is collated locally at the central chlamydia screening office for local audit and is reported annually in aggregate summary to the DoH.

*Even though the Abbott LCx test (Abbott Laboratories, Abbott Park, IL, USA) was withdrawn from the UK market in early 2003, one programme area in phase 1 tested specimens via ligase chain reaction (LCR) from April to August 2003 because of an overstock of available test kits and reagents.

Standardised information about the demographic and behavioural characteristics of the population screened, location of screening, laboratory test method used, and test result is collected uniformly across all local programme areas by the use of a test request form and is reported in disaggregate nationally to CDSC. Data reporting to CDSC is approved by the PIAG.

Sample selection

In this paper, tests reported to CDSC by 15 June 2004 are included. Of those, we selected only tests performed outside of GUM clinics and which were taken for opportunistic screening purposes only, as they most closely reflect the efforts to extend chlamydia testing services to people who might not normally have been tested and who potentially represent a "hidden reservoir" of asymptomatic infections within the young adult population. Tests were categorised as opportunistic screening if the reason for the test was for screening purposes. Tests performed for diagnostic reasons or because a client was a contact of a chlamydia positive were not included. An additional 4% (n = 674) of tests were excluded from analysis because of unknown or missing data for test result, sex, age, type of test, or inconsistent sample type (for example, male tests with self collected vulvo-vaginal swabs).

Data analysis

We performed cross sectional descriptive analyses of the population tested and assessment of factors associated with infection. Distributions of demographic, behavioural, and testing characteristics within the population were tabulated. χ^2 tests and univariate odds ratios were calculated. Multivariate analyses were performed using logistic regression to explore the inter-relation of factors associated with infection within the male and female populations separately, as we hypothesised that the factors associated with infection between the two populations might be different.[2]

We used chlamydia positivity, rather than prevalence, as the dependent variable in our univariate and multivariate analyses, as studies have shown that positivity is a valid surrogate measure of prevalence.[27 28] Further, since this is a largely naive population to screening and the testing period is 12 months or less, the likelihood of repeat testers is minimal and would not have an appreciable impact on our estimates.

All data analysis was performed in SPSS 12.0 for Windows (SPSS Inc, Chicago, IL, USA) with two tailed significance levels of $p < 0.05$.

RESULTS

Opportunistic screening in phase 1 of the NCSP occurred in a staged approach with the number of programme areas and the number of venues within each programme area offering chlamydia screening increasing from the first quarter of operations to the last (table 1). For example, in the first quarter of the NCSP, four programme areas were offering screening at 74 venues outside of GUM clinics; by the end of the first full year of reporting, almost 250 non-GUM venues across all 10 phase 1 programme areas were offering opportunistic screening to young people. A total of 16 413 opportunistic screening tests were performed outside GUM settings during the first full year of the NCSP. Following the phased approach, over 1000 chlamydia screens (6% of the total) were done in the first quarter, and the last quarter of the first year accounted for almost 50% of all screening tests (table 2).

We found 10.1% positivity among women less than 25 years of age opportunistically screened at settings outside of GUM clinics in the first year of the NCSP (table 2). The population of women screened was primarily white and tested at contraceptive clinics. Over half of the female population was under 20 and the other half 20–24 years of age. Behavioural risks among women were common: 44% of the reporting population indicated a new sex partner in the last 3 months and/or two or more sex partners in the last year. SDA and PCR were the most commonly used diagnostic platforms in local laboratories. Urine was the most common specimen type, but nearly 30% of tests were done on self collected vulvo-vaginal swabs.

We found 13.3% positivity among men less than 25 years of age opportunistically screened at settings outside of GUM clinics in the first year of the NCSP (table 2). The population of men screened was primarily white, with 45% of tests done at contraceptive clinics and 26% done at colleges and universities. The male population was slightly younger than the female population—62% under 20 years of age. Behavioural risks among men were more common: 56% of the reporting population indicated a new sex partner in the last 3 months and 60% reported two or more sex partners in the past year. Urine was collected from all men.

Women ages 16–19 years were 43% more likely to test positive for chlamydia than those 20–24 years old (table 2). Women of black Caribbean ethnicity were nearly twice as likely to test positive. Behavioural risks were also associated with infection in women, even after controlling for covariates. Women tested with SDA were more likely to test positive and this factor also held after multivariate adjustment (table 2).

Among men, the groups more likely to test positive were somewhat different from those for women (table 2). After controlling for all factors in multivariate analysis, slightly older males, those 20–24 years of age, were more than twice as likely as those under 20 to test positive. Similar to women, black Caribbean or mixed ethnicity males were also more than twice as likely to be infected. Among men, behavioural risks were not statistically associated with an increased risk of infection, either in unadjusted or adjusted analyses (table 2). Additionally, men screened at colleges and universities and at young people's clinics had a reduced likelihood of infection than those tested in contraceptive clinics. Like their female counterparts, men screened using the SDA test had a significantly higher likelihood of testing positive (table 2).

To understand why higher positivity was found with the SDA test, an exploratory analysis was performed, dividing the population into those tested with SDA and those tested using another NAAT. Groups with higher positivity tended to be over-represented in the population tested with SDA (data not shown). For example, there were larger proportions of black and mixed ethnic groups and people reporting a new sex partner among people tested with SDA ($p < 0.05$), and these groups were almost twice as likely to test positive for chlamydia than white people or those who did not report a

Table 1 Number of programme areas and venues* offering opportunistic screening for *Chlamydia trachomatis* by quarter, National Chlamydia Screening Programme in England, 1 April 2003–31 March 2004

Quarter	Number of programme areas	Number of screening venues
1st, Apr–Jun 2003	4	74
2nd, Jul–Sep 2003	5	121
3rd, Oct–Dec 2003	9	184
4th, Jan–Mar 2004	10	247
Total	10	302

*Does not include GUM clinics.

Table 2 Characteristics and risk factors for chlamydial infection among men and women opportunistically screened outside GUM clinics, National Chlamydia Screening Programme in England, 1 April 2003–31 March 2004

		Screening tests among women				Screening tests among men			
	Total tests No (col %)	No	No (%) CT+	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	No	No (%) CT+	Unadjusted OR (95% CI)	Adjusted OR†† (95% CI)
Total	16 413	15 241	1538 (10.1%)		model n=10 041	1172	156 (13.3%)		model n=792
Age									
Under 16 years	1349 (8.2)	1284	96 (7.5%)	0.84 (0.67 to 1.05)	referent	65	1 (1.5%)	0.06 (0.01 to 0.46)*	not in model
16–19 years	7201 (43.9)	6544	792 (12.1%)	1.43 (1.28 to 1.60)†	1.85 (1.41 to 2.42)†	657	66 (10.0%)	0.45 (0.32 to 0.64)†	referent
20–24 years	7863 (47.9)	7413	650 (8.8%)	referent	1.38 (1.04 to 1.82)*	450	89 (19.8%)	referent	2.51 (1.64 to 3.86)†
Ethnicity									
White	11 138 (67.9)	10 286	973 (9.5%)	referent	referent	852	94 (11.0%)	referent	referent
Black Caribbean	413 (2.5)	365	66 (18.1%)	2.11 (1.61 to 2.78)†	2.04 (1.50 to 2.76)†	48	14 (29.2%)	3.32 (1.72 to 6.41)†	2.76 (1.29 to 5.93)*
Black African	408 (2.5)	373	37 (9.9%)	1.05 (0.75 to 1.49)	1.10 (0.76 to 1.60)	35	7 (20.0%)	2.02 (0.86 to 4.74)	1.45 (0.54 to 3.91)
Black British/other	380 (2.3)	316	48 (15.2%)	1.71 (1.25 to 2.35)†	1.77 (1.28 to 2.46)†	64	13 (20.3%)	2.06 (1.08 to 3.92)*	1.45 (0.69 to 3.04)
Asian subcontinent	262 (1.6)	253	15 (5.9%)	0.60 (0.36 to*1.02)	0.84 (0.49 to 1.43)	9	1 (11.1%)	1.01 (0.13 to 8.15)	0
Chinese/other Asian	201 (1.2)	193	13 (6.7%)	0.69 (0.39 to 1.22)	0.81 (0.42 to 1.55)	8	0 (0.0%)	0	0
Other ethnic group	210 (1.3)	202	13 (6.4%)	0.66 (0.37 to 1.16)	1.12 (0.61 to 2.05)	8	1 (12.5%)	1.15 (0.14 to 9.47)	0
Mixed	517 (3.1)	491	73 (14.9%)	1.67 (1.29 to 2.16)†	1.59 (1.20 to 2.09)†	26	8 (30.8%)	3.58 (1.52 to 8.47)*	2.72 (1.01 to 7.31)*
Unknown	2884 (17.6)	2762	300 (10.9%)	1.17 (1.02 to 1.34)*	1.25 (0.88 to 1.78)	122	18 (14.8%)	1.40 (0.81 to 2.41)	0.85 (0.24 to 3.04)
Risk behaviours‡									
New sex partner									
Yes	5077 (45.0)	4583	586 (12.8%)	1.69 (1.48 to 1.92)†	1.32 (1.14 to 1.53)†	494	74 (15.0%)	1.43 (0.95 to 2.14)	1.14 (0.71 to 1.84)
No	6207 (55.0)	5825	466 (8.0%)	referent	referent	382	42 (11.0%)	referent	referent
2 or more sex partners									
Yes	5061 (45.8)	4547	589 (13.0%)	1.78 (1.56 to 2.03)†	1.57 (1.35 to 1.82)†	514	76 (14.8%)	1.47 (0.96 to 2.24)	1.23 (0.76 to 1.99)
No	5994 (54.2)	5654	436 (7.7%)	referent	referent	340	36 (10.6%)	referent	referent
Specimen type									
Urine	9799 (59.7)	8627	899 (10.4%)	referent	referent	1172	156 (13.3%)	NA	NA
Cervical swab	2101 (12.8)	2101	217 (10.3%)	0.99 (0.85 to 1.16)	1.22 (1.00 to 1.48)				
Vulvo-vaginal swab	4513 (27.5)	4513	422 (9.4%)	0.89 (0.79 to 1.00)	1.16 (0.98 to 1.37)				
Laboratory test									
PCR	7041 (42.9)	6384	542 (8.5%)	referent	referent	657	63 (9.6%)	referent	referent
SDA	7629 (46.5)	7169	828 (11.5%)	1.41 (1.26 to 1.58)†	1.49 (1.28 to 1.75)†	460	86 (18.7%)	2.17 (1.53 to 3.08)†	2.11 (1.33 to 3.35)†
TMA	813 (5.0)	783	70 (8.9%)	1.06 (0.82 to 1.37)	not in model	30	5 (16.7%)	1.89 (0.70 to 5.10)	not in model
LCR	930 (5.7)	905	98 (10.8%)	1.31 (1.04 to 1.64)*	not in model	25	2 (8.0%)	0.82 (0.19 to 3.56)	not in model
Quarter									
Apr–Jun 2003	1032 (6.3)	1015	115 (11.3%)	referent	not in model	17	1 (5.9%)	referent	not in model
Jul–Sep 2003	2408 (14.7)	2316	250 (10.8%)	0.95 (0.75 to 1.20)		92	21 (22.8%)	4.73 (0.59 to 37.81)	
Oct–Dec 2003	5301 (32.3)	5013	492 (9.8%)	0.85 (0.69 to 1.06)		288	38 (13.2%)	2.43 (0.31 to 18.87)	
Jan–Mar 2004	7672 (46.7)	6897	681 (9.9%)	0.86 (0.70 to 1.06)		775	96 (12.4%)	2.26 (0.30 to 17.25)	
Clinic type (no of venues)									
Contraceptive clinics (96)	10 316 (62.9)	9787	1068 (10.9%)	referent	not in model	529	106 (20.0%)	referent	not in model
General practices (131)	1697 (10.3)	1615	161 (10.0%)	0.90 (0.76–1.08)		82	9 (11.0%)	0.49 (0.24 to 1.02)	
Women's clinics§ (21)	218 (1.3)	218	17 (7.8%)	0.69 (0.42 to 1.14)		0	0	0	
Termination of pregnancy (5)	378 (2.3)	376	39 (10.4%)	0.95 (0.67 to 1.32)		0	0	0	
College, university, school (15)	801 (4.9)	500	25 (5.0%)	0.43 (0.29 to 0.65)†		301	14 (4.7%)	0.20 (0.11 to 0.35)†	
Military facilities (4)	84 (0.5)	28	4 (14.3%)	1.36 (0.47 to 3.93)		56	9 (16.1%)	0.76 (0.36 to 1.61)	

Table 2 Continued

	Total tests No (col %)	Screening tests among women: No	Screening tests among women: No (%) CT+	Screening tests among women: Unadjusted OR (95% CI)	Screening tests among men: No	Screening tests among men: No (%) CT+	Screening tests among men: Unadjusted OR (95% CI)	Screening tests among men: Adjusted OR†† (95% CI)
Young people's (16)	1987 (12.1)	1830	150 (8.2%)	0.73 (0.61 to 0.87)†	157	12 (7.6%)	0.33 (0.18 to 0.62)†	
Other¶ (14)	934 (5.7)	887	74 (8.3%)	0.74 (0.58 to 0.95)*	47	6 (12.8%)	0.58 (0.24 to 1.41)	

CT+, *Chlamydia trachomatis* positive; OR, odds ratio; CI, confidence interval; PCR, polymerase chain reaction; SDA, strand displacement assay; TMA, transcription mediated assay; LCR, ligase chain reaction; NA, not applicable.
*Statistically significant at p <0.05 level.
†Statistically significant at p <0.001 level.
**Female model includes females under 25 years of age, ethnicity, behavioural risks, specimen type, and laboratory test.
††Male model includes 16–24 year old men only, ethnicity, behavioural risks, and laboratory test.
‡Only people responding to the question are included in totals.
§Includes gynaecology, infertility, colposcopy, and antenatal services.
¶Includes chlamydia screening office, outreach activities, and unknown clinic types.

new sex partner in the last 3 months (table 2). Further, there were higher concentrations of 20–24 year old females in the population tested with LCR, PCR, and TMA and the positivity in this group was less than 16–19 year olds.

DISCUSSION

The phased implementation of the National Chlamydia Screening Programme in England has begun. The number of phase 1 programme areas, the number of venues within programme areas, and the total number of screens performed all increased over time, reflecting our phased approach. Because the programme has just begun, it is important to place in context the screening volume and its impact on coverage. Economic models have shown that one of the most critical aspects to ensure the success of a widespread screening programme is uptake.[14 15 29–31] Recent estimates from the United States by Levine and colleagues suggest that screening coverage was highest in areas that experienced reductions in prevalence after several years of aggressive and comprehensive screening.[32] Data from the first few years of routine chlamydia testing in Sweden also reflect the impact of high screening volumes.[9] Continued efforts to increase screening coverage in England are focused not only on expanding the number of programme areas involved, but also increasing the volume of testing at the screening venues within those programme areas. This will be monitored closely as the NCSP continues to expand.

The first year of screening has also detected similar levels of infection among people consenting to be screened as was found in the original chlamydia screening pilot.[20] Screening programmes in other countries reported chlamydia prevalences ranging from 6% in Sweden[9] to 12% in the north western region of the United States[10 11] in their first year of implementation. Although those same programmes screened a larger number of women than thus far accomplished in England, the similar rates of infection at the start affirms that the opportunistic approach—selectively screening those thought to be at higher risk—has proved to be a successful strategy in disease detection. The data from the first year of the NCSP justify our continued focus on young women and men attending healthcare settings as performed in the original pilot.

Another unique outcome of the first year results is the demonstration that opportunistic screening can and does occur in a wide variety of settings. Encouragingly, the second highest volumes of screening were from 131 general practices (in five of the programme areas) and 16 young people's services (in six programme areas), both of which are not traditionally centred around sexual health service provision. Much has been made recently about the ability or willingness of GPs to become involved in the NCSP. Oakeshott *et al* suggest in a recent article that without remuneration GPs would not only not participate in screening but also that the programme would not succeed.[33] Unlike the research pilot of opportunistic chlamydia screening in which GPs were paid on a per test basis,[19] the NCSP funding in phase 1 did not include the same payments to GPs (as it is not a research project). The NCSP first year data seem to suggest that GPs are willing to offer chlamydia screening to their clientele without reimbursement incentives from the NCSP. Over 10% of all screening tests were done within general practice, and that proportion increased throughout the first year and continues to do so in preliminary data from the first quarter of the second year (data not shown). We are encouraged by these numbers, as strong efforts have been made by both the national management team, as well as local chlamydia screening coordinators and their teams, to engage primary care and to ease the implementation of screening in those settings. Creative delivery strategies utilised in phase 1

programme areas address some of the barriers to screening within general practice,[33] and include: (1) allowing patients to self select for screening and self complete the test request form (saving time); (2) training of practice nurses to make appropriate invitations for screening (reducing the need for expensive medical consultant involvement); (3) covering administrative time for specimen and data collection (augmenting costs); (4) shifting the responsibility for notification of results and follow up to a local chlamydia screening office (reducing workload burden within general practice); and (5) empowering GPs to holistically attend to the physical and sexual health needs of their young adult population (enhancing the skills and capabilities of general practice staff). The lessons learnt about implementing screening in primary care from the first phase of the programme have informed the development of guidelines for chlamydia screening in general practice as well as model local enhanced service contracts outlining set standards and outcomes for screening in this setting. The devolved nature of general practice provision in England means that efforts to encourage local involvement of GPs in chlamydia screening will become a major challenge of the programme in future years. Indeed, phase 2, and subsequent phase 3, implementation areas will encourage more widespread primary care involvement than previous phases.

Data from the NCSP's first year confirm that the epidemiological profile of both the men and women screened is nearly identical to that found in numerous studies in the United Kingdom[1 17 36] and in Europe,[37] with highest chlamydia positivity among women 16–19 years of age and men 20–24. The age related differences in chlamydia positivity between women and men screened was expected given the results of other studies.[1 9 11 36] Additionally, people who have acquired a sex partner recently or who have had several sex partners were at increased risk of infection. However, the association between behavioural risks and infection among men did not reach statistical significance in univariate analysis or multivariate modelling. This could be the result of a small sample size for men (less than 1200 male tests reported), an under-reporting of sexual risk taking among the female population, or an actual difference in the sexual behaviour of men versus women. There is evidence from the Natsal study of sexual behaviour in Britain to support a behavioural difference between men and women: men reported a greater number of lifetime and recent sex partners, as well as more frequent partner change, than women.[38]

The sexual behaviour data reported through the NCSP have provided additional benefit by further refining our analysis of risk behaviours that are associated with people testing positive for chlamydia. This will allow us to better understand the behavioural components contributing to the spread of STIs,[39] and monitor behavioural changes in the population that may affect our disease control efforts. Other established STI surveillance networks, principally through the statutory KC60 returns from GUM clinics, do not collect sexual behaviour data. The collection of these data in the NCSP is the first large scale programme targeting sexual health to include behavioural surveillance. The use of this information allows us an additional tool in prevention efforts to address, and eventually arrest, the observed increases in STIs in England.

The noted increase positivity among those tested with the SDA platform is an unexpected mystery. The concentration of higher risk people in the SDA tested population and lower risk people in the population tested using other NAATs might help explain the variations in positivity between the four different nucleic acid amplification tests. However, inter-laboratory variation in the use of the testing platforms, adjusted sensitivity and specificity of each NAAT in a "real world" setting, or the utilisation of lower cut-off threshold for positive confirmation within the laboratory could also influence the performance and outcome of the SDA test. It would be worthwhile to further analyse this difference. The DoH has recently funded the Microbiological Diagnostic Assessment Service to carry out a comparative evaluation of the sensitivity, specificity and performance of PCR, TMA, and SDA in three laboratories in England (Department of Health, personal communication). This evaluation may also provide additional context for explaining our findings.

Finally, researchers have suggested that targeted annual screening of 15–24 year old females, combined with treating 50% of partners of chlamydia positive females and increasing condom use, could dramatically reduce the prevalence of chlamydia in the population.[29] The NCSP includes dedicated funding and guidelines for a strong partner follow up activities in local programme areas[21] to ensure women do not become re-infected from an untreated partner and that partners of positive women do not continue to spread infection to others. The NCSP provides for the testing and free treatment of all sexual contacts, regardless of age, through application of rigorous national partner notification standards.[40] In future years, the marrying of partner notification data with screening volume and coverage data will provide an enhanced summary of the NCSP's impact on the population. We hope to expedite disease reductions through the combined approach of screening and comprehensive treatment and follow up.

It is clear from our results that we have some way to go to demonstrate reductions in disease similar to what was experienced in Sweden and the United States; however, the data from this first year of screening are encouraging. New lessons are being learnt on the process and outcomes of opportunistic screening and methods for enhancing its implementation in a diverse range of healthcare settings. Insights are being gained into the best methods for engaging men in sexual health; innovation in treatment and partner notification in sites outside of GUM clinics; and sharing of information on best practice across the breadth of the health service system in England. The collection of an expanded and disaggregate sexual health dataset is improving our understanding of the distribution and determinants of genital chlamydial infection. The NCSP will undoubtedly continue to

Key messages

- The phased implementation of the National Chlamydia Screening Programme has begun: 16 413 chlamydia screens to young men and women during the first year confirm the feasibility of opportunistic screening in non-GUM settings
- The NCSP has demonstrated 10% positivity among women and 13% positivity among men opportunistically screened; this is similar to the findings from the original screening pilot and affirms the opportunistic approach is a successful strategy for disease detection
- 30% of specimens collected from women were self taken vulvo-vaginal swabs (VVS), demonstrating the feasibility and acceptability of VVS as an alternative to urine collection for women
- The NCSP is the first national sexual health initiative to include routine behavioural surveillance, which improves our understanding of the behavioural factors driving STIs and enhances our ability to design appropriate prevention messages

make inroads into the prevention and control of this infection in England.

ACKNOWLEDGEMENTS

Funding is provided by the Department of Health (England), London. The opinions of the authors do not necessarily represent the views of the Department of Health (England).

For all their efforts in bringing chlamydia screening to their communities, the authors would like to thank the clinical, laboratory and administrative personnel from the phase 1 programme areas: Camden and Islington, Cornwall, Hull and East Riding, Lambeth/Southwark/Lewisham, Leeds, Nottingham, Portsmouth, Southend on Sea, the Wirral, and York.

CONTRIBUTORS

DSL is the lead scientist for the NCSP, collated, extracted and analysed the data, and wrote the paper; KAF is the chair of the National Chlamydia Screening Steering Group; SR is the national medical adviser of the NCSP; SA and PC are the national coordinators of the NCSP; each provided additions to the manuscript as co-authors.

Authors' affiliations

D S LaMontagne, K A Fenton, HIV and Sexually Transmitted Infections Department, Health Protection Agency, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK
S Randall, Department of Health, Sexual Health and Substance Misuse Team, Room 580D, Skipton House, 80 London Road, London, and Ella Gordon Unit, St Mary's Hospital, Portsmouth PO3 6AD, UK
S Anderson, P Carter, Department of Health, Sexual Health and Substance Misuse Team, Room 580D, Skipton House, 80 London Road, London SE1 6LH, UK

Competing interest: All authors declare no competing interests in the preparation or submission of this manuscript.

REFERENCES

1 **Health Protection Agency**, SCIEH, ISD, National Public Health Service for Wales, CDSC Northern Ireland, and UASSG. *Renewing the focus. HIV and other sexually transmitted infections in the United Kingdom in 2002.* London: Health Protection Agency, 2003.
2 **Stamm WE**. Chlamdyia trachomatis infections of the adult. In: Holmes KK, Sparling PF, Mardh PA, *et al*, eds. *Sexually transmitted diseases*, 3rd ed. United States: McGraw-Hill Health Professions Division, 1999:407–22.
3 **Idahl A**, Boman J, Kumlin U, *et al*. Demonstration of Chlamydia trachomatis IgG antibodies in the male partner of the infertile couple is correlated with a reduced likelihood of achieving pregnancy. *Hum Reprod* 2004;**19**:1121–6.
4 **Mausner JS**, Kramer S. *Epidemiology—an introductory text*, 2nd ed. Philadelphia: WB Saunders, 1985.
5 **Handsfield HH**, Jasman LL, Roberts PL, *et al*. Criteria for selective screening for Chlamydia trachomatis infection in women attending family planning clinics. *JAMA* 1986;**255**:1730–4.
6 **Britton TF**, Delisle S, Fine D. STDs and family planning clinics: a regional program for chlamydia control that works. *Am J Gynecol Health* 1992;**6**:80–7.
7 **Addiss DG**, Vaughn ML, Hillis SD, *et al*. History and features of the Wisconsin Chlamydia trachomatis control program. *Fam Plan Perspect* 1994;**26**:83–9.
8 **Addiss DG**, Vaughn ML, Ludka D, *et al*. Decreased prevalence in Chlamydia trachomatis infection associated with a selective screening program of family planning clinics in Wisconsin. *Sex Transm Dis* 1993;**20**:28–35.
9 **Herrmann B**, Egger M. Genital Chlamydia trachomatis infections in Uppsala County, Sweden, 1985–1993: declining rates for how much longer? *Sex Transm Dis* 1995;**22**:253–60.
10 **Mertz KJ**, Levine WC, Mosure DJ, *et al*. Trends in the prevalence of chlamydial infections—the impact of community-wide testing. *Sex Transm Dis* 1997;**24**:169–75.
11 **Scholes D**, Stergachis A, Heidrich FE, *et al*. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infections. *N Engl J Med* 1996;**334**:1362–6.
12 **Ostergaard L**, Andersen B, Moeller JK, *et al*. Home sampling versus conventional swab samples for screening of Chlamydia trachomatis in women: a cluster-randomized 1-year follow-up study. *Clin Infect Dis* 2000;**31**:951–7.
13 **Marrazzo JM**, Celum CL, Hillis SD, *et al*. Performance and cost effectiveness of selective screening criteria for Chlamydia trachomatis infection in women: implications for a national chlamydia control strategy. *Sex Transm Dis* 1997;**24**:131–41.
14 **Paavonen J**, Puolakkainen M, Paukku M, *et al*. Cost-benefit analysis of first-void urine Chlamydia trachomatis screening program. *Obstet Gynecol* 1998;**92**:292–8.
15 **Kretzschmar M**, Welte R, van den Hoek A, *et al*. Comparative model-based analysis of screening programs for Chlamydia trachomatis infections. *Am J Epidemiol* 2001;**153**:90–101.
16 **Wilson JMG**, Jungner G. *Principals and practice of screening for disease.* Geneva: World Health Organization, 1968.
17 **Chief Medical Officer's Expert Advisory Group**. *Main report of the CMO's Expert Advisory Group on Chlamydia trachomatis.* London: Department of Health, 1998.
18 **Department of Health**. *The national strategy for sexual health and HIV.* London: DoH, 2001.
19 **Pimenta JM**, Catchpole M, Rogers PA, *et al*. Opportunistic screening for genital chlamydial infection I: acceptability of urine testing in primary and secondary healthcare settings. *Sex Transm Infect* 2003;**79**:16–21.
20 **Pimenta JM**, Catchpole M, Rogers PA, *et al*. Opportunistic screening for genital chlamydial infection II: prevalence among healthcare attenders, outcome, and evaluation of positive cases. *Sex Transm Infect* 2003;**79**:22–7.
21 **Department of Health**. *National chlamydia screening programme in England—programme overview, core requirements and data collection*, 2nd ed. London: DoH, 2004.
22 **Fenton KA**. National chlamydia screening programme in England: the first steps. *Sex Transm Infect* 2004;**80**:000–00.
23 **Department of Health**. *The national chlamydia screening programme in England. Programme overview, core requirements and data collection.* London: DoH, Issue 2. April 2004.
24 **Gillick v West Norfolk, Wisbech AHA** [1986] AC112, [1985] 3 WLR830, [1985] 3 All ER 402 HL.
25 **Clinical Effectiveness Workgroup (AGUM and MSSVD)**. *Clinical effectiveness guideline for the management of Chlamydia trachomatis genital tract infection.* London: British Association for Sexual Health and HIV, 2002.
26 **Society of Sexual Health Advisers**. *The manual for sexual health advisers.* London: Society of Sexual Health Advisers, 2004.
27 **Dicker LW**, Mosure DJ, Levine WC. Chlamydia positivity versus prevalence. What's the difference? *Sex Transm Dis* 1998;**25**:251–3.
28 **LaMontagne DS**, Fenton KA, Pimenta JM, *et al*. Using chlamydia positivity to estimate prevalence: evidence from the Chlamydia Screening Pilot in England. *Int J STD AIDS* 2004;(in press).
29 **Welte R**, Kretzschmar M, Keidl R, *et al*. Cost-effectiveness of screening programmes for Chlamydia trachomatis. *Sex Transm Dis* 2000;**27**:518–29.
30 **Kretzschmar M**, van Duynhoven YTHP, Severijnen AJ. Modeling prevention strategies for gonorrhea and chlamydia using stochastic network simulations. *Am J Epidemiol* 1996;**144**:306–17.
31 **Honey E**, Augood C, Templeton A, *et al*. Cost effectiveness of screening for Chlamydia trachomatis: a review of published studies. *Sex Transm Infect* 2002;**78**:406–12.
32 **Levine WC**, Dicker LW, Devine O, *et al*. Indirect estimation of chlamydia screening coverage using public health surveillance data. *Am J Epidemiol* 2004;**160**:91–6.
33 **Centers for Disease Control and Prevention**. *Sexually transmitted disease surveillance 2002 Supplement: chlamydia prevalence monitoring project annual report 2002.* Atlanta: CDC, Division of STD Prevention, October 2003.
34 **Oakeshott P**, Hay P, Pakianathan M. Chlamydia screening in primary care. *Br J Gen Pract* 2004;**54**:491–3.
35 **McNulty CAM**, Freeman E, Bowen J, *et al*. Barriers to opportunistic chlamydia testing in primary care. *Br J Gen Pract* 2004;**54**:508–14.
36 **Adams EJ**, Charlett A, Edmunds WJ, *et al*. Chlamydia trachomatis in the United Kingdom: a systematic review and analysis of prevalence studies. *Sex Transm Infect* 2004;(in press).
37 **Wilson JS**, Honey E, Templeton A, *et al*. A systematic review of the prevalence of Chlamydia trachomatis among European women. *Hum Reprod Update* 2002;**8**:385–94.
38 **Fenton K**, Korovessis C, Johnson AM, *et al*. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet* 2001;**358**:1851–4.
39 **Garnett GP**. The geographical and temporal evaluation of sexually transmitted disease epidemics. *Sex Transm Infect* 2002;**78**(Suppl 1):114–19.

Sexually Transmitted Diseases, May 2004, Vol. 31, No. 5, p.283-289
DOI: 10.1097/01.OLQ.0000124613.85111.6B

Re-evaluating Selective Screening Criteria for Chlamydial Infection Among Women in the U.S. Pacific Northwest

D. SCOTT LA MONTAGNE, MPH,* L. ELIZABETH PATRICK, MC,,† DAVID N. FINE, PHD,† AND JEANNE M. MARRAZZO, MD, MPH,‡ ON BEHALF OF THE REGION X INFERTILITY PREVENTION PROJECT

*From the *Health Protection Agency, Communicable Disease Surveillance Centre, London, U.K., formerly of the Center for Health Training, Seattle, Washington; the †Center for Health Training, Seattle, Washington; and the ‡University of Washington, Division of Infectious Diseases, Seattle, Washington*

Objectives: **Screening women for *Chlamydia trachomatis* (CT) infection using selective screening criteria has been operational in the northwestern United States (Region X) since 1988. Changes in the field, including declines in CT prevalence, introduction of sensitive laboratory tests, and budgetary pressures necessitate reevaluating the selective screening approach to ensure program credibility and efficiency.**

Goals: **The goals of this study were to assess 1) performance of screening criteria in Region X, 2) predictors of CT infection, and 3) optimization of these criteria.**

Study Design: **We conducted cross-sectional analysis of 409,882 CT test records of women from 1998 to 2000 using multivariate logistic regression and sensitivity and efficiency analyses.**

Results: **Young age (<25 yrs), cervical signs of infection, and recent exposure to or history of chlamydial infection were strongly associated with testing positive. Behavioral risks showed a weak association with infection. Currently used selective screening criteria were sensitive but not efficient. Criteria weighted toward young age, exposure to chlamydia, or cervicitis would increase criteria efficiency by nearly 25% in some settings while detecting >90% of infections.**

Conclusion: **Evaluating selective screening criteria can result in modifications that could increase screening efficiency.**

CHLAMYDIA TRACHOMATIS (CT) is a prevalent and potentially devastating infection for women, with over 700,000 cases reported annually in the United States; however, up to 3 million total cases are estimated when underreporting and underdiagnosis are taken into account.[1] Because infection is most often asymptomatic,[2–4] untreated genital chlamydial infection can lead to pelvic inflammatory disease,[5–8] ectopic pregnancy,[7,9] and infertility.[9–12] Recent evidence has suggested that prior CT infection can be linked to ovarian cancer.[13]

Detection of infection is challenging because most women do not develop symptoms that prompt clinical evaluation. Because many women annually attend gynecology or family planning (FP) clinics for routine Pap smears, contraceptive services, and reproductive health checkups, clinic-based CT screening programs were developed.[14,15] One of the first large-scale CT screening programs in the United States began in 1988 at FP clinics in the Pacific Northwest, U.S. Public Health Service (USPHS) Region X, which includes the states of Washington, Idaho, Oregon, and Alaska.[14–16] To both minimize costs and to increase the probability of detecting infection among asymptomatic women, selective screening criteria (SSC) were developed.[17] The SSC initiated in 1988 were based on risk factors for infection, including young age, clinical signs, having sex with an infected partner, sexual behaviors such as frequent multiple sex partners, and previous diagnosis of a sexually transmitted infection (STI).[18–21] Using SSC, women attending for annual pelvic examinations in publicly funded family planning clinics in Region X are routinely tested for CT. For ease of implementation in clinical settings outside sexually transmitted disease (STD) clinics and to allow for funding of diagnostic CT testing in non-STD settings, the selective screening criteria in Region X include 2 elements normally interpreted as indications for diagnostic testing and/or presumptive treatment: manifestations of cervicitis (mucopurulent secretion, cervical friability, and abnormal cervical ectopy) and evidence of recent exposure to CT.

Beginning in 1993, the Centers for Disease Control and Prevention (CDC) began administration of Infertility Prevention Projects based in each federal health region using selective screening criteria that were locally developed; this effort has been the cornerstone of the CDC's programmatic efforts to reduce the morbidity and associated sequelae from this infection. Each of the 10 projects receives funding from CDC to administer chlamydia screening. Areas in the United States and other countries that have been performing clinic- and population-based screening for chlamydial infection have reported declines in prevalence,[22–24] and 2 randomized, controlled trials of screening have shown a 50% reduction in the diagnosis of pelvic inflammatory disease.[25,26]

Many studies have evaluated the performance and cost-effectiveness of this CT control strategy,[27–30] and most have concluded that in settings of moderate prevalence, selective screening programs are cost-effective.[18] The most recent (1995) evaluation of Region X's selective screening criteria used data from 1990 to 1993.[19] At that time, enzyme immunoassay (EIA) with direct fluorescence antibody (DFA) testing was the standard CT diag-

Funding for this study was made possible through the Centers for Disease Control and Prevention, Division of STD Prevention, Infertility Prevention Project and the Department of Health and Human Services, Office of Family Planning. The authors thank all the clinical staff who participated in this screening program for their timely and accurate data collection and reporting; without them, evaluating the success of the program would be impossible.

Correspondence: David N. Fine, PHD, Center for Health Training, 1809 7th Avenue, Suite 400, Seattle, WA 98101-1341. E-mail: scott.lamontagne@hpa.org.uk

Received for publication September 15, 2003, revised December 10, 2003, and accepted December 11, 2003.

nostic test. Recently, highly sensitive nucleic acid amplification tests have been increasingly used and shown to be a factor in observed increases in prevalence in Region X, other parts of the United States, and in Sweden.[31–33] Some investigators have suggested that periodic reevaluation of selective screening should be performed when circumstances in the field change significantly.[18,34]

The current reevaluation of the SSC in use in Region X centers on 3 questions: 1) What is the current performance of the selective screening criteria now used in Region X? 2) Have risk factors for the presence of chlamydial infection changed since the last SSC evaluation in 1995? 3) Can the performance of the selective screening criteria be optimized?

Methods

We analyzed 409,882 CT test records (excluding 4355 or 1% where test result or test type was unknown) for women attending 252 family planning, 123 STD and 251 "other" clinics, including community/migrant, college health, public health nursing, and adolescent clinics, in Region X from 1998 to 2000. STD clinics contributed 34,288 records, FP clinics 304,183 records, and "other" clinics 71,471 records. Women attending STD clinics were universally tested for infection. Women attending family planning and other clinics were tested according to the Region X SSC, which were: 1) age ≤24 years, or 2) age >24 years plus any 1 of the following: nonspecific cervicitis, mucopurulent cervicitis (MPC), friability of the cervix, cervical ectopy, clinician-diagnosed pelvic inflammatory disease (PID), patient-reported or clinician-assessed recent exposure to chlamydia or any other STD, including sex with a symptomatic sex partner in the past 60 days, *C. trachomatis* or any other STD in the prior 12 months, or new sex partner or 2 or more sex partners in the previous 60 days. Diagnostic tests used in Region X were EIA (SyvaMicrotrak), ligase chain reaction (LCR; Abbott LCx), nonamplified DNA probe (PACE2; Gen-Probe), and cell culture.

To define the performance of the current selective screening criteria in Region X, we analyzed all tests for the sensitivity and efficiency of the criteria. Sensitivity was defined as the percentage of positives detected, and efficiency was the percentage of tests that met the criteria.[35] Thresholds of 60% efficiency and 90% sensitivity were used as ideal benchmarks for criteria performance. The ideal scenario was to identify the most positives (a high percentage for sensitivity) while testing the fewest number of people (low percentage for efficiency). Sensitivities and efficiencies for clinic type and test type were calculated separately to explore variations in criteria performance in settings of lower prevalence or locations where use of the more sensitive nucleic acid amplification tests had increased.

To define risk factors associated with chlamydial infection, we analyzed data from women universally tested at STD clinics. Data were gathered on a standardized laboratory test request form in use across all clinics since 1993. Patients self-reported demographics and behavioral risks in response to questions posed by clinicians during the clinic visit. Clinicians reported results of cervical examinations using standard definitions within the program for mucopurulent endocervical discharge, cervical friability, abnormal cervical ectopy, and PID, each reported separately.[16] Laboratories reported test type and results. With CT positivity as the dependent variable, univariate odds ratios for each independent variable were calculated. Variables significant in univariate analysis to a level of $P < 0.05$ were included in a multivariate logistic regression model (forward stepwise procedure with Wald statistical correction). The final model included a variable for type of diagnostic test to explore whether risk factors differed between those tested with amplified and nonamplified laboratory methods.

Using the results of the risk analysis, we developed 5 different sets of selective screening criteria to evaluate for sensitivity and efficiency using the benchmarks of 60% and 90%, respectively. Because no new variables were under consideration for inclusion in sets of SSC, the focus of the sensitivity and efficiency analysis was to assess whether the current SSC in Region X could be simplified. Therefore, the resultant SSC were modifications of the existing Region X criteria and could be applied retrospectively to our study population to address whether the current criteria could be optimized. Additionally, the criteria endorsed by the third U.S. Preventive Services Task Force (USPSTF) were also applied to our study population and compared with the performance of other selective screening criteria. This Task Force recommended screening for: 1) all sexually active women 25 years and younger; and 2) asymptomatic women over 25 years of age at increased risk, defined as new or multiple sex partners, prior history of an STD, or inconsistent condom use.[36]

All analyses were performed using SPSS 8.0 statistical software (SPSS, Chicago, IL). Measures of significance were 2-sided and used a significance level of $P < 0.05$.

Results

Chlamydia positivity was highest in STD clinics (7.3%) and was approximately 4.0% in FP and other clinics (Table 1). Women less than 25 years of age comprised 70% of the FP clinic population and 64% of the "other" clinics' population; women attending STD clinics were slightly older. EIA and LCR were the most frequently used laboratory tests. Almost 50% of tests in STD clinics were EIA, whereas in FP clinics, more than 45% of tests were LCR. The higher proportion of LCR tests within FP clinics reflects the wider dissemination of nucleic acid amplification tests in that setting. For all clinical settings, 97% of samples were clinician-acquired cervical swabs and 2.5% were urine samples (data not shown), reflecting the linkage of the screening program to annual pelvic examinations for women. Behavioral risks were common: 21% to 39% of the population (depending on clinic type) reporting a new sex partner in the last 60 days, and nearly one fourth of the STD clinic attendees reporting 2 or more sex partners over the same period. Not surprisingly, condom use was low; less than 25% of women used condoms at last sex, regardless of clinic type. Women who attended STD clinics were more likely to demonstrate clinical signs associated with increased likelihood of chlamydial infection such as mucopurulent cervicitis or cervical friability (Table 1).

Univariate analysis confirmed that the factors associated most strongly with chlamydial infection among STD clinic attendees were young age, clinical signs, and recent exposure to chlamydia or other STDs (Table 2). Over 80% of all women who tested positive were less than 25 years of age, regardless of clinic type (data not shown). Behavioral risks such as new sex partner, multiple sex partners, or history of chlamydial infection were associated with positivity, but not as strongly. Nonwhite race was also associated with infection, but Hispanic ethnicity was not. Women submitting urine samples were slightly more likely than those submitting cervical swabs to test positive, and those tested with culture were less likely to test positive than those tested with LCR, consistent with the lower sensitivity of culture in detecting CT (Table 2). When stratifying by test type, variables associated with infection did not differ between women tested with EIA and those tested with LCR (data not shown).

Factors associated with an increased risk of chlamydial infection in univariate analysis were explored in multivariate models.

TABLE 1. Characteristics of Women Tested by Type of Clinic, Region X, 1998–2000

Characteristic	STD Clinics (n = 34,228, %)	FP Clinics (n = 304,183, %)	Other* Clinics (n = 71,471, %)
Percent positive for chlamydia	7.3	4.1	3.8
Age (yrs)			
<20	28.0	37.3	35.8
20–24	28.1	33.4	29.4
25–29	15.9	14.7	13.4
>29	28.0	14.6	21.5
Race			
White	75.9	84.0	74.9
Black	12.3	4.4	8.7
American Indian/Alaska Native	2.2	1.1	3.9
Asian/Pacific Islander	3.9	4.2	5.2
Other or More than one race	5.7	6.3	7.3
Ethnicity			
Hispanic	12.0	15.6	24.7
Test type			
EIA	47.1	43.0	36.0
LCR	21.9	45.6	36.8
DNA probe	11.1	6.9	25.1
Culture	20.0	4.5	2.1
New sex partner (past 60 days)	38.6	24.7	21.5
More than 1 sex partner (past 60 days)	23.5	10.2	7.9
Symptomatic sex partner	11.7	2.6	2.7
No condom use (last sex)	78.6	76.6	76.0
Cervical signs (MPC, friability, ectopy)	17.4	8.5	11.5

*Other clinics include community, migrant, college health, public health nursing, and adolescent clinics.
STD = sexually transmitted disease; FP = family planning; EIA = enzyme immunoassay; LCR = ligase chain reaction; MPC = mucopurulent cervicitis.

Among all women attending STD clinics, factors remaining significantly associated with infection, in order of relative strength, were young age, exposure to CT, sex with a symptomatic sex partner, cervical friability, and exposure to nongonococcal urethritis. Weaker, but statistically significant, associations were found with mucopurulent cervicitis, concurrent diagnosis of PID, exposure to *Neisseria gonorrhoeae*, multiple sex partners, and history of chlamydial infection in the last year. Women tested with either EIA or LCR were more likely to be positive than those tested with DNA probe or culture, but no statistically significant difference between EIA and LCR was found (Table 2).

Evaluation of the sensitivity and efficiency of selective screening criteria revealed that the current Region X criteria were more sensitive than the target benchmark, detecting 95.6% of infections, but were less efficient than the 60% benchmark, requiring testing 85.6% of women (Table 3). The sensitivity of these criteria remained high and exhibited little variation across all clinics (range, 94.5–97.5%). Even after stratifying by test type within clinical settings, the sensitivity of the current SSC in Region X showed little variation (range, 90.8–98.7%). The efficiency of the current criteria varied little between clinic types (range, 80.8–87.3%) and did not achieve our study's efficiency benchmark of 60%. When exploring the variation by test type, for all test types except DNA probe, the range of the criteria's efficiency was constant (82.6–89%). The efficiency of the current criteria was most variable when women were tested by DNA probe: 67.9% at other clinics, 88.1% at family planning clinics, and 91.0% at STD clinics. Although SSC were not used in STD clinics where universal testing was used, the criteria would have been no more efficient there than at sites that selectively screened.

Five sets of SSC developed from factors significantly associated with infection through univariate analysis and multivariate modeling showed marked differences in efficiency and sensitivity when compared with each other and with SSC from the USPSTF and those currently used in Region X. The sets of criteria were developed using an additive approach, beginning with just age (Table 3, criteria 3), which had good efficiency (56.1% in STD clinics, 65.1% in "other" clinics, and 70.7% in FP clinics), but reduced sensitivity, detecting approximately 85% of infections. The other criteria added additional components to increase the likelihood of detecting infection in women over 24 years of age using the evidence generated from the analysis of risk factors (Table 3, criteria 4–6). Combining testing, all young women and women over 24, if there were clinical signs, eg, cervicitis or ectopy (Table 3, criteria 4), increased the sensitivity of the criteria, detecting almost 90% of all positives, with a slight reduction in efficiency, requiring testing of 64% to 74% of women. There were only incremental differences on varying the selection criteria for women over 24 using combinations of clinical signs, risk behaviors, and/or recent exposure to an infected partner (criteria 5 and 6). An additional diagnostic model was developed (Table 3, criteria 7), because the current SSC in Region X allowed for diagnostic tests to be included, principally, cervical signs of infection or recent exposure. Not surprisingly, this model performed best in STD clinics, detecting 93.3% of positives, with the greatest efficiency, testing less than 70% of the women attending. However, the relative performance of this model was similar to the other criteria. The recently recommended criteria by the third U.S. Preventive Services Task Force had the lowest efficiency (Table 3), in part because the criteria recommend testing women who do not use condoms regularly, which comprised over 75% of our study population.

Discussion

Our study confirmed that the factors most strongly associated with chlamydial infection are young age, clinical findings suggestive of infection, report of contact to CT, and reported sex with a

TABLE 2. Univariate and Multivariate Factors Associated With Chlamydial Infection Among Women Attending STD Clinics, Region X, 1998–2000

	Univariate Factors (N = 34,228)	Multivariate Factors (model n = 24,780)
	Odds Ratios (95% confidence interval)†	
Age (yrs)		
≤17	8.0 (6.7–9.4)	7.8 (6.3–9.6)
18–19	6.7 (5.6–7.9)	6.3 (5.1–7.8)
20–24	5.0 (4.3–5.9)	4.8 (3.9–5.8)
25–29	2.6 (2.2–3.2)	2.6 (2.0–3.2)
>29	Referent	Referent
Race		
White	Referent	Referent
Black	1.2 (1.1–1.4)	1.5 (1.3–1.8)
American Indian/Alaska Native	1.8 (1.4–2.2)	1.7 (1.2–2.4)
Asian/Pacific Islander	2.1 (1.8–2.5)	2.3 (1.9–2.9)
Other/Multiracial	1.0 (0.9–1.2)	1.2 (0.9–1.5)
Ethnicity		
Hispanic	Referent	Not included in model
Non-Hispanic	1.0 (0.9–1.1)	
Specimen type		
Cervical swab	Referent	Referent
Urine	1.4 (1.1–1.8)	1.1 (0.8–1.6)
Test type		
DNA Probe	Referent	Referent
EIA	0.9 (0.8–1.1)	1.3 (1.1–1.5)
Culture	0.7 (0.6–0.8)	1.0 (0.8–1.2)
LCR	1.2 (1.0–1.4)	1.6 (1.3–1.9)
Clinical exam findings		
Normal appearance of cervix	0.5 (0.5–0.6)	0.8 (0.7–0.9)
MPC	3.5 (3.1–3.8)	1.8 (1.5–2.1)
Friability	3.1 (2.7–3.4)	2.3 (1.9–2.7)
Ectopy	3.2 (2.6–3.9)	1.1 (0.8–1.4)
PID	1.7 (1.4–2.1)	1.5 (1.1–2.0)
Exposure risk factors		
Exposure to CT	7.8 (7.0–8.7)	3.9 (3.3–4.5)
Exposure to GC	3.7 (2.9–4.6)	1.5 (1.1–2.0)
Exposure to NGU	2.3 (1.9–2.9)	2.0 (1.6–2.6)
Exposure to unspecified STD	1.0 (0.8–1.1)	Not included in model
Sex with symptomatic partner	4.3 (3.9–4.8)	2.2 (1.9–2.5)
Behavioral risk factors		
CT last 12 months	2.5 (2.2–2.9)	1.3 (1.1–1.5)
Other STD last 12 months	1.1 (1.0–1.3)	Not included in model
Condom use at last sex (yes)	0.9 (0.8–1.0)	Not included in model
New sex partner	1.4 (1.3–1.5)	1.2 (1.0–1.3)
Multiple sex partners	1.5 (1.4–1.6)	1.5 (1.4–1.6)

†All odds ratios rounded to the nearest 10th percent and calculated at significance level $P < 0.05$.
EIA = enzyme immunoassay; LCR = ligase chain reaction; MPC = mucopurulent cervicitis; PID = pelvic inflammatory disease; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NGU = nongonococcal urethritis; STD = sexually transmitted disease.

symptomatic partner. Behavioral risk factors were weakly associated with infection, especially among women tested with more sensitive laboratory tests. Additionally, behavioral risk factors did not add efficiency to the selective criteria for screening. There were variations in the predictors' performance by test type, but differences were slight and did not outweigh the consistent performance of young age, clinical findings, and recent exposure, as recent studies have confirmed.[37–43]

With the exception of universal screening, none of the selective criteria developed from our models were able to detect >92% of CT-positives outside an STD setting. Our analysis found some added efficiency in including exposure variables, eg, exposure to CT or sex with symptomatic partner, and cervical findings as indications for screening older women. Although these items are usually considered indications for diagnostic testing and/or presumptive treatment in STD clinics and other clinical settings, the inclusion of signs of cervicitis or exposure to an STD in Region X SSC has been maintained over the years for ease in clinical decision-making in non-STD settings. Our results showed that there was very little difference in criteria efficiency or sensitivity when these items were used in a diagnostic model or as part of screening criteria (Table 3, criteria 6 and 7). Behavioral risks such as a new sex partner or multiple sex partners increased the population screened to nearly 80% while only yielding a slight increase in the proportion of infections found.

As an example, Figure 1 illustrates the predictive performance of changing the current SSC to items that reflect greater efficiency with minimal reduction in sensitivity, as suggested in the models in Table 3. In our study population, chlamydia positivity was 5.3% among females tested in FP clinics. The goal of SSC is to detect those women most likely to be positive. Age was the best predictor of infection. If that were the first

TABLE 3. *Sensitivity and Efficiency of Different Selective Screening Criteria for Chlamydial Infection Among Women by Clinic Type, Region X, 1998–2000**

	STD (n = 34,228)		FP (n = 304,183)		Other* (n = 71,471)	
	Study Thresholds = 60% Efficiency/90% Sensitivity†					
Criteria Set	Eff. (%)	Sens. (%)	Eff. (%)	Sens. (%)	Eff. (%)	Sens. (%)
Current criteria in region X‡	87.3	97.5	86.5	95.4	80.8	94.5
US preventive Services Task Force recommendation§	93.3	97.5	95.2	98.2	93.4	97.7
Age ≤24 yrs‖	56.1	82.1	70.7	85.4	65.1	84.4
Age ≤24 or age >24 yrs if any clinical signs, eg, cervicitis¶	63.7	89.5	73.8	88.8	69.6	88.3
Age ≤24 or age >24 yrs if any clinical sign or behavioral risk, eg, recent partner change**	77.1	93.5	79.6	92.1	72.2	90.0
Age ≤24 or age >24 yrs if any clinical sign or recent exposure to a sexually transmitted disease††	67.0	92.0	74.7	89.9	70.7	89.3
Diagnostic model‡‡	69.3	93.3	78.8	91.9	75.8	91.9

STD = sexually transmitted disease clinic; FP = family planning clinic.
*Other clinics include community, migrant, college health, public health nursing, and adolescent clinics.
†See notes in text for definitions.
‡Screen 1) all women age ≤24 yrs, all pregnant women, and all women receiving an intrauterine device (IUD), and 2) women >24 yrs if any clinical sign (cervicitis, MPC, friability, ectopy, or PID), any recent exposure (to chlamydia, gonorrhea, nongonococcal urethritis, or other STD, or reported sex with a symptomatic partner in the last 60 days), diagnosed chlamydial infection or other STD in the last year, or behavioral risk (new sex partner, 2 or more sex partners in the last 60 days).
§Screen 1) all women age ≤25 yrs, and 2) women >25 years if more than 1 sex partner, or diagnosed chlamydial infection or other STD in the last year, or inconsistent condom use.
‖Screen 1) all women age ≤24 yrs.
¶Screen 1) all women age ≤24 yrs and 2) women >24 yrs if any clinical sign (cervicitis with or without mucopus, cervical friability, or PID).
**Screen 1) all women age ≤24 yrs, and 2) women >24 yrs if any clinical sign (cervicitis with or without mucopus, or PID), or behavioral risk (new sex partner or 2 or more sex partners in the last 60 days).
††Screen 1) all women age ≤24 yrs and all pregnant women, and 2) women >24 yrs if any clinical sign (cervicitis with or without mucopus, friability, ectopy, or PID), or any exposure (to chlamydial infection in the last 60 days or sex with a symptomatic sex partner).
‡‡Test 1) all women if any clinical sign (cervicitis with or without mucopus, friability, ectopy, or PID) and all pregnant women, and 2) screen women age ≤24 yrs, and 3) test all women if any exposure (to chlamydia, gonorrhea, or nongonococcal urethritis, or sex with symptomatic sex partner), or history of a positive chlamydia test in the last year.

criterion for screening, 85% of all positives (10,621 of 12,437) would have been detected, whereas testing two thirds of the female population (Fig. 1) over the 3-year period of our study. Using additional selection criteria for women over 24, eg, clinical signs or conditions, or recent exposure to chlamydia, 15% of this older age group would have been tested, but the positivity in this group was 4.6% (Fig. 1). Therefore, these additional criteria would have identified a subset of women at highest risk. The remaining population of women over 24 had the lowest positivity, 1.6%, which some have suggested is below the threshold to make screening for chlamydial infection cost-effective.[18,24,28–30,36] However, the number of positives missed would have been less than 1 positive per clinic per year.

The current selective screening criteria used in the Region X Infertility Prevention Project are very inclusive; 80% to 87% of women screened in the last 3 years satisfied these criteria. This region, as the first large-scale population-based chlamydia screening program implemented in the United States, has been using these criteria for nearly 10 years. Even with the marked reductions in prevalence observed in this population and the increasingly widespread use of highly sensitive nucleic acid amplification tests, the current SSC were sensitive, although not particularly efficient. They required testing over 85% of women in various clinics to capture over 95% of all positives. Although Miller and colleagues recently suggested that 50% efficiency and 80% sensitivity were good benchmarks for selectively screening women for chlamydial infection,[35] the Region X Infertility Prevention Project Advisory Committee argued that failing to detect nearly 20% of all positives was unacceptable (Committee minutes, January 2002, unpublished data).

For most of the screening scenarios investigated, criteria efficiency ranged from 56% to 95%, and criteria sensitivity ranged from 82% to 98% across the 3 clinical settings. The limited variation in criteria sensitivity likely reflects the relative stability over time of those factors associated with infection. The wide range of efficiency might suggest that criteria should be tailored to the clinical setting in which screening is occurring. In Region X, the SSC have always been consistent across all 4 states and non-STD clinics. This has facilitated program implementation and training of clinical staff through provision of clear, consistent messages and clinical protocols. Our study suggests that STD clinics might benefit most by using selective screening for chlamydial infection, although potential tradeoffs in reducing the comprehensive diagnostic services currently offered in many of these settings would need to be considered carefully.

Finally, our study showed that the current criteria in use in Region X could be optimized. A selective screening approach that first tests all women 24 years and younger, then tests women over 24 years if they have cervical signs implicative of infection or report recent exposure to CT or sex with a symptomatic partner (Table 3, 6), would have been over 10% more efficient with only a modest 5% decrease in sensitivity. Had this been used in the STD clinic population, efficiency would have increased over 25% while still detecting 92% of all positives.

There are at least 3 potential limitations with our evaluation.

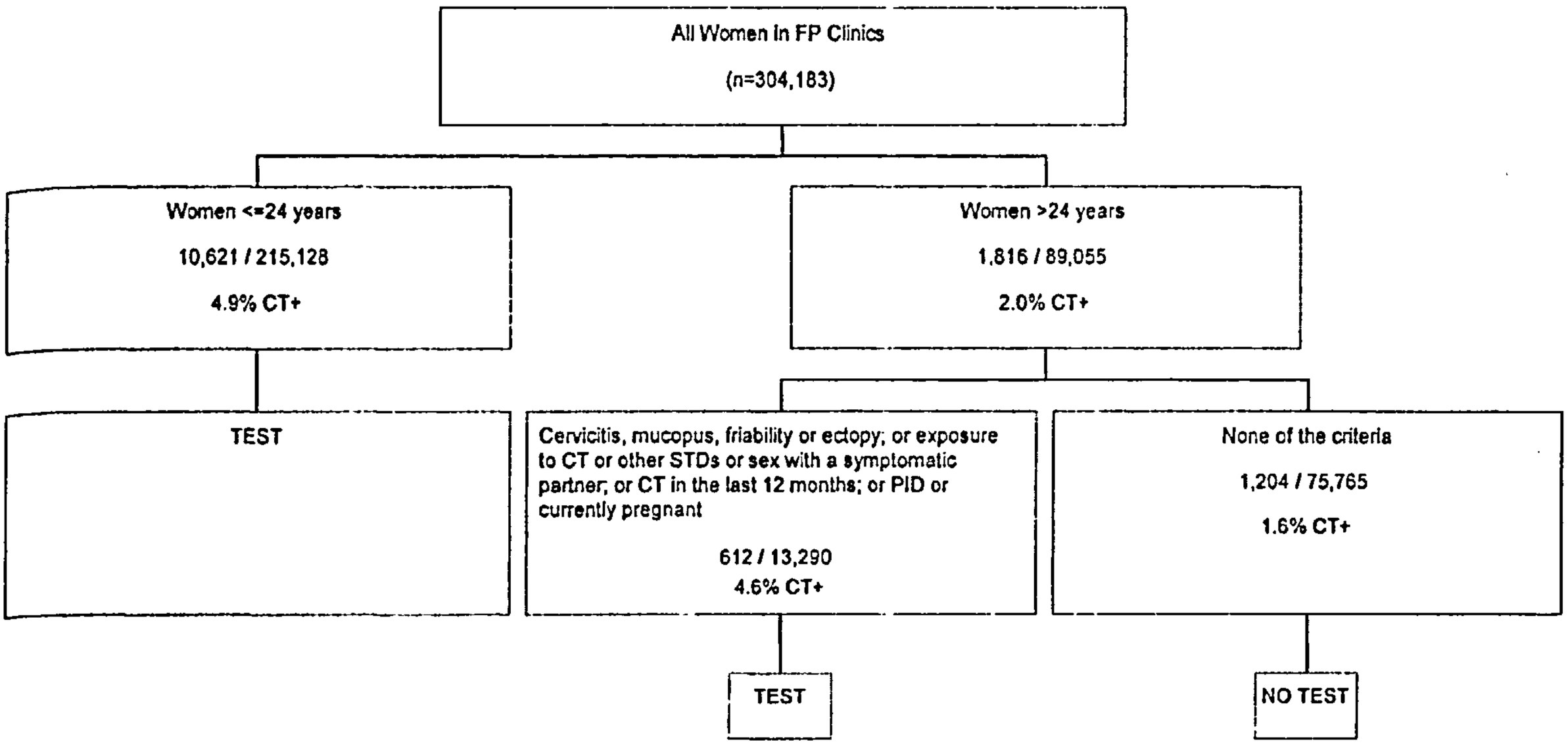

Fig. 1. Predictive performance of modified selective screening criteria,* Region X, 1998 to 2000. *The modified selective screening criteria in Region X are: 1) screen all women 24 years and younger; and 2) for women >24 years of age, test for chlamydial infection if at least 1 of the following exists: cervicitis, mucopurulence, friability, ectopy, pelvic inflammatory disease (PID), reported exposure to *Chlamydia trachomatis* (CT), sex with a symptomatic partner in the past 60 days, CT infection in the last 12 months, PID, pregnancy, or planned intrauterine device insertion.

First, selection bias could have been introduced by excluding a small proportion of tests among the screened population, not accounting for women who were tested frequently during the 3-year study period or by clinics not testing eligible women. However, less than 1% of all tests performed on women were excluded; women who are repeatedly tested would generally be included in the screening criteria (mostly because of age), and the Project has had a high participation rate among clinics since the program's inception in 1988. Second, almost all women in our study had a cervical sample used as the diagnostic specimen for CT; urine for nucleic acid amplification testing (NAAT) has become more widespread. However, the performance of NAAT performed on cervical samples is comparable to that on urine,[44] so use of urine as the diagnostic modality in this study is unlikely to have changed our conclusions. Finally, the poor performance of our behavioral risk factors could be reflective of not having asked the right questions to detect asymptomatic infections in women over 24. It is possible that there are other characteristics of the over 24-year-old population of women that could aid in the development of more SSC for this group.

Based on the results of our evaluation, the Region X Infertility Prevention Project has modified their selective screening criteria for women tested for chlamydial infection at family planning and other non-STD clinics and began testing women accordingly in January 2003. The criteria eliminated include the 2 items reflecting risk behavior (new sex partner or more than 1 sex partner in the past 60 days), recent exposure to a partner with an STI that is not CT, and history of an STI that is not CT. These modified selective screening criteria in Region X are: 1) test all women under 25 years old; and 2) for women ≥25 years of age, test for chlamydial infection if at least 1 of the following exists: signs of mucopurulent cervicitis, PID, reported exposure to chlamydia, sex with a symptomatic partner in the past 60 days, chlamydial infection in the last 12 months, PID, pregnancy, or planned IUD insertion.[16*] As funding for large-scale screening initiatives becomes increasingly strained, incremental efficiency gained in selective screening criteria should translate into program savings.

References

1. Department of Health and Human Services. Sexually transmitted disease surveillance 2000. Atlanta: Division of STD Prevention, Center for Disease Control and Prevention, 2001.
2. McCormack WM, Alpert S, McComb DE, et al. Fifteen-month follow-up study of women infected with *Chlamydia trachomatis*. N Engl J Med 1979; 300:123–125.
3. Schachter J, Stoner E, Moncada J. Screening for chlamydial infections in women attending family planning clinics. West J Med 1983; 138:375–379.
4. Brunham RC, Paavonen J, Stevens CE, et al. Mucopurulent cervicitis—The ignored counterpart in women of urethritis in men. N Engl J Med 1984; 311:1–6.
5. Westrom L, Joesoef R, Reynolds G, et al. Pelvic inflammatory disease and fertility. A cohort study of 1844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis 1992; 19:185–192.
6. Hillis SD, Owens LM, Marchbanks PA, et al. Recurrent chlamydial infections increase the risk of hospitalization for ectopic pregnancy and pelvic inflammatory disease. Am J Obstet Gynecol 1997; 1:103–106.
7. Cates W Jr, Wasserheit JN. Genital chlamydial infections: Epidemi-

*Accurate pregnancy and IUD data were not available during the study period, but have been a part of the screening criteria in Region X based on standard gynecologic clinical standards recommended by the American College of Obstetrics and Gynecology.

ology and reproductive sequelae. Am J Obstet Gynecol 1991: 164: 1771–1781.
8. DeMuylder X, Laga M, Tennstedt C, et al. The role of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in pelvic inflammatory disease and its sequelae in Zimbabwe. J Infect Dis 1990; 162:501–505.
9. Miettinen A, Heinonen PK, Teisala K, et al. Serologic evidence for the role of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in the etiology of tubal factor infertility and ectopic pregnancy. Sex Transm Dis 1990; 17:10–14.
10. Mabey DCW, Ogbaselassie G, Robertson JN, et al. Tubal infertility in the Gambia: Chlamydial and gonococcal serology in women with tubal occlusion compared with pregnant controls. Bull World Health Organ 1985; 63:1107–1113.
11. Tjiam KH, Zeilmaker GH, Alberda AT, et al. Prevalence of antibodies to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in infertile women. Genitourin Med 1985; 61:175–178.
12. Robertson JN, Ward ME, Conway D, et al. Chlamydial and gonococcal antibodies in sera of infertile women with tubal obstruction. J Clin Pathol 1987; 40:377–383.
13. Ness RB, Goodman MT, Shen C, et al. Serologic evidence of past infection with *Chlamydia trachomatis*, in relation to ovarian cancer. J Infect Dis 2003; 187:1147–1152.
14. Lossick J, DeLisle S, Fine D, et al. Regional program for widespread screening for *Chlamydia trachomatis* in family planning clinics. In: Bowie WR, Caldwell HD, Jones RP, et al., eds. Chlamydial Infections: Proceedings of the Seventh International Symposium on Human Chlamydial Infections. Cambridge: Cambridge University Press, 1990:575–579.
15. Britton TF, Delisle S, Fine D. STDs and family planning clinics: A regional program for chlamydia control that works. Am J Gynecol Health 1992; 6:80–87.
16. Region X Infertility Prevention Project Manual. Seattle: Center for Health Training, 2002.
17. Handsfield HH, Jasman LL, Roberts PL, et al. Criteria for selective screening for *Chlamydia trachomatis* infection in women attending family planning clinics. JAMA 1986; 255:1730–1734.
18. Marrazzo JM, Celum CL, Hillis SD, et al. Performance and cost-effectiveness of selective screening criteria for *Chlamydia trachomatis* infection in women: Implications for a national chlamydia control strategy. Sex Transm Dis 1997; 24:131–141.
19. Marrazzo JM, Fine D, Celum CL, et al. Selective screening for chlamydial infection in women: A comparison of three sets of criteria. Fam Plann Perspect 1997; 29:158–162.
20. Han Y, Coles FB, Hipp S. Screening criteria for *Chlamydia trachomatis* in family planning clinics: Accounting for prevalence and clients' characteristics. Fam Plann Perspect 1997; 29:163–166.
21. Stamm WE. *Chlamydia trachomatis* infections of the adult. In: Holmes KK, Sparling PF, Mardh PA, et al., eds. Sexually Transmitted Diseases, 3rd ed. McGraw-Hill Health Professions Division, 1999: 407–422.
22. Mertz KJ, Levine WC, Mosure DJ, et al. Trends in the prevalence of chlamydial infections—The impact of community-wide testing. Sex Transm Dis 1997; 24:169–175.
23. Herrmann B, Egger M. Genital *Chlamydia trachomatis* infections in Uppsala County, Sweden, 1985–1993: Declining rates for how much longer? Sex Transm Dis 1995; 22:253–260.
24. Kretzschmar M, Welte R, van den Hoek A, et al. Comparative model-based analysis of screening programs for *Chlamydia trachomatis* infections. Am J Epidemiol 2001; 153:90–101.
25. Scholes D, Stergachis A, Heidrich FE, et al. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infections. N Engl J Med 1996; 334:1362–1366.
26. Ostergaard L, Andersen B, Moeller JK, et al. Home sampling versus conventional swab samples for screening of *Chlamydia trachomatis* in women: A cluster-randomized 1-year follow-up study. Clin Infect Dis 2000; 31:951–957.
27. Howell MR, Quinn TC, Brathwaite W, et al. Screening women for *Chlamydia trachomatis* in family planning clinics—The cost-effectiveness of DNA amplification assays. Sex Transm Dis 1998; 25: 108–117.
28. Townsend JRP, Turner HS. Analysing the effectiveness of chlamydia screening. J Oper Res Soc 2000; 51:812–824.
29. Welte R, Kretzschmar M, Leidl R, et al. Cost-effectiveness of screening programs for *Chlamydia trachomatis*—A population-based dynamic approach. Sex Transm Dis 2000; 27:518–529.
30. Honey E, Augood C, Templeton A, et al. Cost effectiveness of screening for *Chlamydia trachomatis*: a review of published studies. Sex Transm Infect 2002; 78:406–412.
31. Dicker LW, Mosure DJ, Levine WC, et al. Impact of switching laboratory tests on reported trends in *Chlamydia trachomatis* infections. Am J Epidemiol 2000; 151:430–435.
32. Department of Health and Human Services. Chlamydia prevalence monitoring project annual report—2001. Atlanta: Division of STD Prevention, Centers for Disease Control and Prevention, 2002.
33. Gotz H, Lindback J, Ripa T, et al. Is the increase in notifications of *Chlamydia trachomatis* infections in Sweden the result of changes in prevalence, sampling frequency, or diagnostic methods? Scand J Infect Dis 2002; 34:28–34.
34. Mosure DJ, Berman S, Dicker LW, et al. A re-evaluation of selective screening criteria for women attending family planning clinics in the US. In: Stephens RS, et al., eds. Chlamydial Infections: Proceedings of the Ninth International Symposium on Human Chlamydial Infection. San Francisco: International Chlamydia Symposium, 1998: 333–336.
35. Miller WC, Hoffman IF, Owen-O'Dowd J, et al. Selective screening for chlamydial infection: Which criteria to use? Am J Prev Med 2000; 18:115–122.
36. United States Preventive Services Task Force. Screening for chlamydial infection: Recommendations and rationale. Am J Prev Med 2001; 20:90–94.
37. Fenton KA, Korovessis C, Johnson AM, et al. Sexual behaviour in Britain: Reported sexually transmitted infections and prevalence genital *Chlamydia trachomatis* seroprevalence. Lancet 2001; 358: 1851–1854.
38. Grun L, Tassano-Smith J, Carder C, et al. Comparison of two methods of screening for genital chlamydial infection in women attending general practice: Cross sectional survey. BMJ 1997; 315:226–230.
39. Gaydos C, Howell R, Pare B, et al. *Chlamydia trachomatis* infections in female military recruits. N Engl J Med 1998; 339:739–744.
40. Hiltunen-Back E, Haikala O, Kautiainen H, et al. A nationwide sentinel clinic survey of *Chlamydia trachomatis* infection in Finland. Sex Transm Dis 2001; 28:252–258.
41. Todd CS, Haase C, Stoner BP. Emergency department screening for asymptomatic sexually transmitted infections. Am J Public Health 2001; 91:461–464.
42. Penney G, Thomson M, Norman J, et al. A randomized comparison of strategies for reducing infective complications of induced abortions. Br J Obstet Gynaecol 1998; 105:599–604.
43. Ryan G, Abdella T, McNeeley G, et al. *Chlamydia trachomatis* infection in pregnancy and effect of treatment on outcome. Am J Obstet Gynecol 1990; 162:34–39.
44. Black CM, Marrazzo J, Johnson RE, et al. Head-to-heat multicenter comparison of DNA probe and nucleic acid amplification tests for *Chlamydia trachomatis* infection in women performed with an improved reference standard. J Clin Microbiol 2002; 40:3757–3763.

International Journal of STD & AIDS 2005; 16: 323–327

ORIGINAL RESEARCH ARTICLE

Using chlamydia positivity to estimate prevalence: evidence from the Chlamydia Screening Pilot in England

D S LaMontagne MPH FRIPH[1], **K A Fenton** MBBS MSc[1], **J M Pimenta** PhD[2], **M Catchpole** FRCP FFPH[1,2], **P A Rogers** MSc[2], **S Randall** MD FRCOG[2], **W G Hewitt** BSc DipClinMicro[2], **H Mallinson** PhD[2], **G S Underhill** MBBS FRCPath[2], **L McLean** BSc RM[2], **T Gleave** MSc RGN[2], **V Harindra** FRCP[2], **A K Ghosh** MD[2], **J M Tobin** FRCOG MFFP[2]

[1]Health Protection Agency, Communicable Disease Surveillance Centre, HIV and STI Department, 61 Colindale Avenue, London NW9 5EQ; [2]The Chlamydia Pilot Steering Group, UK

Summary: Studies have suggested that positivity can be used to estimate the prevalence of *Chlamydia trachomatis* in large-scale chlamydia screening programmes. A recent pilot of opportunistic screening in England estimated that the prevalence among 16–24-year-old women in Portsmouth and Wirral was 9.8% and 11.2%, respectively. This study assessed the continued validity of positivity as an approximate for prevalence. We re-analysed data from the Chlamydia Screening Pilot to estimate positivity, calculated as total positive tests divided by total tests, and compared these estimates with the previously reported prevalence, measured as the number of women testing positive divided by the total number of women screened. Overall positivity was 9.4% in Portsmouth and 11.0% in the Wirral; these estimates were not statistically different from prevalence, regardless of health-care setting, age group or symptoms. We conclude that positivity can be used as a proxy for prevalence.

Keywords: *Chlamydia trachomatis*, chlamydia, screening, positivity, prevalence

Introduction

Chlamydia trachomatis is the most common bacterial sexually transmitted infection in the United Kingdom; over 82,000 cases were diagnosed in genitourinary (GU) medicine clinics in 2002.[1] The highest rates of chlamydia infection are among 16–19-year-old women and 20–24-year-old men.[1] Untreated chlamydial infection can lead to serious sequelae in women, including pelvic inflammatory disease (PID),[2] ectopic pregnancy,[3] and infertility.[4,5]

Prevalence of genital chlamydial infection in women in the UK varies widely depending on the age group under study, clinical setting, and laboratory test method.[6–9] Two recent studies, both using urine samples and ligase chain reaction (LCR) testing (LCx, Abbott Laboratories, Chicago, IL, USA), illustrate this variation. A national household probability survey of adults 18–44 years of age in England showed a prevalence of 3.0% (95% confidence interval [CI]: 1.7–5.1) among both 25–34-year-old men and 18–24-year-old women.[10] A pilot of opportunistic screening based in clinical settings in two health authorities in England among women aged 16–24 years found a prevalence of 9.8% in Portsmouth (95% CI: 9.3–10.3) and 11.2% on the Wirral (95% CI: 10.3–12.1).[11] Taken collectively, these studies provide evidence that genital chlamydial infection, often found to be asymptomatic, affects a large proportion of the sexually active population and constitutes a reservoir of hidden disease with potential long-term negative reproductive health sequelae.

The results of an opportunistic screening trial – the 'Chlamydia Screening Pilot' – informed the national policy in England and led to the phased implementation of opportunistic chlamydia screening for sexually active women and men under 25 years of age at selected clinical services facilities throughout the country.[12] As necessary with any large-scale screening programme, monitoring of activities, outcomes, and impact is of key importance. In the Chlamydia Screening Pilot, prevalence was reported as an outcome measure. To count individuals for the outcome measure, all testing

Correspondence to: D Scott LaMontagne
Email: scott.lamontagne@hpa.org.uk

episodes from the same participant were linked based on personal identifying details, such as name, date of birth, and residential postcode.[13] Although all patients attending for health care as part of the National Health Service (NHS) are allocated a unique identifying number (NHS number), this was not captured in the screening trial, as patients do not routinely use their number. As such, matching testing episodes to individuals in the pilot was a time-consuming and difficult process. Given the challenges in measuring and monitoring chlamydia prevalence in a large population-based cohort,[11,13] the Department of Health (England)-funded National Chlamydia Screening Programme has proposed to use positivity, rather than prevalence, as an outcome measure.[14] Positivity has been used in the United States (USA) as a surrogate measure for prevalence in clinic-based screening programmes and has been shown to be a useful tool in monitoring programme performance.[15] This approach has been validated in only one published study, concluding that positivity was a useful proxy measure.[16] However, in that study, data were collected from limited health settings, so questions regarding the generalizability of these conclusions remain. Re-examining the Chlamydia Screening Pilot data provides an ideal opportunity to crossvalidate this method, while informing the appropriateness and utility of using positivity to monitor the National Chlamydia Screening Programme in England..

Methods

Using data collected as a part of the Chlamydia Screening Pilot, we selected all test records with a known test result from individual 16–24-year-old women tested for genital chlamydial infection via a urine sample at family planning (FP), GU medicine, general practice (GP), and youth clinics ($n = 16{,}595$). Tests from other clinical sites, those with equivocal or inhibitory results, and tests of cure were excluded. We calculated positivity, defined as the number of positive tests divided by the total number of tests, and 95% CIs using SPSS 11.5[17] and STATA 8.0.[18] Positivity by single years of age, health-care setting, symptomaticity, and geographic area were also calculated. We compared positivity estimates with prevalence. Prevalence for each health-care setting and by symptomaticity within the health-care setting has been published elsewhere;[11] however, prevalence by single years of age within only the four health-care settings of interest for this study (FP, GP, GU medicine and Youth clinics) was recalculated because the published age-specific prevalence included all health-care settings.

Definitions

Positivity: Using test records, the number of positive tests (numerator) divided by the number of tests (denominator) among women 16–24 years of age for GP, FP, GU medicine, and Youth clinics combined.

Prevalence: The total number of women 16–24 years of age with a positive test during the full 12-month duration of the Chlamydia Screening Pilot (numerator) divided by all 16–24-year-old women (patients).[11] If a woman attended and tested positive at more than one health-care setting, she was counted as a part of the prevalence estimates at each setting. Age was defined as age at first test.

Symptomaticity: The original definitions of symptom categories[11] were applied to the test records used for this analysis. Diagnostic tests were those performed on patients with either reported symptoms of chlamydial infection and attended for this reason or attended for GU medicine screening. Tests performed for another reason but with symptoms reported on the intake form were classified as 'other reason but reported symptoms.' Test records that were asymptomatic, i.e., no symptoms were reported, were categorized as 'opportunistic screening.'

In addition to calculating CIs to assess differences between positivity and prevalence, two-sided binomial probability tests (using STATA 8.0) were also performed to further test our hypothesis, using the prevalence within each strata as the comparison measurement for the positivity within the same strata.

Results

We found an overall positivity of 9.4% (95% CI: 8.9–9.9) in Portsmouth and 11.0% (95% CI: 10.1–11.9) in the Wirral (Table 1). This was slightly lower than the prevalence in these areas, 9.8% (95% CI: 9.3–10.3) and 11.2% (95% CI: 10.3–12.1), respectively, but was not statistically different.[11] Positivity by health-care setting did not differ from prevalence within these settings. For example, positivity among GP attenders in the Wirral was 8.8% (95% CI: 7.4–10.1) compared with prevalence at this location of 8.7% (95% CI: 7.4–10.2). Absolute differences between positivity and prevalence within health-care settings ranged from –1.43 to 0.04 and the percentage difference between the two ranged from –8.58% to 0.47%, neither of which was statistically significant. There were fewer attenders to youth clinics in Portsmouth than the Wirral, reflected in the greater variation between positivity and prevalence estimates and associated CIs (Table 1).

Additionally, positivity by single year of age did not vary from prevalence in either the Wirral or Portsmouth (Figure 1). Positivity tended to be slightly lower than prevalence for most age cohorts. The age distribution curve of positivity followed the same pattern for prevalence in both the Wirral and Portsmouth. Positivity was highest among women aged 19 and 20 years in the Wirral and women 18 and 19 years old in Portsmouth.

Positivity by reason for test within GP, FP, GU medicine, and youth clinic health-care settings was similar to the prevalence in these locations (Table 2).

Table 1 Positivity and prevalence among 16–24-year-old women by health-care setting, Chlamydia Screening Pilot, Portsmouth and the Wirral, England, 1999–2000

Health-care setting	No. of women	No. of tests	Positivity (95% CI)	Prevalence* (95% CI)	Absolute difference	Percent difference	No. of women with repeat tests (%)	Percentage of repeat tests that were positive
Portsmouth								
GP	7391	7616	8.53 (7.9–9.2)	8.49 (7.9–9.1)	0.04	0.47%	441 (5.9%)	17.1%
FP	2880	3204	9.52 (8.6–10.5)	9.81 (8.8–10.9)	−0.29	−2.96%	236 (8.1%)	11.8%
GU medicine	936	1258	13.28 (11.4–15.2)	13.42 (11.6–15.4)	−0.14	−1.04%	90 (9.7%)	15.0%
Youth	147	164	15.24 (9.7–20.8)	16.67 (11.6–23.4)	−1.43	−8.58%	14 (9.5%)	60.0%
Total	11,354	12,242	9.4% (8.9–9.9)	9.8% (9.3–10.3)				
Wirral								
GP	1501	1588	8.75% (7.4–10.1)	8.74% (7.4–10.2)	0.01	0.11%	74 (4.9%)	9.8%
FP	967	1052	9.89% (8.1–11.7)	10.11% (8.4–12.1)	−0.22	−2.18%	91 (9.4%)	15.8%
GU medicine	507	616	16.88% (13.9–19.8)	17.57% (14.7–20.9)	−0.69	−3.93%	51 (10.1%)	19.6%
Youth	1009	1097	12.03% (12.0–14.0)	12.74% (10.8–14.9)	−0.71	−5.57%	114 (11.3%)	20.8%
Total	3984	4353	11.0% (10.1–11.9)	11.2% (10.3–12.1)				

*Prevalence previously published (see reference 11)
GP=general practice; FP=family planning; GU=genitourinary; CI=confidence interval

There were slight variations in the estimates based on the use of health-care setting for positivity calculations, whereas the prevalence estimates were based on the health-care setting of the first test. However, in locations with higher levels of testing, positivity estimates were more stable and reflective of prevalence. The results of all two-sided binomial probability tests were not significant, providing additional statistical evidence that suggests no difference between positivity and prevalence in our study population.

Discussion

Our study found slight and non-statistically significant differences between positivity and prevalence regardless of geographic area, health-care setting, age, or reason for test. The methodology to use positivity as a surrogate measure for prevalence was first suggested by Dicker *et al.*[16] and validated using data from women tested via cervical swab who attended FP and STD clinics in the USA at a time when non-amplified, less sensitive testing methods were employed. However, since that time, large-scale opportunistic screening programmes have changed to include widespread use of non-invasive urine samples, a broader range of clinical settings for testing, especially GP and primary care, and advances in laboratory technologies that are more sensitive in detecting chlamydial infection. Given these changes, the question is whether chlamydia positivity can still be used as a valid and stable surrogate measure for prevalence. Because the Chlamydia Screening Pilot used only urine specimens and highly sensitive detection methods on a very large population of women, the majority of whom attended GPs, the data gathered provided a 'natural experiment' to retest the suggested methodology.

Our results robustly confirm that positivity can be used as a proxy measure for prevalence. Our estimates of positivity were comparable to prevalence in all health-care settings under study, including GP. In general, positivity underestimated prevalence; however, the absolute differences in the underestimations were slight, not statistically significant, and did not change the interpretation of the data. Single-year age estimates of positivity were less than, but not statistically different from, prevalence. There are some slight variation in numerators and denominators when selecting tests or selecting women by age for these estimates. For prevalence, the age at the first test was used; positivity used the age at every test. The effect is to bias the prevalence numerators towards younger ages. Since positivity uses age at test, there will result a smaller numerator within the younger ages, potentially reducing the percent positive. Lastly, if there is a high proportion of women with repeat tests (more than 7% of our study population), the denominator of the positivity estimate

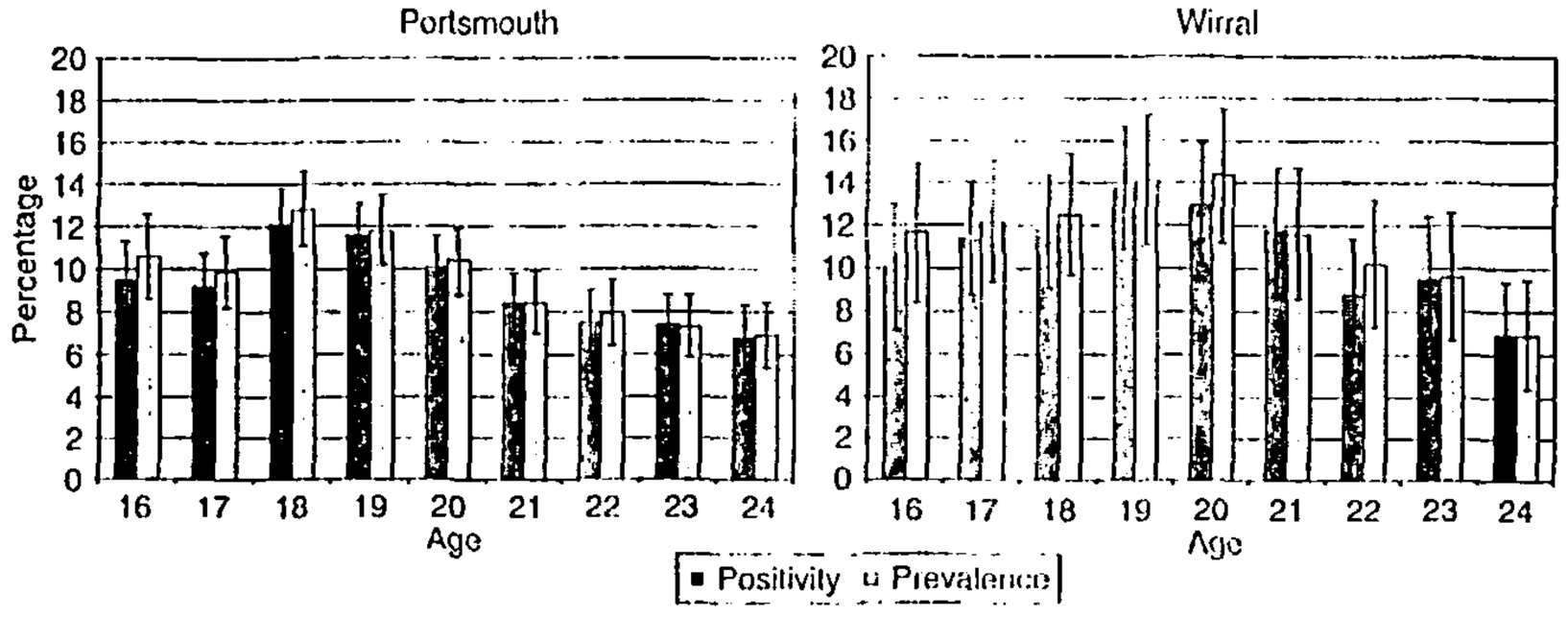

Figure 1 Chlamydia positivity among women compared with age-specific prevalence (see body of the text for definitions of positivity and age-specific prevalence). [Chlamydia Screening Pilot, Portsmouth and the Wirral, England, 1999–2000]

Table 2 Positivity among 16–24 year old women by reason for test* and health-care setting, [Chlamydia Screening Pilot, Portsmouth and the Wirral, England, 1999–2000]†

Health-care setting	Diagnostic		Other reason but reported symptoms		Asymptomatic	
	No. of tests (+)	Positivity (95% CI)	No. of tests (+)	Positivity (95% CI)	No. of tests (+)	Positivity (95% CI)
Portsmouth						
GP	337 (53)	15.7% (11.8–19.6)	2118 (220)	10.4% (9.1–11.7)	3910 (317)	8.1% (7.3–9.0)
FP	71 (11)	15.5% (6.9–24.1)	1015 (103)	10.1% (8.3–12.0)	1946 (179)	9.2% (7.9–10.5)
GU medicine	925 (128)	13.8% (11.6–16.1)	29 (3)	10.3% (–1.4–22.1)	280 (32)	13.2% (7.7–15.2)
Youth	4 (0)	0.0%	38 (5)	13.2% (1.9–24.4)	117 (20)	17.1% (10.2–24.0)
Wirral						
GP	151 (24)	15.9% (10.0–21.8)	422 (41)	9.7% (6.9–12.6)	743 (57)	7.7% (5.8–9.6)
FP	14 (0)	0.0%	315 (32)	10.2% (6.8–13.5)	671 (67)	10.0% (7.7–12.3)
GU medicine	273 (40)	14.7% (10.4–18.9)	248 (53)	21.4% (16.2–26.5)	74 (9)	12.2% (4.5–19.8)
Youth	16 (2)	12.5% (– 5.7–30.7)	276 (41)	14.9% (10.6–19.1)	638 (69)	10.8% (8.4–13.2)

*Reason for test was defined in the original study (Pimenta *et al., Sex Transm Infect* 2003;79:22-7") and repeated among testing episodes for this analysis (see Methods)
CI=confidence interval; GP=general practice; FP=family planning; GU=genitourinary

would be increased, contributing to a reduction in the percent positive.

Dicker and colleagues suggest that positivity would overestimate prevalence if a high proportion of the population was tested frequently.[16] In this study, positivity was less than prevalence at FP, GU medicine, and youth clinics in both the Wirral and Portsmouth, suggesting underestimation of prevalence. In these settings, the percentage of tests that were repeat was greater than 8%; seeming to support the conclusions by Dicker *et al.* in the relationship between frequent testing with underestimations of prevalence.

Dicker *et al.* also conclude that positivity would underestimate prevalence if there was a high percentage of repeat tests that were positive.[16] However, in all settings in our study, the percentage of repeat tests that were positive was higher than prevalence (ranging from 9.8% to 60%). The converse finding could be the result of factors that make these two studies different. First, the test volume in our study is significantly less than the multi-year data used by Dicker and colleagues. The result is smaller numerators and denominators, from which percentages become more pronounced. For example, 14 women attending youth clinics in Portsmouth had multiple tests (31 tests in total). Among the 17 repeat tests (second or third tests only) for these 14 women, 10 (or 60%) were positive. Second, the opportunity for women to be tested more than once was reduced by the limited 12-month duration of Chlamydia Screening Pilot and the screening protocol that advised re-testing only if the woman changed sex partners. Lastly, in the Chlamydia Screening Pilot, women testing positive were actively followed up to ensure treatment compliance. The multiple contacts by the health-care provider for treatment might have built relationships with higher risk women, creating an environment of trust and security, such that they might be more likely to re-attend through these established links. Regardless of these differences and potential limitations, we found no statistically significant or interpretive difference between positivity and prevalence.

The results of the Chlamydia Screening Pilot guided the development and direction of the National Chlamydia Screening Programme in England, which is currently being implemented in phases across the country. In large-scale screening programmes, assessing programme impact is necessary to ensure that there is public health benefit to the population. For chlamydia screening, this

often has been put in terms of cost-effectiveness, declines in prevalence over time, and decreases in incident cases of PID. The cost-effectiveness evaluation of the Chlamydia Screening Pilot is ongoing and two randomized control trials have shown that chlamydia screening can decrease PID incidence.[19,20] Therefore, the principal measurement of programme impact for the National Chlamydia Screening Programme in England will be illustrating a decline in infection over time where the screening programme is in operation.[14]

It is important to note the difficulties in precisely measuring and monitoring prevalence in the community through a national screening programme for genital chlamydial infection. The principal limitation is not all sexually active women are tested; thus, the infection status of women not tested remains unknown. At best, prevalence estimates can be made for only the population tested and only if individual patients can be uniquely identified to prospectively track multiple testing and/or infection episodes across clinical settings attended and geographic areas lived in. To monitor that level of prevalence within a large-scale national programme would require a Herculean effort. As noted previously, the NHS assigns patient identification numbers that are unique to the individual, but these numbers are not widely used by patients and clinical facilities are limited in their capacity to search the national database for these identification numbers. Therefore, it is envisioned that most local programmes monitoring chlamydia screening activities will need to use positivity within clinic settings as an alternate technique for investigating changes in prevalence.

Monitoring positivity, in lieu of prevalence, would also minimize the reporting burden for clinical providers participating in the National Chlamydia Screening Programme to uniquely identifying individuals tested and would still allow for rigorous assessment of the programme's impact on decreasing disease in the population. This method will also allow for more rapid epidemiological assessment of populations affected and changes in the burden of disease.

Acknowledgements: The authors would like to thank the original participants in the Chlamydia Screening Pilot whose tireless efforts made the project a success and the members of the Chlamydia Pilot Steering Group who approved the secondary analysis of the pilot data presented in this paper. Sources of support: none declared.

References

1 Health Protection Agency, SCIEH, ISD, National Public Health Service for Wales, CDSC Northern Ireland and the UASSG. *Renewing the Focus: HIV and Other Sexually Transmitted Infections in The United Kingdom in 2002*. London: Health Protection Agency, November 2003
2 Weström L, Joesoef R, Reynolds G, *et al*. Pelvic inflammatory disease and fertility. *Sex Transm Dis* 1992;19:185–92
3 Hillis S, Owens L, Marchbanks P, *et al*. Recurrent chlamydial infections increase the risks of hospitalization for ectopic pregnancy and pelvic inflammatory disease. *Am J Obstet Gynecol* 1997;176:103–7
4 Mabey DCW, Ogbaselassie G, Robertson J, *et al*. Tubal infertility in the Gambia: chlamydial and gonococcal serology in women with tubal occulsion compared with pregnant controls. *Bull World Health Organ* 1985;63:1107–13
5 Miettinen A, Heinonen PK, Teisala K, *et al*. Serologic evidence for the role of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis* in the etiology of tubal factor infertility and ectopic pregnancy. *Sex Transm Dis* 1990;17:10–4
6 Grun L, Tassano-Smith J, Carder C, *et al*. Comparison of two methods of screening for genital chlamydial infection in women attending general practice: cross sectional survey. *Br Med J* 1997;315:226–30
7 Clay J, Bowman C. Controlling chlamydial infection. *Genitourin Med* 1996;72:145
8 Hopwood J, Mallinson H. Chlamydia testing in community clinics – a focus for accurate sexual health care. *Br J Fam Plan* 1995;21:87–90
9 Rogstad KE, Davies A, Murthy SK, *et al*. The management of *Chlamydia trachomatis*: combined community and hospital study. *Sex Transm Infect* 2000;76:493–4
10 Fenton KA, Korovessis C, Johnson AM, *et al*. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital *Chlamydia trachomatis* infection. *Lancet* 2001;358:1851–4
11 Pimenta JM, Catchpole M, Rogers PA, *et al*. Opportunistic screening for genital chlamydial infection II: prevalence among healthcare attenders, outcome, and evaluation of positive cases. *Sex Transm Infect* 2003;79:22–7
12 Department of Health. *A Pilot Study of Opportunistic Screening for Genital Chlamydia trachomatis Infection in England (1999–2000). Summary Report*. London: Department of Health, 2002
13 Pimenta JM, Catchpole M, Rogers PA, *et al*. Opportunistic screening for genital chlamydial infection I: acceptability of urine testing in primary and secondary healthcare settings. *Sex Transm Infect* 2003;79:16–21
14 *Department of Health Chlamydia Screening Programme Roll Out Core Requirements*. London: 2003, 1–37
15 Department of Health Sexually Transmitted Disease Surveillance 2001 Supplement: Chlamydia Prevalence Monitoring Project Annual Report – 2001. Atlanta: Centers for Disease Control and Prevention, 2002, 1–37
16 Dicker LW, Mosure DJ, Levine WC. Chlamydia positivity versus prevalence. What's the difference? *Sex Transm Dis* 1998;25:251–3
17 SPSS (computer program). Version 11.5. Chicago, IL: SPSS, Inc, 2002
18 STATA (computer program). Version 8.0. College Station, TX: Stata Corporation, 2003
19 Scholes D, Stergachis A, Heidrich FE, *et al*. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infections. *N Engl J Med* 1996;334:1362–6
20 Ostergaard L, Andersen B, Moeller JK, *et al*. Home sampling versus conventional swab samples for screening of *Chlamydia trachomatis* in women: a cluster-randomized 1-year follow-up study. *Clin Infect Dis* 2000;31:951–7

(Accepted 15 May 2004)

ORIGINAL ARTICLE

Modelling the healthcare costs of an opportunistic chlamydia screening programme

E J Adams, D S LaMontagne, A R Johnston, J M Pimenta, K A Fenton, W J Edmunds

Sex Transm Infect 2004;80:363–370. doi: 10.1136/sti.2004.009654

See end of article for authors' affiliations

Correspondence to: Elisabeth J Adams, Statistics, Modelling and Economics Department, Communicable Disease Surveillance Centre, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ, UK; elisabeth.adams@hpa.org.uk

Accepted for publication 1 April 2004

Objectives: To estimate the average cost per screening offer, cost per testing episode and cost per chlamydia positive episode for an opportunistic chlamydia screening programme (including partner management), and to explore the uncertainty of parameter assumptions, based on the costs to the healthcare system.

Methods: A decision tree was constructed and parameterised using empirical data from a chlamydia screening pilot study and other sources. The model was run using baseline data from the pilot, and univariate and multivariate sensitivity analyses were conducted.

Results: The total estimated cost for offering screening over 12 months to 33 215 females aged 16–24 was £493 412. The average cost (with partner management) was £14.88 per screening offer (90% credibility interval (CI) 10.34 to 18.56), £21.83 per testing episode (90% CI 18.16 to 24.20), and £38.36 per positive episode (90% CI 33.97 to 42.25). The proportion of individuals accepting screening, the clinician (general practitioner/nurse) time and their relative involvement in discussing screening, the test cost, the time to notify patients of their results, and the receptionist time recruiting patients had the greatest impact on the outcomes in both the univariate and multivariate sensitivity analyses.

Conclusions: Results from this costing study may be used to inform resource allocation for current and future chlamydia screening programme implementation.

Genital *Chlamydia trachomatis* infection is the most common sexually transmitted infection (STI) diagnosed in genitourinary medicine (GUM) clinics in the United Kingdom.[1] It is mainly asymptomatic and may lead to pelvic inflammatory disease (PID) in a proportion of untreated cases, which in turn may cause ectopic pregnancy and infertility in women.[2] Asymptomatically infected individuals may not have adequate opportunity or seek to be tested, leaving a reservoir of hidden infections and risk of sequelae. Therefore, screening at-risk populations can identify and treat asymptomatic infection, reduce sequelae, and perhaps impact the associated long term healthcare costs.[3 4]

The decision to implement opportunistic chlamydia screening may be based in part upon results from economic analysis, which have been undertaken using various screening assumptions.[5 6] A review of other cost effectiveness studies by Honey *et al*[7] found that depending on the model assumptions, screening females for chlamydial infection can be cost effective under various baseline prevalence estimates, especially when age is used to select women and DNA testing methods are used. In England, chlamydia screening is currently being implemented in phases across the country.[8] It is, therefore, timely to assess the cost of such a screening programme and examine in detail the relative contribution of the cost elements, using a combination of data such as the time involvement of personnel, variable costs, and overhead costs. As screening encompasses more sites across the country, information from this study may be particularly useful as it directly feeds back into programme implementation, and may help other sites that are planning and undertaking screening programmes elsewhere.

In this study, a decision analytical model was used to estimate the average cost per test offer, cost per testing episode, and cost per chlamydia positive episode, based on the costs incurred by the healthcare system. The model structure gives the ability to change the model assumptions and run a series of "what if" scenarios (for example, what if the role of practice nurses is emphasised over doctors' roles in discussing screening). It also allows for detailed analyses of uncertainty on how patients move through the screening process for both patient flow and the costs of the programme. The results from this analysis may help to advise on appropriate resource allocation to minimise screening costs and improve the efficiency of future screening programmes in the United Kingdom and elsewhere.

METHODS

Screening methodology

Data on patient flow came from a pilot study funded by the Department of Health (England) to evaluate the costs, acceptability, and feasibility of opportunisitic chlamydia screening; these methods have been fully described elsewhere.[9 10] This analysis included 16–24 year old females who were offered screening when attending GUM clinics, family planning clinics, antenatal clinics, termination of pregnancy clinics, and general practitioner (GP) surgeries. The study was undertaken between 1 September 1999 and 31 August 2000 in Portsmouth and Wirral, England. Although some men were also offered screening opportunistically at GUM and youth clinics those data are not included here. In the pilot study, research nurses were responsible for managing patients and their partners. In this analysis, we have estimated the costs of a health adviser who would have a similar role with patient and partner management. Women who accepted a test offer were asked to submit a urine sample for ligase chain reaction (LCR) testing (LCx *Chlamydia trachomatis* assay, Abbott Laboratories Diagnostic Division). Patients in the pilot study with an insufficient diagnosis were advised to get another test, and patients with an equivocal result were given the option to be treated or retested. The

Abbreviations: CI, credibility interval; GP, general practitioner; GUM, genitourinary medicine; LCR, ligase chain reaction; PID, pelvic inflammatory disease; STI, sexually transmitted infection

model used in this analysis assumed that patients with a final diagnosis of positive, insufficient, or equivocal were asked to attend for treatment (azithromycin or doxycycline; alternative regimen used for pregnant women). The positive patients were also asked to report any sexual partners from the past 3 months. For the reported partners, contact was attempted (either by the patient or the health adviser), and the partner(s) was asked to attend, receive prophylactic treatment, and give a urine sample for LCR testing. A small subset of partners was tested using other methods (n = 20); these were not included in this analysis.

Decision analysis model

Two linked decision trees (Precision Tree, version 1.0.4, Palisade Corporation) were constructed to simulate the flow of female screening episodes from initial test offer to patient treatment and partner reporting (fig 1A), and contacting partners and partner management (prophylaxis and testing) (fig 1B). Two of the nodes have branches with the same outcomes (or next steps), which are linked in the model (that is, all insufficient/equivocal diagnoses are treated as positives and go to the treatment node, and individuals may have reported partners without receiving treatment). Each node of the model returns the number of patient episodes and the expected average value of the model at that point.

Patient data extraction

In the pilot screening model, patient testing and management spanned across various healthcare settings. The methodology of the pilot study stated that patients would be tested in a variety of settings but treatment and partner notification would be undertaken in GUM clinics, by health advisers or at the site of testing. This analysis combined the number of patient episodes through each step of the tree across healthcare settings, instead of using individuals as the unit of measurement. Since some women were tested more than once and in various clinical settings,[9] each time they were offered a test they would have been included in the total number of patient episodes. This was thought to better estimate the true costs to the screening programme. However, this may contribute to a different acceptance rate than if the results were estimated based on the number of women who accepted testing, instead of counting each occasion they were offered a test. Data were also combined from Portsmouth and Wirral to give an average estimate of the value of such a screening strategy.

Two researchers (DSL, ARJ) extracted the data for each branch of the decision tree using different methods to check for accuracy (Stata, version 8.2, Stata Corporation, and SPSS, version 11.0, SPSS Inc). In both methods, screening episodes from men, women aged <16 years or >24 years and any test of cure episodes were excluded from the analysis. For both extraction methods, a stepwise approach was used following the decision trees (figs 1A, B) with the test records filtered at each node.

Costs

The overall healthcare costs of screening were estimated from direct costs from the pilot study (preliminary invoiced expense forms supplied by the Department of Health, Economics and Operational Research Division) and additional costs borne by the healthcare system (that is, clinicians involved in screening who did not receive remuneration from the screening programme, etc). Incorporating both types of

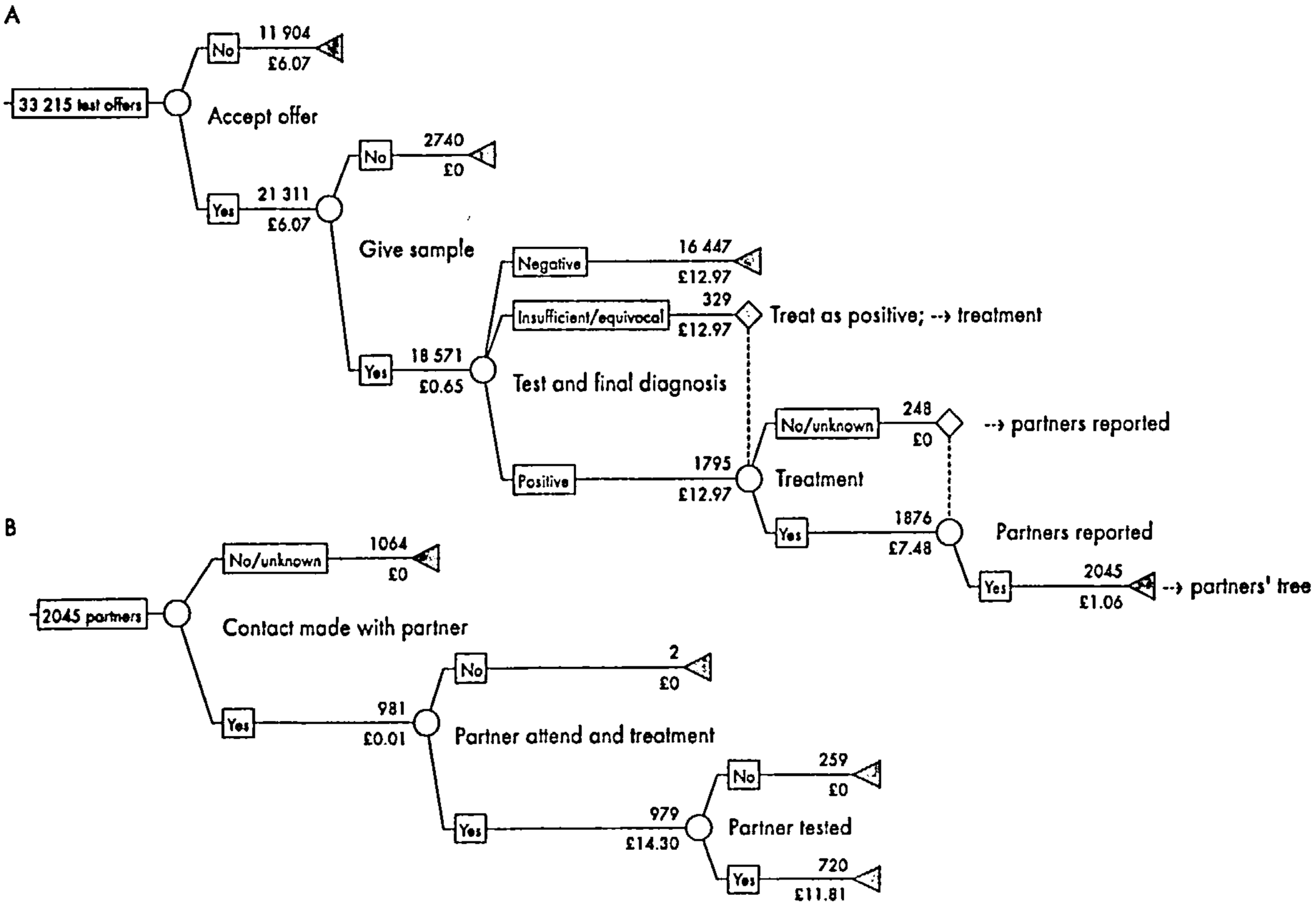

Figure 1 Schematic diagram of the screening trees used in the analysis. (A) Patient tree; (B) partner tree. For each branch option, the number who flowed through that branch is given above the line, and the baseline cost is below. Triangles indicate a branch termination, and broken lines indicate a flow to another node.

Table 1 Total annual overhead costs used in the analysis based on invoiced expenses from the chlamydia screening pilot study

Item	Cost (£)*
Total personnel overheads	**36 974**
Programme administrator	11 138
Consultant coordinator	14 362
Administration and clerical	11 474
Total capital overheads	**17 164**
Refrigerators	4421
Computers and printers	4851
Office furnishings	2621
Accommodation: rent/alterations	5271
Total running overheads	**22 329**
Travel and transportation	1244
Telephone and fax	323
Stationery and postage	12 178
Advertising	671
Other costs	7913

Source: Preliminary cost data provided by the Department of Health, Economics and Operational Research Division, and data from the questionnaire on time and patient flow.
*Costs inflated to £UK at 2001 rates.

costs was thought to more closely estimate the true costs of a chlamydia screening programme, by taking on the wider healthcare costs (but excluding the social costs and costs to the patient). The included costs were not all paid for directly by the screening study itself, and therefore would not necessarily be funded in a nationally implemented programme.

The planning and set-up costs of the screening programme were included and were based on the pilot invoiced expenses. Costs deemed to be associated with the research side of the pilot screening programme were excluded from the analysis (that is, personnel costs for analysis relating to the study evaluation, since the pilot was a research study to evaluate the feasibility and effectiveness of chlamydia screening). Recruitment of staff and laboratory upgrade costs (from EIA to NAAT testing) were also excluded.

In the pilot, a fee was paid to the clinicians for each chlamydia test initiated. However, this cost was excluded from the analysis, as it is unlikely to continue in the phased implementation of the national programme. Instead, their time costs have been accounted for in the analysis by estimating the cost of a consultation with a healthcare clinician to offer screening to a potential patient (see below).

All costs were inflated to reflect 2001 prices (£ sterling), using the Hospital and Community Health Services inflation indices for either prices or pay.[11] The adjusted costs included all overhead costs and some of the unit costs (noted in tables 1 and 2).

Overheads

There was an overhead fixed cost for the screening infrastructure, personnel and running the programme (table 1). These costs were taken from the expenditure reports and include one off and recurring costs.

While the patient flow data were taken over a 12 month period, the screening study and associated costs were incurred roughly over 2 years. Therefore, the total costs were annualised to allow for comparison with the study period data. One-off costs, including refrigerators, computers, and office furnishings, were assigned an estimated lifespan of 5 years, and an annual cost per item was estimated[11] using a discount rate of 3.5%.[11] Only one of the sites supplied these one-off costs, so these total annualised costs were doubled to account for both sites. The personnel (that is, administrators, screening coordinator, etc) and running (that is, telephones, travel/transport, etc) overhead costs from both the Portsmouth and Wirral sites (including set up and pilot costs) were halved to estimate an annual cost per item. An overhead cost per patient screening episode was estimated from the total overhead costs.

Costs at each branch

Variable costs were added at each step in the decision tree (table 2). To estimate these, costs of materials and personnel were summed (derived from the mean Portsmouth and Wirral costs when data were available). Personnel costs were derived from the estimated salary of a typical healthcare worker who would see a patient or partner (receptionists, GPs, practice nurses/health advisers, and GUM consultants), and included qualification costs, ongoing training and other additional costs such as overhead costs, to estimate the actual opportunity costs.[11 14] In the pilot, women were screened at various clinical settings and would have spoken to various healthcare personnel. This analysis assumed that the salary of a practice nurse or health adviser (both assumed to be a grade F nurse in the NHS pay scale[11]) would give a lower cost estimate, and that of a GP clinician an upper estimate. The relative involvement of both clinicians was assumed to be 50%, but was allowed to vary in the sensitivity analysis (see below). These annual costs were used to derive the cost per patient related minute (except for receptionist, which was just a cost per minute), using data on the average number of weeks worked per year, and the average number of hours per week.[11]

These data were then combined with estimates of the time spent on different screening and related activities. To obtain this, a questionnaire was sent to the primary research nurses involved in the original chlamydia screening pilot in both sites, asking about the time spent on specific activities during the screening process. These estimates were not directly measured while the pilot was conducted, and therefore are based on retrospective accounts. The baseline estimates represent an average when data from both sites were available.

The total cost of a patient (or partner) flowing through various parts of the tree (with different outcomes) will simply be the sum of the branch costs through which she or he flows.

Outcome: estimated average cost of screening

Three main outcomes were estimated: the average cost per screening offer; cost per testing episode (giving a urine sample and testing, regardless of the outcome), and cost per positive episode. The cost estimates are additive, such that the cost per testing episode includes the cost per screening offer and the cost per positive episode includes the cost per testing episode. These are simply the weighted average of all possible outcomes (and associated costs) for that decision node and all subsequent nodes. For example, the cost per offer is the weighted average of the cost of all the occasions a test offer was not accepted and the cost of all occasions a test was accepted and all of their subsequent downstream costs. Likewise, the cost per testing episode is the weighted average of those testing negative and those with a diagnosis of positive, insufficient, or equivocal. For all outcomes, these costs include those of accepting a test, the laboratory costs of testing, and the costs of notifying them of their results, and also include the weighted costs of those testing positive that may include the additional costs of treatment and partner notification for a proportion of positives.

All outcomes included the costs of partner management (contacting, treatment, and testing) as these are all part of the screening structure and contribute to the cost of the outcomes. These outcomes were assessed from the healthcare

Table 2 Total variable costs at each node of the decision tree (in bold) and their constituent inputs

Item	Baseline	Unit	Minimum	Maximum	Distribution*	Source†	Comment
Overall: personnel							
Receptionist	0.13	£/Minute				Assumption	
GP	1.01	£/Minute‡				Ref 11	
Practice nurse/health adviser§	0.42	£/Minute‡				Ref 11, 14	
Medical GUM Consultant	1.40	£/Minute‡				Ref 11, 14	
(1) Accepting the test	**3.77**	**£/Episode**	**1.50**	**5.42**			
Information leaflet	0.31	£/Item				A	Cost inflated to £UK at 2001 rates
Receptionist time	1.8	Minute	0.5	3	Uniform	A	Screening selection and invitation
GP/nurse time to discuss screening	4.5	Minute	2	7	Triangular	A	Depends on setting/clinician
% GP time compared to nurse time	50	%	0	100	Uniform	Assumption	
(2) Giving a sample	**0.65**	**£/Episode**					
Sample container	0.50	£/Item				B	Cost inflated to £UK at 2001 rates
Request form	0.15	£/Item				B	Cost inflated to £UK at 2001 rates
(3) Testing and final diagnosis	**12.97**	**£/Episode**	**10.71**	**15.25**			Cost inflated to £UK at 2001 rates
LCR test materials and personnel	11.81	£/Item	10.49	13.14	Uniform	B	Average of both sites, cost inflated to £UK at 2001 rates
Health adviser time to notify patient	2.8	Minute	0.5	5	Uniform	A	
(4) Treatment	**7.46**	**£/Episode**					
Azithromycin	7.33	£/Treatment				Ref 17	Recommended dosage[17]
Doxycycline	4.98	£/Treatment				Ref 17	Recommended dosage[17]
Health adviser time for treatment	5	Minute				A	Partner notification not included
% receiving azithromycin compared to doxycycline	15.6	%	0	100	Triangular	C	
(5) Partners reported	**1.06**	**£/Episode**	**0.85**	**1.27**			
Health adviser time for eliciting partner information	2.5	Minute	2	3	Uniform	A	
(6) Partners contacted	**0.01**	**£/Partner episode**	**0.00**	**0.13**			
Health adviser time to contact partner	1	Minute	0	10	Triangular	A	
% partners contacted by health adviser compared to patient contacted	3	%				C	
(7) Partner attendance and treatment	**14.30**	**£/Partner episode**	**7.16**	**10.74**			
Time for partner clinic visit	12.5	Minute	10	15	Uniform	A	
% partners seen by health adviser compared to GUM consultant	70	%	40	100	Uniform	Assumption	
(8) Partner tested	**11.81**	**£/Partner episode**	**10.49**	**13.14**	Uniform	B	See No 3 above.

*Distributions used in the sensitivity analysis. Uniform distributions were used to represent a large degree of uncertainty (any value over the range selected randomly); triangular distributions were used when the most likely value was known (the value drawn for each simulation was more likely to be closer to the mean value).
†A, data from interview with primary research nurses in Portsmouth and Wirral; B, preliminary pilot expenses provided by the Department of Health, Economics and Operational Research Division; C, pilot database.
‡Patient related minute.
§Mid-scale grade F nurse.

provider perspective, incorporating the costs of the screening programme and the associated wider healthcare costs. The baseline costs were used in the primary analysis.

Sensitivity analyses

Sensitivity analyses were undertaken to assess which costs and patient flow values were most important to the outcomes, and to explore the range of possible outcomes (given some parameter uncertainty) for this screening programme. The costs of such a screening programme are variable and may depend on the personnel involved in counselling and testing (that is, whether a general practitioner, health adviser, or GUM consultant discusses screening with a patient), the cost of the LCR test (which often varies between laboratories), and the numbers of patients and their partners who flow through the screening and partner decision trees.

Parameter values were drawn from specified distributions. The patient flow through the model was based on data from the pilot and was binomially distributed (proportion at each branch and the total number). The cost and the time components were mainly drawn from uniform distributions to represent a large degree of uncertainty (with any value randomly drawn from the range). Triangular distributions were assigned when there was considerable evidence that the mean closely approximated the baseline value. Then, the value used for each simulation was more likely to be drawn from a value closer to the mean. The baseline and maximum and minimum values used are given in table 2 along with the assigned distribution.

The screening programme modelled here is just one of many possible options. Therefore, univariate sensitivity analyses were performed, which varied one of the model assumptions at a time, and we then compared results to the baseline model outcomes. The input parameters were varied between the minimum and maximum values given in table 2. Additionally, several other "what if" scenarios were tested, in which one or two of the parameters were changed. This included (a) changing the relative time a receptionist rather than GP spent with a patient during screening recruitment (that is, if a receptionist spends 3 minutes recruiting each patient then a GP spends only 3 minutes per patient; or no receptionist involvement then 10 minutes of GP time per patient), (b) excluding the cost of a consultation with a clinician for non-test acceptors, (c) varying the test acceptance rate from 34% to 94% (roughly a 50% change from the baseline of 64%), (d) including a lower LCR test cost estimate of £9, thought to be more realistic of the test costs for a larger scale screening programme, and (e) changing the chlamydia prevalence of tested patients. The prevalence range was based on a lower estimate of 3% found in 18–24 year old females in a population based survey,[15] and on an upper estimate of 18%

found in females aged 16–24 attending GUM clinics.[9] The estimate for prevalence was driven by data from the decision analysis model, and it was assumed that positivity was an approximate estimate for prevalence.[16] It was estimated by: (positive + equivocal + insufficient tests)/total tests. In this analysis the baseline prevalence was estimated to be 11.4%, based on the above equation and data on screening episodes, and differed slightly from the estimated prevalence in the pilot study.[10]

A probabilistic multivariate sensitivity analysis was also performed using @risk (version 4.0.5, Palisade Corporation) running within Excel (version 2000, Microsoft). The analysis was run 1000 times, and at each simulation parameter values were randomly drawn using Latin Hypercube sampling. The parameters that varied were the input costs and times with ranges given in table 2, the distribution of individuals flowing through the tree (drawn from binomial distributions described above), and the acceptance rate (triangular distribution: minimum 34%, mean 64%, maximum 94%). Distributions for the outcome variables (cost/offer, cost/tested, cost/positive) were generated along with non-parametric 90% credibility intervals (CIs)—that is, 90% of the model simulations fell within the upper and lower CI.

RESULTS

The estimated overall annual cost of the opportunistic screening programme based on offering screening to 33 215 women aged 16–24 was £493 412. Of these costs, 80% (£394 429) were the variable patient costs, 5% (£22 515) were associated with partner management costs, and 15% (£76,468) were overhead costs for running the programme. Thirty nine per cent of the costs were personnel costs (including overheads and variable costs). About a third (37%) of the total costs were associated with the test kit cost (excluding testing personnel). These estimates are specific to the number of screening episodes examined in this analysis.

The estimated average cost per test offer given the flow of individual testing episodes in the pilot was £14.88 (90% CI 10.34 to 18.56), which included all of the downstream costs of testing, notifying patients of results, treatment and partner notification for positives, and all of the partner management costs. The average cost per testing episode was £21.83 (90% CI 18.16 to 24.20) including all downstream costs and partner management. The estimated average cost per positive episode was £38.36 (90% CI 33.97 to 42.25), which included a proportion of positive episodes having treatment and partner management. If the partner management costs were ignored, the average cost per screening offer, testing episode, and positive episode were reduced to £14.18 (90% CI 10.01 to 17.80), £20.57 (90% CI 17.18 to 22.63), and £27.35 (90% CI 24.29 to 29.98), respectively. If the partner tree was examined alone, the expected average cost per partner contact was £11.01 (90% CI 9.12 to 13.23), a weighted average of the costs of contact made with a proportion of partners, and partner treatment and testing for a proportion of partners.

Sensitivity analyses

In the univariate sensitivity analysis, varying the proportion accepting the test offer had the greatest expected impact on the cost per screening offer compared to the baseline result (fig 2). As the test acceptance increased, so did the cost per offer, and vice versa as the acceptance decreased (£18.98 for 94% acceptance; £10.74 for 34% acceptance). The relative role of the receptionist in explaining screening (compared to GP involvement) also had a large impact (25% difference from baseline) on the cost per offer. As the receptionist spent more time explaining screening and the clinicians spent less time, the average cost per offer declined from £18.59 to £13.98. Similarly, as the time associated with primary care clinicians (doctors or nurses) explaining screening to patients decreased, so did the average cost per offer.

Several of the parameters had a moderate impact on the outcomes (12% or less change from the baseline results). These included the relative involvement of GP versus practice nurse explaining screening to patients, excluding the healthcare worker consultation for non-test accepter, the test cost, and the prevalence of chlamydial infection. A two way analysis of the prevalence and the proportion accepting a test indicated that the prevalence had little impact on the outcomes, compared to the proportion accepting a test that had a large impact on the cost per test offer (fig 3).

The distribution of the results from the multivariate sensitivity analysis is shown in figure 4. The estimated average cost per positive individual was less certain (had a wider range of possible values) than the cost per offer and cost per individual tested. The multivariate sensitivity analysis results indicated that the parameters that impacted most on the outcomes were (in order of importance): the proportion accepting a screening offer, the relative importance of GP versus nurse involvement in discussing screening and patient recruitment, the GP/nurse time to discuss screening before test acceptance, the total laboratory test cost, the time to notify patients of their results, and the receptionist time spent selecting and recruiting patients.

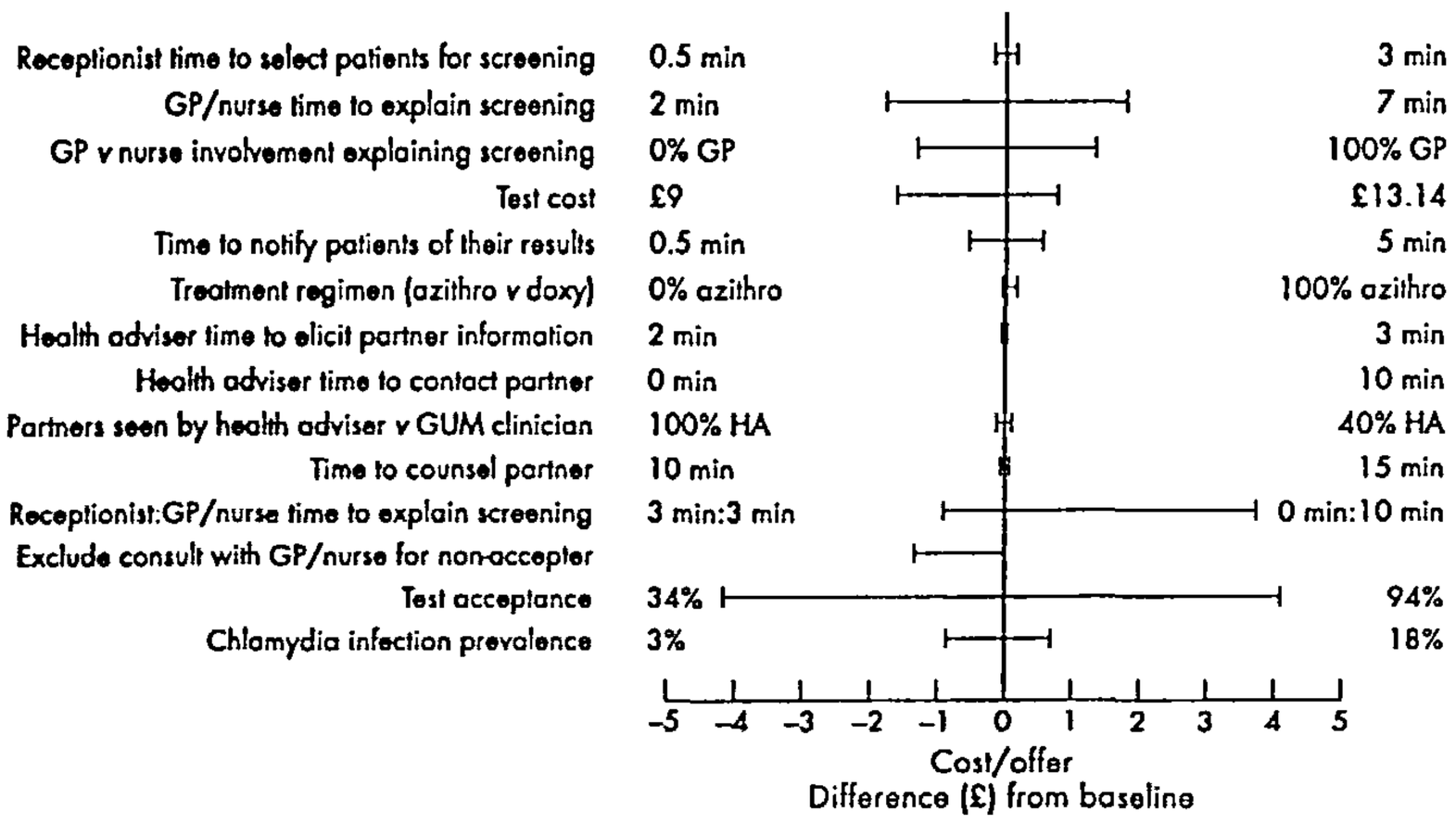

Figure 2 Results from the univariate sensitivity analysis. The difference (£) from the baseline cost per test offer for various parameters tested individually from their minimum to maximum values. A negative difference denotes a cost savings from the baseline.

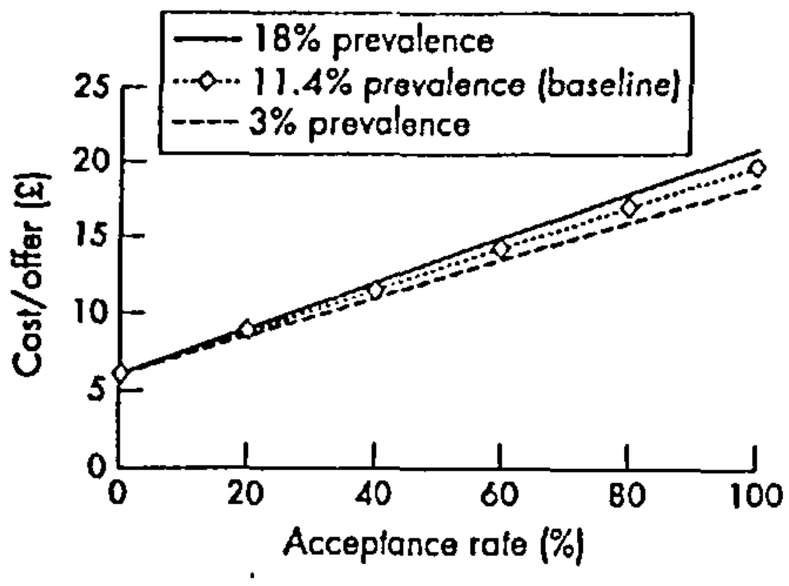

Figure 3 Results from the two way sensitivity analysis of prevalence and acceptance rate; change in the cost (£)/offer.

DISCUSSION

This analysis provides estimates of the average cost of screening from the healthcare perspective. The average cost per screening offer was about £15 including partner management. It was an additional estimated £7 more (£21 total) per person tested, and £16 more than that per person positive (total about £38).

Varying the proportion that accepted a test had the largest effect on the cost per offer, since the participants largely drive the overall costs of the screening programme. While a high test acceptance rate accounts for higher costs, it may help identify the greatest number of infections if the correct population is tested. Identifying cases through screening with the aim to reduce transmission and prevent sequelae may save money in the longer term. This is an area of ongoing research, and can be better addressed with cost effectiveness studies.

Since the laboratory test cost was important in the sensitivity analysis (in part because more than one third of the total screening cost came from LCR testing), determining the most accurate value for this variable will provide a better estimate of the overall costs of screening. Variations in laboratory cost may be explained by differences in the LCR test kit cost and laboratory personnel, and some local variation is expected. There are also various laboratory options, for the testing process including leasing equipment, buying equipment, and renting reagents, that can be examined to see if test costs can be reduced to drive down the overall laboratory costs.

Partner management contributed only 5% of the overall costs, yet it is an important part of a screening programme. While screening females will detect their infection, partner notification will identify male partners at risk who may not otherwise be tested, and treating partners may prevent both re-infection and onward transmission of chlamydia. The costs of partner management were included in the screening model, and it does not appear to make a difference to the cost per screening offer or cost per testing episode if it is included or not, although it does impact the cost per positive episode.

The infrastructure in place for screening may remain (for example the overheads), irrespective of the numbers being tested and treated, at least in the short run. Roughly 25% of the overhead costs were one-off costs such as capital items (refrigerators, office furnishings, computer equipment) that would probably not need to be spent again if more tests were done. These costs would, however, be necessary if a new site were to implement a screening programme. Screening start-up costs may be used for these capital costs, unless they could be accommodated and streamlined within the current healthcare infrastructure. This could be explored in future analyses.

Results from the multivariate and univariate sensitivity analyses highlight areas of uncertainty in the data that influence the costs of screening. For example, the time spent by clinicians explaining screening had a large impact on the costs because of its high variability and impact on all screening offers. Refining this and other estimates may give more precise estimates of the costs involved. However, some of the costs incurred in the pilot study, such as clinician time explaining screening, may not be incurred in future screening paradigms[8] because patients will be expected to self select for screening and there would be minimal involvement of staff for recruitment. Time and motion studies can be conducted to better understand the flow of people through screening and the costs involved in each step. This information can be used to streamline the process and reduce costs within the existing infrastructure.

The costs and resources will be dictated at a local level to a certain extent, so variation in the outcomes would be

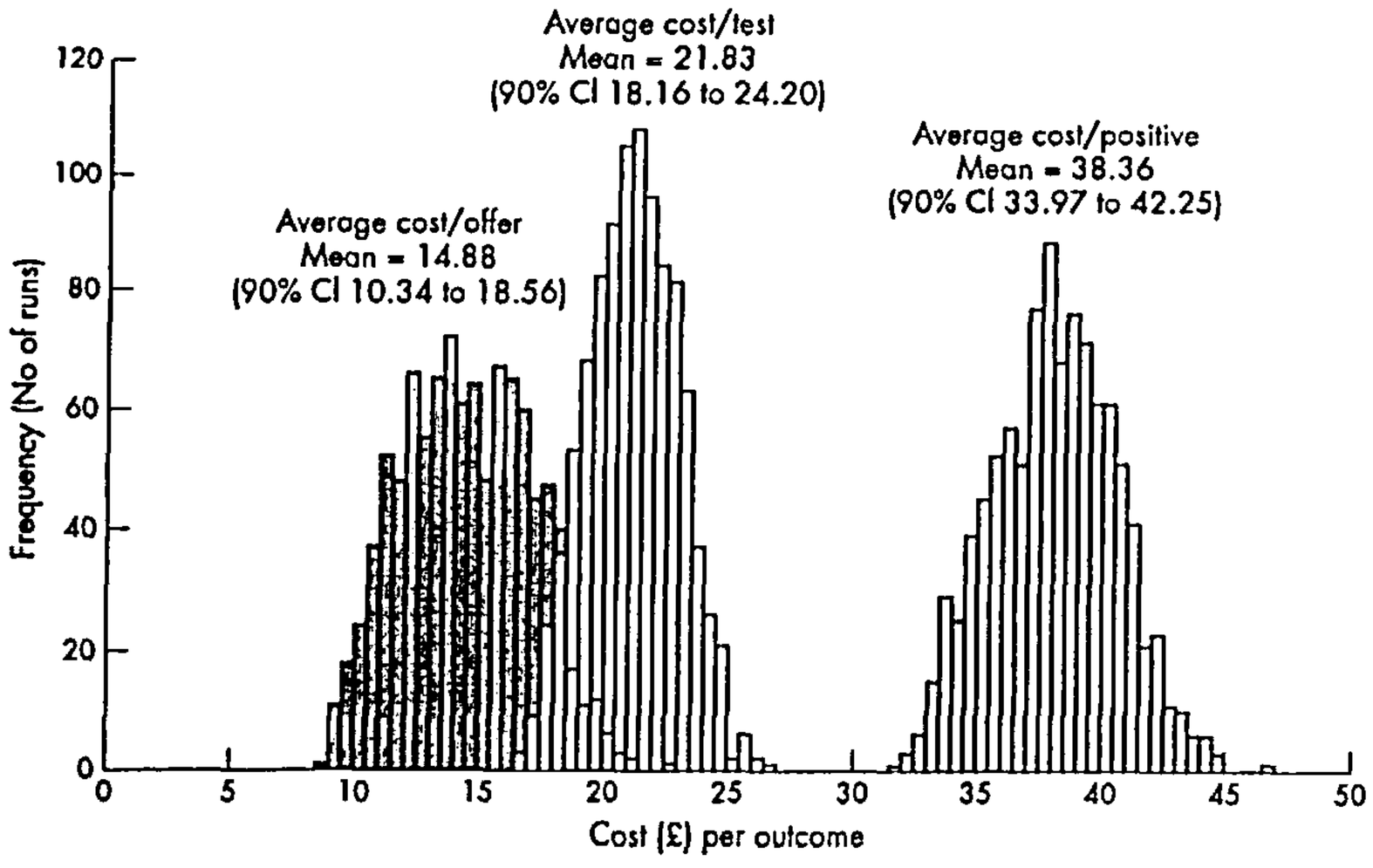

Figure 4 Results from the multivariate sensitivity analysis; frequency distribution of outcomes for 1000 runs, including partner management costs.

expected if this analysis were done for other sites. However, the results from this analysis may also provide a point of reference for evaluating future screening proposals.

There are several reasons why this analysis adds greatly to the information about the cost of genital chlamydia screening. Firstly, the model input data on the patient and partner flow were taken directly from the pilot study. Secondly, much of the cost data also came directly from the pilot invoiced expenses, so is thought to accurately represent the current costs of a screening programme. Thirdly, the individual patient data allow direct estimates of the mean and variance in proportions at each node. This, combined with the flexible model structure and ability to simulate alternative scenarios, provides a powerful tool to explore the average costs of screening, the uncertainty in these estimates, and the cost under different scenarios.

Cost effectiveness studies of chlamydia screening address a different issue from the one in this analysis, but they require similar screening costs. In this analysis, the detailed costs at each step of the tree are examined, and include costs from the wider healthcare system such as personnel who have contact with potential patients in settings where screening is offered (receptionists, nurses, general practitioners), overhead costs of running a screening programme, screening set-up costs, and partner management costs. These may be included in other studies estimating the cost effectiveness of screening, depending on the assumptions about the infrastructure and organisation of the screening programme. Some studies have estimated the time and relative involvement of healthcare workers for different outcomes (PID, ectopic pregnancy, infertility),[4 18 19] but this is the only recent analysis to explicitly estimate the time and costs at each step of a screening programme. The method presented here provides a more precise estimate of the cost of patients with a specific outcome flowing through the screening tree.

This analysis was done from the health provider perspective. It included screening costs and also those of other healthcare personnel involved in the screening process. However, there are other costs that are not included, such as patient costs and the wider societal costs. For example, there may be costs to a positive patient in terms of time lost from work to travel to a clinic to receive treatment, and similar costs for a partner. Another large chlamydia screening study is collecting patient costs as part of their study, which should provide more information when the results are published.[20]

Only the screening costs were included in this analysis, and none of the averted costs from preventing infection and sequelae were estimated. For example, preventing PID or ectopic pregnancy may be a result of screening and treating asymptomatic infection through a screening programme. Other costs and modelling studies have included these sequelae and the estimated costs saving from averting infection and/or complications.[5 6 21 22] Results from this analysis combined with the identified costs of sequelae will be used in further modelling and economic studies.

This analysis provided the average expected cost of screening, based on detailed data, and provides a novel framework for estimating the costs and uncertainty of a screening programme. The uncertainty analyses provided information about the relative importance of different components of the screening model that may direct what information should be collected in future studies. Results may help advise in the phased chlamydia screening implementation planned for future areas in England, and for screening programmes elsewhere.

Key messages

- This study estimates the healthcare costs of opportunistic chlamydia screening in clinical settings in England. It is based on empirical data from a recently completed chlamydia screening pilot study and uses decision analytical modelling techniques to explore the uncertainty of results and the impact of changing key assumptions in the screening paradigm.
- The average cost per screening offer is approximately £15 (under baseline assumptions); these are costs incurred by both the screening programme and the healthcare system in which screening occurs. Sensitivity analyses highlight the elements of screening where costs could be targeted for reduction, including lowering the laboratory test costs and reducing clinician involvement in screening.

ACKNOWLEDGEMENTS

Thanks to Jeremy Townshend, Liam Toohill, and colleagues at the Department of Health, Economics and Operational Research Division for supplying the preliminary invoiced expenses data, research nurses in Portsmouth and Wirral for completing interviews about the patient flow, and everyone else involved in the chlamydia screening pilot study in Portsmouth and Wirral. Thanks to Philippe Mayaud for comments on the paper.

CONTRIBUTORS

EJA contributed to designing and planning the study, created the decision tree model, collected and analysed the costs and related data, conducted interviews with the research nurses, conducted the cost and sensitivity analyses, interpreted results and prepared the manuscript as the lead writer; DSL and ARJ helped develop the decision tree model, extracted and analysed the empirical data from the pilot study and were involved in the data analysis and interpretation; JMP helped develop the decision tree model, was a primary investigator of the pilot study, and helped with interpretation of the data and results; KAF contributed to the study development and helped with interpretation of the analysis; WJE helped conceive and design the study, contributed to the model design, cost estimates and interpretation of data, and all authors read and provided comments on the manuscript and approved the final paper.

Authors' affiliations

E J Adams, W J Edmunds, Statistics, Modelling and Economics Department, Communicable Disease Surveillance Centre, Health Protection Agency, London, UK
D S LaMontagne, K A Fenton, HIV/STI Department, Communicable Disease Surveillance Centre, Health Protection Agency, London, UK
A R Johnston*, Institute of Environmental Science and Research Ltd, Kenepuru Science Centre, Porirua, New Zealand
J M Pimenta*, Epidemiology, GlaxoSmithKline R&D, Middlesex, UK

*Formerly of the Health Protection Agency.

REFERENCES

1 Health Protection Agency, SCIEH, ISD, National Public Health Service for Wales, CDSC Northern Ireland, and UASSG. *Renewing the focus. HIV and other sexually transmitted infections in the United Kingdom in 2002.* London: Health Protection Agency, 2003.
2 Cates Jr W, Wasserheit J. Genital chlamydial infections: epidemiology and reproductive sequelae. *Am J Obstet Gynecol* 1991;164:1773–81.
3 Addiss DG, Vaughn ML, Ludka D, *et al.* Decreased prevalence in Chlamydia trachomatis infection associated with a selective screening program of family planning clinics in Wisconsin. *Sex Transm Dis* 1993;20:28–35.
4 Scholes D, Stergachis A, Heidrich F, *et al.* Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med* 1996;334:1362–6.
5 Townshend JRP, Turner HS. Analysing the effectiveness of Chlamydia screening. *J Oper Res Soc* 2000;51:812–24.
6 Welte R, Kretzschmar M, Leidl R, *et al.* Cost effectiveness of screening programs for Chlamydia trachomatis: a population-based approach. *Sex Transm Dis* 2001;27:518–29.

7 **Honey E**, Augood C, Templeton A, *et al.* Cost effectiveness of screening for Chlamydia trachomatis: a review of published studies. *Sex Transm Infect* 2002;78:406–12.
8 **Department of Health**. *Chlamydia screening programme roll out core requirements*. London: DoH, 2003:1–37.
9 **Pimenta JM**, Catchpole M, Rogers PA, *et al.* Opportunistic screening for genital chlamydial infection. I: Acceptability of urine testing in primary and secondary healthcare settings. *Sex Transm Infect* 2003;79:16–21.
10 **Pimenta JM**, Catchpole M, Rogers PA, *et al.* Opportunistic screening for genital chlamydial infection. II: Prevalence among healthcare attenders, outcome, and evaluation of positive cases. *Sex Transm Infect* 2003;79:22–7.
11 **Netten A**, Curtis L. *Unit costs of health and social care 2002*. Kent: Personal Social Services Research Unit, 2002.
12 **Drummond M**, O'Brien B, Stodddart G, *et al. Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press, 1997.
13 **HM Treasury**. *The green book, Appraisal and evaluation in central government*. London: TSO, 2003.
14 **Centre for Innovation in Primary Care**. *Consultations in general practice—what do they cost?*. London: Centre for Innovation in Primary Care, 1999.
15 **Fenton KA**, Korovessis C, Johnson AM, *et al.* Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet* 2001;358:1851–4.
16 **Webster DL**, Mosure D, Levine W. Chlamydia positively versus prevalence—what's the difference? *Sex Transm Dis* 1998;25:251–3.
17 **British Medical Association and the Royal Pharmaceutical Society of Great Britain**. *British National Formulary* 2003:46.
18 **Postma MJ**, Welte R, van den Hoek JA, *et al.* Cost-effectiveness of partner pharmacotherapy in screening women for asymptomatic infection with Chlamydia trachomatis. *Value Health* 2001;4:266–75.
19 Howell M, Kassler W, Haddix A. Partner notification to prevent pelvic inflammatory disease in women. *Sex Transm Dis* 1997;24:287–92.
20 **ClaSS Study Group**. Evidence is not (yet) enough for evidence based policy for chlamydia screening. *BMJ* 2001;322:364–5.
21 **Marrazzo J**, Celum C, Hillis S, *et al.* Performance and cost-effectiveness of selective screening criteria for Chlamydia trachomatis infection in women: implications for a National Chlamydia Control Strategy. *Sex Transm Dis* 1997;24:131–41.
22 Howell M, Quinn T, Gaydos C. Screening for Chlamydia trachomatis in asymptomatic women attending family planning clinics: a cost-effectiveness analysis of three strategies. *Ann Intern Med* 1998;128:277–84.

BJOG: an International Journal of Obstetrics and Gynaecology
December 2004, Vol. 111, pp. 1408–1412
DOI: 10.1111/j.1471-0528.2004.00207.x

Management of genital chlamydial infections at termination of pregnancy services in England and Wales: where are we now?

D. Scott LaMontagne,[a] Jeanne M. Pimenta,[b] Kevin A. Fenton,[a] Harry Mallinson,[c] Jenny Hopwood[d]

Objective To determine the range of policies and practices related to the management of genital chlamydial infection employed at termination of pregnancy services in England and Wales.

Design Cross-sectional descriptive study.

Setting England and Wales.

Population Termination of pregnancy providers.

Methods Survey questionnaire administered to termination of pregnancy providers.

Main outcome measures Policies and practices for the management of genital chlamydial infection in women seeking termination of pregnancy with comparison to the national guidelines of the chief medical officer (CMO) and the Royal College of Obstetricians and Gynaecologists (RCOG).

Results One hundred and thirty-eight (48%) practices responded to the survey, with representation across England and Wales. Policies for screening and/or treatment of chlamydial infection existed for 70% of providers. We found three practice patterns for the management of genital chlamydial infection among termination of pregnancy attenders: 70% of providers tested their own attenders prior to termination and treated if necessary; about 25% of providers administered prophylaxis without testing; and a small number of providers (<5%) neither tested nor treated attenders.

Conclusion These patterns may be the result of differences in the CMO and RCOG guidelines. Given the impact of untreated genital chlamydial infection in women attending for termination, consistent recommendations from the CMO and RCOG may encourage uniform practice for the management of chlamydial infection in this vulnerable population.

INTRODUCTION

Chlamydia trachomatis is the most common bacterial sexually transmitted infection in England and Wales.[1] Untreated infection can lead to pelvic inflammatory disease, infertility and ectopic pregnancy.[2] Data from termination of pregnancy (TOP) services indicate a prevalence between 4.9% and 14.0% (weighted average prevalence of 7.6%).[3–14] In 2001, over 70,000 diagnoses among males and females attending genitourinary medicine (GUM) clinics were recorded, an increase of 158% since 1993.[1] Factors associated with infection in these populations include young age (<25 years), non-white ethnicity and presence of other genital tract infections.[3,5,15]

Around 180,000 medical or surgical terminations of pregnancy (TOP) are performed each year[16] and may place women at greater risk of ascending upper genital tract infection.[17,18] The incidence of pelvic inflammatory disease in chlamydia-infected women following TOP is between 25% and 63%.[17] The chief medical officer's (CMO) Expert Advisory Group on *Chlamydia trachomatis* has advised screening all women attending for TOP, treatment of those found to be positive and contact tracing of partners for testing and treatment where needed.[19] Guidelines from the Royal College of Obstetricians and Gynaecologists (RCOG) allow for either (1) prophylaxis for attenders without testing for chlamydial infection or (2) screening attenders and treatment if indicated.[20] There is no mention of partner follow up in the RCOG guidelines. Furthermore, the Department of Health's recent phased roll out of the national Chlamydia Screening Programme recommends opportunistic screening of all women attending for termination of pregnancy, with appropriate treatment and partner notification for women who test positive.[21]

In this study, we explored current local policy and practice for chlamydia testing and treatment among TOP providers in England and Wales. We examined variations

[a]*HIV/STI Department, Health Protection Agency, Communicable Disease Surveillance Centre, London, UK*
[b]*GlaxoSmithKline R&D, Worldwide Epidemiology, Middlesex, UK*
[c]*Liverpool Public Health Laboratory, University Hospital Aintree, Liverpool, UK*
[d]*Chlamydia Office, St Catherine's Hospital, Birkenhead, UK*

Correspondence: Mr D. S. LaMontagne, HIV/STI Department, Health Protection Agency, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK.

in policy and practice by region of the country, service size and the degree to which the national recommendations regarding testing and treatment for infection have been implemented in termination of pregnancy services.

METHODS

The most recent (1999) list of termination of pregnancy service providers was obtained from the Department of Health (England) and included the name, location, and annual number of terminations performed for each service. This was used as the sampling frame to identify participating services. All services on the Department of Health list were contacted by telephone to confirm current service provision and to verify contact details.

A survey questionnaire was designed, which requested detail on current policies for screening and treating genital chlamydial infection; assessment of testing and treatment services to client populations; information on follow up for women testing positive; and perceived barriers to implementing chlamydia screening. The survey requested provider practice for those persons attending for surgical termination separately from those persons attending for medical termination. Questionnaires were sent to either the director of gynaecology or the lead clinician at each service with a response paid envelope addressed to the study administrator. A second mailing was sent to non-responders after four weeks. Larger centres (performing more than 100 terminations annually) were contacted directly by telephone two weeks after this to encourage survey completion. The cutoff for responding was 10 weeks after the original mailing.

Data were entered into a secure, password-protected Microsoft Access database. A categorical coding frame for each free text question was developed. Several survey questions were recoded for meaningful analysis. Service size was categorised by the annual number of terminations reported: fewer than 200 terminations per year (small services); 201–600 (medium sized services); or more than 600 annual terminations (large services). Respondents were categorised into either NHS or non-NHS (private and non-specialised combined) services based upon the primary source of funding reported. Data were analysed using SPSS 11.5 (SPSS, Chicago, Illinois) and STATA 7.0 (Stata, College Station, Texas). Descriptive statistics and bivariate analyses with χ^2 test (as appropriate) were generated.

Ethical approval for the study was not required as the study was a policy survey related to information at the service and not patient level.

RESULTS

In total, 380 services in England and Wales reported terminations in 1999. Seventy-eight services were excluded due to duplication on the list, service closure, incomplete contact information or changed service mix that no longer included terminations. Eighteen services were excluded as they were represented by the British Pregnancy Advisory Service or Marie Stopes International. As national policies exist for these organisations, one survey questionnaire was sent to the central office of each organisation. In total, 284 services were invited to participate in the study. Responses were acquired from 156 (55%) services. Eighteen providers indicated that they no longer provided a service. Results are presented for 138 services (48% response rate).

All regions except the West Midlands were evenly represented in services of different size (Table 1). One hundred and twenty services (87%) were NHS funded and 16 (12%) were non-NHS funded. Two respondents (1%) did not provide funding information. Eleven respondents reported more than one funding source: eight provided more than 200 terminations funded by the NHS and were classified as such; the other three were classified as non-NHS.

Ninety-six services (70%) reported a written policy for screening and/or treatment of genital chlamydial infection. For providers with policies regarding chlamydia screening, the most common content areas within the policy included testing (82/96), treatment (67/96) and referral of positives to GUM clinics (65/96) (Table 1).

Actual practice showed no difference between attenders receiving a medical termination *vs* those receiving a surgical termination (data not shown). For medical terminations, providers in Yorkshire and Humberside and East Midlands were more likely to employ prophylaxis without testing ($P < 0.05$). For surgical terminations, services in Yorkshire and Humberside and the North East were more likely to provide prophylaxis without testing ($P < 0.05$).

NHS services were more likely than non-NHS services to have a screening and/or treatment policy (75% *vs* 38%, $P < 0.05$); screen all or some of their surgical termination attenders (74% *vs* 50%, $P < 0.05$); and treat all or some of their medical termination attenders (97% *vs* 71%, $P < 0.05$). Additionally, NHS services were more likely to report more than 50% of their attenders were screened for chlamydial infection (91% *vs* 30%, $P < 0.05$).

Medium and large services were more likely than small services to have a written policy for screening and/or treatment (79% *vs* 51%, $P < 0.05$). More small services did not screen women attending for surgical terminations (41% *vs* 26% [medium] *vs* 22% [large], $P < 0.05$). Small services were less likely than medium or large services to telephone test results to women who were screened (12% *vs* 33% *vs* 51%, $P < 0.05$). Small services were also less likely to report a formal policy of onward referral of chlamydia positive patients (50% *vs* 69% [medium] *vs* 84% [large], $P < 0.05$).

Both the RCOG and CMO guidelines recommend screening attenders and treating those who are positive. Over one-third of services administered treatment without

Table 1. Characteristics of 138 services that responded. Values are given as *n* (%).

Service provider characteristics	Number and percentage of services	
Region		
East Midlands	15 (11)	
Eastern	13 (9)	
London	13 (9)	
North East	11 (8)	
North West	20 (15)	
South East	16 (12)	
South West	18 (13)	
Wales	15 (11)	
West Midlands	3 (2)	
Yorkshire and Humberside	14 (10)	
Annual number of terminations (n = 135)		
≤200 (small)	39 (28)	
201–600 (medium)	48 (35)	
600 or more (large)	48 (35)	
Existing policy (n = 136)	96 (70)	
Policy covers		
Testing for genital CT infection	*82 (85)*	
Specimen collection and delivery	*45 (47)*	
Receipt of laboratory results	*50 (52)*	
Treatment of women testing positive	*67 (70)*	
Counselling regarding STIs	*43 (45)*	
Partner notification	*26 (27)*	
Referral to GUM services	*65 (68)*	
Treatment of all attenders	*14 (15)*	
Termination practice*		
Surgical terminations	133 (96)†	
Medical terminations	109 (79)†	
Actual screening and treatment practice for CT	Surgical TOP	Medical TOP
Neither screens nor treats	3 (2)	5 (5)
Prophylaxis without screening	35 (26)	25 (23)
Screening and treatment	95 (71)	79 (73)

CT = *Chlamydia trachomatis*; STIs = sexually transmitted infections; GUM = genitourinary medicine.
Totals and percentages may not add to total respondents due to non-responses on some questions. Percentages may exceed 100% due to rounding or multiple responses.

* Surgical and medical termination categories are not mutually exclusive; 106 providers are represented in both categories.

† Excludes two services that did not respond to testing and treatment practice questions and three services that did not provide surgical terminations.

‡ Excludes 1 service that did not respond to testing and treatment practice questions and 28 services that did not provide medical terminations.

screening (Table 1, next to last row). Eighty percent (28/35) of surgical termination providers reported administration of treatment during or after the procedure and 60% of these reported that they administered the RCOG recommended first-line therapy. Medical termination providers, which provided prophylaxis without testing for chlamydial infection, showed a similar pattern of treatment.

Among TOP providers that screen (Table 1, final row), 93% screened all attenders, regardless of surgical or medical termination. Half of the services that screen administered antibiotic treatment for those testing positive (52% and 56% of surgical or medical termination) and half treated all those screened (48% and 44%). Among services that screen for chlamydial infection then treat, if positive, over 90% of providers tested attenders before the termination procedure, regardless of the procedure, and over 80% administered treatment on-site. Treatment mostly occurred during or after termination (70% surgical and 63% medical terminations). Adherence to the RCOG-recommended first-line therapy was reported by 42% of surgical and 48% of medical termination providers.

Very few providers performed partner notification activities themselves (<5%). Approximately half the services (48% of surgical termination providers and 51% of medical termination providers) referred women who test positive onto GUM.

Cervical swabs were used exclusively by over half of screening services, and a combination of swabs and urine was employed by nearly a third, regardless of type of termination procedure. Fewer than 10% of providers were using urine only for specimen collection. Full employment of nucleic acid amplification tests was less than 25%; an additional 50% of providers used only non-amplified tests, such as enzyme immunoassays; and about 20% used a combination of these.

The most common factors reported to limit the delivery of chlamydia testing were lack of financial support (46/138) and time constraints in clinic (38/138). Several service providers stated that prophylactically treating all TOP attenders was easier, more reliable and more cost effective (data not shown).

DISCUSSION

Our study found significant heterogeneity in the behaviour of termination of pregnancy services in their approach to testing and treating for genital chlamydial infection. Three distinct patterns emerged: (1) TOP providers that screened attenders prior to termination and treated if necessary; (2) providers that administered prophylactic antibiotics without testing; and (3) providers that did not screen or treat. A possible explanation for these patterns might be uncertainty in best practice due to the overlapping and diverging recommendations of the RCOG and the CMO.

Among the nearly 70% of providers that engaged in screening before termination, over 90% tested everyone. The RCOG and CMO guidelines are most similar on this point but the RCOG guidelines do not explicitly recommending testing *all* patients. Consistency in this policy directive between the two bodies may be warranted. Most screening providers tested prior to termination, as

recommended, and collected an appropriate sample. However, less than half were using the more sensitive nucleic acid amplification test that is the current diagnostic standard.[21] As TOP providers are likely to become increasingly involved in routine testing for genital chlamydial infection, it is necessary that laboratory capability also improves to provide the best diagnostics for this population.

For all services, differences in the treatment regimen administered were apparent. Inconsistency in the recommended treatment regimens between the RCOG and CMO policies may be influencing these providers' practices. The majority of these providers were in compliance with one guideline or the other, but this lack of explicit and consistent direction for treatment is of some concern. Lack of consistency between guidelines was demonstrated in that about 25% of the providers offered prophylaxis to TOP attenders without testing, a practice that is only encouraged by the RCOG guideline.[20] Additionally, less than two-thirds indicated using the RCOG recommended treatment regimen.

Although very few providers reported they neither screened nor treated any TOP attender, the fact that any provider reported this practice is disturbing. There is significant evidence of the health risks associated with untreated genital chlamydial infection[17,18] and these risks are much greater for women who have a termination.

Our study has several limitations. Only about one-half of all providers responded to our survey. This is an important source of bias, the direction of which is not possible to predict. Secondly, we do not know to what extent the responses of the central offices for the British Pregnancy Advisory Service and Marie Stopes International represent the practice of providers within their networks. Finally, there may have been practice changes in the intervening years between our survey and this publication, especially in light of the large amount of national coverage for the Department of Health's phased roll out of the national Chlamydia Screening Programme in England.

In conclusion, we found that over 95% of responding TOP providers reported practice consistent with either the RCOG or CMO guidelines on *Chlamydia trachomatis*, although there were discrepancies. Specifically, guidelines need clarifying on (1) whether antibiotic prophylaxis should be offered to all TOP attenders without testing; (2) what is the appropriate treatment regimen for both prophylaxis without testing and test then treat policies; and (3) what should be the laboratory test standard for all women submitting a sample for chlamydia testing. Additionally, the absence of any guidance regarding partner notification and contact tracing for women testing positive in the RCOG recommendations should be addressed. Synchronising the RCOG and CMO guidelines would be beneficial in harmonising a universal standard for chlamydia testing and treatment for all women, increasing the compliance of providers and may encourage providers to begin a testing programme within their service.

Acknowledgements

We would like to thank the Department of Health for providing a list of termination services in England and Wales; Maria Solomou for questionnaire administration, data entry and data management; Pauline Rogers for helpful comments on the questionnaire; and Neil Macdonald for questionnaire design wizardry.

Contributions

D.S.L. analysed and interpreted the data and authored the manuscript. J.M.P. and K.A.F. developed protocol and questionnaire, implemented the study and commented on the manuscript. H.M. and J.H. assisted with protocol and questionnaire development and commented on the manuscript.

Conflict of interest

J.M.P. is currently employed by GlaxoSmithKline but carried out this work while employed by the Health Protection Agency (formerly known as the Public Health Laboratory Service). GlaxoSmithKline was not involved in the decision to publish.

References

1. PHLS, DHSS and PS, and the Scottish ISD(D)5 Collaborative Group. *Sexually Transmitted Infections in the UK: New Episodes seen at Genitourinary Medicine Services, 1991 to 2001*. London: Public Health Laboratory Service, 2002.
2. Stamm WE. *Chlamydia trachomatis* infections of the adult. In: Holmes KK, Sparling PF, Mårdh P-A, et al, editors. *Sexually Transmitted Diseases*. New York: McGraw-Hill, 1999:407–422.
3. Hopwood J, Mallinson H, Jones I. There is more to a test than technology—evaluation of testing for chlamydia infection in a charitable sector termination service. *Br J Fam Plan* 1998;**23**:116–119.
4. Blackwell A, Thomas P, Wareham K, Emery S. Health gains from screening for infection of the lower genital tract in women attending for termination of pregnancy. *Lancet* 1993;**342**:206–210.
5. Southgate L, Treharne J, Williams R. Detection, treatment and follow up of women with *Chlamydia trachomatis* infection seeking abortion in inner city general practices. *BMJ* 1989;**299**:1136–1137.
6. Smith N, Nelson M, Hammond J, Purkayastha S, Barton S. Screening for lower genital tract infections in women presenting for termination of pregnancy. *Int J STD AIDS* 1994;**5**:212–213.
7. Ridgway GL, Mumtaz G, Stephens RA, Doriel J. Therapeutic abortion and chlamydial infection. *BMJ* 1983;**286**:1478–1479.
8. Simms I, Hopwood J, Mallinson H, Rogers P, Webb A. Changing screening strategies for genital chlamydia in family planning services: a good public health strategy? *Eur J Contracept Reprod Health Care* 2000;**5**:91–95.
9. Tobin J, Bateman J, Banks B, Jeffs J. Service audit of the process of referral to genitourinary medicine of patients found to be chlamydia positive in a family planning service. *Br J Fam Plan* 1999;**24**: 160–163.
10. Blackwell AL, Emery SJ, Thomas PD, Wareham K. Universal prophylaxis for *Chlamydia trachomatis* and anaerobic vaginosis in women attending for suction termination of pregnancy: an audit of short-term health gain. *Int J STD AIDS* 1999;**10**(8):508–513.
11. Uthayakumar S, Tenuwara W, Maiti H. Is it evidence-based practice? Prophylactic antibiotics for termination of pregnancy to minimize post-abortion pelvic infection. *Int J STD AIDS* 2000;**11**(3):168–169.
12. Hopwood J, Mallinson H, Gleave T. Evaluation of near patient testing

for *Chlamydia trachomatis* in a pregnancy termination service. *J Fam Plan Reprod Health Care* 2002;27(3):127–130.
13. Pimenta JM, Catchpole M, Rogers PA, et al. Opportunistic screening for genital chlamydial infection. II: Prevalence among healthcare attenders, outcome, and evaluation of positive cases. *Sex Transm Infect* 2003;79(1):22–27.
14. Mallinson H, Hopwood J, Skidmore S, Fenton K, Phillips C, Jones I. Provision of chlamydia testing in a nationwide service offering termination of pregnancy: with data capture to monitor prevalence of infection. *Sex Transm Infect* 2002;78:416–421.
15. Harvey J, Webb A, Mallinson H. *Chlamydia trachomatis* screening in young people in Merseyside. *Br J Fam Plan* 2000;26(4):199–201.
16. Office of National Statistics. *Population Trends. National Statistics 101* [Autumn 2000]. London: HMSO, 2000.
17. Moller BR, Mardh PA, Ahrons S, Nussler E. Infection with *Chlamydia trachomatis*, *Mycoplasma hominis* and *Neisseria gonorrhoeae* in patients with acute pelvic inflammatory disease. *Sex Transm Dis* 1981;8(3):198–202.
18. Barbacci MB, Spence M, Kappus EW, Burkman RC, Rao L, Quinn TC. Postabortal endometritis and isolation of *Chlamydia trachomatis*. *Obstet Gynecol* 1986;68(5):686–690.
19. Chief Medical Officer's Expert Advisory Group. *Main Report of the CMO's Expert Advisory Group on Chlamydia trachomatis*. London: Department of Health, 1998.
20. Royal College of Obstetricians and Gynaecologists. *The Care of Women Requesting Induced Abortion*. London: RCOG Press, 2000.
21. Department of Health. *Chlamydia Screening Programme Roll Out—Core Requirements*. London: Department of Health, 2003.

Accepted 2 April 2004