

Reply to Gonzalez-Serna et al

We thank Gonzalez-Serna and his colleagues for initiating a discussion on our paper that models the impact of the test-and-treat policy on the human immunodeficiency virus (HIV) epidemic in Los Angeles County. Gonzalez-Serna et al contest the relevance of our findings that test-and-treat could potentially increase multidrug resistance (MDR) in Los Angeles by 89% [1]. Using observational data from British Columbia, Canada, they show that MDR and total drug resistance prevalence in British Columbia decreased over a period during which antiretroviral treatment (ART) prevalence increased by 60%. There are several reasons why this finding might not be particularly relevant for evaluating the impact of test-and-treat in Los Angeles or other regions of the world.

First, British Columbia is a distinct setting with vastly different demographics and healthcare characteristics than Los Angeles. There is evidence that MDR prevalence in Canada is generally much

lower than in the United States [2]. As with any mathematical model, our results are a product of the assumptions we make about parameter values and initial conditions, which are setting-specific. Because MDR prevalence in Los Angeles is higher at baseline than in British Columbia, the force of infection of transmitted resistance is higher, causing faster growth. Model results may be different with dynamics based on British Columbia characteristics.

Second, these findings from British Columbia are inconsistent with findings in other parts of the world [3–6]. A recent World Health Organization report highlights the growth of drug-resistant HIV in low- and middle-income countries over the past decade, and shows a positive association between ART coverage and prevalence of transmitted drug-resistant HIV [7].

Third, a recent Canadian surveillance report shows that the results Gonzalez-Serna et al report from British Columbia might not even generalize to other provinces in Canada. This report surveys 6 Canadian provinces and shows that prevalence of resistance increased by approximately 70% from 1999 to 2008 and there was no reduction in MDR [8]. Furthermore, a considerable proportion of transmitted drug resistance in both the United States and Canada remains undetected [9].

Fourth, early-stage HIV (ESH) treatment—a hallmark of test-and-treat—stayed relatively stable in British Columbia from 1995 to 2008 [10]. It is likely that ESH will coincide with lower levels of adherence, a strong predictor of increases in acquired drug resistance.

Gonzalez-Serna et al also note a decrease in clinical significance of MDR, as dozens of different drug classes are now available. They suggest that pandrug resistance is the appropriate resistance measure instead of triple-therapy resistance, which we use. Even if this were true, MDR will likely raise HIV treatment costs for cash-strapped patients or healthcare systems. In addition, with expansion of early

treatment, MDR detection might be more difficult as patients are asymptomatic and might not be monitored closely. Without close monitoring of resistance, patients could unknowingly develop MDR and thus delay initiation of second-line treatment. Therefore, the clinical significance of MDR may be greater with a larger ESH treatment prevalence.

We agree with Gonzalez-Serna et al (and state in the main text) that test-and-treat is likely to bring epidemiologic benefits even with MDR growth, and we do not recommend abandoning this policy. However, Gonzalez-Serna et al downplay potential implications of MDR growth. We believe a prudent approach would be to evaluate the cost-effectiveness of test-and-treat compared to other policies, and if adoption of test-and-treat is warranted, it should be accompanied by initiatives to control and closely monitor MDR such as expanded MDR surveillance and interventions to improve adherence.

Notes

Financial support. A. J. and R. V. received institutional funding through the National Institutes of Health (R01 NIH grant). E. D. receives institutional funding through the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant number R01HD054877).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases **2013;57(3):479–80**

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DOI: 10.1093/cid/cit261