Commentary: Chlamydia trachomatis screening: what are we trying to do?

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Chlamydia trachomatis is a sexually transmitted infection that can cause pelvic inflammatory disease (PID) which can lead to infertility and ectopic pregnancy. Infection is often asymptomatic, detectable with a urine test, and cured by single dose therapy. These characteristics are similar to another infection Neisseria gonorrhoeae. In the US, a N. gonorrhoeae control programme began in the mid-1970s, and between 1975 and 1996, rates of N. gonorrhoeae fell from 467.7 to 121.8 per 100 000 population.1 The prevalence of C. trachomatis infection among persons who were tested (test positivity) fell when C. trachomatis screening was introduced in Sweden,2 British Columbia,3 and the Northwestern United States.1 A study found screening was associated with lower rates of PID,4 and several systematic reviews concluded that sexually active women under age 25 years should be screened for C. trachomatis every year.5 Now Low et al., in another review of the evidence conclude that ‘there is an absence of evidence supporting opportunistic chlamydia screening…the most commonly recommended approach’.5

What is going on?

Rates of reported C. trachomatis infection have since increased in Sweden,6 and British Columbia.3 The prevalence among persons tested has also increased in the Northwestern United States,7 and did not fall when C. trachomatis screening was introduced in nine other regions.1 Trends in PID are difficult to evaluate because the diagnosis is non-specific and there are other causes of PID, but rates appeared to decrease among inpatients (by 68%) and outpatients (by 47%) between 1985 and 2001 in the United States.8 Most of this decrease occurred by 1995, before screening recommendations were published. Thus, in the present context, it is appropriate to reexamine the evidence, and remind ourselves what we are trying to do.

PID could be prevented by either preventing C. trachomatis infection in the first place, or by curing infections before they progress to PID. This distinction is important. If screening is intended to interrupt progression, then, presumably, treating recently acquired infections would prevent more PID than treating longstanding infections. Screening routinely once per year would mean the average asymptomatic infection would be about 6 months old. Screening high-risk women more frequently could decrease the average duration of infection and increase the likelihood of preventing PID. For example, women who are diagnosed with a C. trachomatis infection could be asked to return in 3 months for rescreening.

If lowering the incidence of C. trachomatis is important, then screening and treatment should be done in a way that lowers the likelihood of new infection. If everyone is screened annually, with screening spread evenly across 250 working days in a year, every day 0.4% of all infections in a community would be cured. That small drop in prevalence leaves plenty of opportunity for re-infection of persons who were treated or new infection in previously uninfected persons. If everyone were screened and treated on the same day, the risk of re-infection or new infection would be considerably less. Alternatively, screening could focus on likely sexual networks, or screening programmes could emphasize treatment of past partners and screening of future partners.

Low et al. found two studies that evaluated screening to cure infection before it progressed to PID.5 Scholes et al. screened 645 women, treated 44 for C. trachomatis infection, and after 1 year of follow-up, the group had 12 fewer cases of PID than expected based on the comparison group of unscreened women.4 This study did not address the prevention of incident infections. Curing 44 infections among the 36,547 women in the health maintenance organization (with partners that were not screened and were not necessarily part of the same health plan) is unlikely to influence the incidence. Nevertheless, these findings suggest that treating four infected women will prevent one case of symptomatic PID. Ostergaard et al. used a different definition of PID, but had similar success; testing 867 female students, detecting 43 infections and preventing nine reported
cases of acute PID among the 443 interviewed at follow-up. This study also screened some of the boys attending the same schools, so the screening might have influenced incidence as well. As Low et al. point out, these results now seem too good to be true. An impact of that magnitude should be easily detected, but no decrease in hospitalizations for PID was found when following 7053 female army recruits who were screened (643 infections treated) compared with 21021 who were not screened. Furthermore, rates of PID in the US appeared fairly stable from 1996 to 2001 as C. trachomatis screening rates increased.

Low et al. found three studies that evaluated the effect of population-based screening on indicators of C. trachomatis prevalence (not incidence). Ostergaard et al. found that students who were screened for C. trachomatis were less likely to be infected a year later (2.9%) than students who were not originally tested (6.6%). However, the intervention group included only students who were tested at the beginning, so their infections at follow-up were mostly incident infections, whereas the comparison group contained both incident and prevalent infections. Cohen et al. assessed changes in test positivity at three high schools where screening was offered five times in 3 years. About one-half of the enrolled students were tested each time. The prevalence among students tested (not incidence) fell significantly among males (5.9–3.2%), but not females (12.1–10.3%). Hodgins et al. compared six pairs of villages that were randomly assigned to C. trachomatis screening and education vs usual care. In the screening villages, 16% of males and 29% of females aged 15–39 years were screened at baseline. Over the ensuing year, new C. trachomatis infections were reported less often in four of the six intervention villages compared with control villages. This finding could be due to chance. If the intervention had no effect, the probability of finding that at least four of six intervention villages had fewer infections would be 0.34.

With such a small number of studies, in such diverse populations, it is risky to draw conclusions about which approach to screening works best. Low et al. suggest that a registry-based approach will result in more screening. They note that registry-based screening worked well for cervical cancer screening in the UK. However, similar levels of screening have been reached in the US using an opportunistic approach. Furthermore, cervical cancer screening works by interrupting disease progression, not by reducing the incidence of human papillomavirus infection. If screening is intended to reduce the incidence of C. trachomatis infection it must be considered in the context of the existing control programme, which might include education on symptom recognition, access to care, and treatment of partners. As such, how should the success of screening be measured—number of women tested, number of infections treated, prevalence of C. trachomatis, incidence of C. trachomatis, incidence of PID or incidence of long-term sequelae such as tubal-factor infertility and ectopic pregnancy?

These questions would be moot if rates of C. trachomatis infection were declining the way they did for N. gonorrhoeae. But screening for N. gonorrhoeae in the US was accompanied by a massive control effort, including partner notification by health department personnel, that is absent for C. trachomatis. In 1976, there were 1 million N. gonorrhoeae infections reported; 319 029 infected patients were interviewed by health department personnel about their partners, 221 068 partners were examined, 82 277 partners were treated for newly diagnosed infection, and 98 760 partners received prophylactic treatment. At that time, STD control programmes worked on two diseases. Now, in addition to syphilis and gonorrhea, STD programmes deal with HIV, herpes, human papillomavirus, trichomoniasis and C. trachomatis, so competition for resources is intense. As Low et al. point out, further research is certainly necessary to identify interventions that reduce the incidence of C. trachomatis or reduce progression to PID among women who are already infected. So far, programmes to control C. trachomatis have not been met with the same success as programmes to control N. gonorrhoeae. Perhaps this is related to differences in characteristics of the two infections or in the sexual networks of infected persons. Perhaps it is related to differences in the intensity of the efforts mounted by the respective programmes.

References


