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MAJOR ARTICLE

Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide for Human Immunodeficiency Virus Preexposure Prophylaxis at a Boston Community Health Center

Julia L. Marcus,[1,2] Kenneth Levine,[2] Whitney C. Sewell,[1] Patricia Solleveld,[1,3] Kenneth H. Mayer,[2,3] and Douglas S. Krakower[1,2,3]

[1]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA, [2]The Fenway Institute, Boston, Massachusetts, USA, and [3]Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA

Background. Efforts to end the human immunodeficiency virus (HIV) epidemic may be threatened if limited preexposure prophylaxis (PrEP) resources are funneled from tenofovir disoproxil fumarate with emtricitabine (TDF/FTC) to tenofovir alafenamide with emtricitabine (TAF/FTC) without proportional clinical benefits.

Methods. The study population was patients at a Boston community health center who were assigned male sex at birth, aged ≥18 years, and prescribed TDF/FTC for PrEP in the 12 months before TAF/FTC approval (October 2019). We determined the frequency of switching to TAF/FTC in the 12 months after approval, including clinically indicated switching (ie, creatinine clearance <60 mL/minute or reduced bone density), potentially unnecessary switching (ie, no indications for switching and no cardiovascular risk factors), and potentially harmful switching (ie, no indications for switching and either obesity or dyslipidemia).

Results. Of 2892 TDF/FTC users, mean age was 38 years, 96.0% were cisgender men, and 78.9% were white. A total of 343 (11.9%) switched to TAF/FTC. Based on documented renal, bone, and cardiovascular risk factors, we identified 24 (7.0%) with clinically indicated switching, 271 (79.0%) with potentially unnecessary switching, and 48 (14.0%) with potentially harmful switching. When indications for switching additionally included hypertension, diabetes, and creatinine clearance 60–70 mL/minute, 27.1% of switching was clinically indicated.

Conclusions. Few who switched to TAF/FTC had documented indications for switching, although some appear to have been switched in anticipation of indications developing. As generic TDF/FTC is further discounted, provider education and patient decision aids are needed to facilitate selection of PrEP medications that is both clinically sound and cost-effective.

Keywords. human immunodeficiency virus; men who have sex with men; preexposure prophylaxis; tenofovir alafenamide; tenofovir disoproxil fumarate.

Tenofovir disoproxil fumarate, in a single pill with emtricitabine (TDF/FTC), virtually eliminates human immunodeficiency virus (HIV) transmission when taken daily as preexposure prophylaxis (PrEP) [1]. In October 2019, the United States (US) Food and Drug Administration (FDA) approved tenofovir alafenamide with emtricitabine (TAF/FTC) to reduce the risk of HIV transmission during sex, excluding populations who are at risk through receptive vaginal sex, in whom clinical studies are ongoing. The DISCOVER study found that TAF/FTC was noninferior to TDF/FTC in decreasing HIV incidence among cisgender men who have sex with men and transgender women, and that both medications are extremely safe when used as PrEP, with TDF/FTC associated with small decreases in renal glomerular function biomarkers and bone mineral density and TAF/FTC associated with minor weight gain and dyslipidemia [2, 3]. Those incremental differences in laboratory markers did not translate into differences in adverse clinical events in the DISCOVER study. However, TAF/FTC is now recommended for people with an estimated creatinine clearance (CrCl) <60 mL/minute, which is the minimum threshold for use of TDF/FTC [2, 4, 5]. Clinicians may also preferentially prescribe TAF/FTC for people with reduced bone density or with comorbidities, such as hypertension and diabetes, that increase the risk of renal dysfunction. Alternatively, some clinicians or patients may prefer TDF/FTC in the setting of higher body mass index (BMI) or dyslipidemia.

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Correspondence: Julia Marcus, PhD, MPH, Department of Population Medicine, Harvard Medical School, 401 Park Dr, Ste 401, Boston, MA 02215, USA (julia_marcus@harvardpilgrim.org).

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Despite evidence to the contrary, Gilead Sciences—which manufactures TDF/FTC (Truvada) and TAF/FTC (Descovy)—has claimed that TAF/FTC is safer [6] and has higher prevention efficacy [7] for PrEP, and has intensively marketed TAF/FTC to clinicians and potential consumers. As a result, clinicians and patients may favor switching from TDF/FTC to TAF/FTC, or initiating PrEP with TAF/FTC, even when a patient's history suggests that TDF/FTC would be clinically equivalent or potentially beneficial. Generic TDF/FTC became available in the US in October 2020 [8] and was initially priced about 15% lower than Truvada and Descovy, at $1455 per month compared with $1600–$1800 per month. Even when considering the greatest possible clinical benefits of TAF/FTC, Walensky et al found that the potential benefits of TAF/FTC mean that it should cost no more than an additional $370 per year relative to generic TDF/FTC when used as PrEP [9], a threshold already exceeded with only the modest initial discount to generic TDF/FTC. After a 6-month exclusivity period for the first manufacturer of generic TDF/FTC, multiple manufacturers began offering generic versions of TDF/FTC in April 2021, driving list prices as low as $30 per month and further widening the cost differential between TDF/FTC and TAF/FTC [10].

Efforts to end the HIV epidemic may be threatened if limited resources are funneled to TAF/FTC without proportional clinical benefits [11], but there are limited data on postapproval use of TAF/FTC. We evaluated the frequency and predictors of switching from TDF/FTC to TAF/FTC in the first 12 months of TAF/FTC availability at the largest PrEP provider in New England.

METHODS

Fenway Health is a Boston community health center that specializes in care for sexual and gender minorities. Our study population included people who were assigned male sex at birth, were at least 18 years of age, were prescribed TDF/FTC for PrEP at Fenway Health in the 12 months before FDA approval of TAF/FTC for PrEP in October 2019, and had at least 1 PrEP prescription in the 12 months after FDA approval. We followed this cohort of TDF/FTC users from October 2019 until TAF/FTC prescription, HIV diagnosis, or 30 September 2020, whichever occurred first.

The primary outcome of our analysis was switching to TAF/FTC in the first 12 months of availability, as identified by prescriptions in electronic health record (EHR) data. To identify factors associated with switching, we extracted data on demographic characteristics (ie, age, gender, race, ethnicity, insurance type), vital statistics (ie, height and weight), diagnoses (ie, sexually transmitted infections [STIs], bone-related conditions, hypertension, diabetes mellitus), and laboratory test results (ie, lipids, creatinine). For height and weight, we used the most recent measurements prior to October 2019 to compute BMI. For STIs, we included any diagnosis of gonorrhea, chlamydia, or syphilis in the 12 months prior to October 2019. For lipids and creatinine, we extracted the most recent measurements in the 12 months prior to October 2019, and used the Cockcroft-Gault formula to estimate CrCl [12]. For bone-related conditions, we included any diagnoses prior to October 2019 that were suggestive of reduced bone density, including osteoporosis, osteopenia, and pathological or stress fractures. For hypertension and diabetes mellitus, we included any diagnoses prior to October 2019.

We used descriptive statistics to characterize the demographic and clinical characteristics of people using TDF/FTC, and computed the overall proportion who switched to TAF/FTC. Switching to TAF/FTC was defined as follows: clinically indicated for those with documented CrCl <60 mL/minute or reduced bone density; potentially unnecessary for those without documented CrCl <60 mL/minute or reduced bone density and with no documented cardiovascular risk factors; or potentially harmful for those without documented CrCl <60 mL/minute or reduced bone density and with at least 1 documented cardiovascular risk factor (ie, BMI ≥30 kg/m^2, total cholesterol ≥200 mg/dL, low-density lipoprotein cholesterol [LDL-c] >160 mg/dL, or high-density lipoprotein cholesterol [HDL-c] <40 mg/dL). Remaining on TDF/FTC was defined as clinically indicated for those without documented CrCl <60 mL/minute or reduced bone density, and potentially harmful for those with documented CrCl <60 mL/minute or reduced bone density. We also assessed the proportion that would have been defined as having clinical indications for switching if indications additionally included hypertension, diabetes, and CrCl 60–70 mL/minute, all of which may presage the development of CrCl <60 mL/minute.

We used Cox proportional hazards regression to identify factors associated with time to switching to TAF/FTC, estimating unadjusted and age-adjusted hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for each covariate of interest. We excluded respondents from analyses if data were missing for a given variable. Other than age adjustment, we did not conduct multivariable analyses to adjust for confounding because our goal was to describe clinical decision making rather than isolate a specific causal effect [13]. To assess whether patterns of PrEP use during the coronavirus disease 2019 (COVID-19) pandemic had influenced our results [14], we conducted a sensitivity analysis with follow-up only through 23 March 2020, the day that stay-at-home orders were implemented in Massachusetts. Analyses were conducted in SAS version 9.4 software (SAS Institute, Cary, North Carolina).

Patient Consent Statement

The institutional review board at Harvard Pilgrim Health Care Institute determined this study to be exempt from review according to federal regulations.

RESULTS

A total of 2892 people were prescribed TDF/FTC in the 12 months before FDA approval of TAF/FTC in October 2019, and had at least 1 PrEP prescription in the 12 months after FDA approval. Mean age was 38 years (range, 18–83 years) and most (96.0%) were cisgender men (Table 1). Most were white (78.9%), 6.3% were Black or African American, 6.1% were multiracial, and 5.7% were Asian; 14.8% were Hispanic. Nearly all (98.3%) had health insurance, with 84.5% privately insured. In the 12 months prior to TAF/FTC approval, 14.5% were diagnosed with an STI. Few (0.6%) had a prior diagnosis indicative of reduced bone density, 11.3% had hypertension, and 3.0% had diabetes mellitus. Of the 86.9% with documented height and weight in the 12 months prior to TAF/FTC approval, mean BMI was 27 kg/m^2 (standard deviation [SD], 5.0 kg/m^2). Of the 84.0% with a creatinine measurement in the 12 months prior to TAF/FTC approval, mean CrCl was 101 mL/minute (SD, 22.3 mL/minute) and 1.8% had a CrCl <60 mL/minute. Of the 33.5% with lipid measurements in the 12 months prior to TAF/FTC approval, mean total cholesterol was 174 mg/dL (SD, 36.1 mg/dL), mean LDL-c was 104 mg/dL (SD 30.4 mg/dL), and mean HDL-c was 47 mg/dL (SD, 13.2 mg/dL).

Table 1. Characteristics of People Prescribed Tenofovir Disoproxil Fumarate/Emtricitabine in the 12 Months Prior to Tenofovir Alafenamide/Emtricitabine Approval, Fenway Health, 1 October 2018–30 September 2019

Characteristic	No. (%)[a]
Total	2892 (100)
Age, y, mean (SD)	38 (11.2)
Gender	
Cisgender man	2774 (96.0)
Transgender woman	42 (1.5)
Another gender	40 (1.4)
Nonbinary	34 (1.2)
Race	
White	2108 (78.9)
Black or African American	167 (6.3)
Multiracial	163 (6.1)
Asian	153 (5.7)
Another race	52 (2.0)
Native Hawaiian or other Pacific Islander	16 (0.6)
American Indian or Alaska Native	14 (0.5)
Hispanic	388 (14.8)
Insurance	
Private	2439 (84.5)
Medicaid	290 (10.1)
Medicare	61 (2.1)
Uninsured	49 (1.7)
Other public	47 (1.6)
STI diagnosis[b]	420 (14.5)
Reduced bone density[c]	16 (0.6)
Hypertension[c]	327 (11.3)
Diabetes mellitus[c]	88 (3.0)
BMI[d], kg/m^2, mean (SD)	27 (5.0)
CrCl[e], mL/min, mean (SD)	101 (22.3)
Total cholesterol[e], mg/dL, mean (SD)	174 (36.1)
LDL-c[e], mg/dL, mean (SD)	104 (30.4)
HDL-c[e], mg/dL, mean (SD)	47 (13.2)

Missing data were <0.1% for gender, 7.6% for race, 9.3% for ethnicity, 0.2% for insurance, 13.1% for BMI, 16.0% for CrCl, and 66.5% for lipids.

Abbreviations: BMI, body mass index; CrCl, creatinine clearance; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SD, standard deviation; STI, sexually transmitted infection.

[a]Data are presented as No. (column %) unless otherwise indicated.

[b]STI diagnosis included syphilis, gonorrhea, or chlamydia in the 12 months prior to October 2019.

[c]Reduced bone density, hypertension, and diabetes mellitus were based on any diagnoses prior to October 2019.

[d]BMI was based on the most recent body weight and height prior to October 2019.

[e]Creatinine and lipids were the most recent in the 12 months prior to October 2019.

In the first 12 months of TAF/FTC availability, a total of 343 (11.9%) switched from TDF/FTC to TAF/FTC. Based on documented renal, bone, and cardiovascular risk factors, we identified 24 (7.0%) with clinically indicated switching to TAF/FTC, 271 (79.0%) with potentially unnecessary switching, and 48 (14.0%) with potentially harmful switching. Among those who did not switch to TAF/FTC, we identified 2514 (98.6%) for whom remaining on TDF/FTC was clinically indicated and 35 (1.4%) for whom remaining on TDF/FTC was potentially harmful. If hypertension, diabetes, and CrCl 60–70 mL/minute were additionally considered clinical indications for switching to TAF/FTC, the proportion with clinical indications increased from 7.0% to 27.1% of those who switched.

In unadjusted Cox regression models, the risk of switching increased with age; people aged 60 years or older had a 2.6-fold (95% CI, 1.7- to 3.8-fold) higher risk of switching to TAF/FTC compared with those younger than 30 years (Table 2). The risk of switching to TAF/FTC was also higher among people who were Hispanic compared with those who were not Hispanic (HR, 1.4 [95% CI, 1.0–1.8]), among people with Medicare compared with those who were privately insured (HR, 2.0 [95% CI, 1.2–3.4]), among those with CrCl <60 mL/minute (HR, 5.2 [95% CI, 3.5–7.9]), and among those with hypertension (HR, 1.6 [95% CI, 1.2–2.1]) or diabetes mellitus (HR, 2.2 [95% CI, 1.4–3.3]). The risk of switching to TAF/FTC was lower among people with total cholesterol ≥200 mg/dL compared with those with total cholesterol <180 mg/dL (HR, 0.4 [95% CI, .2–.7]) and among people with LDL-c between 101 mg/dL and 160 mg/dL compared with those with ≤100 mg/dL (HR, 0.6 [95% CI, .4–.9]). The frequency of switching to TAF/FTC was greater among people with reduced bone density, though CIs were wide (HR, 1.6 [95% CI, .5–5.0]). Gender, race, STI diagnosis, BMI, and HDL-c were not associated with switching to TAF/FTC. Results were similar in age-adjusted models, except that Medicare insurance and hypertension were no longer significantly associated with switching. Results were also similar when follow-up was truncated prior to the implementation of COVID-19–related restrictions (Supplementary Table 1).

Table 2. Factors Associated With Switching from Tenofovir Disoproxil Fumarate/Emtricitabine to Tenofovir Alafenamide/Emtricitabine, Fenway Health, 1 October 2019–30 September 2020

Factor	Did Not Switch to TAF/FTC	Switched to TAF/FTC	Unadjusted HR (95% CI)	Age-Adjusted HR (95% CI)
No. (row %)	2549 (88.1)	343 (11.9)	…	…
Age, y				
<30	658 (90.3)	71 (9.7)	ref	…
30–39	960 (89.1)	117 (10.9)	1.1 (.8–1.5)	…
40–49	471 (88.0)	64 (12.0)	1.2 (.9–1.7)	…
50–59	354 (85.9)	58 (14.1)	**1.5 (1.0–2.1)**	…
≥60	106 (76.3)	33 (23.7)	**2.6 (1.7–3.8)**	…
Gender				
Cisgender man	2445 (88.1)	329 (11.9)	ref	ref
Transgender woman	36 (85.7)	6 (14.3)	1.2 (.5–2.6)	1.4 (.6–3.1)
Another gender	34 (85.0)	6 (15.0)	1.3 (.6–2.9)	1.4 (.6–3.0)
Nonbinary	32 (94.1)	2 (5.9)	0.5 (.1–1.9)	0.6 (.1–2.4)
Race				
White	1865 (88.5)	243 (11.5)	ref	ref
Black or African American	144 (86.2)	23 (13.8)	1.2 (.8–1.9)	1.3 (.9–2.1)
Multiracial	143 (87.7)	20 (12.3)	1.1 (.7–1.7)	1.2 (.7–1.9)
Asian	134 (87.6)	19 (12.4)	1.1 (.7–1.7)	1.2 (.8–2.0)
Another race	45 (86.5)	7 (13.5)	1.2 (.6–2.6)	1.3 (.6–2.8)
Native Hawaiian or other Pacific Islander	15 (93.8)	1 (6.3)	0.5 (.1–4.0)	0.5 (.1–3.9)
American Indian or Alaska Native	14 (100.0)	0 (0.0)	…	…
Ethnicity				
Not Hispanic	1990 (89.0)	246 (11.0)	ref	ref
Hispanic	332 (85.6)	56 (14.4)	**1.4 (1.0–1.8)**	**1.4 (1.1–1.9)**
Insurance				
Private	2154 (88.3)	285 (11.7)	ref	ref
Medicaid	254 (87.6)	36 (12.4)	1.1 (.8–1.5)	1.1 (.8–1.5)
Medicare	47 (77.1)	14 (23.0)	**2.0 (1.2–3.4)**	1.5 (.9–2.6)
Uninsured	43 (87.8)	6 (12.2)	1.0 (.5–2.3)	1.1 (.5–2.4)
Other public	45 (95.7)	2 (4.3)	0.4 (.1–1.4)	0.4 (.1–1.4)
STI diagnosis[a]				
No	2187 (88.5)	285 (11.5)	ref	ref
Yes	362 (86.2)	58 (13.8)	1.2 (.9–1.6)	1.3 (1.0–1.7)
Reduced bone density[b]				
No	2536 (88.2)	340 (11.8)	ref	ref
Yes	13 (81.3)	3 (18.8)	1.6 (.5–5.0)	1.4 (.5–4.1)
Hypertension[b]				
No	2277 (88.8)	288 (11.2)	ref	ref
Yes	272 (83.2)	55 (16.8)	**1.6 (1.2–2.1)**	1.3 (1.0–1.8)
Diabetes mellitus[b]				
No	2482 (88.5)	322 (11.5)	ref	ref
Yes	67 (76.1)	21 (23.9)	**2.2 (1.4–3.3)**	**1.8 (1.1–2.8)**
BMI[c], kg/m^2				
<18.5	20 (95.2)	1 (4.8)	0.4 (.1–3.0)	0.5 (.1–3.7)
18.5–24.9	905 (88.0)	123 (12.0)	1.1 (.8–1.5)	1.2 (.9–1.7)
25.0–29.9	839 (86.3)	133 (13.7)	1.3 (.9–1.8)	1.3 (.9–1.8)
≥30.0	439 (89.2)	53 (10.8)	ref	ref
CrCl[d], mL/min				
<60	22 (50.0)	22 (50.0)	**5.2 (3.5–7.9)**	**4.3 (2.7–6.8)**
≥60	2102 (88.1)	283 (11.9)	ref	ref
Total cholesterol[d], mg/dL				
<180	450 (84.4)	83 (15.6)	ref	ref
180–199	199 (89.6)	23 (10.4)	0.7 (.4–1.0)	0.7 (.4–1.0)
≥200	199 (93.0)	15 (7.0)	**0.4 (.2–.7)**	**0.4 (.2–.7)**
LDL-c[d], mg/dL				
≤100	384 (82.2)	83 (17.8)	ref	ref
101–160	426 (88.6)	55 (11.4)	**0.6 (.4–.9)**	**0.6 (.4–.9)**

Table 2. Continued

Factor	Did Not Switch to TAF/FTC	Switched to TAF/FTC	Unadjusted HR (95% CI)	Age-Adjusted HR (95% CI)
>160	38 (84.4)	7 (15.6)	0.9 (.4–1.9)	0.9 (.4–1.9)
HDL-c[d], mg/dL				
<40	233 (87.9)	32 (12.1)	ref	ref
40–59	450 (86.0)	73 (14.0)	1.2 (.8–1.8)	1.2 (.8–1.9)
≥60	163 (91.6)	15 (8.4)	0.7 (.4–1.3)	0.7 (.4–1.3)

Data are presented as No. (%) unless otherwise indicated. Values in bold indicate $P < .05$. Missing data were <0.1% for gender, 7.6% for race, 9.3% for ethnicity, 0.2% for insurance, 13.1% for BMI, 16.0% for CrCl, and 66.5% for lipids.

Abbreviations: BMI, body mass index; CI, confidence interval; CrCl, creatinine clearance; HDL-c, high-density lipoprotein cholesterol; HR, hazard ratio; LDL-c, low-density lipoprotein cholesterol; STI, sexually transmitted infection; TAF/FTC, tenofovir alafenamide with emtricitabine.

[a]STI diagnosis included syphilis, gonorrhea, or chlamydia in the 12 months prior to October 2019.

[b]Reduced bone density, hypertension, and diabetes mellitus were based on any diagnoses prior to October 2019.

[c]BMI was based on the most recent body weight and height prior to October 2019.

[d]Creatinine and lipids were the most recent in the 12 months prior to October 2019.

DISCUSSION

In this study of adults who were assigned male sex at birth and prescribed TDF/FTC at the largest PrEP-providing clinic in New England, 12% switched to TAF/FTC in the first 12 months of availability. Consistent with the known side-effect profiles of TDF/FTC and TAF/FTC, lower CrCl was associated with switching, while switching was less likely among those with higher total cholesterol or LDL-c. Most switching to TAF/FTC was potentially unnecessary based on documented renal, bone, and cardiovascular risk factors, although some patients appear to have been switched in anticipation of clinical indications developing, and others may have had indications for switching that were not documented. Overall, our results suggest that limited resources are being invested in TAF/FTC without obvious corresponding clinical benefits for most patients, with implications for the cost-effectiveness of PrEP in the US [11].

In a recent preliminary report, Hoover et al found that 29% of TDF/FTC users in a national prescription database switched to TAF/FTC during the first 6 months after FDA approval, and that 36% of new users were prescribed TAF/FTC [15]. Likewise, Gilead Sciences reported a 46% market share for Descovy for PrEP in the US at the end of 2020 [16], suggesting a high proportion of new PrEP users initiating TAF/FTC, a high frequency of switching from TDF/FTC to TAF/FTC, or both. There are several reasons that switching may be less frequent in our clinical setting compared with others. First, Fenway Health was a site for the DISCOVER study and nearly all primary care providers at Fenway have prescribed PrEP [17]. Switching to TAF/FTC may be more common in other clinical settings where prescribers have less familiarity with the evidence on the available medications for PrEP, including data on the robust safety and effectiveness of TDF/FTC [18] and the side effects associated with TAF/FTC [2, 3]. Second, patients at Fenway Health, including those in our cohort, are a largely non-Hispanic white and urban population, and the incidence of switching to TAF/FTC may be higher in other communities. Consistent with findings from Hoover et al, we observed more switching among Hispanic people compared with non-Hispanic people (11.3% vs 8.7%). Finally, only 1.8% of our study population had documentation of CrCl <60 mL/minute, and diagnoses of hypertension, diabetes mellitus, or bone-related conditions were also uncommon. Switching to TAF/FTC may be more frequent in populations with a higher prevalence of renal dysfunction, risk factors for renal dysfunction, or reduced bone density.

We found that lower CrCl was associated with switching to TAF/FTC, while dyslipidemia was associated with a reduced likelihood of switching. Switching to TAF/FTC was also more common among people with reduced bone density, although this association was not statistically significant given small numbers, and among those with diagnoses of hypertension or diabetes. TAF/FTC has been associated with weight gain, and TDF/FTC with weight loss, but we did not observe an association between BMI and switching in our cohort. Overall, our findings are consistent with the small decreases in renal glomerular function and bone density biomarkers associated with TDF/FTC use, and the small increases in dyslipidemia associated with TAF/FTC use. We also found that switching increased with age, reflecting the higher prevalence of renal dysfunction and reduced bone density at older ages. Older patients or their providers may also favor proactive switching to TAF/FTC before those conditions develop. Some TDF/FTC users in our cohort did not have documented creatinine or lipid testing in the 12 months prior to TAF/FTC approval; it is possible that some of those patients accessed laboratory testing outside of Fenway Health, with results accessible to clinicians but not included in the EHR data that we extracted. However, we expect that most test results that were missing from our analyses on creatinine or lipids were also unavailable to prescribers.

The associations of renal and cardiovascular risk factors with switching were reassuring, but most of the switching to TAF/FTC was potentially unnecessary based on documented risk factors. Some of the switching was potentially harmful, although

the body weight and lipid changes among people using TAF/FTC for PrEP have not yet been associated with clinical events [2, 3]. We also identified missed opportunities for switching, with a small proportion of those remaining on TDF/FTC having CrCl <60 mL/minute or reduced bone density. Some patients who switched to TAF/FTC had hypertension or diabetes mellitus, which placed them at higher risk for renal dysfunction, or had CrCl that was close to the threshold of <60 mL/minute. Although those patients did not meet our definition of having a clinical indication for switching, they may have switched in anticipation of such an indication developing. Large observational studies of PrEP users are needed on the rates of progression from hypertension, diabetes, and CrCl 60–70 mL/minute to CrCl <60 mL/minute to elucidate whether such anticipatory switching is warranted. Longitudinal studies of large cohorts of PrEP users can also determine whether switching to TAF/FTC is associated with clinical benefits in the setting of either existing or anticipated clinical indications.

Patients or providers may prefer one PrEP medication over the other independent of clinical indications. Some patients may have asked to switch to TAF/FTC for reasons that we could not assess in structured EHR data, such as novelty, smaller pill size, or perceiving TAF/FTC to have superior efficacy or safety compared with TDF/FTC. Qualitative research could further elucidate reasons why patients and providers prefer TDF/FTC or TAF/FTC. Provider education and patient decision aids that incorporate all the available evidence on safety, effectiveness, and costs could help facilitate decision-making about which PrEP medications—or modalities, as long-acting PrEP becomes available—will best meet patients' needs and preferences [19–21].

Ideally, prescribing decisions would be driven primarily by clinical indications and patient preferences, but the high cost of branded PrEP medications is likely to influence decisions about which medication to use, just as it has influenced PrEP uptake, adherence, and persistence over the past 9 years [22–26]. Out-of-pocket payments for PrEP increased 14.9% annually during 2014–2018, with the highest out-of-pocket payments in the South, which accounts for a disproportionate share of new HIV infections [27]. Assistance programs—including those run by Gilead Sciences, Teva Pharmaceuticals (the first manufacturer of generic TDF/FTC), the federal government, and some states—have covered out-of-pocket costs of PrEP medications for some users [28]. However, not everyone has been eligible for those programs, and the challenge of navigating the patchwork of financing mechanisms has posed its own barrier to PrEP access [29, 30]. As of July 2021, health plans are now required to cover all out-of-pocket costs for at least one PrEP medication, as well as associated provider visits and laboratory testing, as a result of the grade A recommendation for PrEP by the US Preventive Services Task Force [31]. Implementation of the Task Force's recommendation could mitigate some of the cost-related barriers to PrEP for patients, but it will not relieve the costs shouldered by the health care system.

Given the robust evidence base and cost-effectiveness of TDF/FTC, some community advocates, health departments, clinicians, and researchers have recommended that TDF/FTC remain first-line for PrEP [11, 32]. To minimize costs to payers, some major insurers have required prior authorization before covering the use of TAF/FTC, while generic TDF/FTC is covered without prior authorization or any out-of-pocket costs [33]. However, the reportedly large market share of Descovy for PrEP suggests that the impact of such efforts to discourage clinically unnecessary use of TAF/FTC has been limited. The emergence of discounted generic TDF/FTC could facilitate broader and more equitable access to PrEP, but whether this benefit is realized will depend on the complexities of a fragmented health care system (eg, the 340B Drug Pricing Program for community-based clinics [10]) and the extent to which positive marketing about TAF/FTC—and negative advertising about TDF/FTC—succeed in depicting TAF/FTC as a superior medication for PrEP [11, 34, 35].

Our study provides initial data from a PrEP-experienced community health center on the frequency and predictors of switching from TDF/FTC to TAF/FTC for PrEP. Switching was infrequent in our cohort, but it may be more common in different patient populations, in clinical settings where providers are less knowledgeable about PrEP, and as the COVID-19 pandemic eases and PrEP use resumes. Among those who switched to TAF/FTC in our cohort, few had a documented clinical indication to do so, although some patients appear to have been switched in anticipation of indications developing, and others may have had indications for switching that were not documented. Overall, our results suggest that the increasing use of TAF/FTC for PrEP may inflate costs to the health care system without proportional improvements in clinical outcomes for most patients. In 2018, the US health care system spent at least $2.1 billion on PrEP, while covering only 18% of people who could benefit from it [27]. With generic formulations of TDF/FTC now available and deeply discounted, efforts are needed to ensure that providers' and patients' shared decisions about PrEP medications are both clinically sound and cost-effective.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. D. S. K. and J. L. M. conceived the study. K. L. and P. S. assisted with data extraction. J. L. M. analyzed the data and drafted the manuscript. All authors contributed to interpretation of the data, critically

revised the manuscript for important intellectual content, and approved the final version of the manuscript for submission.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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