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Can We Afford to Control the HIV Epidemic with Antiretrovirals? Can We Afford Not to Do So?

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Although major strides have been made in the use of antiretroviral therapy to treat HIV over the past two decades and the rate of new infections has declined, there are still about 2 million new infections globally annually [1]. Recent studies have suggested that the prompt initiation of antiretroviral therapy has dual benefits, both in enhancing the quality and duration of life of those who initiate treatment independent of CD4 count, and in rendering virologically suppressed individuals less infectious to their partners [2-4]. Some presentations at the recent International AIDS Conference in Durban suggest that wider access to antiretroviral therapy has attenuated the rate of new infections in some settings [5]. However, the AIDS epidemic is not monolithic, and while epidemic control may be seen in some settings, other populations have seen marked increases in rates of new infections in recent years, including young heterosexuals in several African countries, men who have sex with men (MSM) and transgender women in many parts of the world, as well as injecting drug users in countries of the former Soviet Union and parts of Asia [1].

While the advent of generic antiretrovirals has driven down the cost of treatment in resource-constrained environments, in developed countries, medication costs are more than $15,000 per year, resulting in an aggregate cost of billions of dollars per year, if all HIV-infected people are to be treated. Additionally, numerous recent studies have suggested that antiretroviral use as pre-exposure prophylaxis (PrEP) can decrease HIV acquisition by high-risk populations [6-10]. Thus the question has arisen as to how to best use antiretroviral medications, whether to focus solely on treatment or to include PrEP as part of a global HIV epidemic control strategy.

In the current issue of *Clinical Infectious Diseases*, Drabo and associates found that for MSM in Los Angeles county that testing every 4 years and immediate initiation of treatment ("test and treat") was the most cost-effective, being less than $20,000 per quality-adjusted life-year (QALY) [11]. Scenarios with HIV testing as frequently as every 6 months followed by immediate treatment were also highly

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cost-effective. This is not surprising, given that the medication increases individuals' life expectancies and renders them less infectious. What also emerged from their study was that providing PrEP for the highest risk HIV-uninfected MSM in addition to a test and treat strategy would increase the QALY to $27,863 per year in the most cost effective scenario, but that this would lead to further decreases in the number of new HIV infections. Their simulations are helpful in helping policy makers and public health authorities think through optimal strategies for HIV epidemic control, but have to be anchored in the real world of an ongoing domestic and international HIV epidemic.

The rationale for early and prompt treatment is clear cut, but currently, 15% of HIV-infected Americans are unaware of their HIV status [12], and close to 50,000 new infections occur each year [13], so any test and treat strategy still needs to focus on wider expansion of testing. Although the U.S. Preventative Service Task Force (USPSTF) has recommended testing all American between the ages of 15 and 65 at least once in their lifetime, and more frequent testing for those at increased risk of HIV [14], many Americans remain untested, or not tested repeatedly if they are high risk. In addition, although 85% of HIV-infected Americans are aware of their status, only approximately 30% are virologically suppressed with antiretrovirals [12]. This means that there are more than 500,000 Americans who are potentially infectious to their partners. Thus, test and treat strategies alone are not sufficient, particularly because HIV treatment entails a lifelong commitment to therapy, requiring ongoing engagement in care to maintain virologic suppression.

The reality that virologic suppression of all HIV-infected people is not iminent, provides the rationale for the addition of PrEP. However, with the current cost of PrEP medication and follow-up exceeding $10,000 per year, its use must be judicious and selective. Therefore candidates for PrEP should be among those at highest risk for HIV infection. However, many of these individuals may not be routinely engaged in care because they are otherwise healthy, and may come from socially marginalized

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populations, not perceiving healthcare settings as culturally competent and congenial. It is incumbent upon clinical providers to become familiar with how to best make individuals from sexual and gender minority populations and those who use injection drugs feel comfortable with their care and to be able to elicit histories of their potential risk-taking behavior. Only when individuals are comfortable in delineating their potential HIV exposures can PrEP be considered. PrEP is not a "wholesale" intervention, but its selective use in discreet populations at highest risk for HIV, particularly urban men who have sex with men from racial and ethnic minority communities, can be clearly cost-effective as demonstrated in the Drabo et al article. In two recent trials of PrEP in MSM the number needed to use PrEP to prevent one new HIV infection was less than 20 [10, 15]. The detection of bacterial STDs in HIV-uninfected MSM and/or their use of specific non-prescription medications (e.g. methamphetamines and poppers) can also help identify a population who would benefit from PrEP [16].

Another opportunity to enhance the cost effectiveness of PrEP will be to reduce the cost of the medication [17]. The first medications being used for PrEP, tenofovir and emtricitibine in a fixed drug combination, will soon be off patent, which could conceivably reduce their costs [18]. However, other recent drugs that have become generic have not had substantial price reductions. Thus, public health authorities will need to work with the pharmaceutical industry in order to ensure that the transition of the original PrEP regimen to a generic formulation may result in a net cost savings. A challenge for the future is that other medications for PrEP, such as the less nephrotoxic tenofovir alafenamide, are also being developed and might provide favorable, but more expensive, PrEP alternatives [19]. It would be unfortunate to have "antiretroviral apartheid" resulting in some individuals receiving cheaper medications with a higher side effect profile while others with better insurance plans or other means of improved access receiving newer, improved formulations. It is conceivable that the development of long-acting injectable antiretroviral medication may result in PrEP alternatives that may lead to

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enhanced adherence, but again the question of whether the cost will result in net savings and the ability to more selectively use PrEP with a lower societal expenditure remains a major question.

Many HIV-infected individuals, as well as those at increased risk, may have social, structural, and behavioral issues that need to be addressed if the therapeutic and prophylactic use of antiretroviral medication is to be effective. These challenges include unstable housing, substance addictions, and depression, which may limit their ability to be highly adherent [20]. Thus, effective use of antiretroviral treatment in controlling the HIV epidemic invariably involves addressing these factors. For PrEP users, it is conceivable that if the factors that potentiate their risk are addressed, their PrEP course may be limited, and they could discontinue PrEP. Although antiretrovirals are not a panacea, their judicious use in a comprehensive program that addresses the full medical and behavioral health needs of those who are HIV-infected or affected can contribute to a net result that will halt the further spread of HIV.

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Potential Conflicts of Interest

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