ture to address other concerns — such as malaria, tuberculosis, maternal and child health, immunizations, and unanticipated infectious disease outbreaks — that affect the geographic areas where patients with HIV are treated. Specifically, the program has contributed to building sustainable health system capacity in host countries by investing in the critical infrastructure of laboratories and training more than 220,000 health care workers.[5] With regard to international public relations, PEPFAR has done as much as or more than any other program in enhancing the humanitarian image of the United States and has firmly established it as a key player in the response to a historic global public health crisis.

Over the past 15 years, PEPFAR has demonstrated the transforming results that can be realized by strong government leadership in the global health arena. It is entirely possible to bring the HIV/AIDS pandemic to an end, and PEPFAR will undoubtedly play an essential role in this endeavor. However, it is vital that support for this transformative program continue both to meet the immediate challenge of HIV/AIDS and to serve as the model for the control and elimination of other globally devastating infectious diseases.

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Treating and Preventing HIV with Generic Drugs — Barriers in the United States

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Combination antiretroviral therapy (ART) has dramatically improved survival rates among people with HIV and is a mainstay of HIV prevention; evidence shows that durable viral suppression prevents the transmission of infection. In addition, preexposure prophylaxis (PrEP) is an emerging approach to preventing HIV acquisition for certain high-risk groups. Generic ART medications offer the potential for treating and preventing HIV with fewer resources. Generic versions of lamivudine, abacavir, and efavirenz became available in the United States within the past 6 years at prices lower than their brand-name counterparts, a generic version of PrEP (emtricitabine and tenofovir disoproxil fumarate) was approved in 2016, and generic versions of tenofovir disoproxil are expected later in 2018. Yet most of the discussion about the availability of generic HIV drugs focuses on low- and middle-income countries.

ART accounts for 60% of the projected $326,500 discounted lifetime medical cost of HIV treatment in the United States.[1] A 2013 study estimated nearly $1 billion in savings in the first year if all eligible U.S. patients for whom brand-name was prescribed efavirenz at the time (when it was a component of a leading ART regimen) switched to a regimen with generic efavirenz.[2] Our analysis of four regimens currently recommended by the Department of Health and Human Services (HHS) shows in more detail the potential cost savings associated with switching to generic regimens (see table). For example, switching from a brand-name to a generic formulation of the three-drug combination of dolutegravir, abacavir, and lamivudine (regimen 1) would yield a 25% reduction in both the wholesale acquisition cost (generating savings of $667) and the federal supply schedule cost (generating savings of $553) for a 30-day supply. The wholesale acquisition cost approximates what private

Costs for a 30-Day Supply of ART Regimens Recommended by the Department of Health and Human Services.*

Recommended Initial Regimens for Most People with HIV	Brand-Name and Generic Components	Wholesale Acquisition Cost	Federal Supply Schedule Cost
		dollars	
Regimen 1 (generic substitution available)			
Dolutegravir/abacavir/lamivudine	Triumeq	2,599	2,206
Dolutegravir + abacavir + lamivudine	Tivicay + abacavir + lamivudine	1,932†	1,653†
Dolutegravir + abacavir + emtricitabine	Tivicay + abacavir + Emtriva	2,322†	1,803†
Regimen 2 (generic substitution available)			
Dolutegravir + tenofovir disoproxil fumarate/emtricitabine	Tivicay + Truvada	3,103	2,113
Dolutegravir + tenofovir disoproxil fumarate + lamivudine	Tivicay + Viread + lamivudine	2,739†	2,108†
Dolutegravir + tenofovir alafenamide/emtricitabine	Tivicay + Descovy	3,103	2,113
Regimen 3 (generic substitution not available)			
Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine	Genvoya	2,756	1,529
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine	Stribild	3,090	1,529
Regimen 4 (generic substitution available)			
Raltegravir + tenofovir disoproxil fumarate/emtricitabine	Isentress + Truvada	2,957	2,148
Raltegravir + tenofovir disoproxil fumarate + lamivudine	Isentress + Viread + lamivudine	2,593†	2,143†
Raltegravir + tenofovir alafenamide/emtricitabine	Isentress + Descovy	2,957	2,148

* Regimen 1 is recommended only for patients who are HLA-B*5701-negative. The price for generics is calculated as the median generic manufacturer price. The wholesale acquisition cost approximates what private insurers pay, and the federal supply schedule cost approximates what government programs pay, excluding negotiated bulk discount prices.
† Cost includes a generic component.

insurers pay for a drug, and the federal supply schedule cost approximates what government programs pay.

Greater use of generic ART in the United States could provide some relief to government programs that already face severe budgetary pressures and serve the majority of people with HIV and those at the highest risk for infection. Moreover, if proposed health policy reforms — such as allowing private insurers to exclude people with preexisting conditions or converting Medicaid to a block-grant program — are enacted and people with HIV lose their current public or private health insurance coverage, there will be more pressure on the AIDS Drug Assistance Program (ADAP). A payer of last resort, ADAP provides access to drugs for low-income people who are uninsured or underinsured. ADAP funding has been flat for the past 15 years despite increased demand as people with HIV live longer and more people are diagnosed with HIV infection. Finding new sources for cost savings is particularly important as states and local communities scale up efforts to increase rates of diagnosis, linkage to HIV care, and viral suppression as part of initiatives such as New York State's Ending the Epidemic, San Francisco's Getting to Zero, and Houston's Roadmap to Ending the HIV Epidemic.

Can the United States realize billions of dollars in savings from the availability of generic ART medications? Although we believe such savings are theoretically possible, numerous legal, clinical, and market factors create barriers to the widespread adoption of generics in the United States as well as uncertainty about actual cost savings.

A key barrier to uptake of generics is modification of brand-name products coupled with aggressive marketing of modified products. Manufacturers have used various strategies to delay generic competition, such as developing coformulations with medications that have longer patent lives (e.g., coformulating tenofovir disoproxil

fumarate with emtricitabine), changing inactive drug components (e.g., adding a new binding agent to the combination of efavirenz, emtricitabine, and tenofovir to resist degradation), filing for approval for additional indications that introduce new patent claims and extend market exclusivity (e.g., obtaining FDA approval to market lamivudine to treat hepatitis B virus), and obtaining patents on pediatric formulations (e.g., patenting the combination of lopinavir and ritonavir). In promoting their brand-name products, manufacturers may emphasize the side effects of older products as compared with newer brand-name alternatives, thereby increasing the general mistrust of generics. For example, efavirenz has been linked to increased suicidality[3]; because of the strength of this evidence, it is no longer a recommended first-line therapy in the current HHS guidelines despite the infrequency of suicides. There continues to be persistent skepticism among clinicians, pharmacists, and patients regarding the performance and safety of generic medications in general as compared with their brand-name counterparts.[4]

Because all first-line ART regimens contain three or four medications, often coformulated, the staggered availability of generic versions of each component will probably require replacing coformulated tablets with multiple individual pills, which creates several obstacles for both clinicians and patients. First, there is a perception — but no strong evidence — that increasing the number of pills in a once-daily regimen will adversely affect adherence and viral suppression. In keeping with systematic reviews on the general acceptability of generics,[4] a recent study found that a substantial minority of French HIV physicians and their patients were unwilling to prescribe or use generic medications — and that the majority were unwilling if switching to generics resulted in an increased pill burden.[5] In addition, patients taking multiple pills could potentially face higher costs if they had separate copayments for each medication rather than one copayment for a combination pill, which could affect their willingness or ability to refill prescriptions on time.

In an era when the "end of AIDS" is conceivable, the availability of generic ART medications might help address some budget shortfalls, particularly in states that didn't expand their Medicaid programs.

Another complication is the fact that the financial incentives for switching to generics vary among payers. HIV care is financed through a complex patchwork of public and private payers, including private insurance, Medicaid, Medicare, and state ADAPs. Payers don't incur identical costs for ART. As shown in the table, although there are cost savings associated with all generic-substitution regimens, not all substitutions yield meaningful price reductions. For example, although switching to a generic formulation of dolutegravir, abacavir, and lamivudine (regimen 1) would lead to a 25% reduction in the cost of a 30-day supply for both private and government payers, doing the same for dolutegravir, tenofovir disoproxil fumarate, and emtricitabine (regimen 2) would yield savings of $364 for private insurers but only $5 for public payers.

Furthermore, some clinics are eligible for the federal 340B drug-pricing program, which provides access to discounted medications, and ADAPs have negotiated rebates, price freezes, and medication prices that are lower than mandatory government rates for Medicaid. Currently, HIV-program pharmacies eligible for 340B pricing can generate substantial revenue by dispensing brand-name ART and obtaining full reimbursement from payers, which provides a disincentive to use generics. ADAP managers also have other priorities in addition to encouraging generic substitution, such as adapting to rapid changes in the federal health insurance landscape, managing funding cuts, and establishing programs that provide access to PrEP for HIV-negative persons.

After more than three decades of progress in HIV prevention and treatment, we have reached an era when the "end of AIDS" is conceivable, and many communities in the United States are mobilizing around ambitious new goals for linkage to and retention in care, rates of durable viral

suppression, and PrEP use. The availability of generic ART medications might help address some budget shortfalls, particularly in states that didn't expand their Medicaid programs, where ADAPs must stretch their budgets to cover uninsured people with HIV and federal funding cuts are anticipated. However, many factors will delay widespread adoption. Although information and education about generics can improve health professionals' and patients' confidence in generic substitution, there is limited evidence on which interventions are most effective at improving perceptions of generic drugs.[4] Generic ART will not be a panacea for government programs serving people with HIV and those at risk. We believe it is important to continue to advocate for sufficient funding for public-insurance programs that can provide access to all medications needed for HIV treatment and prevention.

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