

## Symposium

Is screening for *Chlamydia trachomatis* infection cost effective?

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Chlamydial infections are the most prevalent bacterial sexually transmitted infections recognised throughout the world. According to the WHO, 50–70 million chlamydial infections are detected annually worldwide.<sup>1</sup> In most developed countries, sexually transmitted chlamydial infections are still strikingly common particularly among adolescents, and 10–20 times more common than gonococcal infections.<sup>1</sup> In our recent study, the prevalence of *Chlamydia trachomatis* infection was 5.6% among asymptomatic women attending a family planning clinic and a student health clinic.<sup>2</sup> Chlamydial infections cause major medical, social, and economic problems. Sequelae of *C trachomatis* infection are extremely costly to the healthcare system, and include pelvic inflammatory disease (PID), ectopic pregnancy, tubal factor infertility (TFI), epididymitis, proctitis, and arthritis. Chlamydial infections, like STDs in general, are primarily a woman's healthcare issue since the manifestations and consequences in women are more damaging to the reproductive tract than in men. Expensive medical high technology, such as in vitro fertilisation (IVF), has largely emerged because of reproductive tract damage caused by sexually transmitted chlamydial infections. There is a strong link between past chlamydial infection and TFI or ectopic pregnancy. Emerging evidence suggests that *C trachomatis* infection is a significant risk factor for other adverse pregnancy outcomes—that is, preterm delivery and spontaneous abortion.<sup>3</sup> Recent studies also suggest that *C trachomatis* infection is an independent risk factor for the development of cervical neoplasia.<sup>3–6</sup> Since chlamydial infections are usually asymptomatic, the key to the prevention of chlamydial infections and their sequelae is screening using a high performance diagnostic test. Screening based on first void urine (FVU) testing by gene amplification techniques, in combination with single dose therapy with azithromycin may have a major impact on the prevention and control of asymptomatic chlamydial infections. Disease prevention can be primary, secondary, or tertiary.

Tertiary prevention of acute and chronic chlamydial infections of the upper genital tract has largely failed because substantial tubal damage has already occurred by the time symptoms develop or the patient presents with infertility or ectopic pregnancy. Primary prevention involves preventing both exposure to and acquisition of chlamydial infection through lifestyle counselling and health education. Clearly, more emphasis should be directed to primary prevention by implementing health education programmes among ado-

lescents. Secondary prevention by universal screening, however, is likely to play the most critical role in the prevention of PID and long term sequelae, although this still needs to be proved in randomised controlled intervention trials.<sup>7</sup> Secondary prevention means early detection of subclinical disease by screening or case finding in order to prevent lower genital tract infection from ascending to the upper genital tract. Chlamydial infection fills the general prerequisites for disease prevention by screening since chlamydial infections are highly prevalent, are associated with significant morbidity, can be diagnosed, and are treatable.

Cost analyses are becoming more common among trials which compare therapeutic or procedural healthcare interventions.<sup>8–12</sup> The most widely known form of economic evaluation is cost-benefit analysis.<sup>13</sup> It is restricted to those forms of evaluation that are used to place a monetary value on benefits and outcomes. This makes cost-benefit analysis the most comprehensive and theoretically sound form of economic evaluation. On the other hand, in cost effectiveness analysis the outcomes are not measured in monetary units, but in clinical units such as cases of PID or TFI.<sup>14</sup> Recent studies have addressed the cost effectiveness of identifying and treating *C trachomatis* infections in asymptomatic women.<sup>15,16</sup> Genc and Mardh<sup>15</sup> showed that when the prevalence of chlamydial infection exceeded 6%, screening of women with DNA amplification assay of endocervical swabs (and treatment of positive women with a single oral dose of azithromycin) was the most cost effective intervention strategy. If the prevalence was even higher, screening with enzyme immunoassay of cervical specimens also generated savings and improved the cure rates compared with a “no screening” situation. Diagnosis of *C trachomatis* by tissue cell culture of cervical swabs was cost effective only when the prevalence of infection was greater than 14%. Most of the savings generated by the screening strategy were attributable to prevention of complications and sequelae of chlamydial infection in women. However, the study anticipated that only women who have clinical symptoms of PID are at risk for infertility, ectopic pregnancy, or chronic pelvic pain. Hence, subclinical or silent upper genital tract infections caused by *C trachomatis* were not considered. We recently developed a computer based decision tree model in order to conduct a more thorough cost-benefit analysis of screening versus no screening situation, based on testing of first void urine specimens with PCR among women.<sup>17</sup> The decision tree

model can be used in a wide range of socioeconomic analyses.<sup>18</sup> It is a quantitative technique which measures the overall performance of a specific healthcare intervention, such as a new diagnostic test. We also considered silent or subclinical chlamydial infections in order to improve the reliability of the results. Compared with conventional diagnostic methods, such as cell culture or enzyme immunoassays, PCR and LCR allow testing of FVU samples in both women and men with a high level of sensitivity and specificity.<sup>19-21</sup> According to the model, in the no screening situation systematic FVU screening for *C trachomatis* was not performed, and only symptomatic women were tested using conventional fluorescent antibody (FA) confirmed enzyme immunoassay on cervical swabs (MicroTrak Chlamydia EIA, Syva Co, Palo Alto, CA, USA). *C trachomatis* positive women and their current partners were contacted and treated systematically with a single dose of azithromycin 1 g. In the screening situation a FVU screening policy targeted to women of childbearing age was applied. All screened individuals were tested using *C trachomatis* PCR assay (Amplicor, Roche Diagnostic Systems, Basle, Switzerland) on FVU specimens. Only direct costs due to chlamydial infection were included. The costs per capita of the screening situation and the no screening situation were calculated. The cost of the screening strategy was 16% less per capita if the participation rate in the screening programme was at least 75%. When the sensitivity of the screening test was 90%, the threshold value for the prevalence of *C trachomatis* infection was as low as 3.2% (that is, screening in a low prevalence population would still be cost effective). The cost savings increased with increasing prevalence, and when the prevalence approached 10% (for example, in a high risk population) the net savings were approximately 30% per capita. Sensitivity analyses showed that in addition to lower costs, the screening situation also produced considerable health benefits compared with the no screening situation—that is, the proportion of cured patients increased by about 85% and about 50% less suffered from long term complications.

There is clear evidence that systematic screening of asymptomatic populations decreases the incidence of *C trachomatis* infections. This has been documented both in nationwide screening programmes<sup>22</sup> and in screening programmes performed in other defined populations in which the screening activity has remained stable.<sup>23</sup> Furthermore, recent randomised clinical trial has shown that intervention with selective screening of chlamydial infections effectively reduces the incidence of PID.<sup>7</sup> It still remains to be seen whether such intervention will also have a significant effect on the rate of long term sequelae of chlamydial infections.

Since *C trachomatis* is the major cause of female genital tract infections and infertility

and adverse pregnancy outcome, prevention and control of these infections and their sequelae will have a major impact on the reproductive health of women. Further socioeconomic studies linking the cost of secondary prevention of *C trachomatis* infections and the cost of infertility or adverse pregnancy outcome are warranted.

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