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LETTER

Spontaneous remission of sexually transmitted diseases must be considered in randomised controlled trials

Randomised controlled trials that test biomedical interventions to reduce sexually transmitted infections (STIs) have had very mixed results,^{1–2} as have behavioural trials.^{3–4} It is only in the past 10 years that the field has recognised that chlamydia resolves itself without treatment in 50% of the cases,⁴ although the estimates range from 13% to 60%.^{5–7} The length of time to clear chlamydia infection varies from 60 days in women to up to 15 months in men.⁵ The speed of resolution is also subject to individual-level factors (eg, infection clears sooner in older people), making it difficult to determine sample sizes for randomised controlled trials with STI outcomes.

In a recent five-country trial,¹ the determination of sample size to identify the necessary number of participants to demonstrate a reduction in bacterial STI was based primarily on chlamydia (65.8% of the bacterial infections observed at recruitment; 10.3% prevalence) and trichomoniasis among women (17.2% of infections; 4.89% prevalence). When we examined all the bacterial STIs 1 year later, the rates of chlamydia were more than 60% lower and the rates of trichomoniasis were 40% lower. Potentially, half of the new chlamydia and trichomoniasis infections may have spontaneously resolved, as suggested by the above studies, but the actual incidence rates may have been 25% more than those observed at 12 months

(assuming a consistent rate of infection over time).

The emerging data on spontaneous remission rates raises serious questions on how to design effective evaluations to demonstrate reductions in STIs. Randomised controlled trials must be designed to have shorter periods between assessments. It is also likely that there is a variance in the rates of clearance, although it is unclear in what direction and for whom the variations will apply. Thus, the design of future multisite trials must *cautiously* estimate STI infections, given the emerging data on spontaneous remissions or clearing of infections, and consider much shorter follow-up periods, even for long-term longitudinal trials.

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Funding NIMH provided funding for this multisite study.

Competing interests None.

Patient consent All human subjects signed the informed consent forms that were reviewed and approved by the Institutional Review Boards at UCLA and the China CDC.

Ethics approval UCLA SG-IRB; RTI IRB; Chinese Centers for Disease Control IRB.

Provenance and peer review Not commissioned; internally peer reviewed.

Accepted 16 February 2011
Published Online First 1 April 2011

Sex Transm Infect 2011;**87**:305.
doi:10.1136/sextrans-2011-050009

This paper is freely available online under the BMJ Journals unlocked scheme, see <http://sti.bmj.com/site/about/unlocked.xhtml>

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