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MAJOR ARTICLE

Suboptimal Uptake, Retention, and Adherence of Daily Oral Prexposure Prophylaxis Among People With Opioid Use Disorder Receiving Hepatitis C Virus Treatment

Christopher Brokus,[1,2] Sarah Kattakuzhy,[1,2] Britt Gayle,[1,2] Shivakumar Narayanan,[2] Ashley Davis,[1,2] Amelia Cover,[1,2] Rahwa Eyasu,[1,2] Emade Ebah,[1,2] Onyinyechi Ogbumbadiugha-Weekes,[1,2] Jennifer Hoffmann,[2] Rachel Silk,[1,2] Jasmine Stevens,[1,3] Julia Mount,[1,3] Catherine Gannon,[1,3] Laura Nussdorf,[1] Poonam Mathur,[2] Phyllis Bijole,[4] Miriam Jones,[4] Randy Kier,[4] David Sternberg,[4] Aaron Greenblatt,[5,6] Eric Weintraub,[5] Henry Masur,[1,3] Shyamasundaran Kottilil,[1,2] and Elana Rosenthal[1,2]

[1]DC Partnership for HIV/AIDS Progress, Washington, District of Columbia, USA, [2]Division of Clinical Care and Research, Institute of Human Virology, University of Maryland School of Medicine, Baltimore, Maryland, USA, [3]Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland, USA, [4]HIPS, Washington, District of Columbia, USA, [5]Division of Addiction Research and Treatment, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland, USA, and [6]Department of Family and Community Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA

Background. Daily oral preexposure prophylaxis (PrEP) with tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) prevents human immunodeficiency (HIV) among people who inject drugs (PWID). Despite rising HIV incidence and injection drug use (IDU), PrEP use remains low and there is limited research about uptake, adherence, and retention among PWID.

Methods. The ANCHOR investigation evaluated a community-based care model collocating hepatitis C virus (HCV) treatment, medication for opioid use disorder (OUD), and PrEP in individuals in Washington, DC, and Baltimore, Maryland. PrEP counseling was conducted from HCV treatment day 0 until week 24. Subjects could start any time during this window, were followed for 48 weeks, and were assessed for adherence by self-report and dried blood spot TDF analysis.

Results. One hundred ninety-eight participants were enrolled, of whom 185 (93%) were HIV negative. Twenty-nine individuals (15.7% of HIV-negative cohort) initiated PrEP. One hundred sixteen participants (62.7%) met 2014 Centers for Disease Control and Prevention (CDC) PrEP criteria due to IDU (82 [44.3%]), sex (9 [4.9%]), or both practices (25 [13.5%]). Providers recommended PrEP to 94 individuals (50.8%), and recommendation was associated with PrEP uptake. Median treatment duration was 104 days (interquartile range, 28–276 days), with 8 participants retained through week 48. Adherence was variable over time by self-report and declined by TDF analysis. No HIV seroconversions occurred.

Conclusions. This cohort of people with HCV and OUD experienced low uptake of PrEP despite the majority meeting CDC criteria. High rates of disruption and discontinuation, compounded by variable adherence, made TDF/FTC a suboptimal prevention strategy. Emerging modalities like long-acting formulations may address these barriers, but PWID have been excluded from their development to date.

Keywords. HCV; opioid use disorder; OUD; PrEP; PWID.

The opioid epidemic has created a steep rise in overdose deaths [1] and infectious complications of injection drug use (IDU), including hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections [2, 3]. People who inject drugs (PWID) experience a disproportionate burden of HIV thorough sexual and parenteral routes of transmission, as evidenced by recent outbreaks among PWID from Massachusetts to Washington state [4–7]. While infection rates fell among other vulnerable groups from 2014 to 2018, the annual rate of HIV transmission attributable to IDU increased, undermining decades of success in reducing HIV's impact [2, 8]. Expanding and optimizing preexposure prophylaxis (PrEP) represents one solution to this crisis and could help to achieve the goals of the HIV National Strategic Plan and the "Ending the HIV Epidemic" initiative to prevent new infections in PWID [9].

The Bangkok Tenofovir Study demonstrated that daily oral tenofovir disoproxil fumarate (TDF) as PrEP reduces HIV incidence among PWID by up to 56% [10, 11]. Despite this efficacy, PWID awareness and accurate knowledge about PrEP remain low and trail other at-risk groups [12–18]. Because harm reduction methods like syringe services programs (SSPs) and medication for opioid use disorder (MOUD) have successfully reduced HIV among PWID, community concerns about

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Correspondence: Elana Rosenthal, MD, Institute of Human Virology, University of Maryland School of Medicine, 725 West Lombard Street, Baltimore, MD 21201 (erosenthal@ihv.umaryland.edu)

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PrEP's potential to de-prioritize these methods are valid [19]. However, such programming remains inaccessible and underutilized in areas susceptible to HIV outbreaks, revealing an urgency to understand and enact a role for PrEP in the preventive armamentarium of PWID [20, 21].

In Washington, DC, where HIV prevalence was 1.8% in 2019, interventions such as SSP scale-up and treatment as prevention have been critical in decreasing IDU-related HIV transmission by 99% since 2007 [22]. Despite this progress, in 2018 the number of men diagnosed with HIV attributable to IDU increased for the first time in a decade while viral suppression among HIV-positive PWID was 73% [22]. Previous scholarship found low baseline PrEP familiarity among PWID in Washington, DC, and Baltimore, Maryland, yet demonstrably higher interest if it were made accessible [23, 24]. Eighty-seven percent expressed interest in free PrEP, whereas just 0.9% were currently taking PrEP [22]. Additional research documents a similar discrepancy between willingness and actual use of PrEP among PWID elsewhere in the United States [25, 26].

To date, there has been limited research on PrEP uptake, adherence, and retention in this population. In studies engaging PWID, actual uptake never exceeded 3% while rates of PrEP use among men who have sex with men (MSM) reached 35% in 2017 [27, 28]. Analyses of PrEP adherence and retention in PWID are supported by limited published data and represent a major deficit in implementation efforts. This investigation sought to evaluate PrEP initiation, adherence, and retention among people with OUD receiving HCV treatment in a community-based model for PrEP delivery in Washington, DC, and Baltimore, Maryland.

METHODS

Study Background

The Novel Model of Hepatitis C Treatment as Anchor to Prevent HIV, Initiate Opioid Substitution Therapy, and Reduce Risky Behavior (ANCHOR) study (NCT03221309) is an implementation investigation in a harm reduction drop-in center in Washington, DC, and an opioid treatment program in Baltimore [29]. All participants had chronic HCV, OUD, and active intravenous and/or intranasal opioid use. A first phase enrolled 100 people with IDU within 3 months and a second phase enrolled people with opioid misuse within 1 year. HCV was treated with a direct-acting antiviral (DAA) regimen per standard of care [30, 31]. Baltimore subjects were already taking MOUD; DC subjects could start MOUD during the study. From day 0 to the timepoint of HCV cure determination (week 24), HIV-negative participants were offered initiation of TDF/emtricitabine (FTC) for PrEP.

Patient Consent Statement

The study was approved by the University of Maryland Institutional Review Board. Written consent was obtained for all study participants.

Eligibility and Intake

One hundred ninety-eight patients 18 years or older with chronic HCV and quantifiable viral load, OUD by *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-V*) criteria, and reported opioid misuse within 1 year were enrolled ("ANCHOR cohort") [29]. Patients were excluded if they had decompensated liver disease, contraindications to DAAs, or were pregnant or breastfeeding.

After completing screening, patients who met inclusion criteria were started on DAAs at a day 0 visit. HIV-negative participants were eligible for PrEP initiation. Hereafter, "PrEP subgroup" refers to the subset of participants who initiated PrEP during the study and "No PrEP subgroup" refers to the subset who did not initiate PrEP during the study.

PrEP Initiation

A screening epidemiologic survey evaluated baseline PrEP interest. Patients were asked if they had heard of PrEP, were offered PrEP previously, and would be interested in taking PrEP. Medical providers assessed patient risk behavior and made recommendations based on the 2014 Centers for Disease Control and Prevention (CDC) criteria for PrEP initiation (the guidelines available at the time of study initiation). However, patients not explicitly meeting criteria were not excluded if they wished to start PrEP. Interest in PrEP uptake was assessed at visits from HCV day 0 until week 24. Patients could decide to initiate PrEP any time during this 6-month window.

PrEP Study Visits

If a patient initiated PrEP, an intake visit was completed with screening laboratory tests to ensure eligibility. Medication was dispensed at a unique PrEP day 0 visit. Patients were subsequently seen for a PrEP-specific visit at weeks 4, 12, 24, 36, and 48 after PrEP initiation, or until discontinuation. At each visit, participants were evaluated by a medical provider and labs were drawn to monitor health and safety.

PrEP Medication Dispensation

For the first 100 enrolled participants, TDF/FTC was available from donation through an investigator-initiated grant from Gilead Sciences and dispensed in 30-pill bottles at PrEP visits. At the PrEP day 0 visit, 1 bottle was dispensed; at the week 4 visit, 2 bottles were dispensed; and at the remaining visits, 3 bottles were dispensed.

For the remaining 98 subjects, patients who were interested in starting PrEP were given a monthly TDF/FTC prescription to be filled through insurance at their preferred pharmacy.

Adherence Assessments

PrEP adherence was assessed by patient self-report of pills missed in the previous week and previous month. Among the first 100 participants, adherence was also assessed by dried

blood spot (DBS) at weeks 4, 24, and 36. This assessment measures tenofovir diphosphate (TFV-DP) levels to estimate frequency of dosing [32]. Due to drug–drug interactions between TDF and DAA therapy for HCV, DBSs collected during HCV treatment (PrEP week 4) only indicated tenofovir's presence and could not evaluate dosing frequency.

Treatment interruption was defined as sustained PrEP nonadherence lasting 7 consecutive days or greater with subsequent continuation of medication. Details about interrupted treatment were recorded at each study visit.

If PrEP was discontinued before completion of 48 weeks, an end-of-study questionnaire was conducted to ascertain motivations for discontinuation.

Covariate Assessments

Baseline demographics, drug use behavior, and sexual behaviors were collected in an epidemiologic survey at screening. PrEP eligibility data based on CDC 2014 PrEP guidelines were collected by clinicians on or before HCV day 0.

At day 0, the Darke HIV Risk-Taking Behavior Scale (HRBS) was administered to all participants regardless of PrEP initiation. This validated survey assesses past-month drug and sexual behaviors that can increase HIV risk and assigns subscores and a total score based on engagement in those behaviors. Higher scores indicate greater potential risk for HIV acquisition.

RESULTS

Enrollment

One hundred ninety-eight participants enrolled in ANCHOR, of whom 185 (93%) were HIV-negative. Twenty-nine participants (15.7% of HIV-negative cohort) initiated PrEP.

The HIV-negative cohort had a median age of 57 years (interquartile range [IQR], 52–61 years) and was predominantly male (129 [69.7%]), Black (155 [83.8%]), and heterosexual (145 [92.9%]). One hundred one individuals (54.6%) reported baseline housing instability. There were no significant differences in demographics, housing status, or carceral history when comparing the PrEP and No PrEP subgroups ($P > .05$) (Table 1).

Past PrEP Exposure

At baseline, 68 individuals (36.8% of HIV-negative cohort) had ever heard of PrEP. Twenty-seven (14.6%) had been offered PrEP by a previous provider, and 7 (3.8%) took PrEP before the study. There were no significant differences in having heard of PrEP ($P = 1$), being offered PrEP previously ($P = .77$), or prior PrEP use ($P = .30$) between the PrEP and No PrEP subgroups. Individuals who expressed interest in taking PrEP were more likely to initiate PrEP than those who did not express initial interest ($P < .001$).

Table 1. Baseline Population Characteristics

Characteristic	HIV Negative (n = 185)	PrEP (n = 29)	No PrEP (n = 156)	*P* Value
Demographics				
Age, y, median (IQR)	57 (52–61)	54 (52–60)	58 (52–61)	.20
Male sex	129 (69.7)	21 (72.4)	108 (69.2)	.83
Black race	155 (83.8)	26 (89.7)	129 (82.7)	.42
Heterosexual	172 (93.0)	27 (93.1)	145 (92.9)	1
Baseline epidemiology				
Unstably housed	101 (54.6)	17 (58.6)	84 (53.8)	.69
Drug use, daily or greater frequency	111 (60.0)	21 (72.4)	93 (59.6)	.22
Receptive needle sharing, past year	24 (13.0)	7 (24.1)	17 (10.9)	.07
Receptive IDU equipment sharing, past year	54 (29.2)	8 (27.6)	46 (29.5)	1
>1 sex partner, past year	33 (17.8)	8 (27.6)	25 (16.0)	.18
Condomless vaginal sex, past year	72 (38.9)	12 (41.4)	60 (38.5)	.84
Condomless anal sex, past year	11 (5.9)	2 (6.9)	9 (5.8)	.68
Transactional sex, past year	10 (5.4)	2 (6.9)	8 (5.1)	.66
2014 CDC eligibility				
Met IDU criteria only	82 (44.3)	10 (34.5)	72 (46.2)	.63
Met sex criteria only	9 (4.9)	2 (6.9)	7 (4.5)	.31
Met both criteria	25 (13.5)	9 (31.0)	16 (10.3)	**.006**
2017 CDC eligibility				
Met IDU criteria only	39 (21.1)	5 (17.2)	34 (21.8)	.53
Met sex criteria only	20 (10.8)	4 (13.8)	16 (10.3)	.8
Met both criteria	31 (16.8)	11 (37.9)	20 (12.8)	**.002**

Data are presented as No. (%) unless otherwise indicated. Bolded values represent significant associations ($P < .05$).

Abbreviations: CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus; IDU, injection drug use; IQR, interquartile range; PrEP, preexposure prophylaxis.

HIV Risk Behaviors

When asked about rationale to initiate PrEP, 11 participants (37.9% of the PrEP subgroup) named both drug use and sex as motivations to start, 9 individuals (31%) were uniquely motivated by IDU risk, and 8 individuals (27.6%) were motivated by sexual risk alone.

Self-perception of being at risk for HIV was low in both the PrEP subgroup (3 subjects [10.3% of subgroup]) and the No PrEP subgroup (19 [12.2%]) and was not associated with PrEP uptake ($P = 1$).

Baseline risk behaviors were similar between subgroups. Both populations reported high rates of daily or greater drug use frequency (21 [72.4%] vs 93 [59.6%]; $P = .22$) and moderate rates of receptive needle sharing (7 [24.1%] vs 17 [10.9%]; $P = .07$) and receptive injection equipment sharing (8 [27.6%] vs 46 [29.5%]; $P = 1$) over the past year. Previous year sexual practices, including activity, number of partners, condomless anal or vaginal sex, and transactional sex, did not significantly differ between subgroups ($P > .05$).

HIV Risk Assessment

Among HIV-negative subjects, 116 people (62.7%) met 2014 CDC criteria for PrEP initiation based on risk from IDU (82 [44.3%]), sex (9 [4.9%]), or both (25 [13.5%]). Ninety participants (48.7%) met 2017 CDC PrEP criteria. The PrEP subgroup was more likely to meet both IDU and sexual indication for PrEP initiation by 2014 ($P = .006$) and 2017 CDC guidelines ($P = .002$) compared to the No PrEP subgroup (Table 1).

Regarding baseline HRBS, the PrEP and No PrEP subgroups had comparable scores from drug use risk-taking ($P = .34$), sexual risk-taking ($P = .85$), and composite risk-taking scores ($P = .40$).

Clinicians recommended PrEP to 94 individuals (50.8%) within the HIV-negative cohort. Of those, 21 subjects initiated PrEP (72.4% of PrEP subgroup) and 73 did not (46.8% of No PrEP subgroup). Clinician recommendation was significantly associated with PrEP uptake ($P = .02$). For the 8 PrEP subgroup members without initial recommendation to initiate PrEP, 6 (75%) subsequently met criteria due to emergent risk from IDU (4 [50%]) or sex (2 [25%]) after they started PrEP. The remaining 2 (6.9% of PrEP subgroup) requested PrEP in the absence of self-reported behavioral risk factors.

Retention

Median treatment duration for individuals on PrEP was 104 days (IQR, 28–276 days). Eight participants (27.6% of the PrEP subgroup, 4.3% of the HIV-negative cohort) were retained on PrEP through the week 48 timepoint. Twenty-five (86.2% of subgroup) remained on PrEP at week 4, 21 (72.4%) at week 12, 13 (44.8%) at week 24, and 9 (31%) at week 36 (Figure 1).

The most common cause for discontinuation was side effects, resulting in 7 participants (24.1% of PrEP subgroup) terminating PrEP. In particular, nausea/vomiting was the most frequent side effect, reported by 4 (13.8%). Individuals who discontinued due to side effects ended PrEP earlier than participants who terminated for other reasons ($P = .022$) and had a median treatment duration of 28 days (IQR, 8.5–51.5 days). Other discontinuation reasons included no longer being interested in PrEP (n = 5; median duration, 63 days [IQR, 21–104 days]), lost to follow-up (n = 4; median, 211 days [IQR, 177.3–224.8 days]), medical contraindication (n = 3; median, 84 days [IQR, 43–127.5 days]), housing stability (n = 1; median, 71 days), and death (n = 1; median, 171 days) (Figure 2 and Supplementary Table 1).

Daily Pill Adherence

The number of participants who reported perfect adherence (7 pills/week) was 12 (52.2% of retained participants) at week 4, 10 (47.6%) at week 12, 6 (50%) at week 24, 1 (12.5%) at week 36, and 5 (62.5%) at week 48. Weekly adherence to 4 or more pills was reported by 17 participants (73.9%) at week 4, 15 (71.4%) at week 12, 8 (66.7%) at week 24, 5 (62.5%) at week 36, and 7 (87.5%) at week 48 (Figure 3A).

In adherence measured by DBS analysis, 17 participants (94% of the subset for whom sera were assessed) had detectable TFV-DP at week 4. At week 24, DBS identified 6 individuals (50% of retained participants) with perfect adherence and 2 (25%) at week 36 (Figure 3B).

PrEP Interruptions

Over the course of taking PrEP, 10 individuals (34.5% of the PrEP subgroup) reported a total of 13 treatment interruptions. Median duration of medication interruption was 30 days (IQR, 24–45 days). The most frequent cause was loss or theft of medication, which accounted for 6 interruptions (Figure 4).

HIV Seroconversion

In both the PrEP and No PrEP subgroups, no incident cases of HIV occurred over the study period.

DISCUSSION

In this cohort of 198 people with OUD undergoing HCV treatment, despite high rates of PrEP eligibility, uptake of and retention to TDF/FTC for HIV prevention was low and daily pill adherence was suboptimal.

Though roughly two-thirds of the cohort met CDC PrEP criteria, self-perception of HIV risk was consistently low and was not associated with deciding to start PrEP. Furthermore, while patients were more likely to meet criteria due to IDU-related risk than sex, uptake was significantly higher among people with both IDU and sexual risk (36%) compared to injection risk alone (12%). These data suggest that patients may

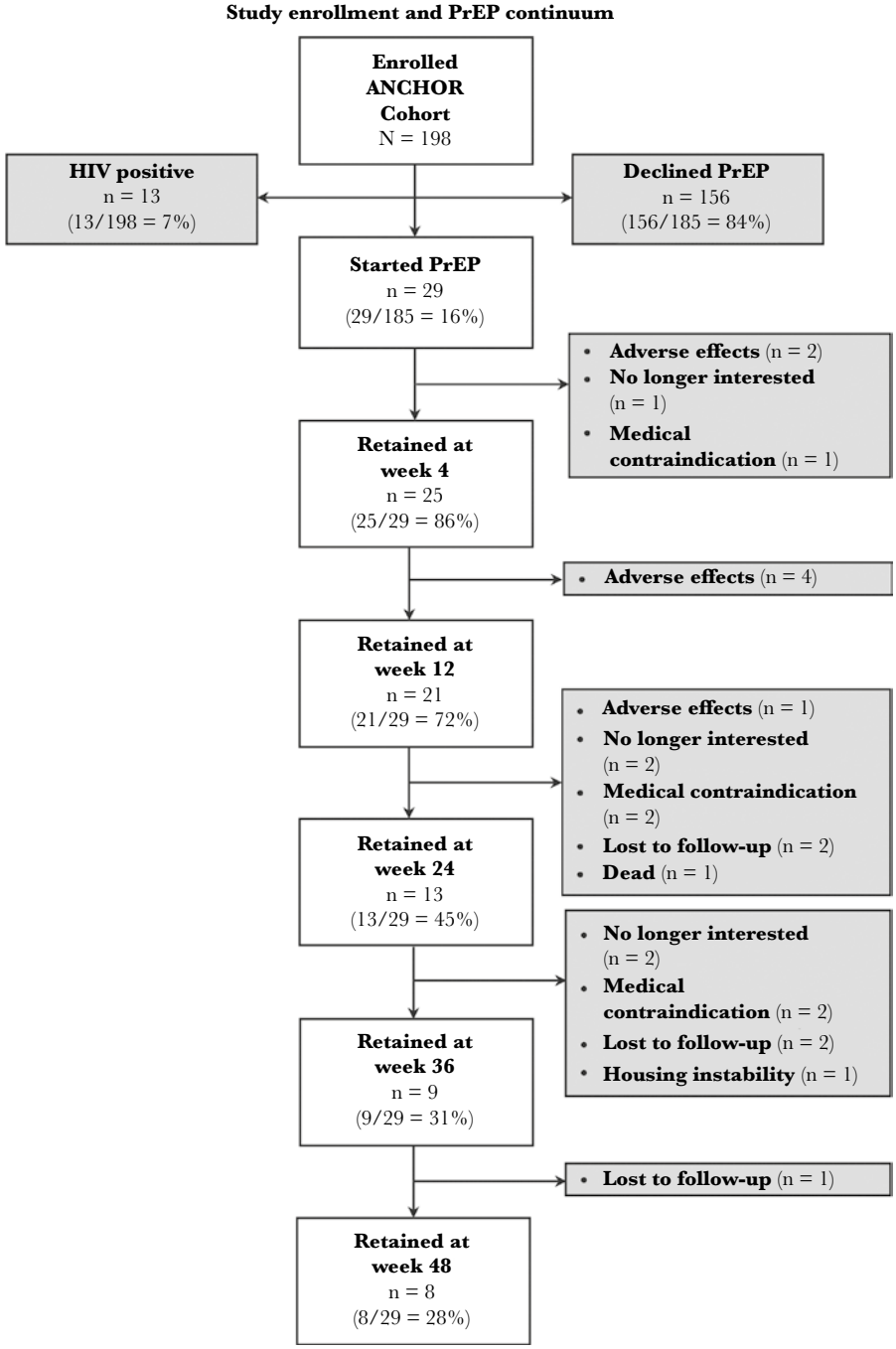

Figure 1. A Novel Model of Hepatitis C Treatment as Anchor to Prevent HIV, Initiate Opioid Substitution Therapy, and Reduce Risky Behavior (ANCHOR) preexposure prophylaxis (PrEP) study enrollment and participant retention along the PrEP continuum. Abbreviations: ANCHOR, A Novel Model of Hepatitis C Treatment as Anchor to Prevent HIV, Initiate Opioid Substitution Therapy, and Reduce Risky Behavior; HIV, human immunodeficiency virus; PrEP, preexposure prophylaxis.

perceive greater threat from sex than IDU or may prioritize other strategies such as SSPs to mitigate IDU-related HIV risk. PrEP discussions among people with OUD should encompass the complexity and overlap of injecting and sexual vulnerability to facilitate engaging in preventive health measures [14, 33].

Of those who met 2014 CDC eligibility, only 16% initiated PrEP. ANCHOR uptake was higher than several studies documenting PrEP use among PWID between 1.8% and 3% [13–17] and aligns with assessments of past or current PrEP use in an urban methadone program [25, 34]. Despite increasing willingness to use PrEP and its delivery in collocated community-based care, PrEP was not a primary component in the prevention framework of PWID. For ANCHOR subjects, PrEP underutilization may originate from attitudes that HIV was not a major concern and from behavioral mitigation like SSP enrollment, which may modulate risk perceptions.

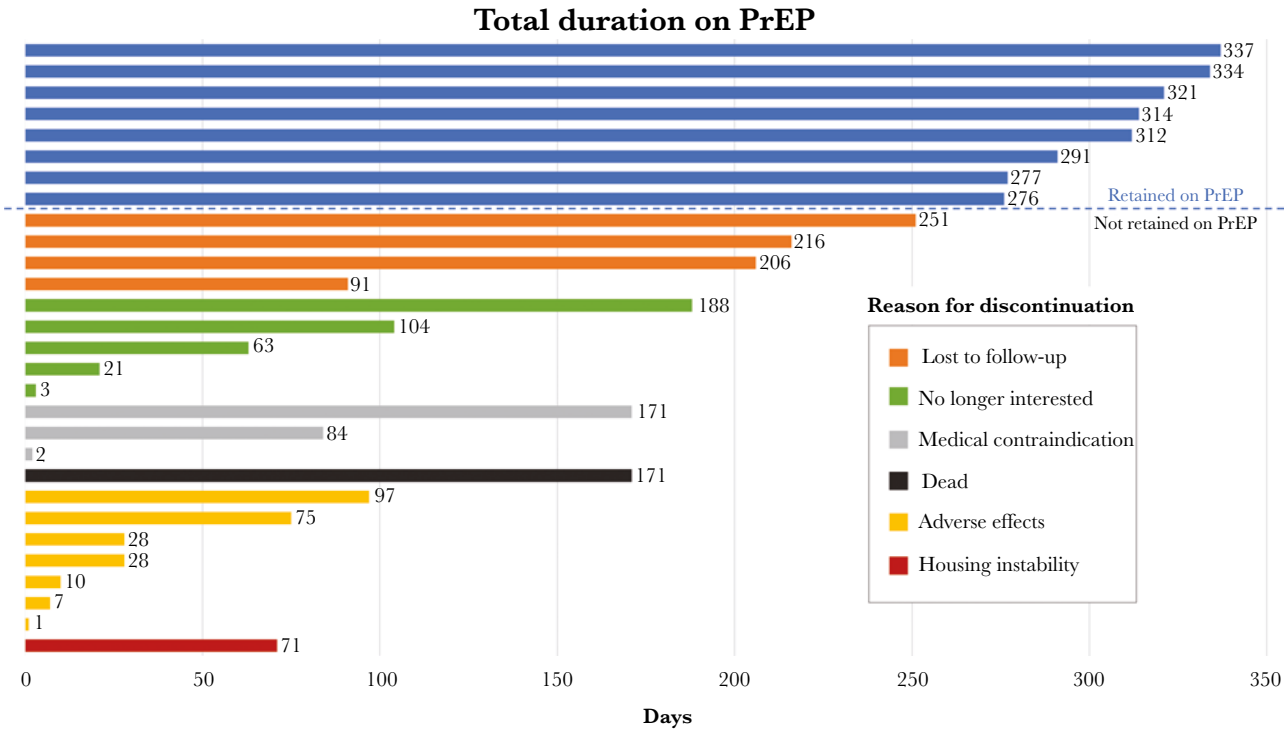

Figure 2. Total duration, in days, on preexposure prophylaxis (PrEP) in the A Novel Model of Hepatitis C Treatment as Anchor to Prevent HIV, Initiate Opioid Substitution Therapy, and Reduce Risky Behavior (ANCHOR) study. Discontinued participants are grouped by reason for cessation of therapy.

Notably, ANCHOR participants were significantly more likely to initiate PrEP when recommended by a clinician, highlighting an active role for providers in bringing patients into learning and decision-making around PrEP initiation. This is in contrast to existing data showing that, despite CDC guidance, providers are least likely to prescribe PrEP to PWID relative to other vulnerable groups [35, 36].

Participants experienced an array of challenges that complicated retention on TDF/FTC over 1 year. Less than one-third of subjects who initiated PrEP completed 48 weeks of treatment, with the largest drop-off between 1 and 3 months. Side effects were the most frequent culprit of discontinuation and resulted in the shortest treatment duration. These difficulties illustrate the importance of counseling on potential side effects and performing targeted interventions to help patients continue PrEP through resolution of side effects, especially in their first month of treatment.

Adherence to PrEP by both self-report and DBS was suboptimal. Participant-dependent report of perfect weekly adherence fluctuated over the treatment continuum, never exceeding 60%. Similar to other studies, self-report held poor predictive value for measuring adherence [37]. Perfect adherence by DBS never exceeded 50%, and the percentage of participants with any quantifiable TFV-DP declined at every timepoint. PrEP adherence remains a critical consideration because of uncertainty surrounding dosing strategy and protective pill coverage for PWID. Notably, research reexamining individual variability in TFV-DP measurements suggests that previous benchmarks of adherence by DBS may have underestimated the pharmacologic forgiveness of this drug at lower-dosing frequencies [38]. Furthermore, while required adherence due to sexual risk has been well-studied in MSM/transgender women populations, the minimum threshold required to prevent HIV by IDU remains unclear. Given the dearth of studies assessing PrEP adherence in PWID and revisions to TFV-DP benchmarks of adherence, ANCHOR offers insight into understanding this crucial stage of the PrEP cascade and demonstrates a need to clarify effective dosing regimens in this population [27].

PrEP interruptions were common, occurring in one-third of the PrEP subgroup. Interruptions potentially exposed these individuals to HIV acquisition and further compounded adherence struggles. Interruptions were predominantly due to lost or stolen medication; other socioecological factors such as incarceration and housing instability also contributed to treatment disruption and nonadherence. These experiences exemplify the structural vulnerability and reality of marginalization this population confronts, echoed in scholarship documenting increased risk of HIV and HCV among PWID experiencing homelessness [39]. Though people with OUD may be at greatest need for a dynamic prevention toolkit, barriers in housing, transportation, and healthcare impede their ability to access, initiate, and remain on daily oral PrEP [2].

New long-acting antiretrovirals such as cabotegravir, islatravir, and lenacapavir have emerged as a potential strategy

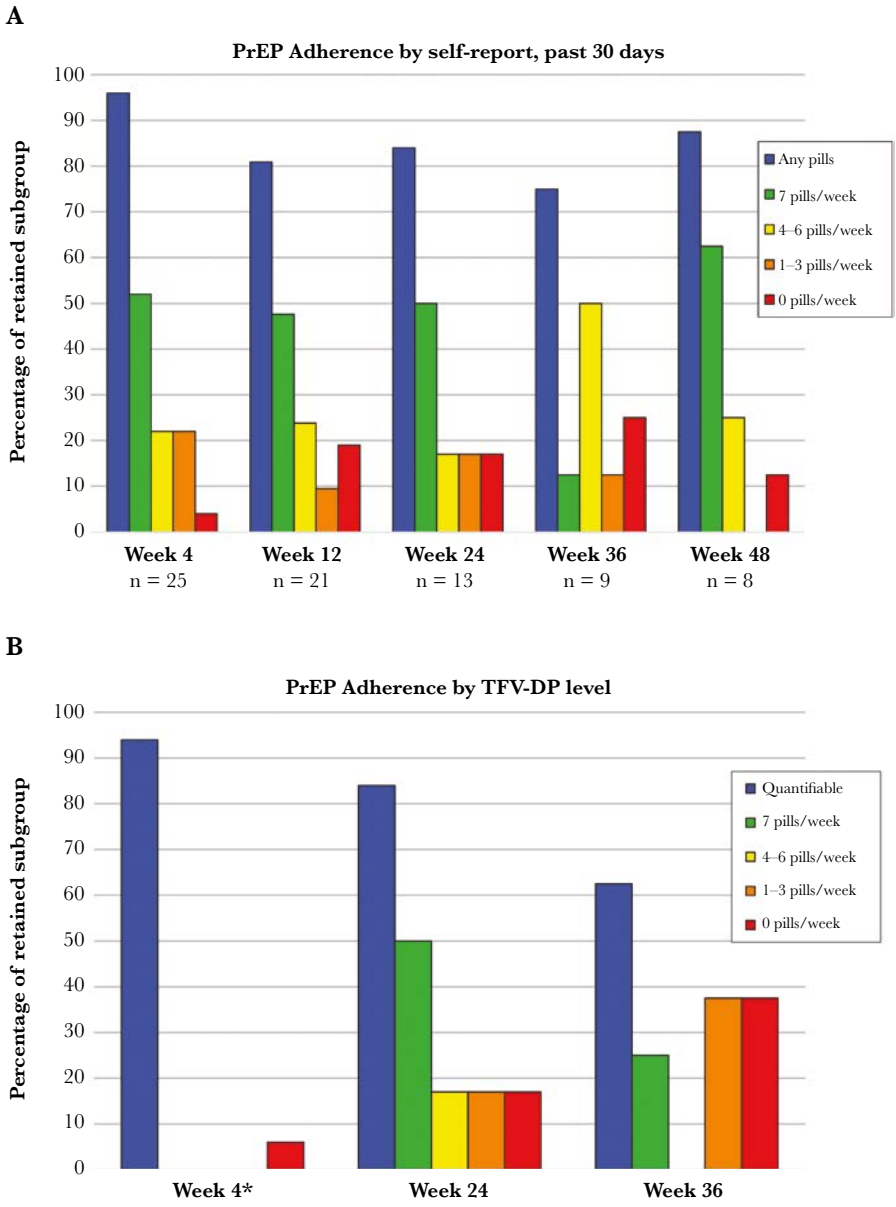

Figure 3. Adherence on preexposure prophylaxis by study timepoint, assessed via self-report (*A*) and dried blood spot analysis of tenofovir level (*B*). *Based on present or not present. Abbreviations: PrEP, preexposure prophylaxis; TFV-DP, tenofovir diphosphate.

to improve PrEP adherence and enhance efficacy, and may help overcome treatment setbacks experienced by the ANCHOR cohort [40–44]. However, investigational studies of cabotegravir and tenofovir alafenamide/FTC as PrEP have excluded PWID to date [42, 45]. Given potential real-world preference for and benefit from long-acting formulations, future investigations should include this population in the development and implementation of these promising technologies.

Delivering HIV prevention in a community-based model collocated with HCV therapy and MOUD was not sufficient in optimizing the PrEP cascade for people who use drugs. Models leveraging peer navigation, media-based PrEP interventions, and social network activation have shown promise in improving MSM engagement in PrEP [46–48]. Precedents examining targeted interventions to increase PWID adherence in HIV care offer further impetus to apply such approaches to PrEP implementation that were not a part of the ANCHOR investigation [49, 50]. Novel PrEP modalities, innovative and community-centered implementation models directly targeting PrEP uptake, and effective patient education and outreach represent future directions to achieve this goal.

Limitations

While this study offers an important contribution to understanding PrEP use among people with OUD, there are limitations. First, this implementation study of the PrEP cascade was

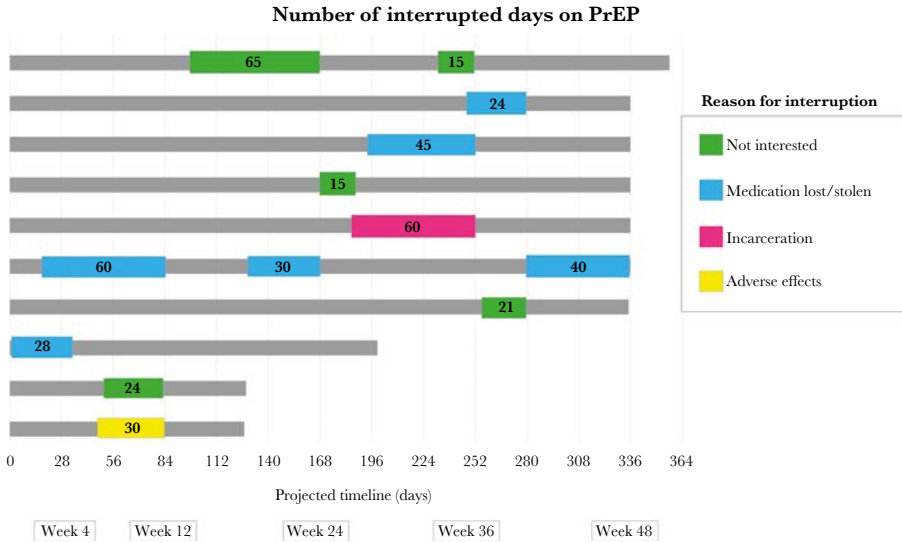

Figure 4. Duration, occurrence, and cause of treatment disruption among the subset of participants who experienced any interrupted days on preexposure prophylaxis. Abbreviation: PrEP, preexposure prophylaxis.

complicated by real-world challenges people who use drugs confront, such as medication procurement and structural vulnerability, which in turn may have impacted outcome variables. Next, ANCHOR principally evaluated a model of care for HCV and OUD, where motivations to start PrEP were secondary to subjects' desire to receive DAA therapy. HCV-negative individuals seeking PrEP may have different motivations and experiences than ANCHOR subjects receiving PrEP in the framework of HCV treatment. Additionally, concomitant DAA therapy and PrEP initiation in the majority of the PrEP subgroup may have caused an elevated rate of early termination from side effects than had PrEP been offered outside HCV treatment. Individuals with OUD may experience gastrointestinal symptoms from opioid withdrawal that can be interpreted as medication-induced [51]. Additional work is needed to clarify optimal approaches to treating HCV and initiating PrEP in similar populations to avoid this retention pitfall. Finally, PWID in the Washington, DC–Baltimore metropolitan area have access to SSPs and may have established best prevention practices in this HIV-endemic region. PrEP delivery and scale-up may hold greater utility and urgency for PWID in localities where harm reduction interventions are sparse, for whom HIV vulnerability may be higher.

CONCLUSIONS

For ANCHOR subjects with OUD receiving HCV therapy, high rates of PrEP eligibility accompanied suboptimal uptake, adherence, and retention. These data highlight a need for better partnerships between providers and PWID to improve PrEP knowledge and implementation in this community. Challenges with daily adherence and persistence in care highlight the necessity for newer PrEP modalities and models that may overcome these struggles, as well as the importance of including PWID in the research that generates them. However, biomedical discoveries alone will not address structural barriers like housing, incarceration, healthcare accessibility, and stigma that hamper the PrEP cascade among PWID. Data from the ANCHOR investigation address a critical gap in the current landscape of prevention research and demonstrate the need to optimize PrEP adherence and retention to prevent HIV in people with OUD.

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

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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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