Annals of Internal Medicine ORIGINAL RESEARCH

Comparative Pricing of Branded Tenofovir Alafenamide–Emtricitabine Relative to Generic Tenofovir Disoproxil Fumarate–Emtricitabine for HIV Preexposure Prophylaxis

A Cost-Effectiveness Analysis

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Background: Tenofovir alafenamide–emtricitabine (F/TAF) was recently approved as a noninferior and potentially safer option than tenofovir disoproxil fumarate–emtricitabine (F/TDF) for HIV preexposure prophylaxis (PrEP) in the United States.

Objective: To estimate the greatest possible clinical benefits and economic savings attributable to the improved safety profile of F/TAF and the maximum price payers should be willing to pay for F/TAF over generic F/TDF.

Design: Cost-effectiveness analysis.

Data Sources: Published literature on F/TDF safety (in persons with and those without HIV) and the cost and quality-of-life effects of fractures and end-stage renal disease (ESRD).

Target Population: Age-stratified U.S. men who have sex with men (MSM) using PrEP.

Time Horizon: Five years.

Perspective: Health care sector.

Intervention: Preexposure prophylaxis with F/TAF versus F/TDF.

Outcome Measures: Fractures averted, cases of ESRD averted, quality-adjusted life-years (QALYs) saved, costs, incremental cost-effectiveness ratios (ICERs), and maximum justifiable price for F/TAF compared with generic F/TDF.

Results of Base-Case Analysis: Over a 5-year horizon, compared with F/TDF, F/TAF averted 2101 fractures and 25 cases of ESRD for the 123 610 MSM receiving PrEP, with an ICER of more than $7 million per QALY. At a 50% discount for generic F/TDF ($8300 per year) and a societal willingness to pay up to $100 000 per QALY, the maximum fair price for F/TAF was $8670 per year.

Results of Sensitivity Analysis: Among persons older than 55 years, the ICER for F/TAF remained more than $3 million per QALY and the maximum permissible fair price for F/TAF was $8970 per year. Results were robust to alternative time horizons and PrEP-using population sizes.

Limitation: Intermittent use and on-demand PrEP were not considered.

Conclusion: In the presence of a generic F/TDF alternative, the improved safety of F/TAF is worth no more than an additional $370 per person per year.

Primary Funding Source: National Institute of Allergy and Infectious Diseases, National Institute on Drug Abuse, National Institute of Mental Health, and Massachusetts General Hospital Executive Committee on Research.

Ann Intern Med. doi:10.7326/M19-3478 Annals.org
For author affiliations, see end of text.
This article was published at Annals.org on 10 March 2020.

Prevention of HIV with preexposure prophylaxis (PrEP) is a cornerstone of the federal plan to end the HIV epidemic (1). Since the first Centers for Disease Control and Prevention (CDC) PrEP guidance in 2012, tenofovir disoproxil fumarate–emtricitabine (F/TDF) has been the only U.S. Food and Drug Administration (FDA)–approved drug combination for PrEP use. In October 2019, on the basis of the results of the DISCOVER trial, tenofovir alafenamide–emtricitabine (F/TAF) became the second approved PrEP drug combination for use in men who have sex with men (MSM) and transgender women (2). In DISCOVER, F/TAF was found to be noninferior to F/TDF in terms of prevention efficacy, had comparably high drug tolerability, and showed statistically significant improvements in markers of renal and bone safety in MSM. Specifically, 48-week results for F/TAF revealed differences in estimated glomerular filtration rate (eGFR) (difference, 4.1 mL/min per 1.73 m^2) and bone mineral density (lumbar spine, 1.6%; hip, 1.3%) (3, 4). Although the manufacturer highlighted these findings as evidence that F/TAF is a superior option for people at risk for HIV who increasingly use PrEP for longer periods (5, 6), the clinical significance of these outcomes remains a matter of debate (7).

In addition to any toxicity differences, another key consideration in decision making is the evolving cost of PrEP options; significantly less costly, generic versions of F/TDF are expected to become commercially available in late 2020 and early 2021. These potential safety, toxicity, and cost tradeoffs have generated an urgent call to be "forward-thinking about what should be first-line PrEP" (8).

We sought to examine how the potentially improved safety profile of F/TAF over F/TDF might translate into observable clinical benefits; compare the potential clinical benefits with the long-term additional costs of F/TAF; understand the effect that the choice

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Editorial comment

between these 2 PrEP options would have on national coverage levels, in the context of the U.S. HIV prevention budget; and estimate the premium that one should be willing to pay for the benefits of switching from F/TDF to F/TAF.

METHODS

Study Design and Overview

We forecast the clinical and economic outcomes of switching all MSM in the United States currently receiving F/TDF-based PrEP to a comparable F/TAF-based regimen. Given the speed of new advances in HIV prevention and treatment, we adopted a short 5-year time horizon. Using the methods of cost-effectiveness analysis, we sought to identify the highest possible price premium that branded F/TAF could command, even under the very best of circumstances, over generic F/TDF. Because this entailed a deliberate search for an extreme upper-bound value, we chose extreme input values, intentionally tipping the scales in favor of F/TAF and portraying this newly approved drug in the most favorable light possible. Accordingly, we erred on the side of overstating the adverse clinical and economic consequences of F/TDF on bone and renal effects compared with F/TAF.

Population and Time Horizon

To determine the value of F/TAF over F/TDF for PrEP in the total population of PrEP users, we considered the age distribution of the 132 340 people currently receiving PrEP in the United States (Table 1), as reported by the CDC. Because F/TAF was FDA-approved for use only in MSM and transgender women (2), we included, proportionately by age, only the 93.4% of PrEP users who are MSM (data are not available on AIDSVu for the number of PrEP users who are transgender women [Table 1]) (9). Recognizing that there might be large differences in the relevant risks and benefits across different age groups, we assessed how our findings might vary when applied to specific age cohorts. We assumed PrEP would be used consistently for a 5-year horizon.

Bone Mineral Density

We obtained gender- and age-stratified data on the risk for incident fractures for patients on long-term TDF, which ranged by site from 5 to 25 fractures per 10 000 patient-years of F/TDF use (Table 1) (10). Although fracture rates were stratified by osteoporosis-related, hip, and nonhip fractures, we summed them and assumed that all fractures occurred at the hip. By choosing the fracture location associated with the largest quality-of-life decrement, this assumption resulted in an exaggerated 30% loss of quality-adjusted life expectancy for a full year for all patients with any type of fracture (11, 12). We used other reports of F/TDF use to confirm that these fracture estimates were consistent with the goal of biasing the analysis against F/TDF-based PrEP (13).

Renal Disease

In a meta-analysis of over 9900 patients receiving F/TDF for PrEP, the majority of creatinine elevations were mild and self-limited, with only 16 and 4 patients experiencing a grade 2 (1.4 to 1.8 times the upper limit of normal) or grade 3 or 4 (≥1.9 times the upper limit of normal) creatinine elevation—outcomes that were not statistically different from those in placebo controls (14). Furthermore, for context, in DISCOVER, patients receiving F/TAF had a baseline eGFR of 123 mL/min per 1.73 m^2, which increased by a median of 1.8 mL/min per 1.73 m^2 at 48 weeks; those receiving F/TDF had a baseline eGFR of 121 mL/min per 1.73 m^2, which decreased by a median of 2.3 mL/min per 1.73 m^2 at 48 weeks (4). To magnify the safety benefit of F/TAF, we assumed an accelerated and irreversible process of end-stage renal disease (ESRD) onset for persons receiving F/TDF. We began the analysis with the prevalence of both stage 2 chronic kidney disease (CKD) and stage 3 or 4 CKD in the population at 0. We justify this simplifying assumption because we are only interested in cases that can be attributed to PrEP and, most specifically, in the incremental cases produced by F/TDF over F/TAF. Preexisting cases—or cases attributable to non-PrEP causes—will cancel out in the calculation of incremental effects. From there, we used the CDC's age-adjusted incidence for dialysis for eGFRs of 60 to 89 mL/min per 1.73 m^2 (stage 2 CKD) and 15 to 59 mL/min per 1.73 m^2 (stage 3 or 4 advanced CKD). For F/TDF, we then inflated the rates of progression to ESRD reported by the U.S. Renal Data System (15). Specifically, we assumed that persons with stage 2 CKD progressed to ESRD at the age-stratified rates reported for persons with stage 3 to 4 CKD; for those with stage 3 to 4 CKD, we doubled the reported annual progression rate (16). Finally, we assumed that progression to hemodialysis was immediate and irreversible, that it lasted all 5 years of the treatment period, and that it produced a persistent reduction in quality of life of 47% (17).

Costs

Of all fractures, those at the hip are the most expensive, owing to the costs of surgical repair and rehabilitation. We therefore assumed all F/TDF-related fractures had the attributable cost of a hip fracture: $70 400 (reported value, updated to 2018 U.S. dollars) in the year of the fracture (18). We assumed that F/TDF-related ESRD resulted in age-dependent annual hemodialysis costs ranging from $92 100 to $95 500 (reported value, updated to 2018 U.S. dollars) (15, 19).

Currently, the Federal Supply Schedule (FSS) price of F/TAF is $16 600 per year (2018 U.S. dollars) (20); however, generic F/TDF is expected to be available in 2020 (21). Historically, prices of oral drugs have decreased an average of 66%, 74%, and 80% in the first 1, 2, and 5 years, respectively, after entry of a generic option (22). For generic F/TDF, we assumed a more modest price reduction of 50% from the price of branded F/TAF (to $8300 per year) that would persist over the 5-year horizon.

Table 1. Input Parameters for Analysis of the Cost-Effectiveness and Budget Impact of F/TAF Versus F/TDF

Parameter	Value			Reference
Cohort				
2018 MSM PrEP users, *n*				
Total	123 610			9
Age 13–24 y	16 069			9
Age 25–34 y	49 442			9
Age 35–44 y	28 429			9
Age 45–54 y	19 777			9
Age ≥55 y	9888			9
Bone mineral density				
Fracture risk on F/TDF, per 10 000 patient-years of use	**Osteoporosis-Related**	**Hip**	**Nonhip**	
Age 13–24 y	7	5	4	10
Age 25–34 y	7	5	4	10
Age 35–44 y	25	11	18	10
Age 45–54 y	25	15	18	10
Age ≥55 y	22	15	15	10
Quality of life in year of fracture	0.7	0.7	0.7	12
ESRD				
Incidence per 1000 patient-years*	**Stage 2 CKD**	**Stage 3 or 4 CKD**		
Age 20–29 y	73	1.3		16
Age 30–39 y	113	3		16
Age 40–49 y	178	11		16
Age 50–59 y	207	25		16
Age 60–69 y	272	55		16
Age ≥70 y	228	107		16
ESRD risk on F/TDF, per 1 000 000 patient-years*	**From Stage 2 CKD**	**From Stage 3 or 4 CKD**		
Age 13–24 y	43	86		15
Age 25–34 y	110	220		15
Age 35–44 y	254	508		15
Age 45–54 y	467	934		15
Age ≥55 y	1196	2392		15
Quality of life with ESRD, for duration	0.53	0.53		17
Costs, $†	**Value**			
Fracture (one-time)	70 400			18
ESRD (annual)				
Age 13–24 y	92 100			19
Age 25–34 y	94 100			19
Age 35–44 y	93 800			19
Age 45–54 y	92 400			19
Age ≥55 y	95 500			19
Drug costs				
Branded F/TAF	16 600			20
Generic F/TDF	8300			Assumption, 22

CKD = chronic kidney disease; ESRD = end-stage renal disease; F/TAF = tenofovir alafenamide–emtricitabine; F/TDF = tenofovir disoproxil fumarate–emtricitabine; MSM = men who have sex with men; PrEP = preexposure prophylaxis.
* See the Methods section of the article.
† Adjusted to 2018 U.S. dollars.

Additional Assumptions

We assumed equal preventive efficacy of both F/TAF and F/TDF, as demonstrated in DISCOVER (3). We also assumed no excess fractures and no progression to ESRD among patients receiving F/TAF. Finally, we deliberately excluded any quantity- or quality-of-life decrements which might arise from the reported risks of F/TAF (for example, worsening of the lipid profile, potential increased atherosclerotic cardiovascular disease risk, and weight gain) (23, 24) and their associated costs (for example, increased statin use). Given the short time horizon of the analysis (5 years), we assumed no mortality and did not apply any discounting.

Statistical Analysis

Clinical Outcomes

To estimate the expected clinical outcomes, we used fracture and ESRD risk to calculate the age-stratified per person probability of a fracture or ESRD event in a given year. We then projected the expected number of fractures or ESRD events over the 5-year treatment horizon.

Cost, Cost-Effectiveness, and Price Premium

To calculate the total costs of the F/TDF regimen, we first multiplied all fracture events over the 5-year

Table 2. Cumulative 5-Year Clinical and Cost Outcomes of F/TAF Versus F/TDF Among MSM in the United States

Age	MSM Receiving PrEP, *n*	F/TAF Outcomes		F/TDF Outcomes				ICER, Δ$/ΔQALYs*
		QALYs	Costs, $*	Excess Cases of ESRD, *n*	Excess Fractures, *n*	QALYs	Costs, $*	
13–24 y	16 069	80 344	1 333 700 000	0.2	128	80 305	675 930 000	16 960 000
25–34 y	49 442	247 210	4 103 700 000	2	393	247 090	2 080 600 000	16 380 000
35–44 y	28 429	142 150	2 359 600 000	5	764	141 910	1 235 800 000	4 681 200
45–54 y	19 777	98 884	1 641 500 000	7	568	98 698	863 930 000	4 163 500
≥55 y	9888	49 442	820 740 000	11	250	49 341	433 240 000	3 836 700
Total†	123 610	618 030	10 259 000 000	25	2101	617 340	5 289 500 000	7 201 200

ESRD = end-stage renal disease; F/TAF = tenofovir alafenamide–emtricitabine; F/TDF = tenofovir disoproxil fumarate–emtricitabine; ICER = incremental cost-effectiveness ratio; MSM = men who have sex with men; PrEP = preexposure prophylaxis; QALY = quality-adjusted life-year.
* All economic outcomes are reported in 2018 U.S. dollars.
† Values may not sum to total because of rounding to 5 significant digits.

horizon by the per-fracture cost and all age-stratified ESRD events over the 5-year horizon by their respective, age-stratified dialysis costs. These total adverse event costs were then summed and added to the F/TDF drug cost over 5 years for all persons receiving HIV PrEP.

We calculated the incremental cost-effectiveness ratio of F/TAF compared with F/TDF as (Δ$/ΔQALY) between the 2 strategies, from the health care sector perspective. Persons receiving F/TAF were assumed to experience no quality-of-life decrement (quality adjustment factor = 1.0). For those receiving F/TDF, quality of life was adjusted downward to reflect the effect of fractures and ESRD (Table 1).

"Willingness to pay" is a common benchmark in cost-effectiveness analysis used to measure value. There is no generally accepted willingness-to-pay threshold. In the spirit of portraying F/TAF in a favorable light, we chose a threshold of $100 000 per quality-adjusted life-year (QALY), a cutoff value that lies at the high end of what is typically regarded as the range of acceptable costs per unit return on investment in the United States (25–27). Holding all other variables at their base values, we identified the price of F/TAF that would just barely achieve an ICER of $100 000 per QALY, thereby identifying the highest price that payers in the United States should be willing to pay for F/TAF compared with F/TDF.

In a series of sensitivity analyses, we examined the effects of alternative costs of generic F/TDF (branded price reductions from 50% to 90%), alternative willingness-to-pay thresholds for the F/TAF price premium, and different treatment horizons (1 to 10 years).

Budget Impact Analysis

We sought to understand the potential magnitude of the financial outlays and coverage levels that could be achieved by a national PrEP scaleup campaign, using both branded F/TAF and generic F/TDF. Because our aim was to estimate the greatest possible number of eligible persons covered, we considered the extreme scenario where the entire current $900.8 million U.S. HIV prevention budget was allocated to PrEP (28). Under this assumption, we estimated the number of people who could be provided PrEP with each regimen, including toxicity and drug costs and excluding the costs of HIV and sexually transmitted infection screening. We compared this estimated coverage with the 492 000 MSM who are projected to be PrEP-eligible in the United States (29).

Role of the Funding Source

This work was supported by awards from the National Institute of Allergy and Infectious Diseases, National Institute on Drug Abuse, National Institute of Mental Health, and Massachusetts General Hospital Executive Committee on Research. The funding sources had no role in the design, analysis, or interpretation of the study; writing of the manuscript; or the decision to submit the manuscript for publication.

RESULTS

Clinical Outcomes

The current population of MSM receiving PrEP by age ranges from nearly 49 500 in the 24- to 34-year age group to nearly 10 000 among MSM older than 55 years (Table 2). Accounting for both age-stratified risk and absolute numbers of patients, we estimate that an immediate switch of these persons from F/TDF to F/TAF will avert 2101 fractures and 25 cases of ESRD over a 5-year horizon. This translates into an overall quality-adjusted life expectancy gain of 690 QALYs (618 030 QALYs with F/TAF vs. 617 340 QALYs with F/TDF).

Costs and Cost-Effectiveness

Assuming F/TAF current costs ($16 600 per year), F/TDF generic costs ($8300 per year), and the offsetting adverse event costs described above, switching all patients to F/TAF-based PrEP will increase total expenditures by $5.0 billion ($40 210 per person over the 5-year treatment horizon). This suggests an ICER greater than $7 million per QALY gained for F/TAF compared with F/TDF. Among patients older than 55 years, the ICER is lower but still exceeds $3 million per QALY (Table 2).

In sensitivity analyses, cost-effectiveness results of this order of magnitude persist across broad variation in the input parameter assumptions, including treatment horizons ranging from 1 to 10 years (base case, 5

Table 3. Permissible Cost of F/TAF Under Alternative Willingness-to-Pay Thresholds and Generic F/TDF Costs

Annual F/TDF Cost (Price Reduction)	Willingness-to-Pay Threshold		
	<$50 000/QALY	<$100 000/QALY	<$150 000/QALY
Total population			
$8300 (50%)	$8610	$8670	$8730
$4150 (75%)	$4460	$4520	$4580
$1660 (90%)	$1970	$2030	$2090
Population aged >55 y			
$8300 (50%)	$8870	$8970	$9070
$4150 (75%)	$4720	$4820	$4920
$1660 (90%)	$2230	$2330	$2430

F/TAF = tenofovir alafenamide–emtricitabine; F/TDF = tenofovir disoproxil fumarate–emtricitabine; QALY = quality-adjusted life-year.

years); PrEP-using population sizes ranging from 100 000 to 1 million (base case, 123 610); and focusing only on the oldest, highest-risk patients. Relaxing any of the pessimistic assumptions regarding the renal and bone safety of F/TDF (for example, assuming similar safety profiles for both treatments) only makes F/TAF even less cost-effective.

Maximum Justifiable Price for F/TAF

Using, as a point of departure, a societal willingness-to-pay threshold of $100 000 per QALY (25–27) and a generic F/TDF cost of $8300 per year (50% generic cost reduction), the superior safety profile of F/TAF, based on the aforementioned assumptions, could justify a price of up to $8670 per person per year for the overall PrEP population; at a willingness-to-pay threshold of $150 000 per QALY and an F/TDF cost of $1660 per person per year (90% generic cost reduction) the highest justifiable cost of F/TAF would be $2090 per person per year (Table 3). For patients older than 55 years, slightly higher F/TAF prices could be justified ($8970 per person per year and $2430 per person per year, respectively), owing to the higher risks for adverse events with F/TDF (Table 3).

Budget Impact Analysis

If the entire U.S. budget for HIV prevention ($900.8 million) were devoted to PrEP, a nationwide rollout using branded F/TAF ($16 600 per person per year) could achieve a coverage level no greater than 54 300 (or 11%) of the estimated 492 000 eligible MSM. This coverage level could be doubled (quadrupled) by switching to a generic F/TDF alternative priced at a 50% (75%) discount to the branded option.

Discussion

It is estimated that 1.2 million Americans are at risk for HIV and eligible for PrEP (29). At the current FSS price of $16 600 per year (2018 U.S. dollars) for branded F/TAF (20), a nationwide PrEP program using this agent would consume the entire $900.8 million federal budget for HIV prevention several times over (28). The relevance of a soon-anticipated generic F/TDF option will be apparent to insurers and other payers, who must decide whether the improved safety of F/TAF justifies its premium price (30). Patients and providers may need to be convinced that this also matters to them: that higher costs may decrease both access and long-term adherence to PrEP, and that the risk for attrition due to higher costs needs to be weighed against any safety benefits of switching to F/TAF.

The DISCOVER trial demonstrated statistically significant differences between F/TAF and F/TDF in surrogate markers of bone and renal safety (3). We sought to quantify how those differences in intermediate markers might translate into meaningful clinical outcomes, in order to understand the magnitude and relevance of these outcomes and how much payers, and society more broadly, should be willing to pay for them. Using the methods of cost-effectiveness analysis with input parameter assumptions that cast F/TAF in a highly favorable light, we found that a markup for F/TAF of up to $370 over the price of generic F/TDF ($8300) could be justified on the basis of those toxicity differences. This implies that, in the presence of a generic alternative, the current price of F/TAF ($16 600 per year) would have to be reduced by over $7900 per year for F/TAF to satisfy generally accepted standards of societal value. If F/TDF can achieve the 75% price reduction that is commonly observed when generic competition ensues (that is, a cost of $4150 per year), the F/TAF price would need to be no higher than $4520 to demonstrate value on the basis of cost-effectiveness. For older patients at unusually high risk for renal disease or bone-related adverse events, the switch from F/TDF to F/TAF would have greater clinical effect and benefit. Even in this population, however, it would be difficult to defend a price greater than $800 over the cost of the generic alternative.

We also find that it is the cost of the drug, more than the frequency or cost of adverse events, that is likely to limit PrEP use and access. At half the drug cost of F/TAF, PrEP with F/TDF could cover about twice the number of people on any given budget. Because DISCOVER demonstrated that the incidence of HIV is 4-fold higher among people not receiving PrEP compared with people receiving it, excess drug costs, resulting in decreased PrEP coverage, potentially translate into the lost opportunity to prevent tens of thousands of new HIV infections.

For almost a decade, F/TDF has been a mainstay of HIV prevention and has been repeatedly shown to be safe, effective, and cost-effective when used as PrEP in high-risk populations (14, 31, 32). The economic value of F/TDF will increase, as emtricitabine loses patent protection and coformulated generic alternatives become available. The successful track record of prevention with F/TDF explains why the recent approval of F/TAF for PrEP has generated such important discussion. Since its approval in October 2019, F/TAF has captured 25% of the market for PrEP prescriptions, and the manufacturer expects 40% to 45% of individuals receiving PrEP to have been switched to F/TAF before generic F/TDF becomes available (33). Anecdotal evidence suggests that many providers are actively switching their PrEP patients to the newest available option, F/TAF, in the absence of any clinically meaningful changes in renal and bone markers while receiving F/TDF. A recent study using data from the Swiss HIV Cohort Study found that switches to F/TAF for HIV treatment occurred in over 50% of patients without any indication for change (34). Investigators in that study cited risks for TDF toxicity as a reason to change the regimen, including eGFR less than 60 mL/min per 1.73 m^2, marked proteinuria, or osteoporosis (as measured by T-score or fragility fractures). Payers are also contemplating who might benefit by initiating PrEP with, or switching to, an agent that has not been shown to be more effective in preventing HIV infection and that offers statistically significant but very small improvements in surrogate markers of safety, at brand-name prices.

Our study has limitations. First, each assumption and uncertain data parameter underlying our analysis was selected to cast F/TAF in the best possible light. In addition to presenting extreme values for bone and renal effects beyond those that have ever been reported—both from a clinical and cost perspective—we intentionally excluded the potential beneficial effects of F/TDF compared with F/TAF. Although hypertension and diabetes are often cited as reasons to favor the renal benefits of F/TAF, mounting evidence suggests the comparatively detrimental effects of F/TAF on lipid profiles, weight gain, and risk for atherosclerotic cardiovascular disease (23, 24). Had we chosen to include these effects in this analysis, the justifiable premium for F/TAF would have been reduced even further.

Second, although we considered a 5-year horizon and daily, rather than on-demand, PrEP, we recognize that consumers may come on and off PrEP on the basis of need and may choose on-demand options. To the extent that adverse events and drug costs are similarly proportional to use, we believe our findings are generalizable to those circumstances.

Third, pricing variables are based on FSS prices available to federal purchasers, which may differ from list prices and net prices of the highly variable discounts or rebates that accrue to Medicaid, commercial insurers, and safety-net providers. Fourth, this analysis does not address barriers to PrEP beyond drug costs, such as stigma, insurance coverage, or other social determinants, nor does it account for public and private programs subsidizing PrEP drug access for uninsured individuals. Finally, we highlight that these findings may not be generalizable to other PrEP-using populations, including cis- or transgender women and people who inject drugs.

In conclusion, PrEP is a key pillar of the U.S. plans to end the HIV epidemic. Generic F/TDF could greatly expand PrEP coverage among the most price-sensitive members of the at-risk population. If branded F/TAF drives out generic F/TDF and inhibits acceptability, access, and uptake, overall rates of PrEP coverage in the at-risk population could decrease, and F/TAF could end up causing more avoidable HIV transmissions than it prevents.

Use of F/TDF for PrEP is effective, cost-effective, and safe; soon, it will also be much less expensive. At current F/TAF prices, F/TAF compared with generic F/TDF will not be cost-effective in the United States, even in populations at highest risk for F/TDF adverse events. Given the very small, albeit statistically significant, differences in surrogate markers, without evidence of clinical significance, there is no urgency and no reason to switch PrEP regimens now, and it would be hard to switch back later. In about a year, when F/TDF is generically available, payers should consider the $370 premium ceiling estimated here in assessing whether to recommend that patients switch to F/TAF.

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Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Massachusetts General Hospital Executive Committee on Research.

Financial Support: By the National Institute of Allergy and Infectious Diseases (R01 AI042006), National Institute on Drug Abuse (R37 DA015612), and National Institute of Mental Health (R01 MH105203), and the Massachusetts General Hospital Executive Committee on Research (Steve and Deborah Gorlin Research Scholars Award to Dr. Walensky).

Disclosures: Dr. Walensky reports grants from the National Institute of Allergy and Infectious Diseases (NIAID) and the Massachusetts General Hospital Executive Committee on Research: Steve and Deborah Gorlin Research Scholars Award during the conduct of the study. Dr. Freedberg reports grants from NIAID during the conduct of the study and grants from NIAID, the French National Agency for Research on AIDS,

UNITAID, and the National Institute of Mental Health (NIMH) outside the submitted work. Ms. McCann reports grants from NIAID during the conduct of the study. Dr. Paltiel reports grants from National Institute on Drug Abuse and NIMH during the conduct of the study. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-3478.

Reproducible Research Statement: *Study protocol:* None required. *Statistical code:* Portions are available through written agreements by contacting Dr. Walensky (e-mail, rwalensky@mgh.harvard.edu) and Dr. Paltiel (e-mail, david.paltiel@yale.edu). *Data set:* All data used in this analysis were obtained from publicly available, published, or online sources. The relevant publication and URLs for each source appear in the References section.

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