Balancing Disease Eradication With the Emergence of Multidrug-Resistant HIV in Test-and-Treat Policies

Anupam B. Jena¹²³

¹Department of Health Care Policy, Harvard Medical School, Boston, ²Department of Medicine, Massachusetts General Hospital, Boston, and ³National Bureau of Economic Research, Cambridge, Massachusetts

(See the HIV/AIDS Major Article by Sood et al on pages 1789–96.)

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A substantial body of evidence has emerged highlighting that early initiation of antiretroviral therapy (ART) for patients with human immunodeficiency virus (HIV) infection has both private and public health benefits. In various studies, early initiation of ART has been associated with greater survival among those infected; fewer combined clinical endpoints such as pulmonary tuberculosis, severe bacterial infection, and death; and, more recently, earlier restoration of CD4+ T cells [1–5]. This growing evidence on the private health benefits of early ART for HIV has led to a trend in recommendations to commence ART earlier and earlier, now to the point that some guidelines suggest that ART be offered to all patients with HIV regardless of CD4 cell count [6]. In addition to the private benefits of early initiation of ART, a number of studies demonstrate an important public health benefit as well, namely, markedly reduced transmission rates of HIV due to reductions in viral load associated with ART [1, 7, 8]. The public health benefit of early ART in reducing disease transmission has formed the basis for widely proposed “test-and-treat” strategies that argue for universal testing for HIV and treatment of individuals who are seropositive, with the hope being near-eradication of HIV. Complex mathematical models of HIV disease dynamics have been used to simulate the impact of test-and-treat policies on the future incidence and prevalence of HIV. Not surprisingly, these studies have found mixed results, with some demonstrating dramatic reductions in HIV prevalence and others suggesting more modest reductions [9–14]. Nearly all studies are unanimous, however, in demonstrating reductions in HIV incidence and death associated with test-and-treat policies.

It is in this context that Sood and colleagues, whose article appears in this issue of Clinical Infectious Diseases, have developed a mathematical model to simulate the impact of test-and-treat policies for HIV among the population of men who have sex with men in Los Angeles County, the county with the nation’s largest incident HIV population. In contrast to many previous studies simulating the impact of test-and-treat policies on HIV disease dynamics, Sood et al calibrate their model to fit existing trends in HIV prevalence in Los Angeles County from 2000 to 2009. The intuition motivating this calibration is that for any model of test-and-treat policies to be scientifically valid, the model must first be able to replicate disease dynamics in an environment where test-and-treat policies are not already occurring. Only then can a model be expected to reasonably predict counterfactual scenarios—such as universal test-and-treat policies—that cannot be studied directly through a randomized controlled trial or natural experiment. After demonstrating that their model fits the data in Los Angeles County closely, the authors use their model to simulate the impact of test-and-treat policies on HIV incidence, prevalence, AIDS-related deaths, and the incidence and prevalence of multidrug-resistant HIV strains.

Several findings emerge. First, like other studies, test-and-treat policies are predicted to substantially reduce, but not eradicate, new HIV infections and AIDS-related deaths. Second, despite the reduction in new HIV infections, there is a substantial increase in multidrug-resistant HIV strains in a 10-year period alone, from nearly 4.8% resistance in 2013 to 9.1% resistance in 2023. The emphasis to quantitatively understand
the impact of test-and-treat policies on multidrug-resistant HIV is an important contribution of this paper. At the very least, it suggests that the public health benefits of test-and-treat policies through reduction of HIV transmission must be balanced against the proliferation of multidrug-resistant strains. The authors do not discuss this, but the increase in drug resistance to 9.1% in 2023 may substantially underestimate multidrug resistance in the years following 2023. Third, Sood and colleagues demonstrate that testing alone may be approximately half as effective in reducing HIV incidence and prevalence as test-and-treat policies, but without additional growth in drug resistance. The intuition is largely behavioral: identifying individuals who are HIV-positive through universal testing alone may reduce incidence of HIV if these individuals take it upon themselves to reduce their sexual activity after being diagnosed with HIV. Because some individuals testing positive for HIV would not be treated in a “test-only” model (ie, those with CD4 counts above treatment thresholds), there would be less selection pressure leading to drug-resistant HIV. This ignores the fact, however, that there appear to be clear private health benefits to treating HIV early, making a “test-only” policy seemingly untenable even if multidrug-resistant HIV incidence is lowered.

The implications of this study—and more importantly, prior modeling studies like this—for the future of HIV research are large. First, important research has emerged on the benefit of antiretroviral chemoprophylaxis before HIV exposure [15–18], and yet much remains to be learned about how routine prophylaxis will impact the epidemiology of HIV infections, AIDS-related deaths, and the development of multidrug-resistant HIV. Modeling exercises such as these may prove useful in anticipating the impacts of preexposure prophylaxis.

Second, despite the complexity of mathematical models that predict the impact of various HIV policies, most are not rich enough to capture the important behavioral economic changes that may be induced by large-scale policies such as universal testing and treating and preexposure prophylaxis. In the United States, variation in state Medicaid eligibility rules for subsidized HIV care has been used to demonstrate that treatment of HIV-positive individuals more than doubles their number of sex partners [19]. It is difficult to predict how large-scale interventions such as universal test-and-treat policies and widespread preexposure prophylaxis will impact sexual behavior, incidence of HIV, and incidence of other sexually transmitted diseases. But better incorporating the impact of these large-scale policies on sexual behavior into existing mathematical models seems warranted. Indeed, in the study by Sood and colleagues, the parameters related to sexual behavior were among the most influential in affecting HIV disease dynamics in Los Angeles County.

Third, the promise of eradicating HIV through test-and-treat and preexposure prophylaxis policies must be balanced by the impact of more prevalent treatment on the growth of multidrug-resistant HIV. Larger-scale treatment of HIV, such as wider use of antibiotics more generally, confers private health benefits to those whose disease is treated, public health benefits to those at risk for HIV who do not acquire the disease, and public health costs to those who acquire multidrug-resistant HIV. HIV treatment policy is therefore intrinsically linked to drug development policy and the demand for new antiretroviral approaches that can deal with the emergence of multidrug-resistant HIV. More widespread treatment of HIV will accelerate the prevalence of multidrug-resistant HIV and the need for novel therapeutic approaches.

Note

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