

## Generic Antiretrovirals and the Uncertain Future of HIV Care in the United States

Generic antiretroviral drugs have contributed to remarkable achievements in the global HIV epidemic. Mortality has decreased by 24% since 2005, new HIV infections have decreased by 20% since 2001, and 8 million persons are receiving treatment (1). In the United States, 10 available generic antiretrovirals have been used infrequently because of greater toxicity and inferior efficacy. However, when generic efavirenz becomes available in 2013, a regimen of generic efavirenz and lamivudine with branded tenofovir will become a credible alternative to branded regimens.

In this issue, Walensky and colleagues (2) mathematically model the effect of the substitution of generic efavirenz and lamivudine in all people living with HIV (PLWHIV) in the United States who were assumed to receive the branded coformulation of these drugs with tenofovir. They found a 50% reduction in drug costs and a savings of \$960 million in care costs in 1 year. They also found reduced treatment efficacy, resulting in 4.4 months of life lost per patient lifetime. Even with substantial variations in the model's assumptions, large-scale cost savings were achieved, and the comparative cost-effectiveness of branded antiretrovirals exceeded the standard threshold of \$100 000 per quality-adjusted life-year. Recent studies in Europe and the United Kingdom also report substantial savings with generic antiretrovirals (3–5).

Can a regimen of combined generic and branded antiretrovirals perform as well as a preferred branded 1-pill, once-daily coformulation? Current HIV treatment guidelines uniformly recommend the use of coformulated antiretrovirals because of convenience, superior patient adherence, patient and clinician preference, and lower insurance copayments. Most available evidence support these recommendations (6). In 1 exception, once-daily regimens of 2 or 3 equipotent antiretrovirals were not inferior to a branded once-daily coformulation (7). Similarly, although guidelines recommend once-daily dosing when possible, 1 of 4 "preferred" initial regimens is dosed twice daily, and 7 of 11 studies in a meta-analysis found no difference between once- and twice-daily regimens (8).

Would even a small reduction in efficacy be acceptable? In the study by Walensky and colleagues, poorer survival with generics resulted from minor differences of uncertain clinical significance between lamivudine and emtricitabine in resistance outcomes and virologic efficacy from limited trial data (9, 10). The best regimen choice in their model was generic efavirenz and coformulated emtricitabine plus tenofovir, a 2-pill, once-daily option with similar efficacy and lower cost. Large-scale effectiveness trials that compare generics, including abacavir, with branded coformulations will be critical in assessing the comparabil-

ity of regimens that contain generic antiretrovirals and defining differences in adherence, virologic success, and health care use. How these studies will be supported is unclear.

Angst and uncertainty about HIV care abound at this time. According to the national version of the "Gardner Cascade," fewer than one third of PLWHIV in the United States have sufficient disease control with treatment, and fewer than half (36%) are reliably receiving care (11). This unacceptably poor performance is worthy of soul-searching. Fortunately, the National AIDS Strategy offers measured and specific guidance to our response to expand HIV testing and improve recruitment and retention in care (12, 13). Nonetheless, our HIV care "system" is a fragile edifice with disparate parts. Public sources, such as Medicaid, Medicare, and the Ryan White Care Act, support 80% of care for PLWHIV, and the Ryan White Care Act covers only care, drugs, and services that are not supported by Medicare and Medicaid. Under the Affordable Care Act (ACA), 32 million uninsured Americans will enter Medicaid starting in 2014, but of 37 states under single-party control, 24 are hostile to ACA and 20 currently plan not to participate in Medicaid expansion (14). Making matters worse, rules for ACA that were recently issued left the definition of "essential health benefits" and drug formulary composition up to states (15). As a result, existing state-to-state disparities in HIV care and access to antiretrovirals will probably persist or worsen.

In addition to these strains, the Ryan White Care Act, which serves more than 500 000 PLWHIV and provides treatment for 200 000 persons, is up for reauthorization in 2013. High-quality HIV care evolved within the HIV multidisciplinary team with guidance, training, and funding from the act. Many care innovations—such as the HIV medical home and HIV prevention and treatment integrated with maternal-child health, mental health, and substance abuse treatment—may be at risk if the act is subsumed into Medicaid under ACA (16). Community health centers are prioritized under ACA, but many lack skills and capacity for HIV care and will require training. The act's budgets will probably be further strained in states opting out of Medicaid expansion (17). Because half of its expenditures are for medications, generic antiretrovirals will be a critical issue in the reauthorization debate and in state Medicaid formulary budgets. Vigilance by HIV advocates will be critical at the federal and state levels to ensure that the act has sufficient flexibility to improve outcomes in states that expand Medicaid eligibility to include most PLWHIV and in states that decline Medicaid expansion. Activism to persuade reluctant states to expand Medicaid

eligibility and to safeguard multidisciplinary HIV care models in the transition into Medicaid will also be crucial.

HIV advocates and caregivers might more readily embrace generic antiretrovirals if, as Walensky and colleagues suggest, the savings were diverted to address other funding needs within the field of HIV medicine, but no such mechanism exists. Perhaps a large, simple trial should be conducted in which generic and branded antiretrovirals are compared and patients in the generic group are allowed to use the cost savings of their regimen to support their annual health insurance premiums, in which case I predict rapid accrual. In any case, Walensky and colleagues' study is a wake-up call to PLWHIV and their clinicians: The era of generic antiretrovirals in the United States has come. The noted infectious diseases physician John G. Bartlett has predicted that the annual cost of antiretrovirals in 10 years will be less than \$200, and he has not often been wrong when forecasting HIV care trends in the United States (18).

Renslow Sherer, MD  
University of Chicago  
Chicago, Illinois

**Potential Conflicts of Interest:** Disclosures can be viewed at [www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-2981](http://www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-2981).

**Requests for Single Reprints:** Renslow Sherer, MD, Section of Infectious Diseases and Global Health, Department of Medicine, University of Chicago, 5841 South Maryland Avenue, MC5065, Chicago, IL 60637.

*Ann Intern Med.* 2013;158:133-134.

## References

1. Joint United Nations Programme on HIV/AIDS. Global Report: UNAIDS Report on the Global AIDS Epidemic 2012. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2012. Accessed at [www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120\\_UNAIDS\\_Global\\_Report\\_2012\\_en.pdf](http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_en.pdf) on 12 November 2012.
2. Walensky RP, Sax PE, Nakamura YM, Weinstein MC, Pei PP, Freedberg KA, et al. Economic savings versus health losses: the cost-effectiveness of generic antiretroviral therapy in the United States. *Ann Intern Med.* 2013;158:84-92.
3. Stoll M, Kollan C, Bergmann F, Bogner J, Faetkenheuer G, Fritzsche C, et al; ClinSurv Study Group. Calculation of direct antiretroviral treatment costs and potential cost savings by using generics in the German HIV ClinSurv cohort. *PLoS One.* 2011;6:e23946. [PMID: 21931626]
4. Gazzard B, Moecklinghoff C, Hill A. New strategies for lowering the costs of antiretroviral treatment and care for people with HIV/AIDS in the United Kingdom. *Clinicoecon Outcomes Res.* 2012;4:193-200. [PMID: 22888265]
5. Sloan CE, Champenois K, Choisy P, Losina E, Walensky RP, Schackman BR, et al; Cost-Effectiveness of Preventing AIDS Complications (CEPAC) investigators. Newer drugs and earlier treatment: impact on lifetime cost of care for HIV-infected adults. *AIDS.* 2012;26:45-56. [PMID: 22008655]
6. Libre JM, Arribas JR, Domingo P, Gatell JM, Lozano F, Santos JR, et al; Spanish Group for FDAC Evaluation. Clinical implications of fixed-dose coformulations of antiretrovirals on the outcome of HIV-1 therapy. *AIDS.* 2011;25:1683-90. [PMID: 21673556]
7. Buscher A, Hartman C, Kallen MA, Giordano TP. Impact of antiretroviral dosing frequency and pill burden on adherence among newly diagnosed, antiretroviral-naïve HIV patients. *Int J STD AIDS.* 2012;23:351-5. [PMID: 22648890]
8. Parienti JJ, Bangsberg DR, Verdon R, Gardner EM. Better adherence with once-daily antiretroviral regimens: a meta-analysis. *Clin Infect Dis.* 2009;48:484-8. [PMID: 19140758]
9. Svicher V, Alteri C, Artese A, Forbici F, Santoro MM, Schols D, et al. Different evolution of genotypic resistance profiles to emtricitabine versus lamivudine in tenofovir-containing regimens. *J Acquir Immune Defic Syndr.* 2010;55:336-44. [PMID: 20739898]
10. Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JM, Miller MD, et al; 903 Study Group. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naïve patients: a 3-year randomized trial. *JAMA.* 2004;292:191-201. [PMID: 15249568]
11. Centers for Disease Control and Prevention (CDC). Vital signs: HIV prevention through care and treatment—United States. *MMWR Morb Mortal Wkly Rep.* 2011;60:1618-23. [PMID: 22129997]
12. The White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States. Washington, DC: The White House Office of National AIDS Policy; 2010.
13. Thompson MA, Mugavero MJ, Amico KR, Cargill VA, Chang LW, Gross R, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. *Ann Intern Med.* 2012;156:817-33. [PMID: 22393036]
14. Davey M. One-party control opens states to partisan rush. *New York Times.* 22 November 2012:A1.
15. U.S. Department of Health and Human Services. Essential Health Benefits, Actuarial Value, and Accreditation Standards: Ensuring Meaningful, Affordable Coverage. Washington, DC: U.S. Department of Health and Human Services; 2012. Accessed at [www.healthcare.gov/news/factsheets/2012/11/ehb11202012a.html](http://www.healthcare.gov/news/factsheets/2012/11/ehb11202012a.html) on 2 December 2012.
16. Martin EG, Schackman BR. What does U.S. health reform mean for HIV clinical care? *J Acquir Immune Defic Syndr.* 2012;60:72-6. [PMID: 22517415]
17. Sherer R. The future of HIV care in the USA. *Sex Transm Infect.* 2012;88:106-11. [PMID: 22158933]
18. Maxmen A. Generic HIV drugs will widen US treatment net. *Nature.* 2012;488:267. [PMID: 22895314]