

Chlamydia

How can chlamydia diagnoses increase when their complications are declining?

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We have to accept that ecological associations do not provide evidence of effectiveness of interventions

Chen and colleagues present, in this issue of *STI* (p 318), some apparently paradoxical data about the recent epidemiology of chlamydial infection in New South Wales, Australia—hospital admissions for pelvic inflammatory disease declined in women and rates of epididymo-orchitis remained constant during a period when notifications of chlamydia increased substantially. Their findings differ from the well documented fall in chlamydia complication rates that accompanied reductions in chlamydia notifications in Sweden^{1,2} and the United States.³

Clinically trained readers of the journal will easily identify possible explanations for this discrepancy: the proportion of women with pelvic inflammatory disease who are admitted to hospital could be decreasing; increased use of azithromycin might have improved compliance and prevented more complications, despite increasing incidence; while trends in notifications do not represent changes in incidence because only a minority of all infections are diagnosed and reported. The authors have recognised and discussed these possibilities.

Chen *et al* used readily available health service databases and obtained aggregated numbers of cases of chlamydial complications and of notifications in New South Wales from 1992 to 2001. It is essential for clinicians and other sexual health professionals to understand both the potential and the limitations of ecological data such as these, because they are often used to make or justify health policy and funding decisions. Often they are the only source of data available.^{4,5} An ecological study is one in which the unit of analysis is a group⁶: the group here is the population of women in New South Wales in which changing rates of chlamydia notifications, and of pelvic inflammatory disease diagnoses, are reported. This example illustrates a well known problem with ecological studies. The “eco-

logical fallacy” would be to suggest that an association at the group level represented a causal relation between the two at the level of the individual. Chen *et al*'s study shows how absurd this inference is: an episode of chlamydia in an individual woman does not protect her from pelvic inflammatory disease. On the contrary, detection and treatment of women with chlamydia prevents pelvic inflammatory disease.^{7,8} If, however, the trend in chlamydia rates had decreased it would be very tempting to claim that screening for chlamydia had led to the fall in pelvic inflammatory disease. This is a plausible explanation, which has often been cited in support of introducing chlamydia screening.^{2,9}

Population level ecological data cannot show that chlamydia screening was directly responsible for the fall in pelvic inflammatory disease rates in Sweden in the late 1980s and early 1990s. In fact, it has been suggested that chlamydia screening in Sweden coincided with falling rates of sexually transmitted infections that were already occurring because of changing sexual behaviour.¹⁰ Chlamydial pelvic inflammatory disease rates in Sweden started falling in the late 1970s: Weström suggested that this was the result of more conservative sexual attitudes and behaviours among young people.¹¹ HIV/AIDS prevention campaigns promoting safer sex from 1987 onwards were credited with falling rates of gonorrhoea and syphilis in England and Wales,¹² and pelvic inflammatory disease in the Netherlands in the 1990s,¹³ because these countries had no chlamydia screening programmes. And despite continued screening, chlamydia rates have actually been increasing in Sweden since at least 1997,¹⁴ in common with countries with no chlamydia control activities. Individual level studies of opportunistic chlamydia screening now suggest that the uptake and frequency of screening in women were not sustained and were insufficient to control transmission.¹⁴ The limited involvement of men, and inadequacies of partner

notification, have also been suggested as factors reducing the effectiveness of screening.¹⁵

This is not to say that ecological studies are without value. A striking example of an ecological study postulating a causal association later shown to be correct was undertaken in the field of STI. Valerie Beral elegantly demonstrated that trends in deaths from cervical cancer in birth cohorts of British women born between 1902 and 1947 exactly paralleled the incidence of gonorrhoea (taken from routine genitourinary clinic data) when those cohorts were 20 years old (fig 1).¹⁶ She also showed that male death rates from syphilis in each social or occupational class were strongly associated with cervical cancer death rates in married women in the same class. This study strengthened the hypothesis that cervical cancer was caused by a sexually transmitted agent, and human papillomavirus types 16 and 18 were recognised as carcinogenic viruses in 1995.¹⁷

Comparison of time trends between a risk factor and a disease is only one kind of ecological analysis. Population data can also be used to examine associations between rates of sexually transmitted infections and socioeconomic characteristics at area level.¹⁸ Ecological studies have, in fact, been proposed as the most appropriate approach to studying the epidemiology of infectious diseases; for sexually transmitted infections the “group” is the sexual partnership.²⁰ Such studies can take into account the characteristics of the partnership as well as the individual. Standard methods of regression analysis have been criticised for failing to take into account the

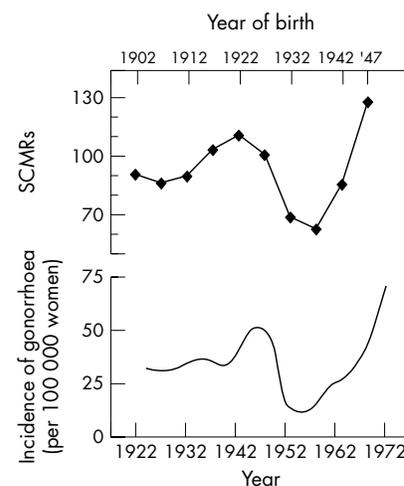


Figure 1 SCMRs from cervical cancer among women born between 1902 and 1942 in England and Wales and incidence of gonorrhoea among women in England and Wales, 1925–72. (From Beral¹⁶) reproduced with permission of author and publishers.)

transmission dynamics of infectious diseases,¹⁹ but multilevel models can now examine variability at the group and individual level simultaneously.²⁰ This avoids the “atomistic fallacy,” which is the opposite of the ecological fallacy, and occurs when factors which explain variability between individuals within groups might differ from those explaining variability across groups.⁶

Analysis of time trends in sexually transmitted infections is important because these trends can point to the need for interventions, and generate hypotheses about explanations for observed changes. They should not be used to make causal inferences. Chen *et al*'s study is welcome because the authors have been suitably cautious in their interpretation of the data, and their study highlights the need for denominator testing data in interpreting trends in surveillance data. The interpretation of ecological data on chlamydia screening outcomes, given that chlamydia is a largely asymptomatic pathogen with no unique outcomes, for which tests have only recently become widely available, and for which incidental antibiotic treatment is common, is particularly problematic. Experience in Sweden shows that opportunistic screening targeted mainly at women, with incomplete coverage and no enforcement of a regular screening interval, does not prevent chlamydia transmission. Unfortunately, early signs suggest that these are the characteristics of the new national chlamydia screening programme in England.¹⁵ Advocates of chlamydia screening, sexual health professionals and policy makers have to accept that ecological associations do not provide evidence of effectiveness,

and that there is no high quality evidence to show the most effective method of screening for chlamydia and achieving sustained control of transmission.^{10–15} This is a question that only randomised controlled trials with long term follow up can answer.

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REFERENCES

- 1 **Egger M**, Low N, Smith GD, *et al*. Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. *BMJ* 1998;**316**:1776–80.
- 2 **Kamwendo F**, Forslin L, Bodin L, *et al*. Programmes to reduce pelvic inflammatory disease—the Swedish experience. [Review] [39 refs]. *Lancet* 1998;**351**(Suppl 3):25–8.
- 3 **Hillis SD**, Nakashima A, Amsterdam L, *et al*. The impact of a comprehensive chlamydia prevention program in Wisconsin. *Fam Plann Perspect* 1995;**27**:108–11.
- 4 **Susser M**. The logic in ecological: I. The logic of analysis [see comments] [published erratum appears in *Am J Public Health* 1994;**84**:825–9]. *Am J Public Health* 1994;**84**:825–9.
- 5 **Susser M**. The logic in ecological: II. The logic of design [see comments]. *Am J Public Health* 1994;**84**:830–5.
- 6 **Diez Roux A**, Schwartz S, Susser E. Ecological variables, ecological studies, and multilevel

- studies in public health research. In: Detels R, McEwen J, Beaglehole R, Tanaka H, eds. *Oxford textbook of public health*. 4th ed. Oxford: Oxford University Press, 2004:493–507.
- 7 **Scholes D**, Stergachis A, Heidrich FE, *et al*. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med* 1996;**334**:1362–6.
 - 8 **Ostergaard L**, Andersen B, Moller JK, *et al*. Home sampling versus conventional swab sampling for screening of chlamydia trachomatis in women: a cluster-randomized 1-year follow-up study. *Clin Infect Dis* 2000;**31**:951–7.
 - 9 **Catchpole M**, Robinson A, Temple A. Chlamydia screening in the United Kingdom. *Sex Transm Infect* 2003;**79**:3–4.
 - 10 **Stephenson JM**. Screening for genital chlamydial infection. *Br Med Bull* 1998;**54**:891–902.
 - 11 **Westrom L**. Decrease in incidence of women treated in hospital for acute salpingitis in Sweden. *Genitourin Med* 1988;**64**:59–63.
 - 12 **Nicoll A**, Hughes G, Donnelly M, *et al*. Assessing the impact of national anti-HIV sexual health campaigns: trends in the transmission of HIV and other sexually transmitted infections in England. *Sex Transm Infect* 2001;**77**:242–7.
 - 13 **Coutinho RA**, Rijdsdijk AJ, van den Hoek JA, *et al*. Decreasing incidence of PID in Amsterdam. *Genitourin Med* 1992;**68**:353–5.
 - 14 **Low N**, Harbord RM, Egger M, *et al*. Screening for chlamydia. *Lancet* 2005;**365**:1539.
 - 15 **Low N**, Egger M. What should we do about screening for genital chlamydia? *Int J Epidemiol* 2002;**31**:891–3.
 - 16 **Beral V**. Cancer of the cervix: a sexually transmitted infection? *Lancet* 1974;**1**:1037–40.
 - 17 **International Agency for Research on Cancer (IARC)**. Summaries and evaluations. Human papillomaviruses (HPV) (www.inchem.org/documents/iarc/vol64/hpv, www.inchem.org/) Available from www.inchem.org/documents/iarc/vol64/hpv.html
 - 18 **Krieger N**, Waterman PD, Chen JT, *et al*. Monitoring socioeconomic inequalities in sexually transmitted infections, tuberculosis, and violence: geocoding and choice of area-based socioeconomic measures—the public health disparities geocoding project (US). *Public Health Rep* 2003;**118**:240–60.
 - 19 **Koopman JS**, Longini IM Jr. The ecological effects of individual exposures and nonlinear disease dynamics in populations. *Am J Public Health* 1994;**84**:836–42.
 - 20 **Diez Roux AV**, Aiello AE. Multilevel analysis of infectious diseases. *J Infect Dis* 2005;**191**:525–33.