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Reply to Srinivas

To the Editor—We thank Dr. Srinivas [1] for his interest in our recent review article [2] and appreciate the opportunity to respond to his thoughtful comments.

We agree that interactions between rifampin and other medications, including antiretrovirals, can be clinically or pharmacologically unpredictable and that close monitoring of patients taking rifampin with other medications is essential [3, 4]. Srinivas brings to light an interesting mechanism—inhibition of hepatic uptake via blockage of organic anion transport—by which rifampin may cause acute paradoxical drug interactions. He further reminds us that the complexity of drug interactions with rifampin is compounded when the companion drug's metabolite is pharmacologically active, as is the case with nelfinavir. It is fortunate, however, that the hepatic transporter blockade drug-drug interaction mechanism he describes appears to be rare, affecting only a few drugs, most of which are not commonly used in resource-limited settings. It is also fair to say that this type of interaction is unlikely to occur with antiretrovirals, the vast majority of which have been evaluated in drug-drug interaction studies with rifampin. In addition, given that the interaction he describes results in higher plasma concentrations of a coadministered drug, the potential impact on antiretrovirals may not be deleterious.

The comments by Srinivas are timely and serve as a much-needed reminder that mechanisms for drug interactions are increasingly complex and that clinicians need to maintain vigilance whenever adding drugs to an existing regimen.

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Use of Mathematical Modeling to Inform Chlamydia Screening Policy Decisions

To the Editor—Regan et al. [1] predict that *Chlamydia trachomatis* prevalence in women in Australia will fall by >70% in 10 years with a screening program that tests 30% of 15–24-year-olds each year. This means that 70% of the target population would remain untested every year and that participants would be tested, on average, once every 3 years. This is an optimistic view of the impact that limited screening coverage would have, given the absence of evidence that opportunistic testing at this level has controlled chlamydia transmission up to now [2]. We think that there are reasons for caution in using predictions from this model to inform decisions on "the most effective chlamydia screening program for Australia" [1, p. 357].

First, the inability to model long-term partnerships explicitly in this compartmental model is a fundamental limitation that makes predictions about reductions in prevalence unreliable. Reinfection of the index case patient from a current untreated sex partner cannot be taken into account in Regan et al.'s model because the model does not keep track of ongoing partnerships and all infected individuals are returned to the susceptible state, after either treatment or natural clearance of infection [1]. Within an ongoing partnership, reinfection can take place if the partner is not treated along with the index case patient. In this model, repeat infections only occur in subsequent partnerships. In reality, early reinfection with chlamydia after screening and treatment of an individual who has untreated partners is common [3]. Regan et al. assert that "screening . . . will be the primary intervention in Australia" [1, p. 357]. They assume that their model provides a conservative estimate of the effect of a chlamydia screening intervention because partner notification would provide additional benefits compared with those of screening alone. This can be shown to be the case when the impact of chlamydia screening is investigated in an individual-based model, because the net effect of screening without partner notification takes into account the reinfection of index case patients in partnerships in which the partner was not screened [4]. Additional partner-notification efforts then have an incremental effect. Regan et al.'s compartmental model, however, overestimates the effect of chlamydia screening because it ignores reinfections that do not contribute to reducing prevalence. After dissolution of the old partnership and formation of a new partnership, the infection could be transmitted to a new sex partner. The impact of ignoring reinfection would be greater when only one sex is screened and at low levels of coverage.

Second, predicted reductions in chlamydia prevalence cannot currently be used as a proxy for the overall effectiveness of a chlamydia screening program. A proxy (or surrogate marker) has to have a known relationship with the outcome [5]. The primary objective of chlamydia screening programs is to prevent complications, such as tubal infertility, that result from chlamydia infections that ascend to damage the upper genital tract [2]. It is not known, however, whether there is a relationship between increasing screening coverage and reducing female reproductive tract morbidity.

Regan et al.'s model is more complex than some other compartmental models of *C. trachomatis* transmission [6] and might be useful for examining the relative importance of different strategies, but it cannot be used to quantify the effects of different levels of screening coverage accurately. The need for empirical studies that demonstrate the impact of chlamydia screening programs on both chlamydia transmission and the incidence of complications remains [2]. Mathematical models that dynamically incorporate the progression to fertility-related complications of chlamydia are needed to help understand the impact of screening programs on primary outcomes [7, 8]. Further methodological studies that directly compare the assumptions and predictions of compartmental and individual-based models to help us understand how reinfection and partner notification affect the incidence and prevalence of chlamydia are also needed. We suggest that it is premature for health policy makers to base decisions about chlamydia screening programs on this mathematical model, which does not represent the dynamics of chlamydia transmission adequately.

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Reply to Low et al.

To the Editor—In our article [1], we described the results from a compartmental model of chlamydia transmission in a heterosexual population. We calibrated our model using the best Australian epidemiological and behavioral data available as well as biological data from the literature. The stated primary aims of our work were to compare various screening strategies in terms of their effectiveness in reducing the incidence and prevalence of chla-