Screening for genital *Chlamydia trachomatis* infection: are men the forgotten reservoir?

Australia is lagging behind other developed countries in efforts to control chlamydial infection

AUSTRALIAN POLITICIANS are concerned about the falling fertility rate and are debating measures, such as cash incentives and paid maternity leave, to reverse the "baby bust".[1] If enacted, these measures are expected to cost several hundred million dollars per year — perhaps several thousand dollars per extra baby. Yet, Australia is at high risk of — if not already undergoing — a silent epidemic of preventable infertility and foetal loss through ectopic pregnancy caused by *Chlamydia trachomatis* infection. This condition can be detected by a $24 test and effectively treated with a single dose of antibiotics.

Some commonly held assumptions about chlamydial infection in men need to be addressed.

Chlamydial notifications have increased fourfold over the past decade (Box). However, as most infections are asymptomatic, the 26 000 cases reported in 2002 probably represent only a fraction of the true incidence and prevalence.[2-4] This trend may be partly due to a reporting artefact or greater numbers or sensitivity of tests.[5] Yet, if these factors were the complete explanation, the graph of notifications should have plateaued long ago. The passage of time and enhanced surveillance data[6,7] indicate that most of the increase is real. The proposed National Sexual Health Strategy was shelved before the last federal election, and state-initiated *Chlamydia* programs designed to enhance case-finding through selective testing by general practitioners (and, therefore, Medicare) were discouraged. Australia is overdue to follow the lead of other developed nations by getting serious about controlling chlamydial infection.[8]

Because infected women are usually asymptomatic, and because they incur the bulk of the serious morbidity, *Chlamydia* programs have traditionally focused on screening women.[9] Selective testing criteria for women include combinations of age under 25 years, reported change of sexual partner, non-use of condoms, unintended pregnancy, and an inflammatory Pap smear result. However, this testing is only secondary prevention — some women identified in this way will already have silent damage to their fallopian tubes and their fertility. True primary prevention mandates that women never acquire chlamydial infection. As there is no vaccine, this means avoiding infection either by behavioural means (use of condoms, non-penetrative sexual practices or sexual abstinence) or by having male partners who are not infected.

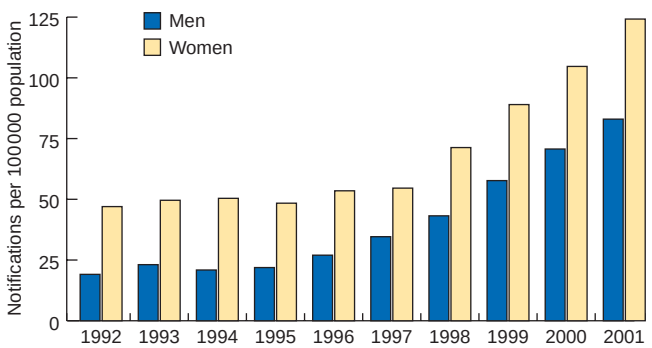
In this light, some commonly held assumptions about chlamydial infection in men need to be addressed. The first is that men are less likely to be infected than women. Recent population-based surveys in Scandinavia, the United Kingdom and the United States have consistently shown similar chlamydial prevalences among heterosexual men and women.[3,4,10] Higher notification rates for women (Box) probably reflect more testing of women than men.[7,11,12] Longer duration of infection in women could also be part of the explanation, although how long untreated chlamydial infection can persist in either sex remains uncertain.[13]

Another apocryphal belief is that the bulk of men with chlamydial infection present for treatment, driven by genital symptoms.[9] However, studies in the community have revealed that most men with urethral chlamydial infection, like women, are symptom-free[3,4,10] — perhaps as many as three-quarters[10] — and that asymptomatic men are less likely than asymptomatic women to present for testing.[10] Although there are few data on the duration of chlamydial infection in men,[13] it may be months or years. A better understanding of the duration of infection would enhance our ability to model potential interventions.

Sweden has a long and much-acclaimed history of screening women for chlamydial infection. This has reduced the prevalence of chlamydial infection and the incidences of both pelvic inflammatory disease and ectopic pregnancy. However, these successes have begun to reverse recently, with the suggestion that Sweden's failure to test men is a significant reason.[8]

Since the advent of urine tests for chlamydia, screening men has become feasible and potentially cost effective (using US parameters).[12] Without this screening, the success possible with interventions aimed exclusively at women may be limited.[8] To determine whether screening of men is justified, more population-based research is required on chlamydial infection in Australian men. The prevalence of infection in different subpopulations would help determine where future screening initiatives are most needed and provide a baseline for evaluating control measures. Factors associated with infection should be identified and assessed as criteria for selective screening. Studies on the natural history of infection and the cost-effectiveness of interventions would also be of global interest.

Chlamydia trachomatis notifications in Australia



Source: National Centre in HIV Epidemiology and Clinical Research (http://www.med.unsw.edu.au/nchecr/)

While definitive screening guidelines cannot be promulgated without such data, clinicians could be remiss if a urine test for *C. trachomatis* was not part of the routine assessment of a young man who reports unprotected sex with a new sexual partner (female or male), regardless of symptoms.

More generally, we should be asking what other factors are contributing to the re-emergence of chlamydial and other sexually transmissible infections in Australia. We also need to debate whether single-sex health models can sometimes ultimately harm women. Most women live in an environment that is also populated by men.

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Helical computed tomography for lung cancer screening

Given the controversy over this strategy, Australia should be involved in its evaluation

LUNG CANCER IS the leading cause of cancer death in Australia and has a dismal prognosis, with 7800 new cases and 6800 deaths each year, and a 5-year post-diagnosis survival of only 12%. New cases increasingly occur in ex-smokers.[1] Helical computed tomography (CT) is a fast and sensitive screening technique that can detect early-stage lung tumours, potentially increasing the proportion of patients who can be offered curative treatment. Newer scanners can perform studies with lower radiation exposure. However, use of this technique is controversial; the studies suggest that it has benefits that are uncontrolled, with no concurrent or randomised comparison group.

Proponents of helical CT screening argue that its high sensitivity and the early results of studies showing that it detects small, early stage and operable cancers demonstrate its clear benefits.[2,3] In the Early Lung Cancer Action Project in the United States, 1000 asymptomatic smokers or former smokers aged over 60 were screened with low-dose helical CT and conventional chest x-rays; 23% had non-calcified pulmonary nodules detected by CT, while only 7% had abnormalities detected by chest x-ray. Of those with nodules on CT, 12% were eventually diagnosed with malignancy, of which 85% were stage I tumours.[4,5] In contrast, only 20% of lung cancers in patients presenting in Victoria in 1995 were localised.[6] Other similar uncontrolled studies in the United States, Japan, Germany and Finland showed that from 5%[7] to over 50%[8] of people screened have an abnormality detected. While many can be investigated with non-invasive tests and reassessment, the substantial rate of false-positive scans requiring potentially hazardous interventions is a real concern.

Others argue that studies with no control group are open to severe biases and give misleading results.[9,10] Non-randomised comparisons between screen-detected and conventionally diagnosed patients that assess outcomes such as tumour size and survival are open to selection, lead time, prevalence–duration and overdiagnosis bias, all of which tend to make the outcomes in the screened group appear more favourable.[11] The experience with previous trials of screening for lung cancer, using chest x-ray and sputum cytology, shows these problems. A randomised trial in Czechoslovakia demonstrated that, in the screening group, 53% of tumours were at an early stage, 25% were operable, and 5-year survival was 23%, compared with figures of 21%, 16% and zero 5-year survival in the unscreened group.[12] However, the death rate from lung cancer over the subsequent 15 years was actually higher in the screened group; this discrepancy arises from the biases noted above. A trial at the Mayo clinic in the United States showed similar results.[13] A Cochrane meta-analysis of trials of lung cancer screening shows no difference in all-cause mortality (relative risk, 1.01; 95% CI, 0.94–1.08), and a higher mortality from lung cancer in the screened groups (relative risk, 1.11; 95% CI, 1.00–1.23).[14]

Randomised trials of helical CT screening have begun. The US National Lung Screening Trial started in 2002 and