

Received: 31 March 2023; revised: 2 October 2023; accepted: 11 October 2023.

References

- Griffith SA, McCoy LE. **To bnAb or not to bnAb: defining broadly neutralising antibodies against HIV-1.** *Front Immunol* 2021; **12**:708227.
- Caskey M. **Broadly neutralizing antibodies for the treatment and prevention of HIV infection.** *Curr Opin HIV AIDS* 2020; **15**:49–55.
- Parsons MS, Chung AW, Kent SJ. **Importance of Fc-mediated functions of anti-HIV-1 broadly neutralizing antibodies.** *Retrovirology* 2018; **15**:58.
- Burton DR, Mascola JR. **Antibody responses to envelope glycoproteins in HIV-1 infection.** *Nat Immunol* 2015; **16**:571–576.
- Mendoza P, Gruell H, Nogueira L, Pai JA, Butler AL, Millard K, et al. **Combination therapy with anti-HIV-1 antibodies maintains viral suppression.** *Nature* 2018; **561**:479–484.
- Gaebler C, Nogueira L, Stoffel E, Oliveira TY, Breton G, Millard KG, et al. **Prolonged viral suppression with anti-HIV-1 antibody therapy.** *Nature* 2022; **606**:368–374.
- Sneller MC, Blazkova J, Justement JS, Shi V, Kennedy BD, Gittens K, et al. **Combination anti-HIV antibodies provide sustained virological suppression.** *Nature* 2022; **606**:375–381.
- Scheid JF, Horwitz JA, Bar-On Y, Kreider EF, Lu CL, Lorenzi JC, et al. **HIV-1 antibody 3BNC117 suppresses viral rebound in humans during treatment interruption.** *Nature* 2016; **535**:556–560.
- Bar-On Y, Gruell H, Schoofs T, Pai JA, Nogueira L, Butler AL, et al. **Safety and antiviral activity of combination HIV-1 broadly neutralizing antibodies in viremic individuals.** *Nat Med* 2018; **24**:1701–1707.
- Caskey M, Klein F, Lorenzi JC, Seaman MS, West AP, Buckley N, et al. **Viraemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117.** *Nature* 2015; **522**:487–491.
- Caskey M, Schoofs T, Gruell H, Settler A, Karagounis T, Kreider EF, et al. **Antibody 10-1074 suppresses viremia in HIV-1-infected individuals.** *Nat Med* 2017; **23**:185–191.
- Chamberland A, Sylla M, Boulassel MR, Baril JG, Côté P, Thomas R, et al., Investigators of the Primary HIV-Infection Cohort of Montreal. **Effect of antiretroviral therapy on HIV-1 genetic evolution during acute infection.** *Int J STD AIDS* 2011; **22**:146–150.
- Ananworanich J, Chomont N, Eller LA, Kroon E, Tovanabutra S, Bose M, et al., RV217 and RV254/SEARCH010 study groups. **HIV DNA set point is rapidly established in acute HIV infection and dramatically reduced by early ART.** *EBioMedicine* 2016; **11**:68–72.
- Evering TH, Mehandru S, Racz P, Tenner-Racz K, Poles MA, Figueroa A, et al. **Absence of HIV-1 evolution in the gut-associated lymphoid tissue from patients on combination antiviral therapy initiated during primary infection.** *PLoS Pathogens* 2012; **8**:e1002506.
- Song H, Bose M, Pinyakorn S, Sanders-Buell E, O'Sullivan AM, Silas D, et al. **Dynamics of human immunodeficiency virus-1 genetic diversification during acute infection.** *Open Forum Infect Dis* 2020; **7**:ofaa429.
- Crowell TA, Ritz J, Coombs RW, Zheng L, Eron JJ, Mellors JW, et al., AIDS Clinical Trials Group A5354/EARLIER (Early ART to Limit Infection and Establishment of Reservoir) Study Team. **Novel criteria for diagnosing acute and early human immunodeficiency virus infection in a multinational study of early antiretroviral therapy initiation.** *Clin Infect Dis* 2021; **73**:e643–e651.
- Moldt B, Parvangada A, Martin R, Pace C, Balakrishnan M, Thomsen ND, et al. **Evaluation of broadly neutralizing antibody sensitivity by genotyping and phenotyping for qualifying participants to HIV clinical trials.** *J Acquir Immune Defic Syndr* 2021; **88**:61–69.
- Moldt B, Gunthard HF, Workowski KA, Little SJ, Eron JJ, Overton ET, et al. **Evaluation of HIV-1 reservoir size and broadly neutralizing antibody susceptibility in acute antiretroviral therapy-treated individuals.** *AIDS* 2022; **36**:205–214.

- Van Zyl GU, Katusiime MG, Wiegand A, McManus WR, Bale MJ, Halvas EK, et al. **No evidence of HIV replication in children on antiretroviral therapy.** *J Clin Invest* 2017; **127**:3827–3834.
- van Zyl G, Bale MJ, Kearney MF. **HIV evolution and diversity in ART-treated patients.** *Retrovirology* 2018; **15**:14.
- Leite TF, Delatorre E, Cortes FH, Ferreira ACG, Cardoso SW, Grinsztejn B, et al. **Reduction of HIV-1 reservoir size and diversity after 1 year of cART among Brazilian individuals starting treatment during early stages of acute infection.** *Front Microbiol* 2019; **10**:145.

DOI:10.1097/QAD.0000000000003792

OPEN

Trends in HIV preexposure prophylaxis utilization and spending among individuals with commercial insurance

Sean Dickson and Katelyn James

In a cross-sectional analysis of HIV preexposure prophylaxis (PrEP) utilization by commercially insured patients from 2019 to 2021, most prescriptions were for branded formulations of PrEP despite the availability of a generic version. Accounting for the modest relative clinical benefit of branded TAF/FTC (tenofovir alafenamide fumarate/emtricitabine) PrEP over generic TDF/FTC (tenofovir disoproxil fumarate/emtricitabine) PrEP, use of generic TDF/FTC PrEP would have reduced commercial insurers' spending by 33%.

Introduction

In October 2019, Descovy (tenofovir alafenamide fumarate/emtricitabine; TAF/FTC) received an indication for HIV prophylaxis, the second drug to do so following Truvada (tenofovir disoproxil fumarate/emtricitabine; TDF/FTC) [1]. Descovy is a prodrug of Truvada whose clinical development was delayed to coincide with the expiry of Truvada patents [1], a technique often called 'product-hopping [2]'. Descovy offers an extremely modest clinical improvement over TDF/FTC; switching all current preexposure prophylaxis (PrEP) patients from TDF/FTC to Descovy would generate a 5-year 0.1% increase in QALYs, meriting only a \$370 annual premium [3]. Generic TDF/FTC was released in August 2020; in 2021, list prices for generic TDF/FTC were less than \$1 per pill while branded Truvada cost \$61 and Descovy cost \$64 [4].

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Table 1. Characteristics of preexposure utilization and excess spending among patients with group commercial insurance in Healthcare Cost Institute Database, 2019–2021.

	2019	2020	2021
Patients with PrEP-eligible prescriptions ^a	34 561	31 966	37 316
Patients concurrently taking ART ^b	3307	2619	2425
Patients taking PrEP	31 254	29 347	34 891
PrEP patients at 340B providers (% of total)	1032 (3.3%)	1045 (3.6%)	1147 (3.3%)
National PrEP patients ^c	266 198	294 883	363 146
Percentage of national PrEP patients in sample	11.7%	10.0%	9.6%
Total PrEP units dispensed	5 772 440	5 422 402	6 492 732
Total PrEP spending	\$323 821 486	\$316 270 267	\$294 771 881
Descovy units dispensed (%) ^d	343 050 (5.9%)	2 248 332 (41.5%)	3,030,877 (46.7%)
Descovy spending	\$19 484 095	\$132 992 628	\$177 106 582
Descovy unit cost	\$56.80	\$59.15	\$58.43
Truvada units dispensed (%)	5 429 390 (94.1%)	2 837 387 (52.3%)	558 811 (8.6%)
Truvada spending	\$304 337 391	\$166 003 019	\$30 866 296
Truvada unit cost	\$56.05	\$58.51	\$55.24
Generic TDF/FTC units dispensed (%) ^e		336 683 (6.2%)	2 903 044 (44.7%)
Generic TDF/FTC spending		\$17 274 620	\$86 799 003
Generic TDF/FTC unit cost		\$51.31	\$29.90
Generic fill rate ^f		10.6%	83.9%
Cost-effective Descovy unit cost ^g			\$30.91
Excess PrEP spending (%) ^h			\$97 571 300 (33.1%)
Total 340B PrEP units dispensed (% of total) ⁱ	204 442 (3.5%)	207 431 (3.8%)	222 140 (3.4%)
340B Descovy units dispensed (%)	16 560 (8.1%)	114 892 (55.4%)	129 716 (58.4%)
340B Truvada units dispensed (%)	187 882 (91.9%)	85 442 (41.2%)	20 679 (9.3%)
340B Generic TDF/FTC units dispensed (%) ^e		7097 (3.4%)	71 745 (32.3%)
340B generic fill rate ^f		7.7%	77.6%

ART, antiretroviral therapy; HCCI, Healthcare Cost Institute; PrEP, preexposure prophylaxis.

^aIncluding Descovy (TAF/FTC), Truvada (TDF/FTC), or generic TDF/FTC.

^bAll patients receiving any additional antiretroviral therapy, per the USP Medicare Model Guidelines v8.0, at any point during the calendar year were excluded as likely using the PrEP-eligible formulations for HIV treatment.

^cData from Sullivan *et al.* [9].

^dDescovy was indicated for PrEP in October 2019.

^eGeneric TDF/FTC was first marketed in August 2020.

^fCalculated as units of generic TDF/FTC divided by the sum of Truvada units and generic TDF/FTC units.

^gCalculated as the sum of the unit cost of generic TDF/FTC plus the amortized annual cost-effectiveness premium for TAF/FTC, \$370.

^hCalculated as the difference between the observed unit cost of Descovy minus the cost-effective unit cost multiplied by Descovy units plus the observed unit cost of Truvada minus the observed unit cost of generic TDF/FTC multiplied by Truvada units.

ⁱThe 340B Program allows certain federally designated providers to purchase drugs a discount, generating revenue when those drugs are reimbursed by insurers at undiscounted rates. Discounts are greater on brand drugs than on generic drugs which has been hypothesized to affect prescribing choice.

Existing estimates of PrEP utilization are generally across market sectors [5]. This article presents the first disaggregation of PrEP utilization by formulation in the commercially insured market and estimates unnecessary spending on Truvada and Descovy instead of generic TDF/FTC. Prior commentary suggested 340B Program providers may over-prescribe Descovy instead of generic TDF/FTC because of greater revenue on the brand product [6]; we compare utilization by 340B status.

Methods

We used Healthcare Cost Institute (HCCI) claims data for employer-sponsored insurance to assess PrEP utilization from 2019 to 2021 by formulation. HCCI data includes approximately 55 million commercially insured individuals across all 50 states, about one-third of all individuals with employer-sponsored insurance [7]. We identified all patients with a claim for Descovy, Truvada, or generic

TDF/FTC in each year and omitted any patients who had any claims for a separate antiretroviral during the calendar year to exclude those under HIV treatment. We identified 340B claims by linking the prescriber practice location to the 340B covered entity database using an established method [8]. To estimate 2021 excess spending on Truvada and Descovy, we first established the cost-effective price for Descovy by amortizing the \$370 annual cost-effectiveness premium identified in the literature for TAF/FTC relative to TDF/FTC to the observed mean unit cost of generic TDF/FTC [3]. We note that the authors of this cost-effectiveness estimate for TAF/FTC over TDF/FTC describe it as ‘an extreme upper bound’ for the incremental value of TAF; therefore, we consider our estimates to be conservative. We then subtracted the cost-effective price for Descovy from the observed mean unit cost of Descovy and also subtracted the observed mean unit cost of generic TDF/FTC from the observed unit cost of Truvada; we then multiplied the excess per-unit costs by total units of Descovy and Truvada to estimate excess spending.

Results

In 2021, 37 316 sample patients used a PrEP formulation; 2425 had other antiretroviral use, leaving 34 891 sample patients (9.6% of national PrEP patients [9]) (Table 1). In 2021, 1147 (3.3%) of patients received PrEP from 340B providers.

In 2019, 5.9% of PrEP units dispensed were for Descovy, increasing to 41.5% in 2020 and 46.7% in 2021. Truvada units were 94.1% in 2019, falling to 52.3% in 2020 and 8.6% in 2021. Generic TDF/FTC grew from 6.2% of units in 2020 to 44.7% in 2021.

340B providers had higher rates of Descovy prescribing (58.4%) than providers overall in 2021. However, 340B providers only accounted for 3.4% of PrEP units dispensed in 2021.

Commercial insurers in the sample spent \$295 million on PrEP in 2021, with \$177 million spent on Descovy, \$31 million on Truvada and \$87 million on generic TDF/FTC (Table 1). Relative to the cost-effective premium on generic TDF/FTC, sample insurers overpaid \$83 million on Descovy (47.1%). Relative to the generic price, sample insurers overpaid \$14 million on Truvada (45.9%).

Discussion

In this analysis of trends in PrEP utilization in the commercial insurance market, providers substantially overprescribe Descovy relative to clinical value. Though differences between Descovy and generic TDF/FTC are not clinically meaningful, Descovy utilization was nearly half of 2021 commercial PrEP utilization and was 60% of spending. Although 340B providers prescribe Descovy at elevated rates, presumably because of the higher revenue realized on branded versus generic PrEP, 96% of Descovy PrEP prescriptions for commercially insured patients are written by non-340B providers; given this low 340B market share, 340B program reforms may have nominal effects on PrEP spending. This low 340B prescribing rate may be attributable to site of care for commercially insured PrEP users, 79% of which access PrEP through primary care [10]; prior work has shown that, in 2012, less than 0.5% of prescriptions dispensed through chain pharmacies were 340B-eligible [11]. Low 340B use may also be attributable to the growth of online PrEP prescribing that would likely be ineligible for 340B use; one such program, MISTR, which focuses on PrEP, reported 150 000 patients in 2023 (though it is unclear how many are being prescribed PrEP) [12]. For the 10% of national PrEP utilization contained in our sample, replacing spending on Descovy and Truvada with generic TDF/FTC would have reduced commercial insurance costs by \$98 million, 33% of their spending on PrEP.

Acknowledgements

Authors' roles: S.D. is responsible for study design, interpretation of results, and drafting of the article. K.J. is responsible for data analysis.

Conflicts of interest

There are no conflicts of interest.

West Health Policy Center, Washington, DC, USA.

Correspondence to Sean Dickson, West Health Policy Center, 1909K St NW, Ste 730, Washington, DC 20002, USA. E-mail: sdickson13@gmail.com

Received: 22 August 2023; revised: 15 November 2023; accepted: 26 November 2023.

References

- Dickson S, Killelea A. **Intentionally delayed pharmaceutical innovation under perverse incentives: Gilead's HIV pipeline as a case study.** *Health Affairs Forefront* 2021. Available at: <https://www.healthaffairs.org/content/forefront/intentionally-delayed-pharmaceutical-innovation-under-perverse-incentives-gilead-s-hiv>. [Accessed 5 December 2023]
- Clayton JD, Redberg RF. **Product hopping—an expensive and wasteful practice.** *JAMA Intern Med* 2020; **180**:1154–1155.
- Walensky RP, Horn T, McCann NC, Freedberg KA, Paltiel AD. **Comparative pricing of branded tenofovir alafenamide-emtricitabine relative to generic tenofovir disoproxil fumarate-emtricitabine for HIV preexposure prophylaxis: a cost-effectiveness analysis.** *Ann Intern Med* 2020; **172**:583–590.
- Ballreich J, Levengood T, Conti RM. **Opportunities and challenges of generic preexposure prophylaxis drugs for HIV.** *J Law Med Ethics* 2022; **50** (S1):32–39.
- Zhu W, Huang Y, Kouritis AP, Hoover K. Oral and injectable PrEP use in the United States, 2013 to 2022. February 2023. Available at: <https://www.croiconference.org/abstract/oral-and-injectable-prep-use-in-the-united-states-2013-to-2022/>. [Accessed 6 July 2023].
- Marcus JL, Killelea A, Krakower DS. **Perverse incentives - HIV prevention and the 340B drug pricing program.** *N Engl J Med* 2022; **386**:2064–2066.
- Healthcare Cost Institute. HCCI's 2.0 Commercial Claims Research Dataset. Available at: <https://healthcostinstitute.org/data>. [Accessed 15 November 2023]
- Dickson S. **Association between the percentage of US drug sales subject to inflation penalties and the extent of drug price increases.** *JAMA Netw Open* 2020; **3**:e2016388.
- Sullivan PS, Woodyatt C, Koski C, Pembleton E, McGuinness P, Taussig J, et al. **A data visualization and dissemination resource to support HIV prevention and care at the local level: analysis and uses of the AIDSvu public data resource.** *J Med Internet Res* 2020; **22**:e23173.
- Song HJ, Squires P, Wilson D, Lo-Ciganic W, Cook RL, Park H. **Trends in HIV preexposure prophylaxis prescribing in the United States, 2012-2018.** *JAMA* 2020; **324**:395–397.
- Clark BL, Hou J, Chou C, Huang ES, Conti R. **The 340B discount program: outpatient prescription dispensing patterns through contract pharmacies in 2012.** *Health Affairs* 2014; **33**:2012–2017.
- Meet The Disruptors: Tristan Schukraft of MISTR on the five things you need to shake up your industry. Authority Magazine. Published 11 April 2023. Available at: <https://medium.com/authority-magazine/meet-the-disruptors-tristan-schukraft-of-mistr-on-the-five-things-you-need-to-shake-up-your-59ff5294423d>. [Accessed 22 August 2023]

DOI:10.1097/QAD.0000000000003809