AIDS and Behavior
https://doi.org/10.1007/s10461-020-03107-6

SUBSTANTIVE REVIEW

Addressing Unhealthy Alcohol Use and the HIV Pre-exposure Prophylaxis Care Continuum in Primary Care: A Scoping Review

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Accepted: 13 November 2020

Abstract

Individuals with unhealthy alcohol use are at increased risk for HIV acquisition and may benefit from receiving HIV pre-exposure prophylaxis (PrEP) in primary care settings. To date, literature synthesizing what is known about the impact of unhealthy alcohol use on the PrEP care continuum with a focus on considerations for primary care is lacking. We searched OVID Medline and Web of Science from inception through March 19, 2020, to examine the extent, range, and nature of research on PrEP delivery among individuals with unhealthy alcohol use in primary care settings. We identified barriers and opportunities at each step along the PrEP care continuum, including for specific populations: adolescents, people who inject drugs, sex workers, and transgender persons. Future research should focus on identification of candidate patients, opportunities for patient engagement in novel settings, PrEP implementation strategies, and stigma reduction.

Keywords HIV · Alcohol-related disorders · Primary prevention · Primary health care · Review

Resumen

Indivíduos con dificultades con el uso del alcohol tienen un alto riesgo de contraer VIH y podrían beneficiarse de recibir profilaxis preexposición (PrEP) de VIH en centros de cuidado primario. Hasta este momento, la literatura que sintetiza lo conocido sobre el impacto de las dificultades con el uso del alcohol en el contínuo del cuidado de PrEP, con un enfoque en los centros de cuidado primario, no es suficiente. Buscamos OVID Medline y Web of Science desde sus principios hasta el 19 de marzo, 2020, para examinar el alcance, el rango, y la naturaleza de la investigación sobre el uso de PrEP en los indivíduos con dificultades con el uso del alcohol en centros del cuidado primario. Identificamos las barreras y las oportunidades en cada paso en el contínuo del cuidado de PrEP, incluyendo para grupos específicos: adolescentes, personas que se inyectan drogas, trabajadores sexuales y personas transgéneros. Futuras investigaciones deben enfocarse en la identificación de pacientes apropriados, oportunidades para atraer la atención de los pacientes en sitios inovadores, para implementar PrEP, y para reducir el estigma.

Introduction

Globally, an estimated 1.7 million adults acquire HIV infection annually, including approximately 38,000 new infections in the United States (US) [1, 2]. Certain populations, including gay, bisexual, and other men who have sex with men (MSM) as well as individuals who inject drugs (PWID), are disproportionately affected. The Centers for Disease Control and Prevention (CDC) estimate that approximately 1 in 6 MSM in the US and approximately 1 in 30 people who inject drugs will be diagnosed with HIV in their lifetimes [3]. Incidence overall and in these subgroups is disproportionately higher in black/African American and Latinx individuals [4]. Pre-exposure prophylaxis (PrEP)—once daily

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10461-020-03107-6) contains supplementary material, which is available to authorized users.

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Published online: 20 November 2020

use of the oral medication FTC/TDF (Truvada®) or FTC/TAF (Descovy®)—is proven to prevent HIV acquisition among at-risk groups, including MSM [5–9] and PWID [10]. In 2015, the World Health Organization expanded its PrEP recommendation to include not only MSM—who report high rates of alcohol use and alcohol use disorder [11–15]—but also populations with an HIV incidence of about 3 per 100 person-years or higher [16]. Similarly, in 2019, the United States Preventive Services Task Force (USPSTF) issued a recommendation that PrEP be offered to persons at high risk of HIV acquisition [17]. Though not commonly considered an HIV risk factor, alcohol use is a common and important contributor to HIV across risk groups [18].

Unhealthy alcohol use, the spectrum of alcohol consumption ranging from drinking over recommended limits to meeting diagnostic criteria for severe alcohol use disorder [19], increases HIV risk in several ways. Unhealthy alcohol use can interfere with decision-making (e.g. the decision to have sex and with whom, or the decision to use drugs), hamper individuals' consideration of the benefits of condom use during sex, limit the dexterity required to apply a condom or to inject safely, or alter perceptions of enhanced sexual experiences in the context of alcohol intoxication (Table 1) [20–24]. Targeted HIV prevention interventions that are safe, effective, and accessible in primary care settings ought to be prioritized for individuals with unhealthy alcohol use [25].

Among those considered to have high risk according to the USPSTF recommendation are MSM with inconsistent use of condoms or heterosexually active women and men with inconsistent use of condoms during sex with a partner who is at risk for HIV. The CDC has recommended PrEP for individuals who have shared injection or drug preparation equipment, have condomless anal or vaginal sex, and/or had a bacterial sexually transmitted infection in the last 6 months [26]. Because alcohol intoxication is associated with reduced condom use and other risk behaviors [23, 27], it follows that unhealthy alcohol use should be considered for determining patients' candidacy for PrEP.

Primary care encounters represent an ideal setting in which to address alcohol use in the context of HIV prevention [28–30]. First, screening for alcohol use may a particularly feasible component of assessing for HIV risk in primary care because it can be accomplished with simple, validated instruments and is recommended by the USPSTF in all adults in ambulatory care [31]. However, uptake of brief interventions for unhealthy alcohol use or evidence-based treatments for alcohol use disorder in these settings is poor and primary care clinicians and trainees may have limited knowledge about PrEP [32, 33]. Over 1.2 million Americans, including approximately 800,000 MSM, are thought to have indications for PrEP use [4, 34]. Yet only an estimated 140,000 people received PrEP prescriptions between 2012, when the US Food and Drug Administration approved TDF/FTC for reducing transmission of HIV among at-risk populations, and the end of 2016 [35]. Second, there have been recent calls for the development of quality measures for care integration of primary care, including HIV primary care, with behavioral health and substance use disorder care [30, 36]. Third, integrating HIV-related care with substance use disorder care is feasible in primary care settings and can lessen barriers to care engagement for individuals with overlapping stigmatized identities that may otherwise be unwilling to seek care [37, 38].

Literature synthesizing what is known about the impact of unhealthy alcohol use on the PrEP care continuum with a focus on considerations for primary care is lacking. Our goal is to review the literature on addressing alcohol use and PrEP in primary care settings, identify gaps in knowledge and implementation, and propose avenues of future inquiry to inform how health systems may better meet the needs of individuals with unhealthy alcohol use to optimize HIV prevention.

Methods

We drew from a scoping review strategy [39] in order to examine the extent, range, and nature of research in this area and to answer the question: what evidence supports the use of PrEP in primary care settings among individuals with unhealthy alcohol use? We searched OVID Medline and

Table 1 Mechanisms by which alcohol impacts HIV acquisition

Risk domain	Risk mechanism
Enhancement of sexual risk	Interferes with decision to have sex
	Interferes with decision to have sex with whom
	Interferes with decision to use drugs with or prior to sex
	Hampers consideration of condom use
	Lessens dexterity needed to apply a condom
	Perceptions of enhanced sexual experience while intoxicated
Enhancement of injection risk	Increases likelihood of injection drug use
	Lessens dexterity needed to inject safely

Web of Science from database inception through March 19, 2020 using a search strategy that included terms pertaining to PrEP and HIV prevention, and terms pertaining to alcohol (Supplemental File). We identified additional studies by scanning systematic reviews and bibliographies. All studies were reviewed by one author (BJO) and eligibility criteria included: (1) the population must include humans with or at risk for unhealthy alcohol use who are in a primary care setting; (2) an intervention involving PrEP must be studied; (3) a comparison group (including a "before" analysis) must be present and (4) outcomes pertaining to HIV risk or infection must be assessed. We used Covidence, a systematic review software, to facilitate organization, screening, and assessment of articles [40].

Scoping reviews are undertaken to map the key concepts underpinning a research area and the main sources and types of evidence available [39, 41]. In this case, the previously characterized PrEP continuum of care provided the contours of the map. We used this framework of PrEP care delivery to structure the reporting of our findings given that each step represents an important opportunity for intervention (Fig. 1) [42, 43]. In appraising the literature on addressing alcohol use and PrEP in primary care settings, we applied this framework to individuals with unhealthy alcohol use to trace what is known about, and where further study is needed regarding, increasing PrEP effectiveness in this key population. We then address aspects of the continuum in special populations with increased risk of HIV acquisition or for whom special care considerations are warranted: adolescents, sex workers, PWID, and transgender persons.

Results

Our search strategy identified 193 unique studies. Following our rapid screening process, 53 unique articles were selected for inclusion in the review. Below, we summarize findings from the included studies based on their focus along the PrEP continuum: (1) PrEP awareness and interest, (2) access to care, (3) likelihood of PrEP prescription, and (4) adherence and retention. We add additional sections on specific populations to summarize evidence pertinent to adolescents, sex workers, individuals who inject drugs, transgender individuals, and Latinx individuals.

PrEP Awareness and Interest

We identified 18 studies that addressed PrEP awareness and interest among individuals with unhealthy alcohol use [28, 44–60]. Alcohol use may impact individuals' awareness of and willingness to engage in PrEP across several domains: overlapping stigma, understanding of the existence of PrEP,

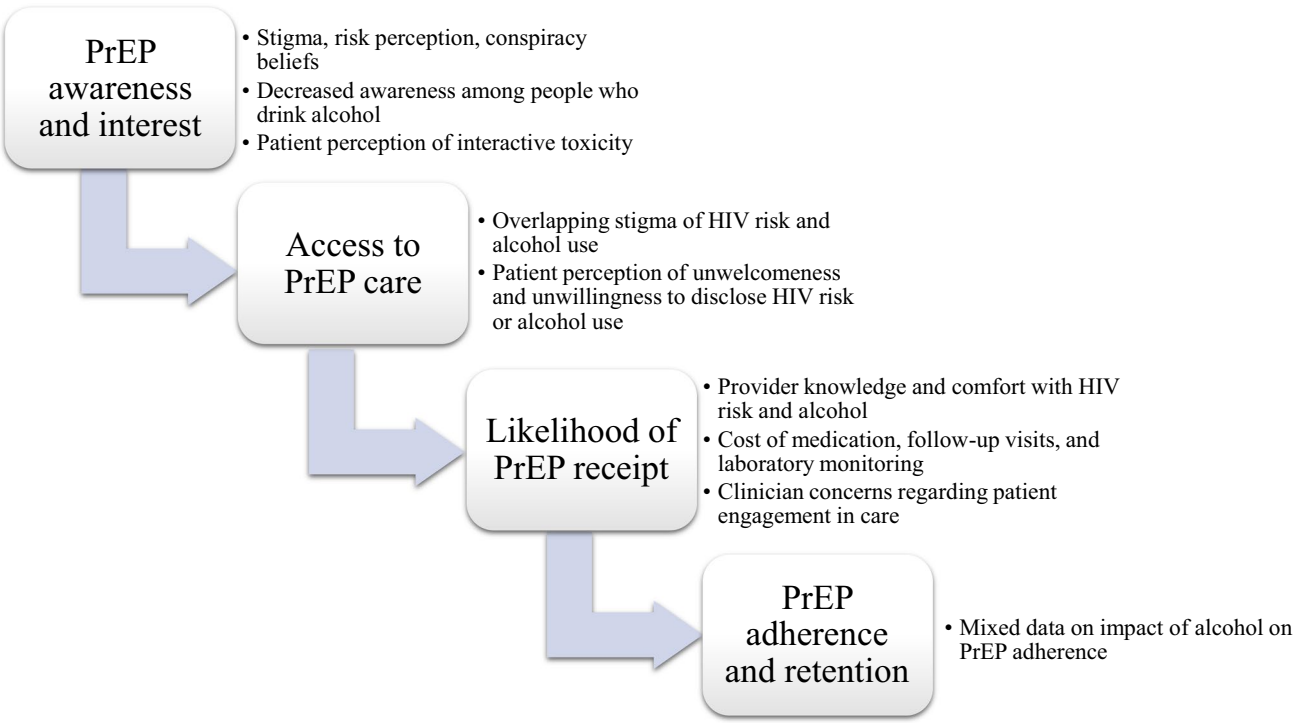

Fig. 1 The HIV pre-exposure prophylaxis (PrEP) care continuum [42, 43] (boxes) and barriers and facilitators specific to individuals with unhealthy alcohol use (bullets)

interest in trying PrEP, concerns about interactions between alcohol and PrEP, and alcohol's impact on interventions to promote PrEP.

Overlapping Stigma

Alcohol use and HIV risk are stigmatized phenomena. Overlapping stigmatized identities (e.g. having an alcohol use disorder and having high HIV risk) can further disrupt care engagement and worsen care disparities beyond the impact of individual stigmatized identities alone. Earnshaw and colleagues have proposed a comprehensive model linking mistrust to HIV risk, suggesting that intersecting stigmas [e.g. driven by homophobia, developmental stage (adolescence), racism, or discrimination against people who use drugs] impact individuals' willingness to trust health care providers and health systems, and to engage in preventive or treatment strategies [48, 49]. Qualitative work performed in Providence, RI, as part of a PrEP acceptability study included 56 semi-structured interviews of MSM and sex workers in 2013–2014. Two thirds of respondents reported recent sex under the influence of alcohol, and those reporting sex work reported more medical mistrust and healthcare discrimination due to issues beyond MSM behavior, including alcohol use [59]. Among adolescents and young adults, overlapping fears of disclosing information regarding alcohol use and HIV risk due to concerns about confidentiality can also impede adolescents and young adults who drink alcohol from asking clinicians about PrEP [54]. Some groups, particularly black MSM, report conspiracy beliefs (e.g. that the CDC is using PrEP as a means to furtively control certain population for their own gain) that are barriers to seeking care that may involve PrEP [61].

Alcohol Use and Awareness of PrEP

Several observational studies in various populations have examined whether alcohol use is associated with awareness of PrEP, with conflicting results (Table 2) [45, 46, 51, 52, 58, 60]. One latent class analysis of approximately 700 gender and sexual minority men in Canada found that those who reported alcohol and other drug use were more likely to be aware of and interested in PrEP [45]. A survey of adolescents, 10% of whom reported alcohol use, and their parents reported high awareness of an interest in PrEP despite the study being conducted before PrEP was approved for use in this age group [58]. However, a study that focused on over 1600 MSM and transgender women in the US found that only 18% of the sample was aware of PrEP, and self-reported unhealthy alcohol use [defined as a score of 8 or greater on the Alcohol Use Disorders Identification Test (AUDIT)] was associated with decreased odds of PrEP awareness [adjusted odds radio (AOR) 0.61, 95% confidence interval (CI) 0.45–0.83] [52]. A neighborhood-level analysis of over 600 young black MSM in the US found that greater neighborhood alcohol outlet density was associated with decreased odds of PrEP awareness after adjusting for other socioeconomic environment features such as vacant buildings density and crime rates (AOR 0.52, 95% CI 0.35–0.80) [46]. In a survey study of over 100 women who inject drugs in the US, PrEP awareness was relatively low (31%), and binge drinking (defined as having four or more drinks in about two hours) was not found to be significantly associated with PrEP awareness [60]. Collectively, these studies suggest that high-risk groups, including MSM with unhealthy alcohol use and women who inject drugs and who also report binge drinking, have low PrEP awareness.

Alcohol Use and Willingness to Engage in PrEP Care

Alcohol use may be associated with decreased willingness to engage in PrEP. A survey of nearly 400 black MSM in the US found that 60% reported being willing to use PrEP and that self-reported high alcohol consumption may decrease the odds of being willing to use PrEP (AOR 0.84, 95% CI 0.72–1.00). This finding is likely driven by perceptions of toxicity that occurs when alcohol and PrEP are used concurrently [62–64]. For example, qualitative focus groups of sub-Saharan African women found that, despite interest in PrEP among female sex workers and women in serodiscordant couples, specific concerns about toxicities between alcohol use (which was reported to often precede sex) and PrEP arose as a barrier [62]. In another study, 300 MSM in the US were surveyed and 75% endorsed at least one interactive toxicity belief between alcohol and PrEP [64]. This is despite a lack of data demonstrating existence of a clinically relevant interaction between alcohol and PrEP, and despite demonstrated safety of PrEP among people who exhibit binge drinking behavior. In the iPrEx study, which evaluated the use of PrEP by MSM and transgender women during a median follow-up of 1.2 years, over 50% of enrollees reported having more than five drinks per day during the study period and there was no significant difference in the occurrence of any adverse events or serious adverse events in the treatment versus placebo arms [8].

Alcohol Use May Negatively Impact Response to Social Marketing Campaigns for PrEP

Finally, alcohol use may impact the success of campaigns whose goal is to expand PrEP access and use. We identified one study of an electronic intervention among African American women in the US in which an avatar-led web-based video that used an education-entertainment strategy to provide information about post-exposure prophylaxis and PrEP, self-reported alcohol use was associated with less

Table 2 Evidence for the impact of unhealthy alcohol use on awareness of pre-exposure prophylaxis (PrEP) for HIV prevention

Study author and publication year	Study design	Population and location	Impact of alcohol use on PrEP awareness	Notes
Underhill [59]	Qualitative (interviews)	56 MSM in Northeast US	Alcohol use may lessen patients' willingness to disclose HIV risk to clinicians	Sex workers less likely to disclose HIV risk than non sex workers
Walters [60]	Cross-sectional	118 women who inject drugs in Northeast US	Binge drinking was not associated with PrEP awareness	Awareness of PrEP was low across the sample (31%)
Shah [58]	Cross-sectional	102 adolescent-parent dyads in Southern US	Sex while intoxicated was not associated with PrEP willingness	10% of the adolescent sample reported sex under the influence of alcohol or drugs
Garnett [52]	Cross-sectional	1673 black MSM and transgender women in Northeast US	Unhealthy alcohol use associated with lesser odds of PrEP awareness (aOR 0.61, 95% CI 0.45–0.83)	Awareness of PrEP was low across the sample (18%)
Edeza [51]	Cross-sectional	22,698 MSM in Latin America	Unhealthy alcohol use not associated with PrEP awareness	Significant predictors of PrEP awareness included reported transactional sex and conomless anal sex
Chen [46]	Cross-sectional; neighborhood-level	61 young black MSM in Midwest US	Neighborhood alcohol outlet density associated with lesser odds of PrEP awareness (aOR 0.52, 95% CI 0.35–0.80)	Alcohol use was not included as an individual-level variable
Card [45]	Cross-sectional; latent-class analysis	7184 sexual and gender-minority men in Canada	Those reporting alcohol, prescription drug use, and stimulant use more likely to report PrEP awareness	Alcohol use not isolated from other drug use in analyses

favorable ratings of the intervention. Studies are needed to characterize how unhealthy alcohol use may impact the success of public health campaigns to promote PrEP expansion and to evaluate PrEP campaigns specifically targeting people with unhealthy alcohol use.

Access to Care

We identified five studies that addressed access to care for individuals with unhealthy alcohol use at risk for HIV [53, 65–68]. Insurers in the US are obligated to cover the cost of PrEP for policyholders since the USPSTF issued its recommendation in 2019 [17]. However, uninsured status is associated with four times lesser odds of receiving PrEP [68]. In European countries, estimated "PrEP gaps" range from 4.3% of those eligible for and willing to use PrEP in Portugal to 44.8% in Russia [66]. In sub-Saharan Africa, where HIV incidence is highest, policies and legal environments create barriers access to care for high risk groups. For example, Nigeria's Same-sex Marriage Prohibition Act prohibits associations between MSM and other persons, which makes healthcare professionals wary of providing services to this population [65]. Even in countries with national health programs that provide universal health care coverage, minority groups eligible for PrEP such as transgender persons are less likely to seek or receive health care likely due to stigma and fear of discrimination or shame [53].

Access to PrEP may be further limited among patients with unhealthy alcohol use, which make up a large percentage of those accessing PrEP (54% in a study in two Northeast US cities [67]). Patients with unhealthy alcohol use face numerous barriers to care, including social and structural vulnerabilities [69, 70], inadequate provider training in evidence-based approaches to care, lack of provider confidence in the effectiveness of care, and lack of patient awareness of treatment modalities [71, 72]. Patients with HIV risk and unhealthy alcohol use—who may also have other socially devalued attributes such as being a sex worker, having a non-heterosexual orientation, or having been incarcerated—face overlapping stigma that may drive them to be less likely to seek, receive, or engage in care [49, 59, 73].

Likelihood of PrEP Prescription

We identified four studies that addressed the likelihood of receipt of a PrEP prescription in primary care [32, 74–76]. For individuals engaged in care who are willing to start PrEP, various barriers may prevent them from receiving a PrEP prescription: provider awareness, comfort, and beliefs surrounding PrEP; and the costs of the medication and accompanying clinical and laboratory services.

Provider Awareness, Comfort, and Beliefs Surrounding PrEP

Provider knowledge has been shown to correlate with adoption of PrEP in practice [33]. In a cross-sectional survey of membership of an academic general medicine society in 2015, 93% reported awareness but only 34.9% reported PrEP adoption; adopters were more likely to perceive PrEP as extremely safe and were less likely to perceive PrEP as being moderately likely to increase risk behaviors ("risk compensation") [74]. Another survey of PrEP awareness and prescribing experience among over 500 primary care providers and HIV specialists in 10 US cities found that PCPs felt less familiar than HIV specialists with prescribing PrEP (28% vs. 76%) or had prescribed it (17% vs. 64%) [76]. Among over 200 internal medicine resident trainees surveyed in 2016, nearly all (96%) had heard of PrEP but only 25% had received any training and 11% had prescribed PrEP [32]. No studies to date have characterized how clinicians approach alcohol use and PrEP in practice.

Cost of PrEP

The cost of PrEP can be prohibitive, as can the cost of follow-up visits and laboratory services recommended to accompany PrEP use. In the US, the cost of PrEP will be covered by insurers by mandate starting in 2021 as a result of its USPSTF recommendation [17]. Clinical practice guidelines generally recommend visits with patients receiving PrEP at least every 3 months, during which time urine and blood testing are recommended, whose costs can be substantial [77]. Maintaining this regimen may be particularly difficult for patients who use alcohol, who are more likely than the general population to have breaks in care and no-shows to scheduled appointments [75]. Clinicians are also more likely to anticipate that patients will have low engagement with care because of their alcohol use and economic vulnerability [71], thereby lessening their confidence in a regimen that includes follow-up visits and laboratory evaluation.

Adherence and Retention

We identified 11 studies that address PrEP adherence among individuals with unhealthy alcohol use in primary care [78–88]. Adherence to PrEP is crucial to its real-world effectiveness [8, 43]. Multiple observational studies have examined the impact of alcohol use on adherence and, despite the plausibility that alcohol use may negatively impact PrEP adherence, evidence has been conflicting (Table 3) [78–88]. Studies involving MSM have suggested that self-reported alcohol use may be associated with decreased PrEP adherence [79, 80, 82, 86, 87] or discontinuation [85]. On the other hand, one study drawing from 125 MSM participating

Table 3 Evidence for the impact of unhealthy alcohol use on PrEP adherence and retention

Study	Study design	Population and location	Impact of alcohol use on PrEP adherence	Notes
Agopian [78]	Cross-sectional	125 MSM in Eastern US	Binge drinking not associated with PrEP adherence or discontinuation	Being <30 years was associated with PrEP discontinuation (aOR 5.00, 95% CI 2.00–12.50) and having health insurance was inversely associated (aOR 0.2, CI 0.04–0.80)
Amico [79]	Prospective cohort	178 MSM in multiple US sites	Drugs and alcohol identified as challenge to PrEP adherence in 32% of participants	Alcohol was not isolated from other drug use in analyses
Grov [81]	Prospective cohort	104 gay and bisexual men	Heavy drinking (5+ drinks in one sitting) not associated with PrEP adherence	Club drug and marijuana use were not associated with missing PrEP doses
Haberer [82]	Prospective cohort	1,147 members of serodiscordant couples in Kenya and Uganda	Heavy alcohol use (positive Rapid Alcohol Problems Screen) was associated with <80% adherence	Median adherence was 99.1% in the overall sample
Hoenigl [83]	Prospective cohort	394 MSM and transgender women in Western US	Alcohol use and other substance use was not associated with PrEP adherence	PrEP adherence measured by blood levels of tenofovir
Marcus [85]	Prospective cohort	972 insured patients initiating PrEP	Drug and alcohol use were associated with discontinuation (aRR 1.88, 9% CI 1.30–2.60)	Alcohol was not isolated from other drug use in analyses
Storholm [86]	Qualitative (interviews)	30 young MSM in Western US	Alcohol use identified as factor of poor PrEP adherence	Primary mechanism identified was alcohol's disruption of daily routines
Van der Elst [87]	Qualitative (interviews and focus groups)	51 MSM from Kenya	Post-coital dosing adherence perceived to be poorer after sex under the influence of alcohol	47% of participants on PrEP reported drinking alcohol before sex
Velloza [88]	Retrospective cohort	350 MSM in Eastern US and Thailand	Heavy alcohol use (score ≥8 on AUDIT scale) was associated with higher concentrations of tenofovir in plasma and hair	21% of sample reported heavy alcohol use

in the 2017 National HIV Behavioral Surveillance System found that binge drinking was not associated with discontinuation; another used monthly interviews to assess gender minority men who were on PrEP and found alcohol use to have no impact on adherence. Three studies have found that alcohol use may improve adherence to PrEP in MSM [83, 84, 88] including one study that examined blood levels of tenofovir [88]. The studies that identified alcohol use as a barrier to adherence tended to be qualitative (and identified alcohol use as a perceived barrier to adherence) [79, 86] or measured alcohol use concurrently with drug use [85]. These findings suggest that more research is needed to clarify the relationship between alcohol and PrEP adherence, and unhealthy alcohol use need not be assumed a barrier to PrEP adherence.

Special Populations

The majority of published evidence for using PrEP in people who consume alcohol come from studies that enrolled MSM. The following special populations warrant special mention given unique treatment considerations and to identify population-specific gaps in the literature.

Adolescents

Adolescents and young adults ages 10 through 25 continue to be left behind in HIV testing and treatment services, despite representing the age group with the highest seroconversion rate [47]. Alcohol use most commonly commences during this age, and although child health providers report screening adolescent patients for alcohol use, adolescents are among the groups most unlikely to receive preventive care, and barriers to screening and follow-up remain [89–91]. Alcohol use has been identified as an independent predictor of HIV acquisition in this age group [92]. Two qualitative studies of adolescent girls in Kenya found that this age group identified concerns about the interactive toxicity between alcohol and PrEP as a barrier to use [62, 63]. However, a survey of adolescents 13–17 years of age and their parents in the US identified that both groups were somewhat to very likely to accept PrEP regardless of sexual activity or alcohol use [58]. Studies that assess access to PrEP and/or adherence to PrEP among adolescents who drink alcohol are lacking.

Sex Workers

Sex workers are particularly vulnerable to the harms of alcohol use and to HIV risk; sexual exchange is often negotiated in alcohol-serving establishments where sex workers may willingly or unwillingly consume alcohol prior to sex [93]. Sex workers may report low PrEP knowledge but high PrEP acceptability in sub-Saharan Africa, with concerns about the toxicity interaction between alcohol and PrEP [63, 94]. Self-reported alcohol use appears to be associated with lower rates of adherence to PrEP among sex workers [95].

Individuals Who Inject Drugs

There is a paucity of research on the use of PrEP among PWID who also drink alcohol. A survey of over 100 women who inject drugs in the US, one third of whom reported binge drinking behavior, found low awareness of PrEP (31%). Binge drinking was not an independent predictor of PrEP awareness in this group. Studies of willingness, access, and adherence to PrEP among this group are lacking.

Transgender Persons

Transgender persons are disproportionately impacted by the harms alcohol and other substance use and have elevated risk for HIV [96]. They are also less likely to engage in primary care or sexually-transmitted infection care than cisgender persons [53]. Transgender women in the US have demonstrated limited awareness of PrEP, and alcohol use is independently associated with lower PrEP awareness in this group [52]. Studies that address willingness, access, and adherence to PrEP among transgender persons who drink alcohol are needed.

Latinx Individuals

Latinx individuals face particular barriers to care as well as increased fear of the government and other institutions, creating additional challenges for initiatives supporting PrEP expansion [97, 98]. Although Latinx populations tend to report lower levels of unhealthy alcohol use than other ethnic groups, certain sub-populations (particularly those of Mexican background and those of lower socioeconomic status) have disproportionately higher alcohol use and limited treatment access and engagement [99]. One survey study of 159 Latinx MSM in the Southern US identified unique manifestations of stigma associated with PrEP use, including that PrEP use implies promiscuity and homosexuality, but did not query alcohol use [100].

Opportunities for Future Research

Research and implementation efforts that apply to people who consume alcohol are needed at each step in the PrEP care continuum. Strategies that identify patients who drink alcohol, are at risk for HIV infection, and are eligible for PrEP are lacking. Machine learning represents a promising approach that has been used to identify potential candidates for PrEP in healthcare settings in the US, Denmark, and Eastern Africa, but is still at the proof-of-concept stage and

risk models have not included alcohol use [101]. Systematic screening for alcohol use and HIV risk in primary care settings, including with technology-based platforms, may also facilitate identification and linkages to alcohol and/or PrEP care for patients who may not be identified otherwise [102]. Biomarkers of alcohol use have been increasingly used for the identification and monitoring of alcohol use and its sequelae [103], and may play an expanded role for identifying individuals who are candidates for PrEP.

Campaigns to promote awareness of and knowledge about PrEP and its safety among people who use alcohol ought to target key patient populations as well as providers. Empowering non-physicians to participate in patient education and screening for PrEP candidacy may help identify difficult-to-reach populations [104]. Pharmacists, for example, have been described as the most accessible health care professionals, including in areas with limited access to health care and among groups who have experienced stigma in traditional health care scenarios, such as those with unhealthy alcohol use [105]. They can screen for unhealthy alcohol use and recommend medication treatments, identify patients at risk for HIV, provide risk-reduction education, and perform adherence assessments for people prescribed PrEP [106]. With respect to provider education, academic detailing, a strategy proven to impact clinical decision making [107–109], may benefit primary care and other front-lines providers who have demonstrated low PrEP adoption [74].

Implementation strategies to enhance provider and organizational readiness and to prescribe PrEP, and specifically for individuals with unhealthy alcohol use, are needed. For example, primary care providers are recommended to screen for and address alcohol use in primary care [31] and generally prefer to integrate PrEP into primary care over referring to a specialist for providing PrEP [110]. However, it is unclear whether an "all trained" model, in which all providers are willing to provide PrEP (and alcohol screening and interventions), or having an onsite PrEP specialist is preferable regarding effectiveness and organizational feasibility. Long-acting injectable cabotegravir, which is showing initial promise for pre-exposure prophylaxis in cisgender men and transgender women who have sex with men [111], may provide new opportunities to integrate the management of unhealthy alcohol use and PrEP in primary care settings given its ease of use.

Finally, given the impact of multiple, overlapping stigmatized identities has on health care access and the healthcare experience for people who drink alcohol and are eligible for PrEP, stigma reduction campaigns should target this population. The use of "person-first" language when addressing or describing individuals at risk, emphasizing the effectiveness of PrEP, the use of sympathetic narratives, and attention towards societal rather than individual causes of alcohol use and HIV risk have been proposed as key steps towards mitigating stigma for people with substance use disorders [112]. Our scoping review identified various points along the PrEP continuum where future study and implementation science can advance knowledge regarding HIV prevention in this population, but may have missed important aspects of care not specified by the PrEP continuum, such as stigma.

Conclusion

Individuals with unhealthy alcohol use who are at risk for HIV infection represent an important target population for efforts to expand PrEP use. This population encounters unique and overlapping barriers along the PrEP care continuum. Population-wide strategies for identifying candidate patients are needed, as are low-barrier strategies to engage at-risk patients in care in various settings, including community health centers and community-based organizations. Certain key populations, including adolescents, PWID, sex workers, and transgender persons may require targeted strategies. Implementation strategies for PrEP expansion in diverse clinical and community environments ought to be evaluated and scaled.

Acknowledgements We thank Melissa Funaro, MLS, for her assistance in conducting the database searches and organizing the literature for this review.

Funding This work was supported by funding from the National Institute on Mental Health (P30MH062294) for the Center for Interdisciplinary Research on AIDS during the conduct of this work. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Center for Interdisciplinary Research on AIDS, the National Institute of Mental Health, or the National Institutes of Health.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

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