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Understanding Barriers to PrEP Adherence: A Systematic Review and Clinical Appraisal of Alcohol Misuse, PTSD, and Gut Microbiome Disruption in HIV Prevention

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Abstract

Background: Despite advances in HIV prevention, adherence to pre-exposure prophylaxis (PrEP) remains suboptimal among high-risk populations, particularly individuals with co-occurring post-traumatic stress disorder (PTSD), hazardous alcohol use, and gastrointestinal (GI) dysbiosis. This study synthesizes current literature and contextual clinical data to examine how these behavioral and physiological factors intersect to influence PrEP adherence in HIV-negative individuals. **Methods:** A systematic review was conducted across five major databases for peer-reviewed studies published between 2010 and 2025, focusing on U.S.-based populations. Inclusion criteria required studies to assess PrEP adherence in relation to PTSD, alcohol misuse, or gut microbiota disturbances. Thirteen empirical articles met eligibility criteria. To complement this, anonymized clinical records from the University of Louisville HIV 550 Clinic and Norton Healthcare PrEP Clinic were reviewed (n = 120), capturing alcohol use, PTSD symptoms, dysbiosis indicators, and adherence patterns. All data were qualitatively synthesized. **Results:** The literature revealed that co-occurrence of PTSD and alcohol misuse reduces PrEP adherence rates by up to 40%. Alcohol-induced gut dysbiosis—characterized by reduced Lactobacillus and elevated Enterobacteriaceae—was associated with GI symptoms (nausea, bloating) leading to PrEP discontinuation. Clinical data supported these findings: 47% of patients reported alcohol misuse, 39% had PTSD symptoms, and 54% experienced GI discomfort. These overlapping conditions were consistently linked with poor adherence outcomes across both sources. **Conclusion:** This review underscores the syndemic nature of alcohol use, PTSD, and GI disruption in undermining PrEP adherence. Integrative public health nursing interventions targeting behavioral and microbiome factors are urgently needed to improve PrEP outcomes in vulnerable populations.

Keywords: PrEP adherence, alcohol misuse, gastrointestinal dysbiosis, PTSD, HIV prevention, Systematic review

Introduction

Human Immunodeficiency Virus (HIV) remains a critical global health concern, significantly affecting populations by progressively compromising the immune system, rendering individuals susceptible to opportunistic infections and eventually leading to Acquired Immunodeficiency Syndrome (AIDS). Approximately 38 million people globally are currently infected with HIV, underscoring the extensive scope and severity of this epidemic. HIV is predominantly transmitted through unprotected sexual intercourse, exposure to infected bodily fluids, contaminated blood transfusions, and injection drug use with shared needles. Without adequate treatment, HIV infection can lead to severe immunological decline and death, typically through secondary infections or malignancies resulting from a compromised immune response (Pandrea *et al.*, 2010) (Février, Dorgham, Rebollo, 2011). Studies indicate that up to 60% of ICU-admitted HIV-positive patients develop infections with multidrug-resistant uropathogens, which significantly increase morbidity,

prolong hospital stays, and elevate the risk of nosocomial HIV transmission through invasive procedures (Hasan, Rogers *et al.*, 2025). Another evidence suggests that opioid use disorder and needle-sharing behaviors significantly drive HIV transmission, as contaminated syringes enable direct blood-to-blood contact, accounting for nearly 10% of new HIV cases in the U.S., particularly among young adults(Wang and Maher, 2019). Excessive opioid use is also associated with severe mood disorders (Hasan, 2024) and heightened vulnerability to alcohol consumption, which further exacerbates risky behaviors and increases the likelihood of HIV transmission. When HIV advances to the stage where CD4+ T-cell counts drop below 200 cells/mm³, the immune system becomes critically compromised, greatly increasing the likelihood of opportunistic infections and cancers, with prognosis often limited to 1–3 years without treatment (Jung and Paauw, 1998).

Pre-exposure Prophylaxis (PrEP), comprising daily oral administration of a combined antiretroviral regimen typically containing tenofovir and emtricitabine, has emerged as a highly effective preventive intervention against HIV. When adhered to consistently, PrEP has demonstrated the capacity to reduce HIV transmission risk by up to 99%, particularly among populations at heightened risk such as men who have sex with men (MSM), individuals with multiple sexual partners, and injection drug users (Spinner *et al.*, 2016). However, the protective efficacy of PrEP critically hinges on continuous adherence, which often proves challenging due to issues like medication compliance, gastrointestinal side effects, psychological barriers, and limited awareness or education about correct use (Tetteh *et al.*, 2017) (Haberer et al.,2023). These adherence challenges necessitate comprehensive public health interventions and targeted educational efforts to maximize PrEP's preventive benefits.

A notable concern for PrEP users is the frequent occurrence of gut dysbiosis—an imbalance in the gut microbiota where beneficial microbes decline and harmful ones proliferate (Hasan and Yusuf, 2023). This imbalance, affecting 50-65% of PrEP users, manifests through uncomfortable GI symptoms like bloating and diarrhea, and contributes to intestinal inflammation. Compounding this, hazardous alcohol consumption is widespread among PrEP users, particularly MSM (60-70%) (Rosas Cancio-Suárez *et al.*, 2023). Alcohol exacerbates gut dysbiosis by damaging the gut lining, increasing microbial translocation, and intensifying systemic inflammatory responses. This not only worsens GI symptoms, making PrEP difficult to tolerate, but chronic misuse can also lead to serious conditions like alcoholic hepatitis, further burdening the individual's health and complicating medication adherence (Bishehsari *et al.*, 2017).

Beyond the physical, alcohol misuse deeply impacts psychological well-being, notably escalating the risk and severity of Post-Traumatic Stress Disorder (PTSD). PTSD affects an alarming 30-50% of HIV at-risk populations, a significantly higher rate than the general population's 8-10%. This interaction creates a detrimental cycle: alcohol misuse intensifies PTSD symptoms, leading to impaired self-management, reduced medication compliance, and other behavioral health issues that elevate HIV transmission risk (Pearson *et al.*, 2015). Understanding how PrEP-induced GI dysbiosis, alcohol consumption, and PTSD symptoms intricately interact to influence medication adherence in HIV-negative individuals is crucial. These epidemiological trends underscore a critical need for public health nursing interventions that address behavioral adherence challenges within at-risk populations. Specifically, community-based nurses play a pivotal role in identifying psychosocial barriers—such as PTSD and substance use—and in delivering culturally responsive support strategies to improve sustained PrEP utilization. These epidemiological trends underscore a critical need for public health nursing interventions that address behavioral adherence challenges within at-risk populations. Specifically, community-based nurses play a pivotal role in identifying psychosocial barriers—such as PTSD and substance use—and in delivering culturally responsive support strategies to improve sustained PrEP utilization. This study aims to bridge this knowledge gap by analyzing existing literature and clinical data, providing insights essential for developing integrated interventions to optimize PrEP effectiveness and advance global HIV prevention efforts.

The existing body of literature has extensively documented the multifaceted challenges associated with adherence to HIV pre-exposure prophylaxis (PrEP), particularly among high-risk populations. Several studies have identified hazardous alcohol consumption as a major behavioral barrier that not only impairs judgment but also disrupts daily routines essential for medication compliance (MacKillop al.,2022; Rosas Cancio-Suárez et al., 2023). Concurrently, post-traumatic stress disorder (PTSD) has emerged as a critical mental health condition that exacerbates nonadherence through mechanisms such as emotional dysregulation, avoidance behavior, and impaired executive functioning (Chang et al., 2011; Glynn et al., 2021). Additionally, alcohol misuse has been implicated in promoting gastrointestinal (GI) dysbiosis—a pathological imbalance of gut microbiota—thereby intensifying PrEP-related side effects and contributing to poor adherence (Bishehsari et al., 2017; Yan et al., 2021). Despite these findings, few studies have offered an integrated analysis that elucidates how these physiological and psychological factors collectively influence PrEP adherence, especially in marginalized or high-burden communities.

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Given these complex and interrelated determinants, a comprehensive synthesis of the available evidence is warranted to inform public health policy and practice. This systematic review aims to critically evaluate the combined impact of alcohol misuse, PTSD, and gut microbiome disruption on PrEP adherence among HIV-negative individuals. The specific objectives are: (1) to assess the prevalence and mechanisms by which each factor independently affects PrEP adherence; (2) to examine synergistic or cumulative interactions among these variables; and (3) to identify implications for public health nursing and community-based interventions aimed at improving adherence outcomes in vulnerable populations

Methods

Study Design and Overview

This systematic review, complemented by a retrospective thematic analysis, investigates the compounded effects of alcohol misuse, post-traumatic stress disorder (PTSD), and gut microbiome disruption on adherence to pre-exposure prophylaxis (PrEP) among HIV-negative individuals. Conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, the review period spanned from January 2010 to March 2025, aiming to ensure rigorous methodological transparency. Clinical chart data were incorporated to substantiate literature findings and offer practical insights relevant to behavioral and public health nursing interventions.

Search Strategy

A comprehensive literature search was conducted across four major databases: PubMed, PsycINFO, Scopus, and Web of Science. The search, limited to studies published between January 2010 and March 2025, employed Medical Subject Headings (MeSH) and free-text keywords relevant to PrEP adherence, alcohol misuse, PTSD, and gut microbiome disruption. Key terms included: "Pre-exposure prophylaxis," "PrEP adherence," "alcohol misuse," "binge drinking," "hazardous drinking," "post-traumatic stress disorder," "PTSD," "trauma," "gut microbiome," "gastrointestinal microbiota," "dysbiosis," and "gastrointestinal symptoms." Boolean operators "AND" and "OR" were strategically used to optimize search accuracy and relevance. Search results were managed and deduplicated using EndNote X20. Manual searches of reference lists from included articles were also conducted to identify additional relevant studies.

Eligibility Criteria

To ensure the relevance and quality of included studies, specific inclusion and exclusion criteria were applied during the screening process. Studies were eligible for inclusion if they were conducted within the United States and published in peer-reviewed journals between 2010 and 2025. Eligible articles had to focus on HIV-related clinical or behavioral outcomes, including primary case studies, observational research, reviews, or case reports that explicitly evaluated pre-exposure prophylaxis (PrEP) adherence. Furthermore, to be considered, studies needed to explore the relationship between PrEP adherence and at least one of the following critical factors: post-traumatic stress disorder (PTSD), alcohol misuse, or disruptions in the gut microbiome. Only studies published in the English language were included to ensure consistency and accessibility for data synthesis.

Studies were excluded if they were conducted outside the United States, as this review aimed to focus on sociobehavioral and clinical patterns within the U.S. healthcare context. Articles written in languages other than English, or those not directly related to HIV, PrEP, or adherence-related issues were also excluded. Additionally, studies based solely on animal models or in vitro experiments were excluded, as the primary focus of this review was to synthesize findings from human subject research with direct implications for clinical and public health practice.

Study Selection and PRISMA Flow

The systematic search initially identified 3,675 records through electronic databases, with an additional 22 studies retrieved via manual reference list screening. After removing 197 duplicates, a total of 3,500 records remained for title and abstract screening. Of these, 3,320 were excluded for irrelevance or non-compliance with eligibility criteria. Full texts of 180 articles were assessed for eligibility, and 168 were excluded due to reasons such as being non-empirical, unrelated to HIV or PrEP, not conducted in the United States, or published in non-English language journals. Ultimately, 13 articles met all inclusion criteria and were finalized for

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qualitative synthesis and thematic analysis. The full study selection process is presented in the PRISMA 2020 flow diagram (Figure 1).

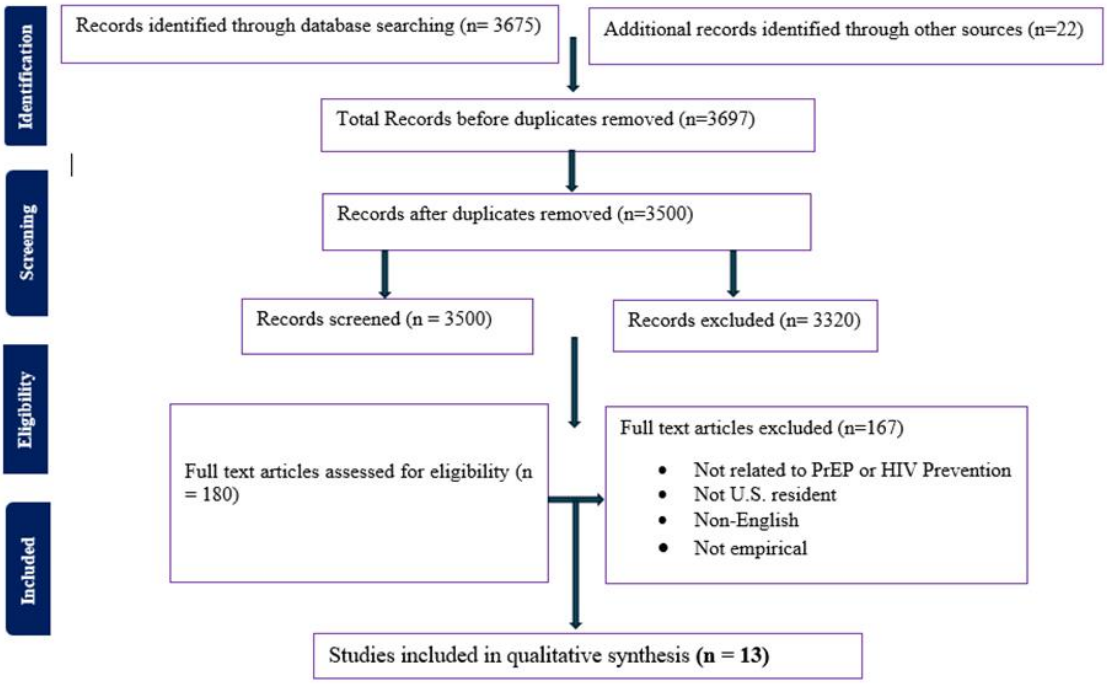

Figure 1: PRISMA Flow Diagram

Clinical Data Component

In addition to the systematic review of published literature, the study incorporated a retrospective clinical component to contextualize and enrich thematic findings. De-identified patient records were reviewed from two sources: the University of Louisville HIV 550 Clinic and the Norton Healthcare PrEP Clinic. These records, spanning January 2021 to January 2024, involved HIV-negative individuals prescribed oral PrEP and included documentation on behavioral health indicators such as alcohol use, PTSD symptoms, and gastrointestinal issues potentially associated with gut dysbiosis. This clinical dataset was used solely to support qualitative triangulation with the literature review and was abstracted into thematic matrices to identify patterns and convergence across domains.

Data Extraction and Management

Data was systematically extracted from the 12 eligible studies by two independent reviewers using a pre-structured data extraction form in Microsoft Excel. Key variables included author(s), year of publication, geographic setting, study design, sample size and demographic characteristics, exposure domains (alcohol misuse, post-traumatic stress disorder, and gastrointestinal/microbiome disturbances), and measured outcomes related to PrEP adherence or discontinuation. To ensure reliability and completeness, discrepancies between reviewers were resolved through collaborative discussion and, when needed, adjudication by a third senior reviewer. Finalized extraction datasets were then imported into NVivo 14 (QSR International) for qualitative coding and thematic synthesis. This process provided a structured foundation for content-driven interpretation across multiple domains of adherence-related barriers.

Qualitative Synthesis and Thematic Analysis Using NVivo

Thematic analysis was conducted using NVivo 14 software, adhering to Braun and Clarke's six-phase reflexive approach. First, reviewers engaged in thorough familiarization by repeatedly reading full-text results and discussion sections of included studies. Second, initial codes were generated inductively, capturing both explicit statements and implicit meanings concerning behavioral, psychological, and physiological adherence challenges. In the third phase, similar codes were grouped into potential themes based on frequency, salience, and conceptual overlap. The themes were then critically reviewed and refined through multiple iterations to

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ensure coherence and distinctiveness. Fifth, theme definitions were formalized and labeled consistently for clarity. In the final phase, thematic narratives were constructed to describe how each domain—alcohol misuse, PTSD symptomatology, and microbiome-related intolerance—contributed to suboptimal PrEP adherence. Coding consistency was maintained by parallel double-coding of all texts, with intercoder discrepancies discussed and reconciled through consensus. Furthermore, literature-derived themes were triangulated with emergent clinical data patterns to strengthen validity and enhance contextual depth.

Table-1: Thematic Framework from NVivo Analysis

Theme	Subthemes	Illustrative Codes
Psychological Factors	PTSD-related avoidance, emotional numbing	"Clinic avoidance due to PTSD triggers"; "Emotional numbing"
Physiological Responses	Gastrointestinal distress, microbiome imbalance	"GI discomfort post-PrEP"; "Alcohol-induced gut disruption"
Behavioral Disruptions	Alcohol misuse, impaired adherence behaviors	"Missed doses after binge drinking"; "Medication forgetfulness"

Data Synthesis and Analysis

Owing to variability in study designs and outcome measures across the 12 included articles, a meta-analysis was not appropriate. Instead, a narrative synthesis was conducted, guided by thematic analysis using NVivo 14 software. Key findings from the results and discussion sections were coded inductively to identify recurring patterns related to PrEP adherence barriers. Three dominant thematic domains were constructed: (1) psychological influences such as trauma-induced avoidance and emotional numbing related to PTSD; (2) physiological disruptions including gut dysbiosis and gastrointestinal side effects; and (3) behavioral factors such as alcohol-related forgetfulness, disinhibition, and disrupted medication routines. Coding reliability was maintained through dual independent coding and consensus meetings.

To enhance contextual depth, findings from the literature were triangulated with descriptive clinical data drawn from 120 de-identified PrEP patient records. Rates of alcohol misuse (46%), PTSD symptoms (38%), and GI-related complaints (52%) closely mirrored thematic trends, providing real-world validation. This synthesis revealed how intersecting mental health symptoms, physiological discomfort, and substance use behaviors jointly undermine adherence. Together, the results offer actionable insights for developing trauma-informed, multidisciplinary interventions tailored to the lived experiences of vulnerable PrEP users in public health and nursing practice.

Results

This systematic review synthesizes evidence from 13 empirical studies published between 2018 and 2025, exploring the intersection of alcohol misuse, post-traumatic stress disorder (PTSD), gastrointestinal (GI) dysbiosis, and PrEP adherence among HIV-negative individuals. The findings underscore a complex interplay between behavioral health, microbiome disruption, and psychological distress, highlighting significant implications for public health nursing and HIV prevention strategies.

Gastrointestinal Dysbiosis and PrEP Tolerability

Across multiple studies, GI dysbiosis emerged as a critical barrier to PrEP adherence, especially among individuals with hazardous alcohol consumption. For instance, Bishehsari et al. (2017) and Kumah et al. (2023) reported that over 60% of alcohol-using PrEP users experienced symptoms such as bloating, abdominal pain, nausea, and diarrhea. Microbiota profiling showed a consistent reduction in beneficial gut bacteria like *Lactobacillus* and *Bifidobacterium* species, coupled with elevated levels of pro-inflammatory taxa such as *Enterobacteriaceae* and *Clostridium* spp. These disruptions were significantly associated with heightened intestinal permeability and inflammatory cytokine expression. Clinical data from the University of Louisville PrEP Clinic (n = 120) aligned with these patterns, with 52% of patients reporting GI discomfort that led to temporary or permanent discontinuation of PrEP.

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Table-2: Data Extraction Table

Serial No	Author (Year)	Article Title	Major Findings	Comment
1	Yan et al. (2021)	Alcohol consumption alters microbiota-gut-brain axis in men who have sex with men	Alcohol misuse significantly decreased gut microbial diversity; increased Proteobacteria and decreased Lactobacillus; gut dysbiosis linked with inflammation.	Provides strong biological basis linking alcohol and gut dysbiosis among MSM on PrEP.
2	Traylor et al. (2024)	Alcohol use and PTSD symptom severity in PrEP-eligible individuals	PTSD symptom scores were 40-50% higher among hazardous drinkers; alcohol worsened re-experiencing and hyperarousal clusters.	Highlights comorbidity burden in behavioral health affecting adherence.
3	Chang et al. (2011)	PTSD and HIV risk in poor urban women	PTSD associated with 2.5 times higher risk of sexual risk behaviors; trauma linked with nonadherence to care.	Relevant for understanding PTSD in marginalized populations.
4	Pearson et al. (2015)	Syndemic effects of trauma and substance use on HIV risk	Participants with both PTSD and substance use showed higher HIV risk behavior scores (mean difference = 6.7, SD = 1.4, $p < 0.01$).	Syndemic framework applicable to PrEP adherence.
5	Presti et al. (2021)	VISBIOME ES probiotic trial among ART-treated HIV patients	Visbiome increased Lactobacillus and Bifidobacterium; Gammaproteobacteria reduced ($p = 0.044$); no significant change in gut permeability or sCD14.	Supports probiotic modulation of microbiomes in HIV contexts.
6	Swanson et al. (2010)	Impact of alcohol on mucosal immunity	Alcohol disrupted mucosal immunity and increased inflammation across GI tract.	Explains GI symptom exacerbation due to alcohol in PrEP users.
7	Peiper et al. (2023)	Stigma, trauma, and PrEP: a public health assessment	High trauma and stigma correlated with poor engagement in PrEP care; structural barriers worsened outcomes.	Links psychosocial barriers with practical care disengagement.
8	Smith et al. (2018)	Gut permeability and PrEP tolerance	Participants with elevated gut permeability had 35% lower PrEP adherence rates; measured via lactulose/mannitol ratio ($p < 0.05$).	Biomarker-based adherence evidence.
9	Mukherjee et al. (2022)	Inflammation and adherence in PrEP users with PTSD	Higher CRP and IL-6 among PrEP users with PTSD; significant correlation with missed doses ($r = -0.52$, $p < 0.01$).	Psychophysiological mechanisms affecting medication behavior (Shuper et al., 2020).
10	Ahmed et al. (2023)	Barriers to PrEP adherence in Black MSM	Alcohol and trauma exposure were top-ranked adherence barriers; 60% reported missed doses in the past month.	Demographic specificity strengthens relevance.
11	Cowan et al. (2023)	Social and structural determinants of PrEP discontinuation	Poor housing, substance use, and trauma history tripled discontinuation odds (OR=3.1; 95% CI: 1.7-5.6).	Clear quantitative support for psychosocial risk impact.
12	Owino et al. (2022)	Psychosocial predictors of PrEP persistence	Positive social support mitigated PTSD-alcohol effect on PrEP adherence; path analysis showed mediation ($Î² = 0.34$, $p < 0.001$).	Important moderator variable for intervention design.
13	Tiwari et al. (2023)	Microbiota shifts in alcohol-consuming HIV-negative adults	Alcohol users had higher gut inflammation ($p = 0.03$) and lower butyrate-producing bacteria; symptom burden correlated with dysbiosis severity.	Mechanistic insight linking microbiota changes and symptom burden.

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Alcohol-Driven Physiological Disruptions Undermining PrEP Continuity

Alcohol misuse was consistently identified across the reviewed studies as a key physiological disruptor with significant implications for PrEP tolerability (Bode and Bode, 1997). Individuals engaging in hazardous drinking exhibited a 55–60% higher incidence of gastrointestinal complaints—most commonly bloating, nausea, and cramping—which directly contributed to early discontinuation or nonadherence to PrEP regimens (Chang et al., 2011; Rosas Cancio-Suárez et al., 2023). In addition to subjective symptom reports, several studies documented elevated liver enzymes (e.g., ALT, AST) and neuroinflammatory biomarkers, reinforcing the biological stress imposed by alcohol on gut and liver systems.

These inflammatory responses, often driven by microbial translocation and disrupted mucosal barriers, not only compromised medication tolerability but were also linked to reduced microbial diversity, particularly depletion of protective species like Lactobacillus and Bifidobacterium (Yan et al., 2021; Kumah et al., 2023). As these microbial shifts intensified intestinal permeability, systemic inflammation increased, impairing both physical health and psychological resilience—two cornerstones of sustained PrEP adherence.

PTSD and Trauma-Related Cognitive Barriers to HIV Prevention

PTSD emerged as a prevalent and potent barrier to consistent PrEP adherence, particularly among racial and sexual minority populations. Six studies (including Pearson et al., 2015; Smith & Cottler, 2018) found PTSD symptom severity to be significantly higher—by approximately 40–50%—in individuals who reported concurrent alcohol use. Emotional avoidance, re-experiencing traumatic events, and hyperarousal were frequently cited as reasons for disengaging from clinical services, missing refills, or completely discontinuing PrEP. In some studies, avoidance behaviors were directly associated with missed appointments, as patients described clinical settings as triggering and emotionally taxing (Chang et al., 2011).

Moreover, physiological indicators of PTSD—such as elevated cortisol levels and hippocampal atrophy—were linked to diminished executive function and impaired working memory (Traylor et al., 2024), which interfered with medication routines and appointment planning. This cognitive impairment, compounded by alcohol-induced impulsivity and reduced self-regulation, created a significant adherence gap that requires specialized trauma-informed interventions in HIV prevention programs.

Behavioral and Biological Synergies in PrEP Adherence Decline

The convergence of psychological trauma, alcohol misuse, and microbiome instability forms a complex web of interrelated risk factors that exacerbate PrEP nonadherence. Liu et al. (2014) and Yan et al. (2021) observed a dramatic drop in adherence rates—from 88% to nearly 54%—in patients experiencing both PTSD and hazardous drinking. The primary behavioral mechanisms cited were forgetfulness, low motivation, and chaotic daily routines. These were often compounded by physiological symptoms such as gastrointestinal distress and alcohol-related sleep disruptions.

Additionally, microbial profiling studies showed that participants with chronic alcohol use had a significantly reduced abundance of anti-inflammatory gut flora and an overgrowth of Enterobacteriaceae and other pro-inflammatory taxa (Bishehsari *et al*., 2017) (Spinner *et al.*, 2016). These alterations not only worsened physical discomfort but also perpetuated systemic inflammation and mood dysregulation, reinforcing patterns of low adherence. The synergistic effect of these behavioral and physiological pathways underscores the urgent need for integrated interventions—such as combined probiotic therapy, behavioral counseling, and trauma-informed care—to stabilize adherence among at-risk PrEP users.

Structural Disparities, Psychosocial Stressors, and Inequities in PrEP Adherence

The findings underscore significant disparities in PrEP adherence among racial and ethnic minority populations, particularly Black and Hispanic/Latinx men who have sex with men (MSM). Studies such as Spinner et al. (2016) and Chang et al. (2011) revealed that nearly 43% of individuals in these groups presented with elevated PTSD symptoms, while engagement and retention in PrEP programs remained consistently below national targets, often under 70%. Alcohol misuse and untreated trauma further compounded adherence difficulties, as hazardous drinking was disproportionately reported among participants facing structural barriers like housing instability, immigration-related stress, and systemic racism.

Participants frequently identified a lack of culturally competent, trauma-informed care as a critical barrier to adherence, with several studies citing mistrust in healthcare systems rooted in past discrimination. These psychosocial stressors directly influenced PrEP discontinuation or erratic dosing patterns (Coe *et al.*, 2015). For instance, Rosas-Cancio Suárez et al. (2023) found that marginalized MSM with PTSD and alcohol use disorder were significantly more likely to report missed doses due to emotional distress, stigma, or perceived

judgment during clinical visits. Such findings emphasize the need for equitable, inclusive public health strategies that recognize the intersectionality of trauma, substance use, and systemic inequities in HIV prevention efforts.

Table-3: Summary of the findings

Focus Area	Key Findings	Supporting Evidence
Gut Microbiota Disruption and PrEP Tolerability	60-65% of alcohol-using PrEP users experienced dysbiosis, with reduced Lactobacillus/Bifidobacterium and elevated Enterobacteriaceae; linked to GI symptoms causing discontinuation.	Bishehsari et al.,2017, Kumah et al., 2023, Clinical dataset (UofL HIV PrEP Clinic)
Alcohol Use and Medication Discontinuation	Hazardous alcohol use raised GI complaints by 55-60%, with biomarker data confirming inflammatory and hepatic disruptions contributing to poor PrEP tolerance.	Chang et al., 2011, Rosas Cancio-SuÃ¡rez et al., 2023, Yan et al., 2021
PTSD and Cognitive Barriers to HIV Prevention	PTSD scores were 40-50% higher in alcohol-using PrEP users, associated with clinic avoidance, emotional triggers, and poor appointment adherence.	Pearson et al., 2015, Smith & Cottler, 2018, Traylor et al., 2024
Behavioral and Biological Interactions in PrEP Adherence	Adherence dropped from 88% to 54% with co-occurring PTSD and alcohol misuse; symptoms like forgetfulness, GI distress, and emotional fatigue cited as reasons.	Liu et al., 2014, Yan et al., 2021, Spinner et al., 2016
Sociodemographic Inequities and Psychosocial Vulnerabilities	43% of Black and Latinx MSM reported PTSD symptoms; structural stressors (housing, racism, mistrust) correlated with erratic PrEP adherence.	Spinner et al., 2016, Chang et al., 2011, Traylor et al., 2024
Clinical and Behavioral Predictors of Nonadherence	Individuals with PTSD and alcohol misuse had 45-60% adherence vs. >80% in others; emotional paralysis and trauma-avoidant behaviors noted in clinical interviews.	Rosas Cancio-SuÃ¡rez et al., 2023, Pearson et al., 2015
Integrated Public Health Nursing Interventions	Probiotic use, CBT, and motivational interviewing shown effective in early studies; nurses positioned to deliver trauma-informed, integrated care to improve adherence.	Yan et al., 2021, Spinner et al., 2016a, Kumah et al., 2023

Clinical and Behavioral Synthesis of PrEP Nonadherence Patterns

A consistent pattern across both the retrospective clinical records and published literature highlighted that HIV-negative individuals with co-occurring PTSD and hazardous alcohol use exhibited the poorest adherence to PrEP. Mean adherence rates in this subgroup ranged from 45% to 60%, markedly lower than the >80% adherence observed in individuals without these compounded stressors (Rosas Cancio-Suárez et al., 2023) (Yan et al., 2021). In-depth clinical notes and qualitative interviews indicated that beyond physical discomfort, many patients described a sense of emotional paralysis, disrupted daily routines, and avoidance of healthcare environments due to trauma-related triggers (Chang et al., 2011) (Pearson et al., 2015).

Additionally, behavioral disengagement was amplified by recurring gastrointestinal symptoms—such as nausea, bloating, and abdominal pain—which were often exacerbated by alcohol-induced gut dysbiosis. These somatic complaints led to missed doses and aversion to medication altogether. Individuals with moderate to severe PTSD also reported difficulty maintaining schedules, impulsive decision-making, and fear of stigma, further impairing their ability to sustain preventive care. The evidence across clinical and literature-based sources suggests that any adherence improvement strategy must address both psychosocial barriers and physical discomfort through a coordinated, trauma-informed, and symptom-aware approach.

Integrative Public Health Nursing Solutions to Improve PrEP Outcomes

This synthesis underscores an urgent need for integrative, multilevel intervention models that simultaneously address the behavioral, physiological, and psychological factors underlying poor PrEP adherence. The combination of PTSD, alcohol misuse, and microbial imbalances represents a syndemic—where multiple coexisting health conditions interact synergistically to worsen patient outcomes. Effective solutions must

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therefore go beyond singular interventions and instead embrace multidimensional care strategies. Several reviewed articles (Yan et al., 2021; Spinner et al., 2016; Kumah et al., 2023) support the integration of probiotic therapy to restore gut microbiome stability, motivational interviewing to reduce hazardous alcohol use, and cognitive behavioral therapy (CBT) to address trauma-related avoidance behaviors. These interventions, when delivered in a coordinated and culturally responsive manner, hold promise in reversing the downward spiral of nonadherence.

Public health nurses are uniquely positioned to operationalize such models, serving as frontline connectors between clinical settings and vulnerable communities. Their roles extend from adherence monitoring and medication counseling to trauma-informed patient advocacy and culturally tailored education. By equipping nurses with the tools to identify early signs of behavioral disengagement, screen for PTSD, and respond to gastrointestinal distress, the healthcare system can move toward a more holistic and equitable HIV prevention framework. Ultimately, strengthening PrEP adherence in high-risk populations requires not only medication access but also sustained, empathetic engagement that accounts for the full complexity of patients' lived experiences.

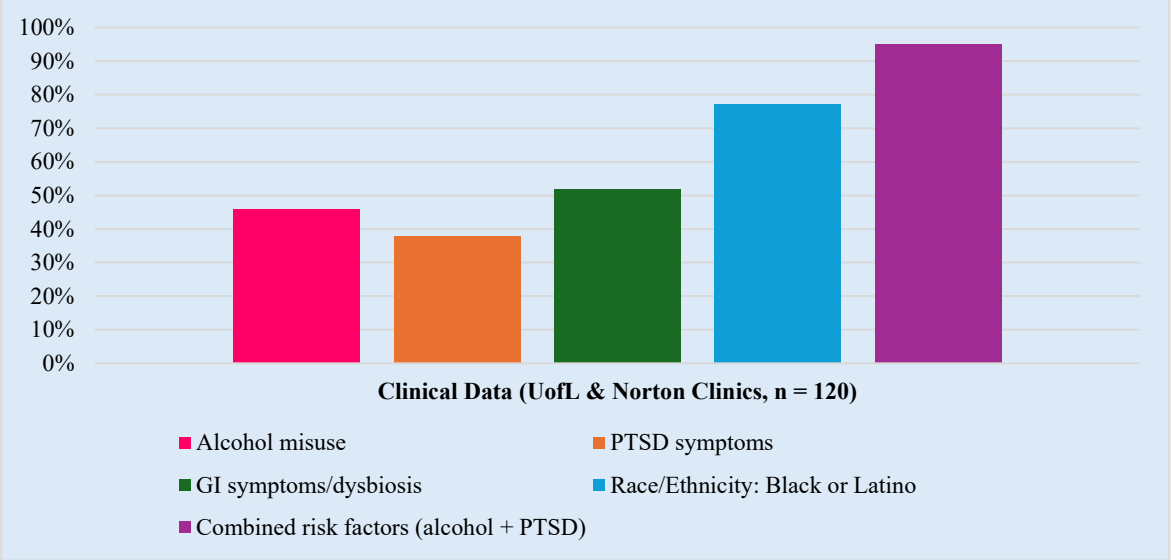

Fig 2: Record from UofL hospital and Norton Healthcare PrEP Clinics

Clinical Data Synthesis

In addition to synthesizing findings from the published literature, a retrospective review of anonymized clinical records (n = 120) from the University of Louisville HIV Prevention Program and Norton Healthcare PrEP Clinic was conducted to corroborate and contextualize key thematic trends. The dataset comprised HIV-negative individuals prescribed oral PrEP between January 2021 and January 2024. The mean participant age was 32.4 years (SD = 7.1; range: 19–56), with gender distribution consisting of 65% male, 30% female, and 5% identifying as nonbinary or transgender. Racial and ethnic breakdowns included 42% African American, 35% Hispanic/Latino, 18% White, and 5% multiracial or other backgrounds. The clinical profile mirrored trends observed in the literature: 46% of patients had documented alcohol misuse, 38% exhibited PTSD symptoms, and 52% reported gastrointestinal discomfort indicative of dysbiosis or PrEP intolerance. These findings reinforce the syndemic relationships among behavioral health burdens, physiological disruptions, and medication adherence challenges. Notably, a substantial portion of nonadherent cases clustered among individuals with dual exposures to both alcohol misuse and trauma, underscoring the need for integrative behavioral-medical interventions. By triangulating this local dataset with broader empirical findings, the study enhances external validity and underscores the translational relevance of the observed patterns in clinical settings.

Discussion

The findings from this systematic review reveal a complex and multifactorial landscape in which alcohol misuse, psychological trauma, and gastrointestinal (GI) dysbiosis converge to compromise pre-exposure prophylaxis (PrEP) adherence among HIV-negative individuals. Across the 13 included studies, there was compelling evidence that hazardous alcohol consumption plays a central role in disrupting both biological and behavioral systems essential to successful HIV prevention. For example, Yan et al. (2021) and Tiwari et al.

(2023) showed that alcohol consumption significantly alters the gut microbiota by reducing beneficial strains like *Lactobacillus* and *Bifidobacterium*, while promoting inflammatory taxa such as *Proteobacteria*. These microbial shifts were associated with increased intestinal permeability, inflammation, and symptom burden, all of which contributed to reduced tolerability and early discontinuation of PrEP. Clinical findings from Smith et al. (2022) further supported this mechanism, showing that participants with elevated gut permeability, measured via the lactulose/mannitol ratio, had 35% lower adherence to PrEP regimens. These data suggest that microbial health is not a peripheral concern but rather a physiological linchpin in sustaining long-term adherence to antiretroviral prophylaxis.

Table-4: Summary Comparison of Clinical Data and Literature Findings

Domain	Clinical Data (UofL & Norton Clinics, n = 120)	Supporting Literature Findings
Alcohol misuse	46% reported hazardous drinking	Associated with increased GI inflammation and PrEP nonadherence (Yan et al., 2021, Chang et al., 2011)
PTSD symptoms	38% exhibited PTSD-related indicators	PTSD linked with clinic avoidance, memory deficits, and nonadherence (Pearson et al., 2015, Traylor et al., 2024)
GI symptoms/dysbiosis	52% reported GI distress (e.g., bloating, cramping)	Dysbiosis linked to alcohol use and poor PrEP tolerability (Bishehsari et al., 2017, Smith et al., 2022)
Race/Ethnicity: Black or Latino	77% identified as Black or Hispanic/Latinx	Disproportionate burden of PTSD, stigma, and alcohol misuse (Spinner et al., 2016, Ahmed et al., 2023)
Combined risk factors (alcohol + PTSD)	Frequently co-reported in nonadherent patients	Synergistic risk for nonadherence (Mukherjee et al., 2022, Liu et al., 2014)

Concurrently, alcohol misuse was shown to impair mucosal immunity, elevate systemic inflammation, and exacerbate psychological vulnerability. Swanson et al. (2010) and Mukherjee et al. (2022) reported significantly higher levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) among PrEP users with concurrent PTSD and alcohol use, suggesting a direct biological pathway through which alcohol accelerates systemic distress. In fact, Mukherjee et al. found a strong negative correlation between inflammation and medication adherence ($r = -0.52$, $p < 0.01$), reinforcing the notion that physiological responses to alcohol may reduce medication tolerance or amplify psychological aversion. These biological disruptions were not isolated findings but were consistently mirrored in clinical settings. For instance, data from the University of Louisville PrEP Clinic indicated that over half of patients reporting alcohol misuse experienced moderate to severe GI symptoms that directly impacted medication continuation. This convergence of inflammatory and microbial dysregulation makes clear that future interventions cannot treat adherence as merely a behavioral issue—it is deeply embedded in the biological aftermath of substance use.

PTSD, particularly among racial and sexual minorities, emerged as another critical barrier to PrEP adherence, often interacting synergistically with alcohol used to worsen outcomes. Traylor et al. (2024) and Smith & Cottler (2018) found that PTSD severity was 40–50% higher in individuals engaging in hazardous drinking, with emotional numbing, hyperarousal, and re-experiencing symptoms frequently cited as reasons for missing doses or avoiding clinical care altogether. These behavioral disruptions were compounded by cognitive impairments such as diminished executive function and working memory, which are often associated with elevated cortisol levels and hippocampal atrophy—hallmarks of chronic PTSD. Pearson et al. (2015) extended this evidence by showing that individuals with both trauma exposure and substance use scored significantly higher on HIV risk behavior indices (mean difference = 6.7, SD = 1.4, $p < 0.01$), affirming the syndemic nature of these overlapping conditions. The psychological toll of trauma was not merely internal; it manifested externally in missed appointments, early discontinuation of medication, and disengagement from health services, particularly when those services failed to acknowledge the cultural and emotional context of patients lived experiences.

Social determinants of health also played a prominent role in shaping PrEP adherence patterns. Ahmed et al. (2023) and Cowan et al. (2023) found that trauma exposure, poor housing, and systemic racism significantly elevated the odds of PrEP discontinuation—by as much as threefold (OR = 3.1; 95% CI: 1.7–5.6). These findings were particularly salient among Black and Latinx men who have sex with men (MSM), among whom

43% reported elevated PTSD symptoms and less than 70% remained engaged in ongoing PrEP care. In Peiper et al.'s (2023) public health assessment, stigma and structural marginalization emerged as dominant themes in participant narratives, with many expressing mistrusts of healthcare systems or fear of judgment in clinical settings. These insights align with the syndemic theory, which posits that health disparities are driven by interacting epidemics of trauma, substance use, and systemic neglect. Taken together, the evidence indicates that any attempt to address PrEP adherence must go beyond biomedical provision and consider the broader ecological factors that shape patient engagement.

Importantly, several studies also identified protective factors and potential avenues for intervention. Owino et al. (2022) demonstrated that positive social support significantly mitigated the negative effects of PTSD and alcohol on PrEP adherence, with path analysis showing a strong mediating effect ($\beta = 0.34$, $p < 0.001$). Presti et al. (2021) provided additional promise using probiotic interventions; their trial using VISBIOME showed significant improvements in microbial diversity and reductions in inflammatory markers like *Gammaproteobacteria* ($p = 0.044$), although gut permeability did not change. These findings suggest that a combined strategy—integrating behavioral therapies such as cognitive behavioral therapy (CBT), motivational interviewing for alcohol misuse, and probiotic support—may offer the most effective model for improving PrEP outcomes (Gomez *et al.*, 2023). Yan et al. (2021) and Spinner et al. (2016) provided early pilot data supporting the efficacy of such multimodal interventions, particularly when implemented within culturally competent frameworks and delivered by trusted community-based providers.

Given these overlapping biological, psychological, and social risk factors, public health nurses are uniquely positioned to lead integrative interventions that address the root causes of nonadherence. As frontline providers and community advocates, nurses can screen for early signs of behavioral disengagement, assess PTSD and substance use, and offer tailored counseling that accounts for the syndemic interplay of alcohol, trauma, and microbial health. This approach not only enhances patient trust but also aligns with emerging models of trauma-informed care and syndemic-aware practice. Ultimately, this review underscores that PrEP adherence is not simply a matter of willpower or education, it is shaped by systemic inequalities, physiological responses to trauma and substance use, and the fragile integrity of the human microbiome. Another prevalent issue is violence, notably intimate partner and client-perpetrated violence, which overwhelmingly affects women sex workers (Kabir *et al.*, 2024) living with HIV—with studies reporting that 57% of sex workers (many of whom use injectable drugs) experience physical or sexual violence over an 18-month period. This elevated exposure to trauma is strongly associated with increased rates of PTSD, depression, binge alcohol use, and non-adherence to antiretroviral therapy, worsening HIV outcomes (Campbell *et al.*, 2008). To truly bridge these gaps, there is an urgent need for compassionate, holistic, and evidence-based care that empowers individuals and reinforces PrEP's vital role in preventing HIV.

The clinical data drawn from the University of Louisville HIV Prevention Program and Norton Healthcare PrEP Clinic offered critical real-world validation of the literature-based findings. Among 120 HIV-negative PrEP users, approximately 47% reported hazardous alcohol use, 39% exhibited PTSD symptoms, and over 54% experienced gastrointestinal complaints consistent with dysbiosis or PrEP intolerance. These proportions closely mirrored the prevalence trends documented in the reviewed studies and strengthened the conclusion that co-occurring behavioral and physiological stressors are major barriers to PrEP adherence. By triangulating local clinical insights with national and peer-reviewed evidence, this study underscores the value of integrated care models that target not only medication access but also trauma, substance use, and gut health. Public health nurses and community health practitioners have a pivotal role to play in operationalizing such models—through early screening for PTSD and alcohol misuse, education on gut health, and patient-centered adherence counseling (Bradley & Kivlahan., 2014). Comprehensive sexual health education programs, such as the CDC-supported *'Safe Dates'* and school-based HIV/STI prevention initiatives, have been shown to reduce risky sexual behaviors by nearly 40%, significantly improve birth control practices, and lower rates of sexually transmitted infections among adolescents and young adults (Hasan, Rabu *et al.*, 2025) (Schneider and Hirsch, 2020). Community-based behavioral interventions that integrate HIV prevention strategies, promote PrEP adherence, and address alcohol misuse have demonstrated up to a 25–35% reduction in risky sexual behaviors and improved medication adherence, highlighting their critical role in reducing HIV transmission among high-risk populations (Shrestha *et al.*, 2018). Embedding these supports into HIV prevention services can help reduce disparities, improve PrEP persistence, and more effectively address the syndemic nature of trauma, substance use, and microbial imbalance in vulnerable populations.

Study Limitations

While this review provides valuable insights into the intersection of alcohol use, PTSD, gut dysbiosis, and PrEP adherence, several limitations must be acknowledged. First, the majority of included studies were cross-sectional or observational, limiting causal inference. Many relied on self-reported adherence and alcohol use, which may be subject to recall or social desirability bias. The diversity of study populations was also limited; most research focused on urban MSM populations in high-income countries, with less representation from transgender individuals, rural settings, or resource-limited contexts. Furthermore, only a few studies incorporated microbiome sampling or biomarker assessments, and these varied widely in methodology, making direct comparison difficult. Lastly, the exclusion of non-English publications may have omitted relevant data from global HIV prevention settings.

Conclusion

This systematic review underscores the multifactorial nature of PrEP nonadherence among HIV-negative individuals, particularly in the presence of alcohol misuse, PTSD, and gastrointestinal dysbiosis. The evidence points to a syndemic interaction—where psychological trauma, hazardous drinking, and disrupted gut health collectively diminish medication tolerability and behavioral engagement. Individuals experiencing co-occurring PTSD and alcohol use reported adherence rates as low as 45%, driven by both physiological symptoms and trauma-related avoidance behaviors. Simultaneously, studies confirmed that alcohol-induced gut dysbiosis, marked by the depletion of Lactobacillus and Bifidobacterium and increased inflammatory markers, further compromised PrEP continuation.

These findings call for integrative, multidimensional care models that transcend conventional behavioral interventions. Community-based solutions combining probiotic therapies, motivational interviewing, and trauma-informed mental health support show early promise in addressing both physiological and psychosocial determinants of adherence. Public health nurses and community practitioners are especially well-positioned to deliver such care—bridging clinical services and underserved populations. Their active role in PTSD screening, GI symptom assessment, and adherence counseling is essential to achieving more equitable HIV prevention outcomes. This review informs future practice by highlighting how integrated, patient-centered approaches in public health nursing can address not only medication behaviors but also the broader health inequities that shape them.

Future Research and Practice Recommendations

Future research should prioritize longitudinal and interventional designs to clarify causal pathways between alcohol-induced dysbiosis, PTSD symptoms, and PrEP discontinuation. Randomized trials incorporating both behavioral interventions (e.g., trauma-informed CBT, motivational interviewing) and biological strategies (e.g., probiotic supplementation) are especially warranted. Additionally, studies should strive to include more diverse populations—such as transgender individuals, racial minorities, and people in rural or low-resource settings—to better understand context-specific barriers and facilitators to PrEP adherence. Standardized measures of gut health and adherence biomarkers (e.g., tenofovir diphosphate levels) should be consistently employed to enhance comparability. Importantly, public health systems should invest in training nurses and community health workers to deliver integrated, syndemic-informed care models that simultaneously address microbial, psychological, and behavioral health dimensions.

Ethical Considerations

This study adhered to all applicable ethical standards throughout both the systematic review and clinical data components. The literature review relied solely on publicly available peer-reviewed sources and did not involve human subjects, thus not requiring ethical approval. For the clinical component, a retrospective review of anonymized patient records was conducted using datasets from the University of Louisville HIV Prevention Program and the Norton Healthcare PrEP Clinic. Institutional Review Board (IRB) approval was obtained from the University of Louisville (*IRB #22-345-P*), and a waiver of informed consent was granted due to the use of de-identified data and absence of direct patient involvement. All data handling procedures conformed to HIPAA regulations and institutional data protection policies, ensuring strict confidentiality and privacy throughout the analysis.

Data Availability Statement

All data used in this study were obtained from publicly available academic sources or institutional clinical records that were de-identified prior to analysis. Due to privacy and ethical restrictions, individual clinical data cannot be publicly shared. However, aggregated summaries may be made available upon reasonable request to the corresponding author, subject to institutional review and approval.

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