

# Pre-Exposure Prophylaxis (PrEP) Safety and Tolerability in Individuals $\geq$ 45 Years Old

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## Abstract

**Background:** The unmet need for PrEP has been exacerbated by the COVID-19 pandemic. While clinical trials have established the safety and efficacy of PrEP, the majority of participants were <45 years old. We aimed to better understand the unique considerations of use in this population through the assessment of real-world data in our cohort of Veterans  $\geq$  45 years old.

**Setting and Methods:** We reviewed all PrEP users, receiving any approved regimen at the Baltimore VA Medical Center in Maryland, USA between 12/3/2014 and 12/3/2019 and found n=59; of those, 18 (30.5%) were  $\geq$  45 years of age.

**Results:** There was no difference between baseline renal function and that  $\geq$  3 months post-PrEP initiation for all patients (creatinine (p=0.63), GFR (p=0.95), proteinuria (p=0.35)). Two patients switched from TDF to TAF due to rising creatinine. Both patients had comorbid hypertension and were on concomitant antiviral treatment, increasing the risk of nephrotoxicity; one patient had concomitant diabetes; neither had documentation of smoking, nor osteoporosis. Two others self-discontinued PrEP due to decreased risk behaviors or were lost to follow-up. Half (9/18) of patients had DEXA scans, with 4 (44.4%) indicating osteopenia, but all of these were noted prior to PrEP initiation and none had documented fractures either pre- or post-PrEP.

**Conclusions:** Our data suggests that TDF/FTC might be a safe and accessible option in this population. With increasing need for PrEP uptake, dedicated studies specific to this population should be conducted to further assess safety, efficacy, and tolerability of TDF/FTC and TAF/FTC.

**Keywords:** PrEP; Safety; Tolerability; Older adults

## Introduction

Pre-exposure prophylaxis (PrEP) is a combination of antiretroviral medications, most commonly prescribed as two co-formulated antiretrovirals, taken as a single tablet daily to significantly reduce the risk of human immunodeficiency virus (HIV) infection in individuals at high risk. When taken as prescribed, PrEP is the most effective biomedical intervention to prevent HIV transmission. As such, PrEP is widely acknowledged as a necessary population health tool to combat the HIV epidemic. With upwards of 40,000 new HIV infections occurring in the United States (U.S.) each year and 20% of individuals with HIV in the U.S. unaware of their status,

preventing new HIV transmissions through the use of proven interventions such as PrEP is critical [1].

Recent U.S. data illustrates that more than 50% of all new HIV diagnoses occurred in only 48 counties, Washington, D.C., and San Juan, Puerto Rico [1]. In response to these disparities, U.S. Department of Health and Human Services (HHS) launched an initiative in 2019 to end the HIV Epidemic (EtHE) in the U.S. by 2030 [1]. This ambitious plan focuses on four key strategies: diagnose, treat, prevent, and respond to avert an estimated 250,000 total HIV infections [1]. However, while PrEP has been available in the U.S. since 2012, a variety of constraints including knowledge about PrEP, perception of HIV risk,

social stigma, provider bias, patient distrust of healthcare systems, lack of access and PrEP side effects, have resulted in inadequate access and uptake among populations that need it the most [2]. The U.S. Centers for Disease Control and Prevention estimates that over 1.2 million U.S. adults, particularly Black adults, could potentially benefit from PrEP, but only a minority of those are currently receiving it [3]. This unmet need has been exacerbated by the Corona virus 2019 Disease (COVID-19) which has created a syndemic health burden for those at high risk for HIV infection [4,5]. Early data indicates that acute HIV cases have doubled during the COVID-19 pandemic and research from Italy suggests that encounters for older individuals with sexually transmitted infections increased after the COVID-19 related lockdown, highlighting the ongoing need for HIV prevention during the current COVID-19 era [6,7].

Previous research has shown that older adult populations are at higher risk of tenofovir-induced renal tubular dysfunction and bone fractures [8,9]. However, the majority of clinical trials establishing the safety, efficacy, and tolerability of PrEP exclude individuals  $\geq$  45 years old; to our knowledge, a lack of a dedicated assessment exists in this age cohort [10]. While a multiple large scale, randomized, placebo-controlled clinical trials have evaluated the safety and efficacy of PrEP in various at-risk populations; the majority of participants were  $<$ 45 years old [11]. As PrEP is increasingly needed and used by older adults, who account for nearly 20 percent of new HIV infections in the U.S., we aimed to better understand the unique considerations of use in this population through the assessment of real-world safety and tolerability data through retrospective analysis.

Our review was conducted at the Baltimore Veterans Affairs Medical Center (VAMC), part of the Veterans Health Administration (VHA), the single largest provider of HIV care in the U.S [12]. The most recent Veterans Health Administration (VA) utilization data (2018) indicates that 79.3% of all enrollees are 45-65+ years of age, with an older average age compared to the general population and with an increased risk for physical health problems [13]. The Baltimore VAMC located in Baltimore, Maryland U.S. is situated in a U.S. Department of Health and Human Services (HHS) designated hot spot for HIV incidence. The Baltimore VAMC also serves individuals from other surrounding hot spot counties including Montgomery and Prince George's County in Maryland.

## Methods

Retrospective electronic medical record chart reviews of all PrEP users defined as any individual with documentation of a prescription for any Food and Drug Administration (FDA) approved PrEP regimen at the Baltimore VA Medical Center between 12/3/2014 and

12/3/2019 was conducted. Chart reviews found a total of  $n=59$  users; of those, 18 (30.5%) were  $\geq$  45 years of age and were included for the purpose of this assessment. All indications for PrEP utilization including sexual risk and injection drug use risks were included.

Patient level data was collected and only accessible through a secure, password protected facility server to ensure confidentiality. Data reviewed and collected included an overview of facility and provider level prescribing statistics and patient level data including: identifiers (name, date of birth) for quality assurance, demographics, past HIV antiretroviral (ARV) use, sexually transmitted infections and substance use disorders, and applicable safety and screening labs with emphasis on renal function and bone density. All protected health information was deidentified prior to analysis to protect patient confidentiality. Extracted data was compiled and stored electronically as an encrypted file on the secured facility server on a password protected computer. This project was reviewed and received an exemption determination by the Institutional Review Board of the University of Maryland and was conducted in compliance with local regulatory requirements.

## Results

Chart reviews noted  $n=59$  PrEP users; of those, 18 (30.5%) were  $\geq$  45 years of age (Table 1). Patients were 45-70 years ( $M=57.1$ ,  $SD=8.1$ ), predominately male (17/18, 94.5%), not Hispanic or Latino (17/18, 94.5%), evenly split between Black and white patients (8/18, 44.4% each). Average duration of PrEP use was 14 months ( $SD=12.3$ ) with the majority most recently taking tenofovir disoproxil fumarate (300 milligrams (mg)) and emtricitabine (200 mg) (TDF/FTC) (13/18, 72.2%) due to men who have sex with men (MSM) risk (12/18, 66.7%). All individuals were on PrEP to reduce risk of sexual HIV acquisition, including one heterosexual individual with a serodiscordant partner.

There was no difference between baseline renal function and renal function  $\geq$ 3months post-PrEP initiation for all 18 patients (creatinine ( $p=0.63$ ), glomerular filtration rate (GFR) ( $p=0.95$ ), proteinuria ( $p=0.35$ )). Two patients switched from TDF/FTC to tenofovir alafenamide (25 mg) and emtricitabine (200 mg) (TAF/FTC) due to rising creatinine. Both patients had comorbid hypertension and were on concomitant antiviral treatment (acyclovir and valacyclovir), increasing the risk of nephrotoxicity; one patient had concomitant diabetes; neither had a history of smoking nor osteoporosis. Two other patients self-discontinued PrEP due to decreased risk behaviors or were lost to follow up. Half (9/18) of patients had record of bone density scans (DEXA scans), with 4 (44.4%) indicating osteopenia, but all were noted prior to PrEP initiation and none had documented fractures either pre- or post-PrEP as determined by chart reviews completed on January 14, 2020.

	N	%	Range	Mean (SD)
Age $\geq$ 45 years	18	30.5	45-70 yrs	57.11 (8.11)
Male	17	94.45		
Female	1	5.55		
Non-Hispanic or Latino	17	94.45		
Black	8	44.44		
White	8	44.44		
TDF/FTC (Truvada)	13	72.22		
Duration (months)			1-34 mon	14 (12.34)
Indication:				
MSM	12	66.67		
Bisexual	2	11.11		
Heterosexual	4	22.22		

**Table 1:** Patient Characteristics of all PrEP users  $\geq$  45 years old receiving any FDA approved PrEP regimen at the Baltimore VA Medical Center in Maryland, U.S. between 12/3/2014 and 12/3/2019.

## Discussion

Our real-world assessment may help to support the overall safety and tolerability of PrEP in adults  $\geq$  45 years old, suggesting that TDF/FTC might be a safe and accessible option for HIV prevention. Although the duration of PrEP utilization in this sample is relatively short (M=14 months (SD=12.34)), it is consistent with previously reported data for PrEP users in the U.S [14].

Our assessment is not without limitations, most notably a small sample size (n=18). Furthermore, our review was conducted prior to the onset of the COVID-19 pandemic. Additional analysis should consider the unique characteristics of this cohort including changes in sex-related behavior risk and barriers to accessing preventative healthcare services (PrEP) during this unprecedented time.

While our assessment may help to support the overall safety and tolerability of PrEP in older adults, other studies have suggested that increased frequency of PrEP safety monitoring should be considered for this population who are more likely to have comorbid conditions [15]. Should this be true, even in the absence of a dedicated PrEP study in older adults, the VA has long been a leader in telehealth innovation and provision and especially given the challenges of the COVID-19 era, the VA healthcare system is uniquely equipped to meet the needs of its patients and continue to ensure quality care delivery. However, with increasing need for PrEP uptake, dedicated studies and ongoing clinical surveillance specific to individuals  $\geq$  45 years old should be undertaken to further assess the safety, efficacy, tolerability of and barriers to uptake of TDF/FTC and TAF/FTC.

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## Conflict of Interest

The authors report no real or perceived vested interests related to this article that could be construed as a conflict of interest. The contents of this presentation do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

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