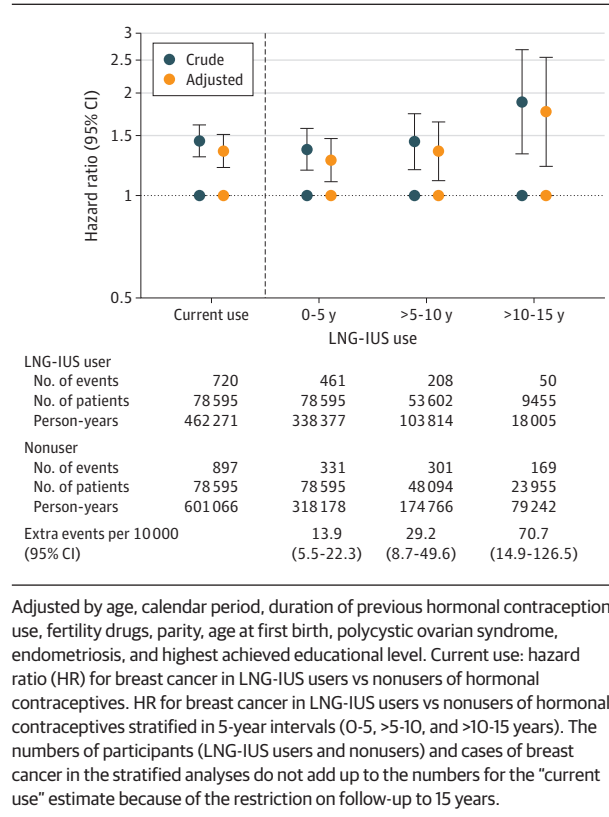


**Figure. Adjusted Hazard Ratios and Excess Breast Cancers per 10 000 Continuous Users of Levonorgestrel-Releasing Intrauterine System (LNG-IUS)**



Adjusted by age, calendar period, duration of previous hormonal contraception use, fertility drugs, parity, age at first birth, polycystic ovarian syndrome, endometriosis, and highest achieved educational level. Current use: hazard ratio (HR) for breast cancer in LNG-IUS users vs nonusers of hormonal contraceptives. HR for breast cancer in LNG-IUS users vs nonusers of hormonal contraceptives stratified in 5-year intervals (0-5, >5-10, and >10-15 years). The numbers of participants (LNG-IUS users and nonusers) and cases of breast cancer in the stratified analyses do not add up to the numbers for the "current use" estimate because of the restriction on follow-up to 15 years.

Given the increase in LNG-IUS use among females at an age with some risk for breast cancer, and its likely long-term use, information about breast cancer risk should accompany discussions about benefits and risks. The HR with short-term LNG-IUS use was similar to that of contraceptive pills<sup>1</sup> (1.2 [95% CI, 1.1-1.3]).

Limitations of this study include that some women may have had the LNG-IUS removed before the end of recommended use, leading to an underestimation of breast cancer risk. Lack of dose-response could indicate low statistical precision or no causal association. Also, unmeasured confounding cannot be excluded.

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**Accepted for Publication:** August 23, 2024.

**Published Online:** October 16, 2024. doi:10.1001/jama.2024.18575

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**Author Contributions:** Dr Mørch had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Acquisition, analysis, or interpretation of data:** All authors.

**Drafting of the manuscript:** Mørch.

**Critical review of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Corn.

**Obtained funding:** Mørch.

**Supervision:** Mørch.

**Other - Principal investigator and initiator of the study:** Mørch.

**Conflict of Interest Disclosures:** None reported.

**Funding/Support:** Sundheds Donationer (health donations) funded this study (2021-0128 to Mørch).

**Role of the Funder/Sponsor:** Sundheds Donationer had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Data Sharing Statement:** See Supplement 2.

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## Trends in Oral and Injectable HIV Preexposure Prophylaxis Prescriptions in the US, 2013-2023

Preexposure prophylaxis (PrEP) with antiretroviral medications is effective in preventing HIV acquisition.<sup>1</sup> Multiple PrEP medications have recently become available in the US, including 3 oral options with comparable safety and efficacy: branded tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) (July 2012), branded tenofovir alafenamide fumarate/emtricitabine (TAF/FTC) (October 2019), and generic TDF/FTC (October 2020).<sup>1</sup> A long-acting injectable option (cabotegravir) became available in December 2021.<sup>1</sup> TDF/FTC and cabotegravir have been approved for use by men and women; TAF/FTC has not been approved for females.<sup>1</sup> The costs of branded medications are substantially higher than those of generic PrEP.<sup>2</sup> Information on PrEP prescriptions by medication type is limited. This study examined trends in PrEP medication prescriptions in the US from 2013 to 2023.



Related article [page 1574](#)



Supplemental content

Table. Characteristics of Persons Prescribed Oral and Injectable PrEP—United States, January 2023 Through December 2023

|                                 | No. (%) <sup>a</sup> |                 |                 |                 |               | P value <sup>c</sup> |
|---------------------------------|----------------------|-----------------|-----------------|-----------------|---------------|----------------------|
|                                 | Total <sup>b</sup>   | Oral PrEP       |                 | Injectable PrEP |               |                      |
|                                 |                      | Generic TDF/FTC | Branded TAF/FTC | Branded TDF/FTC | Cabotegravir  |                      |
| Total                           | 505 730              | 289 869 (53.4)  | 214 102 (39.5)  | 24 768 (4.6)    | 13 709 (2.5)  |                      |
| Sex <sup>d</sup>                |                      |                 |                 |                 |               |                      |
| Male                            | 464 751 (91.9)       | 260 678 (89.9)  | 208 583 (97.4)  | 17 477 (70.6)   | 11 798 (86.1) | <.001                |
| Female                          | 40 558 (8.0)         | 28 953 (10.0)   | 5380 (2.5)      | 7253 (29.3)     | 1895 (13.8)   |                      |
| Unknown                         | 421 (0.1)            | 238 (0.1)       | 139 (0.1)       | 38 (0.2)        | 16 (0.1)      |                      |
| Age, y                          |                      |                 |                 |                 |               |                      |
| 13-24                           | 61 507 (12.2)        | 38 302 (13.2)   | 22 103 (10.3)   | 3134 (12.7)     | 1549 (11.3)   | <.001                |
| 25-34                           | 195 426 (38.6)       | 114 124 (39.4)  | 80 502 (37.6)   | 9958 (40.2)     | 5377 (39.2)   |                      |
| 35-44                           | 131 785 (26.1)       | 74 791 (25.8)   | 56 371 (26.3)   | 6632 (26.8)     | 3898 (28.4)   |                      |
| 45-54                           | 62 559 (12.4)        | 34 493 (11.9)   | 28 015 (13.1)   | 3019 (12.2)     | 1695 (12.4)   |                      |
| 55-64                           | 41 708 (8.2)         | 21 686 (7.5)    | 20 400 (9.5)    | 1695 (6.8)      | 867 (6.3)     |                      |
| ≥65                             | 12 745 (2.5)         | 6473 (2.2)      | 6711 (3.1)      | 330 (1.3)       | 323 (2.4)     |                      |
| Region                          |                      |                 |                 |                 |               |                      |
| Northeast                       | 105 593 (20.9)       | 68 174 (23.5)   | 36 983 (17.3)   | 3101 (12.5)     | 3572 (26.1)   | <.001                |
| Midwest                         | 75 926 (15.0)        | 49 864 (17.2)   | 26 651 (12.4)   | 2718 (11.0)     | 2093 (15.3)   |                      |
| South                           | 193 922 (38.3)       | 93 501 (32.3)   | 99 150 (46.3)   | 13 034 (52.6)   | 4717 (34.4)   |                      |
| West                            | 127 335 (25.2)       | 76 542 (26.4)   | 50 155 (23.4)   | 5802 (23.4)     | 3296 (24.0)   |                      |
| Unknown                         | 2954 (0.6)           | 1788 (0.6)      | 1163 (0.5)      | 113 (0.5)       | 31 (0.2)      |                      |
| Insurance type <sup>e,f</sup>   |                      |                 |                 |                 |               |                      |
| Public                          | 85 986 (21.0)        | 51 857 (22.3)   | 36 323 (20.0)   | 3917 (16.2)     | 1494 (37.9)   | <.001                |
| Private                         | 251 865 (61.6)       | 164 910 (70.9)  | 98 840 (54.6)   | 6902 (28.6)     | 1843 (46.8)   |                      |
| Assistance program <sup>g</sup> | 54 794 (13.4)        | 3103 (1.3)      | 42 447 (23.4)   | 12 908 (53.4)   | 498 (12.6)    |                      |
| Cash                            | 9079 (2.2)           | 6558 (2.8)      | 2670 (1.5)      | 344 (1.4)       | 77 (2.0)      |                      |
| Other                           | 6937 (1.7)           | 6155 (2.6)      | 910 (0.5)       | 97 (0.4)        | 25 (0.6)      |                      |

Abbreviations: PrEP, preexposure prophylaxis; TAF/FTC, tenofovir alafenamide fumarate/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.

<sup>a</sup> Column totals might not add to 100% due to rounding.

<sup>b</sup> Data do not add to row total due to deduplicated persons who used more than 1 type of PrEP medication during 2023.

<sup>c</sup> Corresponding to  $\chi^2$  test for differences in demographics by medication type.

<sup>d</sup> Sex as reported in the person's claims data.

<sup>e</sup> Data do not add to total due to missing information on insurance type.

<sup>f</sup> Approximately 19.2% of payer type information was missing.

<sup>g</sup> Manufacturer and government assistance programs.

**Methods** | Data were obtained from the IQVIA Real-World Longitudinal Prescription Data database (IQVIA), which included more than 95% of US retail pharmacy and more than 75% of mail order pharmacy prescriptions.<sup>3</sup> Prescription claims, medical claims, and demographics databases were linked,<sup>3</sup> allowing us to measure prescriptions for a single patient over multiple years and describe demographic and payer information by medication type.

To identify persons prescribed PrEP, we used a validated algorithm.<sup>3,4</sup> We estimated the cumulative and monthly number of persons aged 13 years or older prescribed PrEP by medication type from January 2013 to December 2023. Cumulative estimates were deduplicated by patient ID. Monthly estimates were deduplicated only by medication type because a person might be prescribed more than 1 type of PrEP in a given month. We used  $\chi^2$  tests to assess whether demographic characteristics (Table) of PrEP users were significantly different by medication type in 2023. Analyses were conducted using SAS version 9.4 (SAS Institute). Alpha of .05

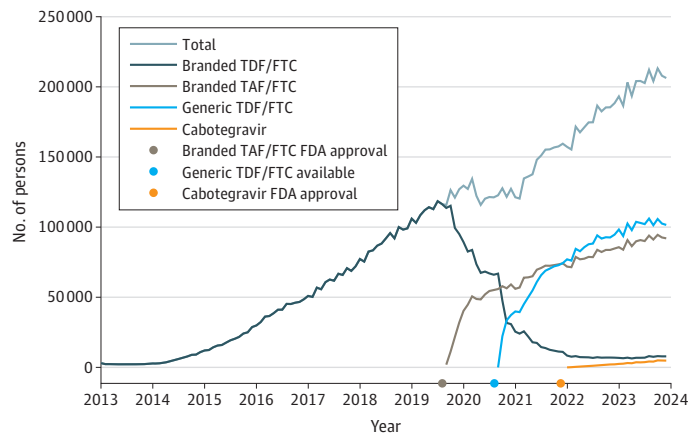
(2-sided) defined statistical significance. This study was determined by the Centers for Disease Control and Prevention to be exempt from institutional review board review. This study was reported using STROBE reporting guidelines.

**Results** | From January 2013 to December 2023, a cumulative 1 126 878 persons were prescribed oral or injectable PrEP, 88.6% of whom were male. The annual number of PrEP users increased from 10 281 in 2013 to 505 730 in 2023.

The monthly use of branded TDF/FTC increased from January 2013 to September 2019, but decreased after branded TAF/FTC and generic TDF/FTC became available (Figure). From December 2021 to December 2023, generic TDF/FTC had the highest monthly share of users among all medications (74 319 vs 74 106 for TAF/FTC; 11 002 for branded TDF/FTC).

A cumulative 99% of persons prescribed PrEP from 2013 to 2023 were prescribed oral PrEP. Since injectable cabotegravir became available in early 2022, it has been prescribed for a cumulative 15 428 persons. From 2022 to 2023,

Figure. Persons Prescribed Preexposure Prophylaxis (PrEP) by Type of PrEP Medication—United States, January 2013 Through December 2023



FDA indicates Food and Drug Administration; TAF/FTC, tenofovir alafenamide fumarate/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.

the percentage of PrEP users prescribed cabotegravir increased from 1.1% to 2.5%.

In 2023, generic TDF/FTC was the predominant form of PrEP prescribed (53.4%) (Table). Significant differences in age and region by medication were found, although differences by sex and insurance were even more pronounced. Of persons prescribed branded TDF/FTC, 29.3% were female compared with 2.5% for branded TAF/FTC ( $P < .001$ ). More users of generic TDF/FTC had private insurance (70.9%) vs those prescribed branded TAF/FTC (54.6%) and TDF/FTC (28.6%) ( $P < .001$ ); 22.3% of those prescribed generic PrEP had public insurance, similar to the percentages using branded medications.

**Discussion** | PrEP use increased between 2013 and 2023, with generic TDF/FTC being the most frequently prescribed medication since 2021. Injectable PrEP use was low likely because of barriers such as the high cost of stocking this expensive medication in clinics. The lower proportion of persons prescribed generic TDF/FTC with public insurance vs private insurance may be attributed to use of 340B programs with prescribing of branded medications required for manufacturer rebates.

New PrEP medications are heavily marketed, yet, generic PrEP dominated the market despite the availability of 3 branded medications. This could be attributed to a 2021 federal guidance directing insurers to cover the cost of generic PrEP medication without patient cost-sharing,<sup>5</sup> suggesting that effective health policy can result in lower health care expenditures.

Study limitations include that IQVIA did not capture prescriptions in organizations, such as Kaiser Permanente and the Veterans Administration, and did not include information about the current gender of PrEP users, so transgender users could not be identified. Also, PrEP use by race and ethnicity was not assessed because this information was missing for most users, and payer information was missing for about 20%.

Studying PrEP prescribing patterns is necessary to monitor progress in the efforts to increase PrEP use and end HIV spread.

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**Accepted for Publication:** September 26, 2024.

**Published Online:** October 14, 2024. doi:10.1001/jama.2024.21493

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**Conflict of Interest Disclosures:** None reported.

**Funding/Support:** This study was funded by the Centers for Disease Control and Prevention (CDC).

**Role of the Funder/Sponsor:** The CDC had a role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Disclaimer:** The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the CDC.

**Data Sharing Statement:** See the [Supplement](#).

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## COMMENT & RESPONSE

### Approach to Hospital Preparedness for Acute Surge Events Due to Emerging Infectious Diseases

**To the Editor** In the research and operations niche of hospital capacity strain and preparedness, although surges have historically been defined according to an unexpected large number of patients (eg, a mass casualty event), many have argued for a more nuanced definition that also includes *any* number of patients with high acuity (or higher acuity than the norm for the treating location) or with unique care needs (such as enhanced personal protective equipment or specialized personnel), or any isolated or simultaneous loss of resources (such as during a natural disaster), and any combination of these, locally or regionally.<sup>1</sup>

A recent *JAMA* Research Letter provided an elegant regional example of why such a nuanced view is necessary.<sup>2</sup> During the last decade's escalation in foreign cyberattacks against US health care systems,<sup>3</sup> 15 California hospitals experienced ransomware-related interruptions in their electronic health record systems and related temporary decreases in their emergency department patient volume, which were the index surge events: loss of resources in their hospitals' information technology infrastructure. But this Research Letter<sup>2</sup> illustrates important secondary surge events in which 37 nearby California hospitals not under attack and with electronic health records operating normally received transient increases in emergency department patients in the weeks after the attack because of either hospital-initiated or patient-driven diversions from the index hospitals.

This outcome is reminiscent of another *JAMA* Research Letter<sup>4</sup> that showed that in the hours after an in-hospital critical illness event on a ward, other patients on the same ward had a sustained elevated risk of a cardiac arrest or intensive care unit transfer. In the cyberattack example, the sequence was as follows: index hospital(s) infrastructure loss, leading to patient diversion, leading to secondary hospital(s) patient surge.<sup>5</sup> The hospital ward example instead had the sequence of acutely elevated index patient acuity (absolutely and in relation to typical local acuity on the ward), leading to diversion of resources in response to and toward that index pa-

tient, leading to reduction of resources for nearby secondary bystander patients.

These studies provide 2 important lessons: (1) capacity strain and surge events come in many forms; and (2) health care delivery systems are highly interconnected both within themselves and externally with modern society at large, hyperlocally, regionally, and even globally. In this increasingly globally connected world facing emerging threats from climate change-related natural disasters, novel pathogens, and cyberattacks, we should approach preparedness research holistically and with nuance.

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**Published Online:** October 14, 2024. doi:10.1001/jama.2024.17700

**Conflict of Interest Disclosures:** Dr Anesi reported grants from the National Heart, Lung, and Blood Institute (K23HL161353) during the conduct of the work; fees from UpToDate for writing COVID-19-related articles; fees for expert witness consulting; and grants from the University of Pennsylvania Perelman School of Medicine Thomas B. McCabe and Jeannette E. Laws McCabe Fund and the Leonard Davis Institute of Health Economics outside the submitted work; and reported that his spouse is employed by the US Food and Drug Administration. No other disclosures were reported.

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**In Reply** We appreciate Dr Anesi's interest in our Research Letter,<sup>1</sup> which reported that ransomware attacks disrupting care delivery in targeted hospitals in California from 2014 to 2020 led to an increase in emergency department visits at nearby facilities.

Although there are some similarities between our work and that of Volchenboum et al,<sup>2</sup> we wish to highlight a key difference. Our findings indicated that patients with emergency health care needs tended to seek care at nearby hospital emergency departments when the targeted facility was compromised. In contrast, Volchenboum et al<sup>2</sup> discussed the concept of negative externalities, in which the health of one patient negatively affected other patients in the same hospital ward. Although adverse health outcomes for patients using emergency departments near targeted facilities are a concern, this