AJPM FOCUS
INCLUSIVITY IN PEOPLE, METHODS, AND OUTCOMES
RESEARCH ARTICLE

Trends in Recommended Screening and Monitoring Tests for Users of HIV Pre-Exposure Prophylaxis Before and During the COVID-19 Pandemic

Ikenna F. Unigwe, PharmD,[1] Robert L. Cook, MD,[2] Jennifer W. Janelle, MD,[3] Haesuk Park, PhD[1]

Introduction: To ensure the health and safety of persons taking pre-exposure prophylaxis to prevent HIV infection, the 2017 Centers for Disease Control and Prevention guidelines recommended initial and follow-up laboratory testing. We assessed the trends in adherence rates to recommended laboratory testing among pre-exposure prophylaxis users and identified factors associated with HIV testing among pre-exposure prophylaxis users from 2016 to 2020 and also examined rate changes during the COVID-19 pandemic in 2020.

Methods: We conducted a retrospective cohort study assessing the rates and trends of recommended laboratory testing among commercially insured pre-exposure prophylaxis users from 2016 to 2020, using the MarketScan database. We examined the proportion of pre-exposure prophylaxis users adhering to the following initial and follow-up laboratory testing: (1) HIV, creatinine clearance, hepatitis B virus, hepatitis C virus, and sexually transmitted infections (chlamydia/gonorrhea and syphilis) within 7 days before pre-exposure prophylaxis initiation; (2) HIV 90 days after initiation; and (3) HIV, creatinine clearance, and sexually transmitted infections 180 days after pre-exposure prophylaxis initiation. We used general linear models to examine trends and multivariable logistic regression to identify predictors of ≥1 HIV test within 180 days after index pre-exposure prophylaxis.

Results: We identified 19,581 new pre-exposure prophylaxis users. Most were male (96%) and aged 18−34 years (55%). Adherence rates to recommended testing increased from 2016 through 2019 (e.g., 9.0%−13.6% for all initial screening tests 7 days before initiation, 42.1%−44.6% for HIV testing 90 days after initiation, 33.8%−40.6% for all follow-up tests within 180 days after initiation), but all rates decreased during the COVID-19 pandemic (12.4%, 33.6%, and 31.6%, respectively). Younger age (aged 13−17 years: AOR=0.44, 95% CI=0.28, 0.71) and ages 18−34 years (AOR=0.80, 95% CI=0.74, 0.86) were associated with a significantly lower likelihood of getting an HIV test within 180 days after initiation than ages 35−44 years, and female sex (AOR=0.64, 95% CI=0.55, 0.74) were associated with a significantly lower likelihood than male sex. Pre-exposure prophylaxis users with a history of sexually transmitted infections had a higher likelihood (AOR=1.27, 95% CI=1.16, 1.40) of getting tested than those without.

Conclusions: Initial screening and follow-up testing rates were lower than those recommended by the Centers for Disease Control and Prevention. Public health efforts are needed to ensure that patients have access to needed laboratory testing during pandemics or natural disasters and to

From the [1]Department of Pharmaceutical Outcomes & Policy, College of Pharmacy, University of Florida, Gainesville, Florida; [2]Department of Epidemiology, College of Public Health and Health Professions & College of Medicine, University of Florida, Gainesville, Florida; and [3]Department of Medicine, College of Medicine, University of Florida, Gainesville, Florida

Address correspondence to: Haesuk Park, PhD, Department of Pharmaceutical Outcomes & Policy, College of Pharmacy, University of Florida, 1225 Center Drive, HPNP Building, Room 3325, Gainesville FL 32610. E-mail: hpark@cop.ufl.edu.

2773-0654/$36.00
https://doi.org/10.1016/j.focus.2023.100134

educate patients and clinicians about the importance of screening and monitoring tests to ensure the safety and health of pre-exposure prophylaxis users.

INTRODUCTION

Oral tenofovir disoproxil fumarate or tenofovir alafenamide with emtricitabine is approved for HIV pre-exposure prophylaxis (PrEP) to prevent HIV transmission and acquisition. There has been an increased uptake of PrEP since its first availability in the U.S.[1] To ensure the health and safety of persons receiving PrEP to prevent HIV infection, the Centers for Disease Control and Prevention 2017 guideline recommends laboratory tests for (1) HIV, creatinine clearance, hepatitis B virus, hepatitis C virus, and sexually transmitted infections (STIs) (chlamydia/gonorrhea and syphilis) within 7 days before PrEP initiation; (2) HIV 90 days after initiation; and (3) HIV, creatinine clearance, and STIs 180 days after PrEP initiation.[2]

There are limited data in the literature about the completion rates of these tests by PrEP users. A previous study using 2011−2015 insurance claims data noted increasing yearly adherence but also reported significant testing disparities between recommended testing frequencies outlined in the guidelines and the actual testing patterns observed in practice.[3] With the increasing use of PrEP in the U.S.[1] and the 2020 coronavirus disease 2019 (COVID-19) pandemic that affected HIV prevention services across the country,[4] there is a need to understand the recent data of these recommended laboratory tests in real-world clinical practices. Thus, we examined trends in adherence rates to recommended laboratory tests and identified factors associated with HIV testing among PrEP users in the U.S. from 2016 to 2020 and also assessed whether adherence rates changed in 2020 during the COVID-19 pandemic.

METHODS

Study Population

This cohort study included commercially insured individuals in the 2016−2020 MarketScan databases aged 13−64 years and prescribed (≥30 days) tenofovir disoproxil fumarate or tenofovir alafenamide with emtricitabine for PrEP from January 1, 2016, to June 30, 2020.[5] To ensure the use of PrEP, we excluded persons with diagnostic codes or prescriptions for HIV or hepatitis B virus for 1 year before first PrEP prescription (index date) or prescriptions (<30 days) for postexposure prophylaxis use.[1,6] We required continuous enrollment 1 year before the index date and 180 days after the index date to enable the assessment of baseline characteristics and outcomes, respectively. The recommended tests were identified using the Current Procedural Terminology codes and Healthcare Common Procedure Coding System, which are used to process insurance claims for medical procedures, supplies, products, and services[7] (Appendix Table 1, available online).

Measures and Statistical Analysis

We calculated the proportion of PrEP users adhering to each recommended test each year. We used general linear models to examine trends for each test and multivariable logistic regression to identify factors associated with ≥1 HIV test within 180 days after the index date, after controlling for demographic characteristics, geography (Appendix Table 2, available online), and history of STI, depression, or substance use disorder. A sensitivity analysis was conducted to assess adherence to the recommended tests 90 days before the index date. This study was approved by the University of Florida IRB. Data were analyzed in 2022.

RESULTS

From 2016 through 2020, 19,581 new PrEP users were identified (96% males; 55% aged 18−34 years) (Table 1). From 2016 through 2019, rates of adherence to recommended testing increased from 9.0% to 13.6% for all screening tests 7 days before the index date, from 42.1% to 44.6% for HIV testing within 90 days after the index date, and from 33.8% to 40.6% for all follow-up tests within 180 days after the index date (Figure 1). By contrast, adherence rates in 2020 decreased to 12.4% within 7 days before the index date (p_{trend}=0.001), 33.6% within 90 days after the index date (p_{trend}=0.17), and 31.6% within 180 days after the index date (p_{trend}<0.001). Seven days before the index date, HIV test adherence rates increased from 34.5% in 2016 to 41.2% in 2019 but decreased to 36.9% in 2020 (p_{trend}<0.001); syphilis testing increased from 28.2% in 2016 to 36.6% in 2019 but decreased to 32.3% in 2020 (p_{trend}<0.001). Similarly, 180-day postindex testing for HIV (60.7%−62.8%) and syphilis (51.6%−53.7%) increased from 2016 through

Table 1. Demographic Differences Among Users of Pre-Exposure Prophylaxis by Year of Initiation, Using Data From MarketScan (N=19,581)

Demographics	2016 (*n*=3,679)	2017 (*n*=4,038)	2018 (*n*=4,858) *n* (%)	2019 (*n*=5,139)	2020 (*n*=1,867)	*p*-value
Age, years						<0.01
13–17	11 (0.3)	14 (0.4)	22 (0.5)	27 (0.53)	6 (0.32)	
18–34	1,800 (48.9)	2,142 (53.1)	2,713 (55.9)	3,010 (58.6)	1,099 (58.9)	
35–44	845 (23.0)	841 (20.8)	963 (19.8)	1,014 (19.7)	377 (20.2)	
≥45	1,023 (27.8)	1,041 (25.8)	1,160 (23.9)	1,088 (21.2)	385 (20.6)	
Sex						<0.01
Male	3,571 (97.1)	3,914 (96.9)	4,669 (96.1)	4,860 (94.6)	1,760 (94.3)	
Female	108 (2.9)	124 (3.1)	189 (3.9)	279 (5.4)	107 (5.7)	
Depression	636 (17.3)	785 (19.4)	953 (19.6)	1,106 (21.5)	476 (25.5)	<0.01
Previous STI	471 (12.8)	481 (11.9)	562 (11.6)	556 (10.8)	223 (11.9)	0.074
SUD	202 (5.5)	258 (6.4)	330 (6.8)	403 (7.8)	141 (7.6)	<0.01
Employment status						0.01
Active full time	3,136 (85.3)	3,382 (83.75)	4,127 (85.0)	4,449 (86.6)	1,616 (86.6)	
Active part time/seasonal	50 (1.4)	75 (1.9)	86 (1.8)	86 (1.7)	32 (1.71)	
Others	493 (13.4)	581 (14.4)	645 (13.3)	604 (11.8)	219 (11.7)	
Region						<0.01
Northeast	833 (22.7)	867 (21.5)	1,140 (23.5)	1,121 (21.8)	361 (19.4)	
North Central	574 (15.6)	591 (14.7)	828 (17.1)	881 (17.2)	305 (16.4)	
South	1,284 (34.9)	1,646 (40.9)	1,937 (40.0)	2,199 (42.8)	870 (46.7)	
West	984 (26.8)	922 (22.9)	944 (19.5)	932 (18.2)	329 (17.6)	

STI, sexually transmitted infection; SUD, substance use disorder.

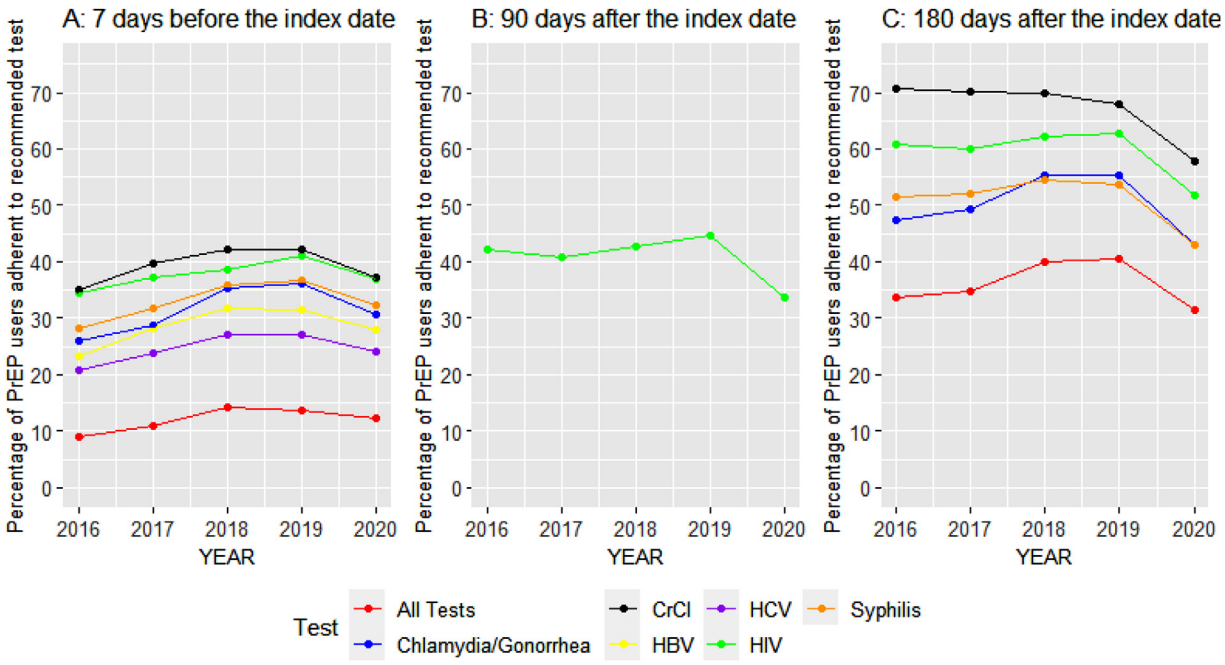

Figure 1. Trends in adherence to recommended screening and monitoring laboratory tests for PrEP users by year from 2016 through 2020.

All tests represent the completion of all recommended tests within the period.

CrCl, creatinine clearance; HBV, hepatitis B virus; HCV, hepatitis C virus; PrEP, pre-exposure prophylaxis.

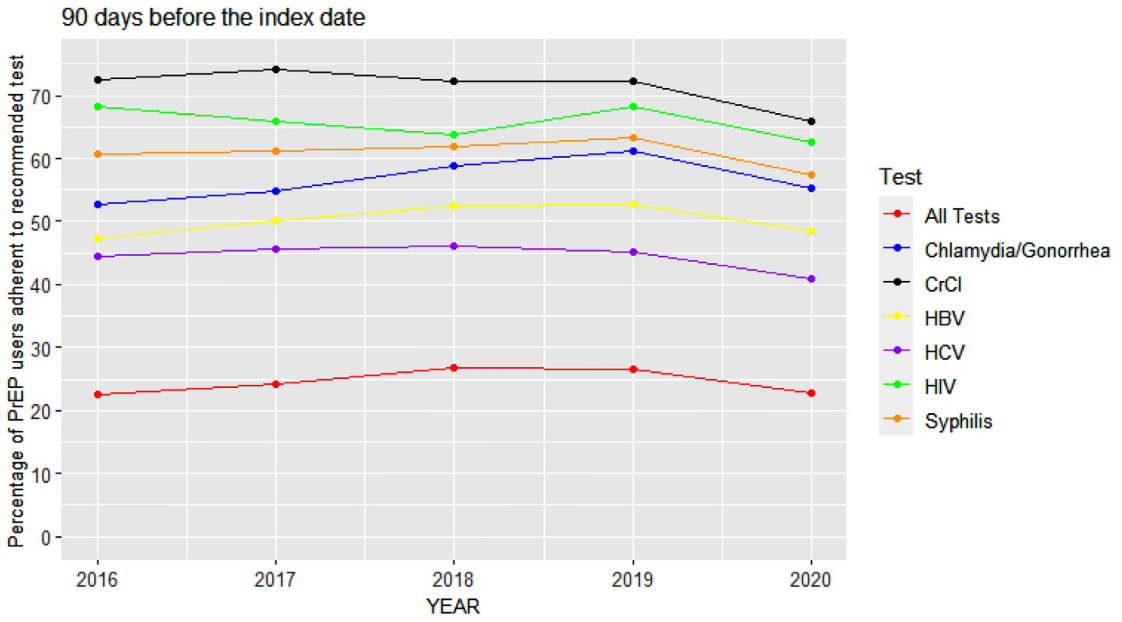

Figure 2. Sensitivity analysis of trends in adherence to recommended screening and monitoring laboratory tests for PrEP users by year, 90 days before the index date, from 2016 to 2020.

All tests represent the completion of all recommended tests within the period.

CrCl, creatinine clearance; HBV, hepatitis B virus; HCV, hepatitis C virus; PrEP, pre-exposure prophylaxis.

2019 but decreased to 51.7% (HIV p_{trend}=0.09) and 43.0% (syphilis p_{trend}=0.04) in 2020.

In sensitivity analysis (Figure 2) assessing the recommended tests 90 days before the index date, rates of adherence to testing increased from 22.6% in 2016 to 26.5% in 2019 for all screening tests 90 days before the index date and decreased to 22.7% in 2020 (p_{trend}<0.001). After controlling for covariates, compared with the rates in 2016, HIV testing 180 days after the index date significantly decreased in 2020 (AOR=0.71, 95% CI=0.63, 0.80) (Table 2). Younger age (ages 13−17 years: AOR=0.44, 95% CI=0.28, 0.71) and ages 18−34 years (AOR=0.80, 95% CI=0.74, 0.86), females (AOR=0.64, 95% CI=0.55, 0.74), and PrEP users in the South (AOR=0.91, 95% CI=0.84, 0.99) and West (AOR=0.89, 95% CI=0.81, 0.97) were associated with significantly lower likelihood of HIV testing within 180 days after the index date than ages 35−44 years, males, and those in the Northeast, respectively. PrEP users with a history of STI 1 year before the index date had a higher likelihood (AOR=1.27, 95% CI=1.16, 1.40) of getting tested than those without. There was no statistically significant difference between PrEP users with a history of depression or substance use disorder and those without.

Table 2. AORs of Risk Factors and HIV Testing Within 180 Days of Pre-Exposure Prophylaxis Initiation

Variable	AOR (95% CI)
Year (ref: 2016)	
2017	0.99 (0.89, 1.09)
2018	1.10 (1.00, 1.20)
2019	**1.13 (1.03, 1.24)**
2020	**0.71 (0.63, 0.80)**
Age category (ref: 35−44), years	
13−17	**0.44 (0.28 0.71)**
18−34	**0.80 (0.74, 0.86)**
≥45	0.93 (0.85, 1.02)
Sex	
Female (ref: male)	**0.64 (0.55, 0.74)**
Employment status (ref: active full time)	
Active part time	**0.56 (0.44, 0.70)**
Others	**0.71 (0.65, 0.78)**
SUD (ref: no)	0.91 (0.81, 1.03)
Depression (ref: no)	1.02 (0.95, 1.11)
Previous STI (ref: no)	**1.27 (1.16, 1.40)**
U.S. geographic region (ref: Northeast)	
North Central	0.90 (0.82, 1)
South	**0.91 (0.84, 0.99)**
West	**0.89 (0.81, 0.97)**

Note: Boldface indicates statistical significance (p<0.05).
STI, sexually transmitted infection; SUD, substance use disorder.

DISCUSSION

Overall rates of adherence to recommended screening and monitoring tests remained suboptimal, although they

increased from 2016 through 2019. Less than 15% of patients completed all screening tests within 7 days before PrEP initiation, and <30% completed all follow-up tests within 180 days after initiation. Reduced testing threatens late detection of HIV infection, antiretroviral resistance, and HIV transmission, demonstrating the need for adherence to the recommended screening and follow-up tests.[3,8]

Completion of individual tests gradually increased from 2016 to 2019, aligning largely with the general improvement in completion rates 180 days after the index date from 2011 to 2015 in a prior study that also used U. S. insurance claims data.[3] Notably, that study reported lower average completion rates, with 5-year mean of 38%, 49%, 39%, and 37% for HIV, syphilis, chlamydia/gonorrhea, and creatinine clearance tests in 2011−2015, respectively; thus, our results from 2016 to 2020 with 5-year mean of 59.5%, 51%, 50.0%, and 67.3%, respectively (data not shown), suggest an improvement 180 days after the index date during the 2016−2020 time period compared with that in the previous 5 years.[3] However, all test rates sharply decreased in 2020, likely owing to the COVID-19 pandemic, indicating potentially negative impacts of the pandemic on HIV preventative care services.[4] Our reduced testing rates align with a previous study reporting a 27%−59% decrease in the total number of HIV tests performed provided by HIV preventive services in the general population in 2020, relative to 2019.[9]

Overall, the HIV testing rate of commercially insured U.S. PrEP users was lower than the estimates from 2 European studies. In a survey of PrEP users among men who have sex with men in Germany, 59.2% of users were tested for HIV every 3 months or more often, compared with 40.8% in our study.[10] An even higher estimate was reported by Tassi et al. among PrEP users in France. Using a historical cohort from the French national health database, 86.3% of users were tested for HIV within 1 month after initiation,[11] suggesting significant room for improvement in the U.S.

Our results found that younger and female PrEP users were less likely to get tested for HIV, which aligns with results of prior studies that showed low HIV testing rates in these subgroups in the general population.[12,13] By contrast, PrEP users with a history of STI were more likely to get tested for HIV because they are considered to be at a high risk for HIV infection. A diagnosis with STI suggests that they did not use condoms, increasing the risk of acquiring HIV and/or spreading it to others. Sores and skin breaks that often accompany an STI also increase the chance of viral penetration into the body.[14]

Limitations

Study limitations included no race and ethnicity data and assessing only commercially insured persons.

CONCLUSIONS

The findings of this study suggest that public health efforts are needed to ensure that patients have access to needed laboratory testing during pandemics or natural disasters and to educate patients and clinicians about the importance of screening and monitoring tests to ensure the safety and health of PrEP users.

ACKNOWLEDGMENTS

We would like to thank Debbie Wilson, who proofread this manuscript and provided very valuable suggestions on modifications. We would also like to thank Augustus Igbokwe, who provided his clinical expertise on HIV pre-exposure prophylaxis screening and monitoring.

Declarations of interest: none.

CREDIT AUTHOR STATEMENT

Ikenna F. Unigwe: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing − original draft, Writing − review & editing. Robert L. Cook: Supervision, Project administration, Writing − review & editing. Jennifer W. Janelle: Methodology, Visualization, Writing − review & editing. Haesuk Park: Project administration, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing − review & editing.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.focus.2023.100134.

REFERENCES

1. Song HJ, Squires P, Wilson D, Lo-Ciganic WH, Cook RL, Park H. Trends in HIV preexposure prophylaxis prescribing in the United States, 2012−2018. *JAMA*. 2020;324(4):395–397. https://doi.org/10.1001/jama.2020.7312.
2. U.S. Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2017 Update − A Clinical Practice Guideline. Atlanta, GA: .Centers for Disease Control and Prevention, 2017.
3. Huang YA, Tao G, Samandari T, Hoover KW. Laboratory testing of a cohort of commercially insured users of HIV preexposure prophylaxis in the United States, 2011−2015. *J Infect Dis*. 2018;217(4):617–621. https://doi.org/10.1093/infdis/jix595.
4. Shoptaw S, Goodman-Meza D, Landovitz RJ. Collective call to action for HIV/AIDS community-based collaborative science in the era of COVID-19. *AIDS Behav*. 2020;24(7):2013–2016. https://doi.org/10.1007/s10461-020-02860-y.
5. MarketScan research databases. IBM. https://www.ibm.com/products/marketscan-research-databases. Accessed April 16, 2022.
6. Wu H, Mendoza MC, Huang YA, Hayes T, Smith DK, Hoover KW. Uptake of HIV preexposure prophylaxis among commercially insured persons-united states, 2010−2014. *Clin Infect Dis*. 2017;64(2):144–149. https://doi.org/10.1093/cid/ciw701.

7. Introduction to billing code systems. American Speech-Language-Hearing Association. https://www.asha.org/practice/reimbursement/coding/code_intro/. Accessed February 20, 2023.
8. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493–505. https://doi.org/10.1056/NEJMoa1105243.
9. Moitra E, Tao J, Olsen J, et al. Impact of the COVID-19 pandemic on HIV testing rates across four geographically diverse urban centres in the United States: an observational study. *Lancet Reg Health Am.* 2022;7:100159. https://doi.org/10.1016/j.lana.2021.100159.
10. Koppe U, Seifried J, Marcus U, et al. HIV, STI and renal function testing frequency and STI history among current users of self-funded HIV pre-exposure prophylaxis, a cross-sectional study, Germany, 2018 and 2019. *Euro Surveill.* 2022;27(14):2100503. https://doi.org/10.2807/1560-7917.ES.2022.27.14.2100503.
11. Tassi MF, Laurent E, Gras G, et al. PrEP monitoring and HIV incidence after PrEP initiation in France: 2016−18 nationwide cohort study. *J Antimicrob Chemother.* 2021;76(11):3002–3008. https://doi.org/10.1093/jac/dkab263.
12. Fields EL, Gayles TA. Considerations for addressing low HIV testing rates among adolescent men who have sex with men. *Pediatrics.* 2020;145(3):e20193996. https://doi.org/10.1542/peds.2019-3996.
13. Yumori C, Zucker J, Theodore D, et al. Women are less likely to be tested for HIV or offered preexposure prophylaxis at the time of sexually transmitted infection diagnosis. *Sex Transm Dis.* 2021;48(1):32–36. https://doi.org/10.1097/OLQ.0000000000001265.
14. Unigwe I, Yang S, Song HJ, et al. Trends in sexually transmitted infections in United States ambulatory care clinics from 2005−2016. *J Clin Med.* 2022;11(1):71. https://doi.org/10.3390/jcm11010071.