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Trends in HIV Preexposure Prophylaxis Use Before and After Launch of the Ending the HIV Epidemic in the US Initiative, 2016–2023

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Abstract

Introduction: The Ending the HIV Epidemic (EHE) in the US initiative was launched by the US Department of Health and Human Services in 2019 with the goal of decreasing new HIV infections 90% by 2030. Increasing the use of HIV preexposure prophylaxis (PrEP) is one of the EHE strategies. We assessed the impact of EHE activities on PrEP use.

Methods: Using IQVIA real-world longitudinal prescription data and the National HIV Surveillance System data, we calculated jurisdiction-level PrEP to diagnosis ratios (PDRs) in the United States from 2016 to 2023. We assessed impact of EHE with a difference-in-difference analysis.

Results: The PDR increased from 3.0 to 14.7 in EHE jurisdictions, from 1.2 to 7.2 in EHE states, and from 2.5 to 13.4 in non-EHE jurisdictions. On average, no additional increase in the PDR was found for EHE counties compared with matched non-EHE counties, (adjusted difference-in-difference: 0.2, 95% confidence interval: –1.0 to 1.3), or for EHE states (adjusted difference-in-difference: 0.4, 95% CI: –1.6 to 2.4).

Conclusions: Overall PrEP use increased markedly, with some EHE jurisdictions achieving greater increases than non-EHE jurisdictions with similar PDRs in 2019. The uneven increase in PrEP use in EHE jurisdictions underscores the need for jurisdiction-specific PrEP implementation

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strategies designed for the needs of each community. It also underscores the need for sufficient funding to accomplish EHE goals.

Keywords

ending the HIV Epidemic initiative (EHE); PrEP; HIV

INTRODUCTION

The Ending the HIV Epidemic (EHE) in the US initiative was launched in 2019 by the US Department of Health and Human Services,^{1,2} with the goal of decreasing new HIV infections 90% by 2030. EHE jurisdictions include 48 US counties, the District of Columbia (D.C.), and the San Juan Municipio, Puerto Rico (EHE local jurisdictions), and 7 states with high rates of HIV diagnoses in rural areas (EHE states). Together, HIV diagnoses in these jurisdictions account for >50% of HIV diagnoses in the United States. The EHE initiative includes strategies to increase HIV testing, prevention, treatment, and responses to outbreaks. The 4 strategies aim to (1) diagnose all individuals with HIV as early as possible after infection, (2) treat people with HIV rapidly and effectively to reach sustained viral suppression, (3) prevent new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs, and (4) respond quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.^{2,3}

PrEP is a safe and highly effective HIV prevention intervention with both oral and long-acting injectable options.⁴ It is indicated to prevent both sexual and injection drug use acquisition of HIV, and its uptake in the United States has increased substantially since its approval.⁵ However, PrEP utilization does not necessarily align with the populations at highest risk of HIV acquisition.⁶ To support states and local communities to increase awareness of, access to, and use of PrEP, the EHE initiative includes a goal to increase PrEP use among persons with indications for it particularly among Black or African American (Black) and Hispanic or Latino (Hispanic) gay, bisexual, and other men who have sex with men, Black women, and persons in other populations disproportionately affected by HIV.² EHE jurisdictions were funded to expand PrEP and postexposure prophylaxis (PEP) efforts, and to expand linkage to PrEP in nontraditional health care venues through programs supported by the Centers for Disease Control and Prevention (CDC). For primary care settings, EHE funds also support expansion of access to HIV testing and provision of PrEP and associated services at federally qualified health centers.²

CDC monitors PrEP use in the United States to assess the effectiveness of activities to increase its use.³ PrEP use can be measured with the PrEP-to-diagnosis ratio (PDR, also referred to as PrEP-to-need ratio), defined as the ratio of the number of persons prescribed PrEP to the number of persons with diagnosed HIV infection in the prior year.^{6,7} To assess the impact of EHE activities on PrEP use, we conducted a difference-in-difference (DID) analysis comparing PDRs in EHE county and state jurisdictions with those in selected non-EHE Jurisdictions during 2016–2023.

METHODS

We analyzed 2016–2023 data in the IQVIA RealWorld Longitudinal Prescription Database (IQVIA data), which included >94% of all prescriptions from retail pharmacies and 74% from mail order outlets in the United States. We used a validated algorithm to estimate the number of persons prescribed PrEP overall and by jurisdictional level.⁵ Annual PDRs were calculated as the number of persons with a PrEP prescription divided by the number of HIV diagnoses in the prior year.⁷ We used 2015–2022 HIV diagnosis data from the CDC National HIV Surveillance System for the denominators of the PDRs.⁸

We described trends in number of persons prescribed PrEP and the PDR in the United States. We further stratified the analysis by EHE jurisdiction type: (1) EHE jurisdictions (n = 50), (2) EHE states (n = 7), and (3) non-EHE jurisdictions. The number of persons prescribed PrEP in non-EHE jurisdictions and the number of persons with diagnosed HIV were calculated by subtracting the numbers in EHE jurisdictions and EHE states from national totals, respectively. To assess trends in the number of persons prescribed PrEP and PDRs over time, we estimated annual percentage change (EAPC) and 95% confidence intervals (95% CIs) using generalized Poisson regression models with year as a continuous variable. We also compared the increases of PDR between 2019 and 2023 by EHE-funded jurisdictions and 50 states.

We conducted DID analyses to compare the change in PDRs before and after the launch of the EHE initiative by EHE status, at both county and state levels, respectively.⁹ For county-level DID analysis, we compared 50 EHE jurisdictions with 50 non-EHE jurisdictions, selected based on having the next largest number of HIV diagnoses in 2016 (“non-EHE counties” thereafter, Appendix Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C496>). Similarly, for comparisons at the state level, we identified 7 non-EHE states with the largest number of HIV diagnoses in rural areas, matching them with the 7 EHE states. (“non-EHE states” thereafter, Appendix Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C496>).

We extracted jurisdictional demographic and social determinant of health (SDOH) indicator data from the US Census Bureau American Community Survey 5-year estimates in 2020.¹⁰ These data included variables for the percentage of a population that is Black or African American, percentage of a population that is Hispanic or Latino, percentage uninsured among persons aged 19–64 years, and percentage of persons living in poverty.^{10,11} We also used data from the 2021–2022 Health Resources and Services Administration (HRSA) Area Health Resources Files to calculate county- and state-level health care provider density, defined as total number of physicians, nurse practitioners, and physician assistants per 1000 population in 2020.¹² We described jurisdiction level demographic and SDOH characteristics, and provider density in 2020 with median and interquartile ranges (IQRs).

In both county-data and state-data analysis, we reported PDR with median and IQR by pre- and post-EHE and by EHE status. We used a mixed-effects model with jurisdiction as random intercepts, and included EHE status, pre- and post-EHE initiation period (2016–2019 vs. 2020–2023), and an interaction term of EHE status by pre- and

post-EHE period as the DID estimator: $DID_{EHE} = (PDR_{EHE, post-EHE} - PDR_{EHE, pre-EHE}) - (PDR_{non-EHE, post-EHE} - PDR_{non-EHE, pre-EHE})$. A DID >0 indicates an additional PDR increase compared with reference jurisdictions. We started the modeling process by testing a parallel trend assumption using the subset of data during the pre-EHE period (2016–2019). The technical details of the DID modeling process exploring unadjusted and adjusted DID models are reported in Appendix 4, Supplemental Digital Content, <http://links.lww.com/QAI/C496>. Finally, we reported DID estimates adjusted for jurisdictional demographic characteristics, SDOH, and health care provider density. We also included a dummy variable to adjust for the impact of the COVID-19 pandemic on HIV diagnoses in 2020, which affected the estimation of PDR in 2021.^{13–15} A sensitivity analysis was conducted by excluding this dummy variable and 2021 data from the model (Appendix 4, Supplemental Digital Content, <http://links.lww.com/QAI/C496>).

All analyses were performed using R version 4.3.0 (R Foundation, Vienna, Austria).

RESULTS

The number of persons prescribed PrEP captured in the IQVIA database increased from 105,051 in 2016 to 505,730 in 2023, with an EAPC of 21.7% (95% CI: 18.2 to 25.2) (Fig. 1A). The PDR in the United States increased from 2.7 PrEP users per HIV diagnosis in 2016 to 13.4 in 2023 with an EAPC of 23.0% (95% CI: 17.8, 28.4) (Fig. 1B). This increasing trend was interrupted by the COVID-19 pandemic during 2020–2021 but recovered by 2022.

Figure 2 shows state-level PDR increases after the launch of EHE, for both EHE and non-EHE jurisdictions. EHE jurisdictions had higher PDR at initiation than non-EHE jurisdictions. The overall median increase of PDR was 6.5 (IQR, 4.0–10.7). The 7 EHE states had much lower PDR at baseline, compared with both EHE and non-EHE jurisdictions, and by the end of 2023, PDRs in 7 EHE states, even though increased, were still lower than the national PDR in 2019 (Fig. 2).

The number of persons prescribed PrEP increased from 62,498 to 265,586, with an EAPC of 19.8% (95% CI: 16.4 to 23.3) in 50 EHE jurisdictions; from 3707 to 25,000, with an EAPC of 27.5% (95% CI: 23.6 to 31.4) in 7 EHE states; and from 38,846 to 215,144, with an EAPC of 23.7% (95% CI: 20.1 to 27.4) in non-EHE jurisdictions (Fig. 1C). The PDR increased from 3.0 to 14.7 with an EAPC of 22.7% (95% CI: 17.5, 28.1) in EHE jurisdictions; from 1.2 to 7.2 with an EAPC of 26.0% (95% CI: 20.7, 31.5) in EHE states; and from 2.5 to 13.4 with an EAPC of 23.7% (95% CI: 18.4, 29.2) in non-EHE jurisdictions (Fig. 1D).

Figure 3 shows the varying magnitude of PDR increases between 2019 and 2023 in EHE jurisdictions. Most EHE jurisdictions achieved an increase, with a median increase of 5.5 (IQR 3.5–8.8). In 2019, 15 out of 50 EHE jurisdictions had a PDR higher than the national average. By the end of 2023, 22 EHE jurisdictions had reached a PDR higher than the national average. The PDR increased in all 7 EHE-funded states, ranging from 2.2 to 5.1, with a median increase of 3.7 (IQR 3.0–4.1), but lagged the average national increase of 6.0 (7.4 in 2019 and 13.4 in 2023) (Fig. 3).

Table 1 shows the characteristics of 50 EHE counties and 50 non-EHE counties with next largest number of HIV diagnoses after EHE counties in 2016, and 7 EHE states and 7 non-EHE states with next largest number of HIV diagnoses in rural areas in 2016 (Appendix Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C496>). Compared with the 50 non-EHE counties, EHE counties had higher median proportions of Black persons (19.6% vs. 12.2%), of Hispanic persons (22.7% vs. 15.4%), and persons in poverty (14.2% vs. 12.1%); similar median proportion of persons without health insurance (13.0% vs. 12.5%); and similar median health care provider density (5.1 per 1000 vs. 5.2 per 1000). Compared with the 7 non-EHE states, EHE states had higher median proportions of Black persons (15.1% vs. 3.9%), persons in poverty (16.0% vs. 11.1%), and proportion of persons without health insurance (14.6% vs. 10.6%); lower proportions of Hispanic persons (4.4% vs. 9.5%); and similar median provider density (3.5 per 1000 vs. 3.8 per 1000) (Table 1).

After adjusting for jurisdictional demographic characteristics, SDOH, provider density, and COVID-19 effects, no additional increases in the PDRs were observed in EHE counties compared with matched non-EHE counties, with an adjusted DID of 0.2 (95% CI: -1.0 to 1.3). Similarly, no additional increases in the PDRs were observed in EHE states compared with matched non-EHE states, with an adjusted DID of 0.4 (95%CI: -1.6 to 2.4) (Table 2).

DISCUSSION

We found PrEP use in the United States has increased markedly since the launch of the EHE initiative. However, the increase was uneven across different jurisdictions. To support achieving the EHE goal of decreased HIV infections, increased PrEP implementation is needed, especially in jurisdictions with low PrEP use and high rates of HIV diagnoses.^{1,2} Our results show no significant additional increase in PrEP use in EHE-funded jurisdictions during the study period compared with non-EHE jurisdictions. However, it is important to note that EHE jurisdictions had overall higher PDRs both at baseline and at the end of the observation period. In addition, they had higher levels of sociodemographic factors that are associated with barriers to HIV prevention compared with non-EHE jurisdictions.

Several factors may hinder the implementation of EHE-funded activities to increase PrEP use. First, the COVID-19 pandemic began in the United States right after the initiation of EHE and resulted in decreases in both clinical services and public health programmatic activities for HIV prevention.^{13–15} Thus, the implementation period of EHE activities might not have been long enough to result in measurable impact. Because the health care system has recovered from COVID-19–related setbacks and with ongoing EHE activities, increased PrEP use is anticipated. Second, PrEP use before the EHE initiative varied across EHE counties. Counties with relatively greater health care and public health capacity and higher baseline PDRs in 2019, such as New York, NY, and San Francisco, CA, showed noticeable increases. In contrast, progress was more limited in counties with fewer health care and public health resources and lower baseline PDRs. The uneven increase highlights the gap in capacity to provide PrEP services across different counties. Given the importance of EHE funding for resource-limited jurisdictions, it is likely that without the support of EHE funding for local public health initiatives and clinical HIV services, PDRs would be even

lower than the observed PDRs. In addition, funding levels required to fully support EHE activities have not been provided.^{16,17}

Increases in the PDR was lower for the 7 EHE states compared with non-EHE states matched for high rates of HIV diagnoses in rural areas. All 7 EHE states had populations with a large proportion of persons experiencing poverty; 5 states had large proportions of uninsured persons above the US average; and 3 states had not expanded Medicaid. All these factors may be associated with challenges to increasing PrEP use.¹⁸ Our findings of low PrEP use in rural areas are similar to those of an earlier study that found that rural areas had too few PrEP providers, referred to as “PrEP deserts.”¹⁹ Novel PrEP delivery strategies, such as telemedicine with mailed PrEP monitoring laboratory tests, long-acting injectable PrEP, and hybrid models that include pharmacies, might be effective PrEP implementation models for rural communities.^{20,21}

Our study has 3 limitations. First, IQVIA data included most PrEP prescriptions in the United States but did not include PrEP prescribed in closed health care systems such health maintenance organizations. As a result, our analysis likely underestimated national PrEP use. Second, we were not able to estimate PDRs by race and ethnicity because IQVIA data were missing this information for about two-thirds of PrEP users. Third, our study was an ecologic analysis so could not assess the impact of specific EHE-funded programs. In-depth studies are needed to evaluate local practices and to address barriers to successful PrEP implementation in EHE jurisdictions.²² In addition, a longer time frame might be needed to realize the impact of the EHE initiative on PrEP use in the United States.

In summary, PrEP use increased during the first 4 years of the EHE initiative, despite interruptions in clinical services and public health activities caused by the COVID-19 pandemic. The uneven increase of PrEP use in different jurisdictions highlights the need for tailored, jurisdiction-specific PrEP implementation strategies and localized capacity for scaling up PrEP, and for sufficient resources to achieve the goals of EHE including increased PrEP use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

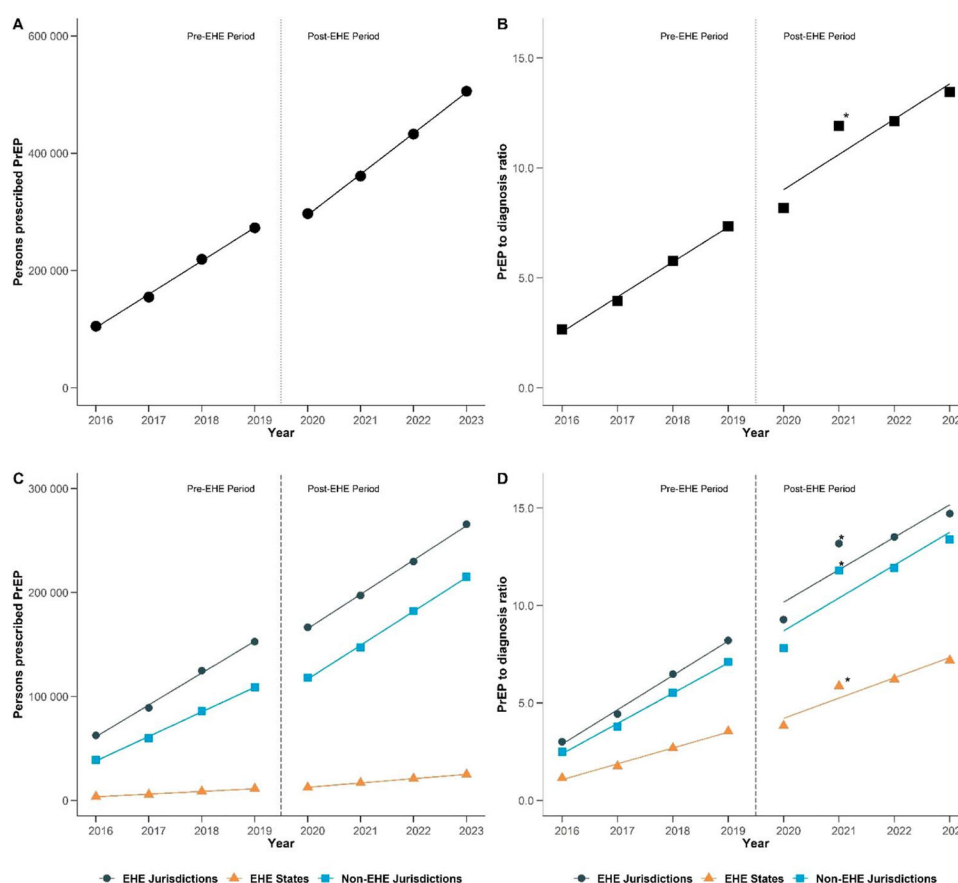
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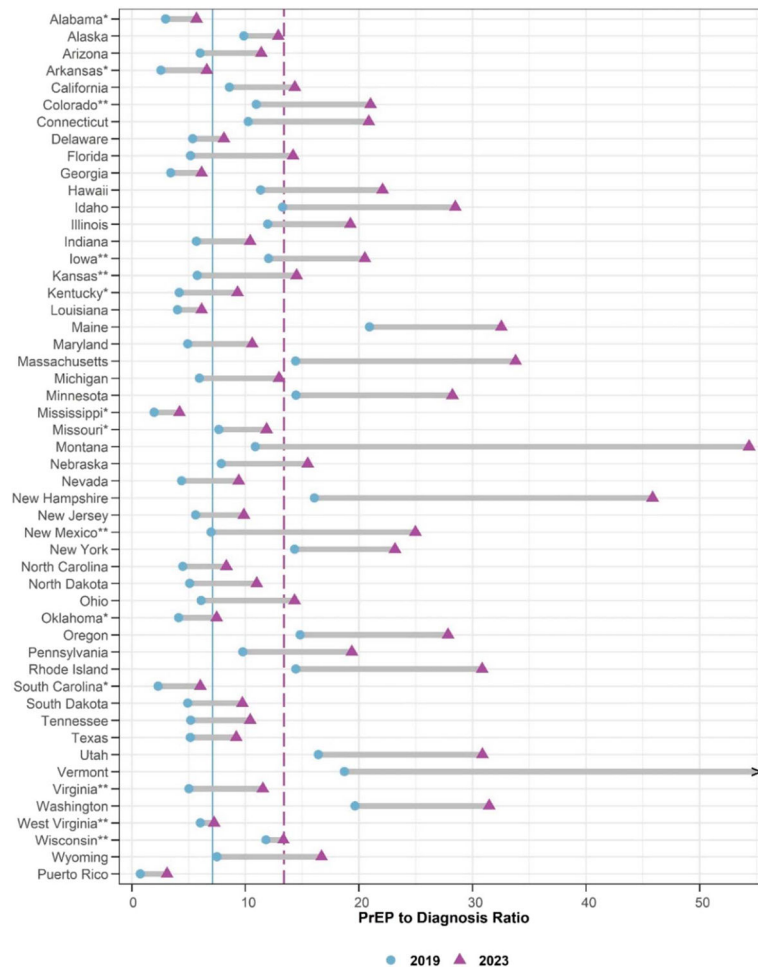
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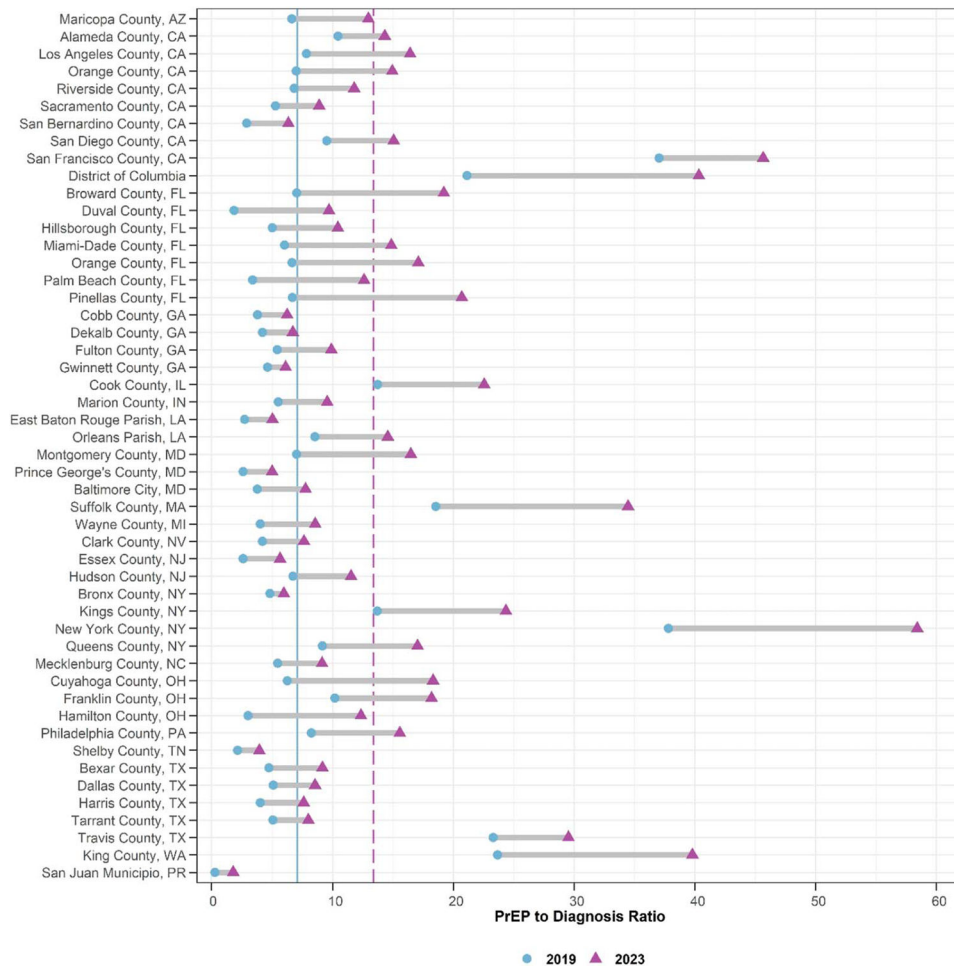
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**FIGURE 1.**

Trends in the number of persons prescribed preexposure prophylaxis (PrEP) and the PrEP-to-diagnosis ratio (PDR) by Ending the HIV Epidemic in the US (EHE) initiative status—United States, 2016–2023. A, Number of persons prescribed PrEP; (B) PrEP-to-diagnosis ratios (PDRs), calculated as number of persons prescribed PrEP divided by the number of HIV diagnoses in the prior year; (C) trends in the number of persons prescribed PrEP; (D) trends in the PDRs. EHE local jurisdictions: 48 counties, D.C., and San Juan Municipio, Puerto Rico. EHE jurisdictions are listed in Appendix Table 3, Supplemental Digital Content, <http://links.lww.com/QAI/C496>; EHE states: Alabama, Arkansas, Kentucky, Mississippi, Missouri, Oklahoma, and South Carolina; non-EHE jurisdictions: jurisdictions that were not EHE jurisdictions or states. PrEP prescriptions and HIV diagnoses in these jurisdictions were estimated by subtracting the number of persons prescribed PrEP and with diagnosed HIV infection in EHE local jurisdictions and EHE states from the US total; solid line: trends in PDRs before and after launch of the EHE initiative; *The COVID-19 pandemic affected HIV diagnosis services in 2020, leading to an underestimation of diagnoses that year and an overestimation of the PDR in 2021.

**FIGURE 2.**

HIV PrEP-to-diagnosis ratios by state—United States, 2019–2023. Reference lines: represent PrEP-to-diagnosis ratios in the United States in 2019 (7.4, blue solid) and 2023 (13.4, purple dashed). *EHE-funded states include Alabama, Arkansas, Kentucky, Mississippi, Missouri, Oklahoma, and South Carolina. **Non-EHE-funded states with the highest number of HIV diagnoses in rural areas include Colorado, Iowa, Kansas, New Mexico, Virginia, West Virginia, and Wisconsin; The PDR of 166 in Vermont is an unstable estimate because <5 HIV diagnoses were reported in 2022.

**FIGURE 3.**

HIV PrEP-to-diagnosis ratios in Ending the HIV Epidemic in the US initiative counties, D.C., and San Juan, PR, 2019–2023. Reference lines represent PrEP to diagnosis ratio in the United States in 2019 (7.4, blue solid) and 2023 (13.4, purple dashed).

TABLE 1.
 Characteristics of the EHE in the US Initiative Jurisdictions and Comparison of Jurisdictions With High Number of HIV Diagnoses by Select Characteristics—United States, 2023

Characteristics	EHE County N = 50 Median (IQR)	Non-EHE Counties* N = 50 Median (IQR)	EHE State N = 7 Median (IQR)	Non-EHE States* N = 7 Median (IQR)
Percentage Black persons	19.6% (10.0%, 29.2%)	12.2% (8.4%, 25.2%)	15.1% (9.6%, 26.3%)	3.9% (3.6%, 5.8%)
Percentage Hispanic persons	22.7% (10.3%, 33.2%)	15.4% (8.2%, 24.8%)	4.4% (4.0%, 6.7%)	9.5% (6.6%, 16.9%)
Percentage persons in poverty status	14.2% (11.6%, 15.9%)	12.1% (8.6%, 15.2%)	16.0% (15.0%, 16.3%)	11.1% (10.5%, 14.3%)
Percentage persons without health insurance	13.0% (9.8%, 16.4%)	12.5% (7.6%, 15.6%)	14.6% (12.8%, 16.9%)	10.6% (8.5%, 12.0%)
Provider density per 1000 population	5.1 (4.2, 7.6)	5.2 (3.3, 7.4)	3.5 (3.4, 3.6)	3.8 (3.5, 4.1)

Data sources: PrEP prescriptions were obtained from the IQVIA database; national and jurisdictional HIV diagnoses were obtained from CDC National HIV Surveillance System (NCHHSTP AtlasPlus <https://www.cdc.gov/nchhstp/about/atlasplus.html>); national and jurisdiction level demographics were obtained from US Census American Community Survey 5-year estimates, 2020; provider density was calculated from the HRSA Area Health Resources Files 2020 data, with total number of physicians, physician assistants, and nurse practitioners divided by the jurisdiction population size.

* Fifty non-EHE counties with next largest number of HIV diagnoses than EHE counties in 2016; 7 non-EHE states with next largest HIV diagnoses in rural areas in 2016 (Appendix Table 1, Supplemental Digital Content, <http://links.lww.com/QAJ/C496>).

TABLE 2.
DID in Preexposure PDRs Pre- and Post-Launch of the EHE in the US Initiative by EHE Status—United States, 2016–2023

	Median PDR (IQR)		Adjusted DID Estimate	
	Pre-EHE Initiation (2016–2019)	Post-EHE Initiation (2020–2023)	aDID (95% CI)	P
High HIV morbidity counties *				
EHE jurisdictions (n = 50)	3.6 (2.1, 6.5)	9.2 (6.3, 14.9)	0.2 (−1.0 to 1.3)	0.77
Top 50 non-EHE jurisdictions with high HIV morbidity (n = 50)	3.1 (1.9, 5.8)	9.2 (5.9, 14.5)	Reference	
High rural HIV morbidity states *				
EHE states (n = 7)	2.0 (1.3, 2.8)	5.3 (4.3, 7.2)	0.4 (−1.6 to 2.4) [†]	0.72
Top 7 non-EHE states with the highest number of HIV diagnoses in rural areas (n = 7)	5.3 (3.5, 9.3)	12.0 (8.4, 24.7)	Reference	

aDID: models were adjusted for jurisdictional level proportions of Black persons, Hispanic persons, persons in poverty, persons without health insurance, impact of COVID-19 pandemic on HIV diagnoses in 2020, and number of health care provider per 1000 population.

* Jurisdictions listed in Appendix Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C496>.

[†]The pre-EHE trends in PDR for both EHE-funded states and non-EHE-funded states did not satisfy the parallel trends assumption required for a valid DID analysis. The model assumes that the difference in trends observed before the intervention persisted during the post-EHE period. This adjustment serves only as an approximation rather than a formal DID estimate (Appendix Table 4c, Supplemental Digital Content, <http://links.lww.com/QAI/C496>, for detailed model and sensitivity analysis).