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EDITORIAL

# What should we do about screening for genital chlamydia?

Nicola Low[a] and Matthias Egger[b]

*Chlamydia trachomatis* is the world's most common bacterial sexually transmitted infection, with an estimated 89 million new cases each year.[1] Genital chlamydia poses a major global public health problem because it is a transmissible cause of severe reproductive morbidity, including pelvic inflammatory disease, impaired fertility and ectopic pregnancy in women.[2] Chlamydia can be cured with antibiotics and transmission prevented by treating sexual partners, but most infections are asymptomatic so they remain undiagnosed. Early diagnosis is possible, with DNA amplification techniques now providing highly sensitive and specific tests[3] that are more acceptable to patients than previous methods because they can be performed on non-invasively collected genital specimens. Probably more than any other single factor, these technological advances in chlamydial diagnosis are driving the current health policy debate about the introduction of national chlamydia screening programmes.[4,5] But do we have enough evidence about the effectiveness of screening and about the natural history of chlamydial disease to be sure that proposed screening programmes will be the most effective and cost-effective way of preventing the long term consequences of infection?

The appropriateness of screening for disease prevention is usually assessed according to principles set out by Wilson and Jungner in 1966.[6] These criteria have been expanded by policy-making bodies such as the UK National Screening Committee to emphasize the rigorous standards of research evidence required to demonstrate effectiveness and the programme aspects of screening.[7] Genital chlamydia has been judged to fulfil these criteria either in whole,[8,9] or in part.[4,10] So how strong is the evidence? The first randomized trial evaluated the effect of chlamydia screening on the incidence of pelvic inflammatory disease in women in a health maintenance organization fulfilling criteria for being at high risk of infection.[11] This approach would be classified as a selective population screening strategy. The incidence of pelvic inflammatory disease at one year was 56% (95% CI: 10–80%) lower in the intervention than the control group. The potential for bias introduced by the study design, however, makes the results difficult to interpret.[10,12,13] In particular, randomization was performed before women were invited for screening, and those allocated to the screening arm were more vigorously recruited.[11] Thus, of more than 36 000 women randomized to intervention and control groups in a ratio of 1:2, only 2607 (7.1%) were included in the analysis, with the ratio of intervention to control groups falling to 1:1.6. More recently, randomized trials in Denmark have also evaluated population screening, inviting school students[14] and young people in the general population[15] to submit self-taken urine or vaginal specimens for chlamydia testing. Amongst women in the school-based study the incidence of pelvic inflammatory disease at one year was reduced by 50%.[14] Over 45% of study participants were, however, lost to follow-up in this study. Whilst evidence from randomized trials is essential, problems with trial quality that could bias the estimated benefits of chlamydia screening could lead to future challenges and debate about the justification for screening programmes, as has recently happened with breast cancer screening.[16–18] Furthermore, the randomized trials evaluated population-based approaches to screening but they have also been cited as evidence in support of opportunistic screening of people using existing health services.[8,19] It is unclear to what extent the results of population-based screening can be extrapolated to opportunistic strategies.

Observational data from chlamydia screening programmes established before randomized trials were performed also provide evidence that screening is associated with reductions in the prevalence of genital chlamydia, pelvic inflammatory disease and ectopic pregnancy.[20–22] Programmes were set up in Sweden[21] and parts of the US[20] during the mid-1980s to conduct opportunistic screening on unselected, mostly female, populations attending a variety of health care settings. Five to 9 years after implementation, proportions of positive samples tested by laboratories in these programmes had decreased by one- to two-thirds.[20,21] However, surveillance data from countries with[23] and without[24] screening programmes have shown similar recent increases in the prevalence of chlamydia (Figure). Changes in population prevalence are clearly influenced by the number of people being tested and, although this has increased in Sweden, the proportion of positive tests has also increased from a nadir of 4.1% in 1994 to 6.1% in 2000.[23] These findings suggest that the opportunistic screening approach to chlamydia control may have reached its limit.

A potential explanation for the resurgence of chlamydia in Sweden could be the failure to include men comprehensively in the screening programme. Opportunistic programmes only reach health service users, and amongst young sexually active people, these are mostly women. In Sweden only 20–25% of chlamydia specimens come from men.[21] Control of chlamydia transmission should occur through partner notification, which

[a] Department of Social Medicine, University of Bristol, UK.

[b] Institute for Social and Preventive Medicine, University of Berne, Switzerland.

Correspondence: Dr Low, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, UK. E-mail: nicola.low@bristol.ac.uk

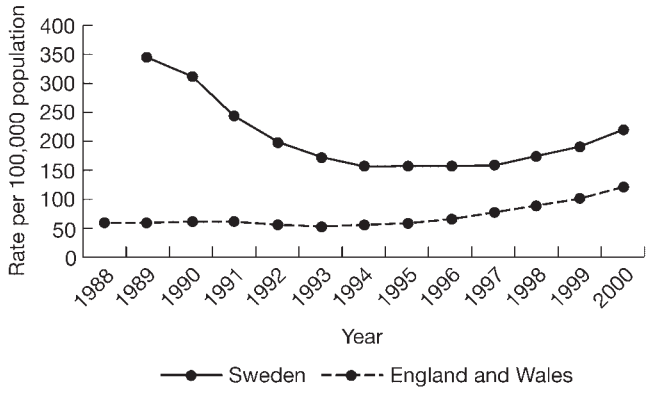


**Figure** Trends in diagnoses of genital chlamydia in Sweden and England and Wales 1988–2000

Source: Sweden (Dr Torsten Berglund, personal communication), England and Wales (Public Health Laboratory Service and Office for National Statistics). The higher recorded prevalence of chlamydia in Sweden probably reflects higher testing rates and differences in national surveillance systems. Genital chlamydia is compulsorily notifiable in Sweden and surveillance data include reports of infections diagnosed in all clinical settings. Chlamydia is not notifiable in England and Wales and surveillance data come from diagnoses made in genito-urinary clinics only.

is compulsory in Sweden. It has also been widely assumed that prevalence of chlamydia is lower in men than women because of lower female to male transmission efficiency and because the majority of infections in men were presumed to be symptomatic and to present early for testing and treatment.[25] Another application of DNA amplification diagnostic techniques has shown this assumption to be false. Several studies have now estimated the prevalence of chlamydia in population-based samples using non-invasive home-collected specimens.[26–29] In the European studies, chlamydia prevalence was 2.2–2.3% in men and 1.5–2.9% in women.[13,26,28] A smaller study from Baltimore found, in our calculation, crude prevalence rates of 3.2% (95% CI: 0.1–7.9%) and 5.2% (95% CI: 2.5–9.3%) in Black men and women, and 3.3% (95% CI: 0.1–8.5%) and 0% (upper CI: 2.6%) in men and women of other ethnic groups.[29] Together, these studies suggest that the circulating pool of asymptomatic untreated chlamydia may be similar in men and women. A strategy combining opportunistic screening in health care settings, which tends to miss a large proportion of men at risk, and partner notification may not be sufficient to produce sustained reductions in chlamydia prevalence.

The case in favour of chlamydia screening for a range of populations and screening strategies has also been made on the grounds of cost-effectiveness.[30–33] Most of the cost savings achieved through screening come from the predicted costs of treatment of complications avoided.[32,34] Economic models are highly sensitive to assumptions about the incidence of complications[34] but these are notoriously difficult to measure. Studies estimating the rate of progression from lower genital tract chlamydia to pelvic inflammatory disease are hindered by small sample size and a lack of objective diagnostic criteria for pelvic inflammatory disease. The most widely cited study found pelvic inflammatory disease in 6 of 20 women with chlamydia (30%, 95% CI: 12–54%).[35] Uncertainty about, and especially overestimation of the incidence of complications, could give misleading results about the cost-effectiveness of screening interventions. Piecing together the natural history of chlamydial disease is fraught with problems,[2,10,34] not least because of the ethics of studying the prognosis of untreated infection. The long term outcomes of laparoscopically confirmed pelvic inflammatory disease have been studied in cohort studies[36,37] with up to 25 years of follow-up.[37] These studies are of limited use, however, because they report only the proportions of women developing infertility or ectopic pregnancy, without taking into account the longitudinal nature of the data, losses to follow up over time or confounding by contraceptive choice or sexual behaviour. Furthermore, in the largest study, chlamydia status at baseline was not known.[37]

Ideally, individual or cluster randomized controlled trials in which the potential for bias has been minimized should compare the effect of different screening strategies with no screening on the incidence of pelvic inflammatory disease and chlamydia. A cluster trial is now being piloted in Scotland (Phil Wilson, University of Glasgow, personal communication). Screening for chlamydia in men also needs to be evaluated and methods of including men in chlamydia screening programmes considered. The ongoing Chlamydia Screening Studies (ClaSS) in the Avon and West Midlands regions of England were set up to determine the prevalence in the sexually active male and female population and to examine the feasibility, acceptability and costs of a mass screening programme. A similar project is ongoing in four regional municipal health services in the Netherlands.[38] Initial results from the Chlamydia Pilot Studies in the Wirral and Portsmouth, England, indicate that opportunistic screening is feasible in a range of settings in the National Health Service, and significant population coverage can be achieved.[39] In order to model more accurately the cost effectiveness of chlamydia screening programmes we also need to improve our understanding of the natural history of chlamydial disease. A linkage study in Uppsala, Sweden, where widespread opportunistic screening was introduced in 1985, will provide information on the incidence of sequelae in women who screened positive for chlamydia, women who screened negative, and women who declined to participate in the programme (Björn Herrmann, University of Uppsala, personal communication). The results from a number of ongoing studies will thus fill some of the important gaps in the evidence base. Surely, in the UK and elsewhere, we should avoid pressure to implement a screening programme prematurely without being sure that this is the most sustainable approach to controlling chlamydia and its reproductive consequences.

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