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Alcohol-Induced Microbial Dysbiosis and Psychosocial Stressors Undermining PrEP Adherence: A Mixed Methods Analysis in HIV-Negative African American Adults

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ABSTRACT

HIV remains a major public health challenge in the Southern United States, with African American communities facing elevated risk. This study investigates how hazardous alcohol use, psychological distress, and gut microbial dysbiosis affect PrEP adherence and evaluates a trauma-informed SBIRT intervention to improve outcomes. This 12-month convergent mixed-methods study was conducted through Kentucky State University with two collaborating clinics. Seventy-eight HIV-negative African American adults on PrEP were recruited via referrals and community outreach and randomized to SBIRT (n = 30), Treatment-as-Usual (n = 30), or a non-hazardous drinking reference group (n = 18). Quantitative data included surveys (AUDIT, PHQ-9, PCL-5), pharmacy refill logs, and stool-based 16S rRNA sequencing. The qualitative arm applied a phenomenological approach with 40 purposively selected participants completing semi-structured interviews at baseline, 3, 6, and 12 months. Interviews were thematically coded in Dedoose and integrated with quantitative analyses (chi-square, ANOVA, Pearson correlations, logistic regression) to examine clinical outcomes and lived experiences influencing PrEP adherence. Among 78 participants, multivariate logistic regression identified hazardous alcohol use (OR=2.9, p=0.008), PTSD (OR=3.6, p=0.003), depression (OR=2.7, p=0.029), and microbial dysbiosis (OR=3.3, p=0.006) as predictors of PrEP non-adherence (<85%). Compared with TAU, SBIRT participants showed higher adherence (80% vs. 53%, p=0.014), greater microbial diversity (Shannon Index 2.6 vs. 1.9, p=0.004), and lower inflammatory biomarkers (IL-6, TNF-α, both p<0.05). They also reported fewer depressive (PHQ-9: 7.8 vs. 11.5, p=0.004) and PTSD symptoms (PCL-5: 29.1 vs. 35.4, p=0.007), alongside safer sexual behaviors. Qualitative analysis confirmed that stigma, trauma, and gut discomfort disrupted adherence, while SBIRT counseling enhanced self-awareness, reduced emotional fatigue, and supported behavioral change. These findings highlight that PrEP adherence can be enhanced through trauma-informed, culturally grounded support in combination with long-acting formulations and probiotic strategies.

INTRODUCTION

In the United States, HIV is a chronic public health concern, and African-American communities in the South are disproportionately affected by new infections. Pre-exposure prophylaxis (PrEP) is one example of a scientific innovation that has been very effective in reducing HIV transmission; nevertheless, its effects have not been uniform across all communities. Across the United States, Black/African American individuals have long shouldered a disproportionate HIV burden despite comprising just ~12–13% of the population yet accounting for nearly 39% of new HIV diagnoses in recent years (Bosh *et al.*, 2021). In Kentucky, this disparity is particularly stark: Black residents make up only about 8–9% of the state's population but account for 30–32% of all HIV diagnoses (Thorpe *et al.*, 2022). Limited access to culturally responsive care, high levels of untreated mental illness, hazardous alcohol use, and persistent stigma collectively undermine consistent PrEP adherence. These intersecting challenges underscore the need for trauma-informed, integrated prevention strategies that reflect the lived experiences of individuals who remain marginalized within the healthcare system (Swendeman *et al.*, 2024). Recent studies show that people's behavioral and psychosocial settings have a significant influence on PrEP participation. According to recent research, especially among young individuals, syringe-sharing practices and opioid use disorder continue to be significant factors in HIV transmission in the US (Wang & Maher, 2019). Non-sterile injection equipment is used to allow direct blood-to-blood contact and is responsible for about 10% of new HIV infections in the country. Meanwhile, long-term opiate abuse is often associated with serious mental disorders (Hasan, 2024b) and heightened susceptibility to alcohol overuse. These coexisting illnesses increase the risk of HIV acquisition by impairing judgment and increasing participation in high-risk sexual and injectable behaviors. Trauma experiences often co-occur and interact with symptoms of depression, PTSD, and high-risk alcohol use in ways that have a substantial impact on adherence patterns (Read *et al.*, 2014), decreasing adherence and contributing

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to drop-off throughout the PrEP treatment continuum. The biological bases of adherence behavior, particularly the function of the gut microbiota, have been the focus of recent scientific investigations. Disturbance in the gut microbial ecosystem, or dysbiosis, has been identified as a potentially significant but little-researched factor in drug tolerance and immunological resilience, especially among African American users, and gastrointestinal side effects continue to be a major cause of PrEP cessation. Given these facts, HIV prevention must take a more comprehensive, person-centered approach that takes behavioral risk, lived experience, and biological feedback mechanisms into consideration (Perler *et al.*, 2021a). This study integrates trauma-informed behavioral interventions within a biopsychosocial framework to address critical gaps in HIV prevention by investigating PrEP adherence in Southern communities through a mixed-methods design.

PrEP, currently available in oral (daily pill) and injectable formulations, mainly comprises tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) or tenofovir alafenamide with emtricitabine (TAF/FTC). Branded formulations like Truvada® and Descovy® have shown up to 92% effectiveness in decreasing the risk of HIV acquisition when used with strong adherence (Grant *et al.*, 2010; Perler *et al.*, 2021). Despite its demonstrated efficacy, significant disparities in PrEP uptake, adherence, and persistence persist across populations. These inequities are shaped not solely by individual behavior but by the multifaceted interaction of social, structural, psychological, and biological determinants (Fields & Tung, 2021). Recent evidence indicates that the adverse effects of PrEP, particularly gastrointestinal symptoms such as nausea, bloating, diarrhea, and abdominal discomfort, are among the most often reported reasons for cessation(Antonini *et al.*, 2023a). The symptoms, often ascribed to PrEP start-up syndrome, have been associated with alterations in the gut microbiota. Fulcher *et al.* (2022) and Perler *et al.* (2021) specifically observed that persons on PrEP have significant microbial alterations, including an increased prevalence of Catenibacterium and Prevotella, and a decrease in taxa such as Finegoldia and Bacteroides (Perler *et al.*, 2021b; Fulcher *et al.*, 2019). Prevotella, prevalent among men who have sex with men (MSM), is connected with inflammatory reactions and insulin resistance, while Catenibacterium is linked to metabolic syndrome. The microbial alterations indicate that PrEP may induce systemic inflammation and gastrointestinal discomfort via microbial dysbiosis (Bragazzi *et al.*, 2022).

Microbial dysbiosis denotes an imbalance in the gut microbiota, marked by diminished microbial diversity and an excess of pro-inflammatory or pathogenic species (Hasan & Yusuf, 2023). In healthy humans, the gut microbiome mostly consists of the phyla Firmicutes and Bacteroidetes, along with lesser amounts of Proteobacteria and Actinobacteria(Yan *et al.*, 2021a). Shifts towards Prevotella dominance and reduced bacterial richness have been seen in males who have sex with men (MSM), even without HIV infection—probably driven by sexual habits, nutrition, and other behavioral variables. These foundational modifications may increase the microbiome's susceptibility to disturbance. Recent studies indicate that approximately 60% of HIV-positive patients admitted to intensive care units (ICUs) acquire infections from multidrug-resistant uropathogens, leading to increased morbidity, prolonged hospitalization, and an elevated risk of nosocomial HIV transmission through invasive clinical procedures (Hasan *et al.*, 2025). Pre-exposure prophylaxis (PrEP), although successful in HIV prevention, has shown an effect on mucosal immunity and microbial ecology, especially when combined with alcohol use. Alcohol autonomously enhances intestinal permeability, elevates bacterial translocation, and produces oxidative stress, hence aggravating microbial dysbiosis (Fulcher *et al.*, 2022). The connection between PrEP and alcohol-related dysbiosis among African American adults, particularly cisgender heterosexual men and women who are heavy drinkers, is little studied. This is a notable deficiency in the literature, since dysbiosis in this demographic may lead to gastrointestinal adverse effects, chronic inflammation, diminished medication tolerance, and noncompliance with PrEP protocols. Co-infections like dengue or COVID-19 may exacerbate the clinical burden of HIV by hastening immunological deterioration, amplifying systemic inflammation, and increasing the chance of unfavorable treatment outcomes (Hasan *et al.*, 2025). Consequently, examining microbiological fingerprints in conjunction with psychological and behavioral factors is essential for enhancing precision preventative interventions in areas disproportionately impacted.

Alcohol intake presents a complex obstacle to HIV prevention among African American people on PrEP. Hazardous drinking compromises judgment and medication compliance while causing substantial physiologic disturbances. Statistical evidence indicates that individuals with alcohol use disorders are significantly more likely to engage in criminal offenses, including violent assaults, domestic abuse, and public disturbances, with alcohol implicated in approximately 40% of violent crimes in the United States (Vinnakota *et al.*, 2022). Chronic alcohol use undermines intestinal barrier integrity, facilitates bacterial translocation, and increases systemic inflammation—mechanisms recognized for disrupting the gut microbiota (Fulcher *et al.*, 2019). These disturbances are clinically significant, as alterations in microbial diversity and an elevated Firmicutes: The ratio of Bacteroidetes has been associated with the deterioration of mucosal immunity and the impairment of the host's antiviral defenses. Simultaneously, PrEP might induce microbial disturbances, especially with extended oral or injectable treatments, thereby exacerbating alcohol-related dysbiosis (Yang *et al.*, 2024). Our analysis revealed that people with larger AUDIT scores had markedly reduced microbial diversity (Shannon Index 1.9

vs. 2.6; p = 0.004) and increased levels of inflammatory markers, including IL-6 and TNF-α. These biological changes were associated with gastrointestinal side effects, including as nausea, bloating, and diarrhea, and were identified as significant predictors of PrEP non-adherence (Rodríguez-Rabassa *et al.*, 2020) (OR = 3.3, 95% CI: 1.5–7.2). Moreover, immunological disruption caused by gut dysbiosis may unexpectedly increase the risk of HIV acquisition, despite pharmacological protection, by augmenting mucosal permeability and the generation of inflammatory cytokines. The intricate relationship between alcohol use and PrEP pharmacodynamics diminishes gut-immune integrity, highlighting the need of including microbial surveillance and behavioral health support into PrEP delivery strategies (Brenchley & Serrano-Villar, 2024). Considering that African American adults have systemic obstacles to addiction treatment and microbiome-focused care, customized treatments that target both behavioral and biological susceptibilities are critically required to maintain the effectiveness of HIV prevention (Pan *et al.*, 2023). Evidence indicates that co-infections with acute viral illnesses, including dengue, influenza, and monkeypox, may significantly worsen HIV-related morbidity (Hasan *et al.*, 2024). Individuals with HIV have increased vulnerability to poor clinical consequences when co-infected with these viruses, partly owing to impaired immune function and systemic inflammation.

These biological issues are exacerbated by significant psychological repercussions. High levels of psychological trauma are often experienced by African Americans, who may be exposed to institutional racism, personal relationship abuse, and community violence. These events are connected with post-traumatic stress disorder (PTSD) and major depressive disorder (MDD), both of which correlate with detrimental health behaviors, including decreased compliance with treatment regimens (Sibrava *et al.*, 2019). Healthcare professionals are increasingly encountering psychological distress (Hasan *et al.*, 2025), including PTSD and chronic stress symptoms, often intensified by the emotional toll of managing HIV patients, observing medication-related side effects, and contending with the stigma and moral dilemmas associated with HIV prevention and care. The COVID-19 pandemic has heightened mental health issues, leading to a surge in the use of illegal substances and alcohol, which has further aggravated high-risk sexual practices and resulted in an increase in new HIV infections among adults (Kabir *et al.*, 2023). In addition to behavioral therapies, education is essential—particularly for sex workers—since it provides them with the information necessary to make educated choices about contraception, manage intricate power dynamics in sexual interactions, and mitigate health risks such as unwanted pregnancies and STIs. Violence, especially in the context of intimate partner and client-perpetrated violence, is a substantial public health issue for women sex workers who are HIV-positive. Evidence indicates that around 57% of this population—many of whom partake in injectable drug use—endure physical or sexual assault during an 18-month timeframe (Kabir *et al.*, 2024). Repeated exposure to interpersonal trauma is significantly correlated with a higher incidence of posttraumatic stress disorder (PTSD), clinical depression, excessive alcohol consumption, and inadequate adherence to antiretroviral therapy, all of which exacerbate HIV-related health outcomes and increase transmission risk (Hasan, 2024a). The use of illicit drugs and excessive alcohol consumption markedly deteriorates HIV outcomes in adults by impairing the immune system, undermining adherence to antiretroviral therapy, promoting high-risk sexual behaviors, and heightening the risk of suicidal ideation (Kabir *et al.*, 2023); recent studies indicate that up to 20% of adults with HIV and co-occurring substance use disorders experience suicidal thoughts (Kabir *et al.*, 2024) or behaviors (Hasan, 2024c). In environments characterized by significant stigma and limited access, thorough contraceptive education improves individual autonomy, facilitates harm reduction, and is essential for promoting reproductive equality and public health outcomes for this often-neglected group (Hasan, Rabu *et al.*, 2025). A study of women survivors of intimate partner violence revealed that individuals with elevated PTSD and depressive symptoms had markedly increased desire to participate in PrEP (OR = 0.22, 95% CI: 0.06–0.76), while concurrently encountering substantial obstacles to maintaining treatment. This contradiction illustrates a significant tension: those most susceptible to HIV often bear the greatest psychological strain, which hinders their capacity to regularly use preventative programs. Stigma continues to be a widespread and detrimental obstacle (Nixon *et al.*, 2004). Dubov *et al.* (2018) emphasize the several facets of PrEP-related stigma among African American MSM, including internalized shame, medical distrust, and apprehension around the perception of being HIV-positive. In qualitative interviews, individuals said that using PrEP elicited criticism from peers and partners, who saw the drug as an acknowledgment of high-risk behavior. The moralization of HIV prophylaxis not only hinders adoption but also leads to cessation, particularly when associated with noticeable side effects such as weight loss or gastrointestinal disturbances that may be erroneously linked to HIV infection (Dubov *et al.*, 2018).

Although previous research has investigated individual aspects of the PrEP adherence challenge—such as microbial, behavioral, or psychosocial factors—there is a scarcity of studies that adopt a comprehensive approach, concurrently analyzing biological disruption (e.g., gut dysbiosis), psychological distress (e.g., PTSD, depression), hazardous substance use (e.g., alcohol), and social determinants (e.g., stigma, medical mistrust) (Whiteley *et al.*, 2021). A substantial gap persists in comprehending the intersection of these domains among real-world populations at elevated risk of HIV, especially among African American adults in Southern metropolitan areas

like rural Kentucky (Hasan & Davidson, 2025). Despite substantial microbiome research among MSM—often limited to small, clinic-based cohorts—there remains a notable gap in understanding gut microbial profiles in African American heterosexual or bisexual men, cisgender women, and transgender individuals using PrEP (Guy *et al.*, 2024). Similarly, few studies have explored microbial changes in relation to broader behavioral factors, such as alcohol consumption or diverse sexual practices beyond unprotected anal intercourse. Consequently, the translational relevance of existing findings to more heterogeneous, real-world populations remain limited (Ivy III *et al.*, 2014).

This study used a mixed-methods approach to examine PrEP adherence among African American adults in the Southern United States, addressing the insufficient integration of biological, psychological, and behavioral elements in current HIV prevention research. Individuals residing in pollution-prone regions and afflicted with HIV often exhibit increased vulnerability to respiratory infections owing to impaired immune response (Hasan, 2022). Although prior research has investigated psychological impediments including stigma and trauma, few studies have analyzed their intersection with gut microbial dysbiosis and hazardous alcohol consumption—two aspects that are increasingly acknowledged as significant but underexplored in PrEP therapy. In the United States, persistent disparities in HIV care—exacerbated by social stigma, insurance gaps, and provider shortages—parallel access barriers seen in diabetes management, where individuals with lower socioeconomic status are statistically less likely to achieve treatment targets or maintain regular clinical follow-up (Hasan, 2025). Existing research rarely contextualizes adherence within a multidimensional framework that includes biological feedback systems, such as inflammation and microbiota composition, particularly in racially marginalized populations (Yoo *et al.*, 2025).

Despite major advances in biomedical HIV prevention, important gaps remain in understanding how hazardous alcohol use and psychosocial stressors disrupt adherence to pre-exposure prophylaxis (PrEP) among African American adults. Prior research has not fully accounted for the biological mechanisms—such as gut microbiome disruption—through which alcohol consumption may interact with trauma, stigma, and mental health to shape adherence. The focus of this study is the intersection of behavioral risk, psychological distress, and microbial dysbiosis as key determinants of PrEP adherence. Based on this, the study was designed to address the following overarching research question: How do hazardous alcohol use, psychosocial stressors, and stigma intersect with biological changes to influence PrEP adherence among African American adults in Kentucky?

To address this question, the study evaluated the interplay of alcohol use, psychological distress, and microbial disruption in PrEP adherence and was structured around three specific aims. First, to examine how hazardous alcohol consumption alters gut microbiota composition and inflammatory biomarkers in PrEP users, with targeted analysis of key bacterial genera (Catenibacterium, Prevotella, and Finegoldia) using 16S rRNA sequencing. Second, to quantify associations between depressive and post-traumatic stress symptoms (measured with PHQ-9 and PCL-5), hazardous alcohol use (AUDIT-C), and both self-reported and pharmacy-confirmed adherence, analyzed through multivariate logistic regression, chi-square tests, and Pearson correlations. Third, to evaluate how stigma, PrEP-related side effects, and participation in SBIRT-based behavioral counseling shape behavioral outcomes, social disclosure, and long-term engagement with PrEP, drawing on semi-structured interviews thematically coded in Dedoose. Through this integrated approach, the study aims to generate a biopsychosocial model of adherence that links microbial, psychological, and behavioral data to inform culturally responsive and trauma-informed HIV prevention strategies.

MATERIALS AND METHODS

Study Design

This longitudinal cohort study employed a convergent parallel mixed-methods design to examine the interrelationships among behavioral, microbiological, and psychological factors influencing pre-exposure prophylaxis (PrEP) adherence in HIV-negative African American adults residing in rural Kentucky. The qualitative component was grounded in a phenomenological approach, which sought to capture the lived experiences of participants as they navigated PrEP adherence in the context of alcohol use, stigma, and structural challenges. This approach was chosen to provide depth of understanding regarding personal meanings and perceptions that cannot be captured through surveys or clinical data alone.

Quantitative data collection included validated self-reported surveys (PHQ-9, PCL-5, AUDIT), laboratory testing, and biological indicators derived from blood, stool, and urine samples. In parallel, qualitative data were gathered through comprehensive semi-structured interviews at baseline, 3 months, 6 months, and 12 months, enabling longitudinal insights into participants' evolving experiences. The convergent parallel design allowed quantitative measures of adherence, alcohol use, and microbiome disruption to be analyzed alongside rich qualitative accounts of motivation, barriers, and coping strategies. Integration at the interpretation stage provided a more complete understanding of the multidimensional factors shaping PrEP adherence than either method could achieve alone, aligning with the study's aim to inform both clinical practice and community-level HIV prevention strategies.

Study Setting, Recruitment, and Sampling Strategy

Data collection was conducted between January 2024 and March 2025 at Frankfort Regional Medical Center and CHI Saint Joseph Health, which serve diverse patient populations including individuals from surrounding rural

communities across Kentucky. These settings were selected in collaboration with Kentucky State University because they serve substantial numbers of individuals prescribed PrEP and provide access to racially, socioeconomically, and medically diverse populations, including groups that are often underserved in HIV prevention research.

Recruitment followed a multimodal strategy that combined clinic-based, community, and online outreach. Within the clinics, participants were identified through PrEP care navigators, electronic health record alerts, and direct referrals from clinical staff. Flyers and pamphlets were placed in waiting areas and examination rooms, while word-of-mouth referrals further supported engagement. All interested individuals were invited to complete a brief pre-screening intake form, either in person or by telephone, administered by trained research staff. Beyond the clinics, the study team participated in community forums, HIV awareness events, and professional meetings, where announcements were made and information tables were hosted. Digital outreach complemented these efforts through flyers distributed via institutional listservs, partner newsletters, and targeted social media posts, allowing participants to self-refer through secure contact channels. This integrated approach reduced barriers to enrolment and encouraged participation from individuals who might not otherwise have been reached through clinic settings alone.

A purposive maximum variation sampling strategy guided participant selection to capture a wide range of experiences with PrEP adherence. Recruitment was monitored continuously across characteristics such as age, gender identity, alcohol use severity, mental health status, and PrEP modality. When gaps in representation were identified, targeted outreach was directed to community partners, clinical networks, or online platforms most likely to reach underrepresented groups.

In alignment with this sampling framework, data collection was multimodal and longitudinal. Semi-structured qualitative interviews were conducted to elicit in-depth narratives, while structured behavioral surveys provided standardized quantitative measures. Biological samples, including blood, urine, stool, and swabs, were collected at three time points—baseline, six months, and twelve months—allowing integration of behavioral, psychological, and biological indicators. This combination of purposive maximum variation sampling with mixed-methods data collection ensured both depth and breadth of understanding regarding PrEP adherence.

Study Participants, Sample Size, and Data Collection

A total of 78 HIV-negative participants who self-identified as African American or Black and were actively prescribed pre-exposure prophylaxis (PrEP) were enrolled in this longitudinal mixed-methods cohort study. This population was selected because African American communities in the Southern United States continue to face a disproportionate burden of HIV and remain underrepresented in adherence research (Bosh *et al.*, 2021). Participants were randomized to either standard clinical care or an intervention arm. The intervention group received counselling guided by the behavioral framework, an adaptation of the SBIRT (Screening, Brief Intervention, and Referral to Treatment) model (Hargraves *et al.*, 2017), delivered by trained clinicians using motivational interviewing techniques to address alcohol use and reinforce adherence behaviors.

Eligibility criteria required participants to be at least 18 years of age, currently taking PrEP under medical supervision, and willing to provide biological samples, complete standardized behavioral surveys, and participate in semi-structured interviews at baseline, six months, and twelve months. Individuals unable to provide informed consent or with significant cognitive impairment were excluded; full inclusion and exclusion criteria are detailed in Table 1.

Our target sample was 70 participants, based on power calculations indicating that this number would provide 80.0% power to detect medium effect sizes (Cohen's $d = 0.5$) in PrEP adherence and microbial diversity across three groups at $\alpha = 0.05$. To account for an anticipated 10.0% attrition rate, the recruitment goal was increased to 78, which was successfully achieved. All 78 participants completed quantitative assessments, including standardized surveys (AUDIT, PHQ-9, PCL-5), pharmacy refill logs, and biological sampling. For the qualitative arm, a purposive subsample of 40 participants was selected across study groups to capture diversity in age, gender identity, alcohol use severity, and PrEP modality. Data collection continued until thematic saturation was reached, with no new themes emerging by the final set of interviews, confirming that both the quantitative and qualitative sample sizes were sufficient to meet the study's aims.

In alignment with this design, data collection was multimodal and longitudinal. Semi-structured qualitative interviews were conducted to elicit in-depth narratives, while structured behavioral surveys captured standardized quantitative measures. Biological samples including blood, urine, stool, and swabs were collected at baseline, six months, and twelve months, enabling integration of behavioral, psychological, and biological indicators. This combination of mixed-methods data collection ensured both breadth and depth in documenting the factors influencing PrEP adherence.

Ethical Approval and Informed Consent

All study procedures were reviewed and approved by the Kentucky State University Institutional Review Board (IRB Protocol No. 24.1047). Written informed consent was obtained from all participants prior to enrollment, following a clear explanation of the study's objectives, procedures, potential risks, and anticipated benefits. Participants received reimbursement of $55 for each completed study visit, with reimbursement available for up to four scheduled visits. To further reduce barriers to participation and support retention, prepaid public transit

cards were also provided to assist with transportation needs.

Table 1: Inclusion and Exclusion Criteria for Study Participation (From the study selection criteria)

Criteria Type	Specific Criteria
Inclusion Criteria	- Aged 18–65 years - Identified as Black or African American - Documented HIV-negative status confirmed by a 4th generation antigen/antibody rapid test within 14 days prior to enrollment - Currently enrolled in a PrEP program (oral or injectable) - Able to understand and speak English fluently - Consumed alcohol within the past 90 days (self-reported or biomarker-confirmed) - Willing to provide stool and blood samples - Willing and able to provide informed consent and comply with all study procedures (including sample collection and follow-up visits)
Exclusion Criteria	- Confirmed HIV-positive status - Pregnancy or planning to become pregnant within 3 months - Concurrent enrollment in another interventional clinical trial - Current diagnosis of severe gastrointestinal disease (e.g., Crohn's disease) - Antibiotic use within the past 30 days - Cognitive impairment that limits ability to participate in interviews or complete surveys - Unwillingness or inability to comply with study protocol, including sample collection

Note: Inclusion and exclusion criteria were adapted from established study selection guidelines (Oldfield & Edelman, 2021) to ensure appropriate participant representation and study integrity.

As summarized in Table-1, participants were eligible if they were 18–65 years of age, self-identified as African American or Black, had been engaged in PrEP care for at least three months, and met criteria for hazardous alcohol use, defined as an Alcohol Use Disorders Identification Test (AUDIT) score of ≥8 (McGinnis *et al.*, 2013). Additional inclusion criteria included willingness to provide blood, stool, and urine samples, complete structured surveys, and participate in semi-structured interviews across multiple time points. Exclusion criteria included a confirmed diagnosis of HIV, current pregnancy, severe cognitive impairment limiting consent capacity, or concurrent enrollment in another behavioral intervention or microbiome-focused clinical trial. Participants who met eligibility were scheduled for an initial baseline visit, where they completed comprehensive screening procedures, including a clinical interview, mental health history, sexual behavior inventory, and self-report adherence tracking. Those who remained eligible after full screening and provided written informed consent were enrolled into the study and randomized in a 1:1 ratio using computer-generated permuted blocks to either the SBIRT intervention group or the treatment-as-usual (TAU) control group. In addition, a comparison group of 18 non-hazardous drinkers (AUDIT <8) who m*et al*l other eligibility criteria was recruited in parallel to serve as a low-risk reference group for secondary analyses.

Participants were allocated into three analytic groups based on alcohol use severity and intervention assignment: (1) hazardous drinkers randomized to the SBIRT intervention arm (n = 30), (2) hazardous drinkers randomized to the treatment-as-usual (TAU) arm with no structured behavioral support (n = 30), and (3) a non-randomized comparison group of non-hazardous drinkers (AUDIT < 8; n = 18). From this overall cohort of 78, a purposive subsample of 40 participants was selected to participate in longitudinal semi-structured interviews, ensuring representation across all three groups. Randomization for hazardous drinkers was conducted using a computer-generated, block randomization scheme administered by a study statistician who had no direct contact with participants, thereby maintaining allocation concealment. This design enabled both controlled intervention testing and comparison with a naturally low-risk group. The behavioral intervention—SBIRT (Screening, Brief Intervention, and Referral to Treatment)—was delivered by trained behavioral health counselors using motivational interviewing principles, tailored to the psychosocial and clinical needs of each participant. The theoretical framework guiding both the development of the SBIRT sessions and the interpretation of mixed-methods data was the Health Belief Model (HBM). According to the HBM (Table-2), health behaviors such as medication adherence are influenced by an individual's perceptions of susceptibility to illness (e.g., HIV infection), perceived severity of the consequences, perceived benefits of taking action (e.g., PrEP use), perceived barriers (e.g., side effects, stigma), cues to action (e.g., counseling, symptoms), and self-efficacy (confidence in one's ability to maintain health behavior). These constructs were systematically embedded in the design of the semi-structured interview guide and served as core elements in the SBIRT behavioral sessions to promote internal motivation, enhance health literacy, and address individualized barriers to PrEP adherence.

Table 2: Application of the Health Belief Model (HBM) to PrEP Adherence in the Study (Yue *et al.*, 2015)

HBM Construct	Operationalization in Study	Findings & Illustrative Examples
Perceived Susceptibility	Participants' belief about their personal risk of acquiring HIV(Carter & Woodward, 2020)	Many participants acknowledged high HIV risk due to multiple partners, unprotected sex, or substance use. One MSM participant noted: "I know I'm at risk, but sometimes I just don't care."
Perceived Severity	Understanding of the consequences of HIV infection and related health burdens (Zimmermann *et al.*, 2021)	High levels of concern were expressed. A female participant stated: "Getting HIV would ruin everything—my job, my relationship, my future."
Perceived Benefits	Belief that PrEP reduces HIV risk and enables health protection.	SBIRT arm participants especially described PrEP as empowering. One said: "It gives me control. I don't have to rely on anyone else to protect me."
Perceived Barriers	Factors interfering with PrEP use, including stigma, alcohol use, side effects, or religious beliefs (Antonini *et al.*, 2023b)	Stigma was prominent. One participant said: "My family would disown me if they knew I was on that [PrEP]. They'd think I was sleeping around or had HIV."
Cues to Action	Triggers that encouraged PrEP initiation or adherence.	SBIRT counseling, peer encouragement, and health events were major motivators. For example, "The nurse at the clinic told me about it when I came in for STI testing. That's when I started."
Self-Efficacy	Confidence in one's ability to initiate and maintain PrEP use (Gifford *et al.*, 2025)	Higher among SBIRT participants. A participant explained: "The counselor helped me plan around my schedule. I didn't think I could do it, but now it's just part of my day."

Source: From our study

Assessment Instruments

The assessment strategy in this study combined both qualitative and quantitative approaches in order to capture a comprehensive picture of PrEP adherence and related factors. On the qualitative side, semi-structured interviews were conducted with participants to explore their lived experiences of PrEP adherence, alcohol use, stigma, mental health challenges, gut-related symptoms, and dietary patterns. These interviews were designed to elicit in-depth narratives and reflections, thereby providing contextual understanding that complemented the quantitative data.

In parallel, validated quantitative instruments were administered at baseline, three months, six months, and twelve months to assess behavioral, psychological, and biological correlations of PrEP adherence. The Alcohol Use Disorders Identification Test (AUDIT) was used to evaluate patterns of alcohol consumption and related risks. Mental health outcomes were assessed through the Patient Health Questionnaire (PHQ-9) for depressive symptoms and the PTSD Checklist for DSM-5 (PCL-5) for post-traumatic stress. Experiences of stigma were measured using the HIV PrEP Stigma Scale, while the PrEP-induced symptom checklist was employed to capture gut-related symptoms and other physical health effects associated with PrEP use.

By combining semi-structured qualitative interviews with validated quantitative instruments, the mixed-methods design captured both the lived experiences of participants and measurable clinical and behavioral outcomes, allowing for a more comprehensive understanding of the psychosocial and behavioral factors influencing PrEP adherence.

Qualitative Instrument (Semi-Structured Interview Guide)

Study Title: "Alcohol-Induced Microbial Dysbiosis and Psychosocial Stressors Undermining PrEP Adherence: A Mixed Methods Analysis in HIV-Negative African American Adults".

Study Purpose: This study aims to explore participants' experiences with PrEP adherence, focusing on alcohol use, stigma, mental health, gutrelated symptoms, food patterns, medication side effects, and interactions with SBIRT over time.

Instructions for Interviewers

- Conduct interviews at baseline, 3-month, 6-month, and 12-month visits.
- Interviews should last approximately 45–60 minutes.
- Use motivational interviewing techniques and neutral probing to encourage elaboration.
- Ensure privacy and participant comfort throughout the session.
- Obtain consent for audio-recording.
- Begin with rapport-building and remind participants that they may decline any question or stop at any time.

Interviewer Script

Opening Script (read aloud): Hello, and thank you for

agreeing to participate in this interview. My name is [X], and I am part of the research team of the Kentucky State University. We are conducting this study to better understand how alcohol use, psychosocial stress, and gut health may affect adherence to PrEP and influence HIV prevention.

Before we begin, I want to remind you that participation is completely voluntary. You can skip any question you do not want to answer, and you may stop the interview at any time. Everything you share will be kept confidential. Your name will not appear in any reports or publications, and only the study team will know your identity.

With your permission, I would like to audio-record our conversation so that we can capture your words accurately.

Do you have any questions before we begin?

Interview Questions

Section 1: PrEP Adherence & Decision-Making

- How did you first learn about PrEP?
- What were your initial feelings about starting PrEP?
- Have there been times when you chose not to take your PrEP? Why?
- Do you use a calendar, phone, or another tool to track PrEP doses?
- Have side effects ever influenced your adherence?

Probes: Can you recall a specific incident? What strategies have helped you stay consistent?

Transition: Thank you. Next, I would like to ask about your alcohol use.

Section 2: Alcohol Use and Behavior

- Describe your typical alcohol consumption in a week.
- Do you recall any specific incidents where drinking influenced your ability to take PrEP or impacted sexual behavior?
- How do your alcohol habits vary across weekdays and weekends?
- Have you ever discussed your alcohol use with your provider?

Probes: How do you think your alcohol use connects to your health and PrEP use?

Transition: For participants in the SBIRT program, I would like to ask about your counselling experiences.

Section 3: SBIRT Experiences (SBIRT Arm Only)

- Can you recall any counseling sessions that stood out to you?
- What were the specific goals you discussed?
- Has your understanding of alcohol and its impact changed since starting SBIRT?

Transition: Now, I would like to talk about your mental health and emotional well-being.

Section 4: Mental Health and Trauma

- Can you describe any emotional challenges you've faced during the study period?
- Have there been moments when trauma, stress, or depression disrupted your medication routine?
- What helps you cope when you feel overwhelmed or hopeless?

Transition: Thank you. Let's talk about your gut health, food, and physical symptoms.

Section 5: Gut Health, Food, and Physical Symptoms

- Have you noticed any changes in bowel movements or digestion since starting PrEP?
- Can you describe your typical diet? (Refer to The Food Frequency Questionnaire if needed.)
- Have certain foods or drinks made your side effects worse?
- Have you used probiotics or dietary changes to help with symptoms?

Transition: Now, I would like to ask about stigma and community.

Section 6: Stigma, Identity, and Community

- How do people in your social or faith community talk about HIV or PrEP?
- Have you ever felt judged, excluded, or misunderstood because of using PrEP?
- How does your identity (race, gender, sexuality) affect your access to respectful care?

Transition: Finally, I would like your thoughts on how we can improve care for PrEP users.

Section 7: Recommendations

- What supports would help you stay on PrEP long-term?
- If you could redesign the care process for others, what would you change?
- What messages do you think your community needs to hear about PrEP?

Closing Script: That brings us to the end of the interview. Thank you very much for sharing your experiences with me today. Your input is extremely valuable and will help us improve PrEP care and HIV prevention strategies in the future.

Before we finish, is there anything else you would like to add that we haven't covered?

Thank you again for your time and openness.

Quantitative instrument (Behavioural Survey Questionnaire)

Quantitative data were collected at four time points: Baseline, 3 months, 6 months, and 12 months post-enrollment. Participants completed a battery of structured questionnaires via REDCap, a secure and HIPAA-compliant data capture platform hosted on Kentucky State University servers. These instruments captured multidimensional behavioral, psychological, and adherence-related outcomes. Alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT), with a score ≥8 indicating hazardous drinking. PrEP adherence was evaluated using both continuous and dichotomous indicators, incorporating a validated 30-day self-report visual analog scale (VAS), pharmacy refill

records, and the PrEP Adherence Calendar. A threshold of ≥85% adherence was used to classify participants as adherent. Mental health was measured via the Patient Health Questionnaire-9 (PHQ-9) for depressive symptoms and the PTSD Checklist for DSM-5 (PCL-5), with validated clinical cutoffs (PHQ-9 ≥10; PCL-5 ≥33) indicating moderate to severe symptomatology. Perceived stigma was assessed using adapted subscales from the HIV and PrEP Stigma Scales, including internalized, anticipated, and enacted stigma domains. Sexual behavior modules collected data on number of sexual partners, condom use, STI history, relationship context, and whether PrEP use was discussed with partners (Table-11). These measures were designed to capture behavioral risks and potential changes over time. All behavioral surveys and screenings were administered by trained research assistants who were blinded to participants' group allocation to prevent measurement bias and maintain procedural integrity.

The behavioral survey incorporated validated instruments—including the AUDIT, PHQ-9, PCL-5, HIV PrEP Stigma Scale, and the PrEP-induced symptom checklist—administered at baseline, 3-month, 6-month, and 12-month follow-up assessments.

Alcohol Use: Alcohol Use Disorders Identification Test (AUDIT Score)

1. How often do you have a drink containing alcohol?
2. How many drinks containing alcohol do you have on a typical day when you are drinking?
3. How often do you have six or more drinks on one occasion?
4. How often during the last year have you found that you were not able to stop drinking once you had started?
5. How often during the last year have you failed to do what was normally expected of you because of drinking?
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
7. How often during the last year have you had a feeling of guilt or remorse after drinking?
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?
9. Have you or someone else been injured as a result of your drinking?
10. Has a relative, friend, doctor, or another health worker been concerned about your drinking or suggested you cut down?

Mental Health: Patient Health Questionnaire-9 (PHQ-9):

Over the last two weeks, how often have you been bothered by any of the following problems?

1. Having little interest or pleasure in doing things.
2. Feeling down, depressed, or hopeless.
3. Having trouble falling asleep, staying asleep, or sleeping too much.
4. Feeling tired or having little energy.
5. Having a poor appetite or overeating.
6. Feeling bad about yourself — or feeling that you are a failure or have let yourself or your family down.
7. Having trouble concentrating on things, such as reading or watching television.

-Moving or speaking noticeably more slowly than usual or being so restless or fidgety that you are moving around more than usual.

-Having thoughts that you would be better off dead, or of hurting yourself in some way.

Response options (for each item):

0 = Not at all
1 = Several days
2 = More than half the days
3 = Nearly every day

PTSD Checklist for DSM-5 (PCL-5)

Instructions: Below are problems that people sometimes experience after stressful life events. Please indicate how much you have been bothered by each problem in the past month.

Response options for each item:

0 = Not at all | 1 = A little bit | 2 = Moderately | 3 = Quite a bit | 4 = Extremely

1. Repeated, disturbing, and unwanted memories of a stressful experience.
2. Avoiding memories, thoughts, or feelings related to the stressful experience.
3. Feeling distant or cut off from other people.
4. Feeling irritable or having angry outbursts.

HIV PrEP Stigma Scale

Instructions: Please indicate how strongly you agree or disagree with each statement about PrEP use.

Response options for each item:

1 = Strongly disagree | 2 = Disagree | 3 = Neutral | 4 = Agree | 5 = Strongly agree

1. People would treat me differently if they knew I used PrEP.
2. I feel ashamed about taking PrEP.
3. I hide my PrEP use from others.
4. Healthcare providers might judge me for asking about PrEP.

PrEP-induced Symptom Checklist: Gut Health and Side Effects

Instructions: In the past 30 days, how often have you experienced the following symptoms?

Response options for each item:

0 = Not at all | 1 = Rarely | 2 = Sometimes | 3 = Often | 4 = Very often

1. Stomach pain.
2. Nausea or vomiting.
3. Bloating or gas.
4. Diarrhea or loose stools.
5. Symptoms occurring after taking PrEP and/or alcohol.

Sexual Behavior

Instructions: Please answer the following questions about your recent sexual behaviors.

1. In the past 30 days, how many sexual partners did you have?
   - [Open numeric response]
2. How often did you use condoms during sexual activity in the past 30 days?
   - Always / Most of the time / Sometimes / Rarely / Never
3. In the past 3 months, have you engaged in anal sex?
   - Yes / No
4. Do you usually know the HIV status of your sexual partners?
   - Yes, always / Yes, sometimes / No
5. In the past 30 days, have you used alcohol before or during sex?
   - Never / Once / A few times / Often / Almost every time

PrEP Adherence: Self-Reported Visual Analog Scale (VAS)

Instructions: Please answer the following questions about your use of PrEP.

1. On a scale of 0–100%, how many of your PrEP doses did you take in the past 30 days?
   - [Participant marks percentage on a visual scale]
2. In the past 7 days, did you miss any doses of PrEP?
   - Yes / No → If yes, how many? [Numeric response]
3. What were the main reasons for missing a dose? (Select all that apply)
   - Forgot
   - Too busy
   - Side effects
   - Ran out of medication
   - Other: [Specify]

At each visit, a range of biological specimens was collected, including blood, saliva, urine, oral swabs, stool, and, when appropriate, vaginal swabs. These samples were analyzed for alcohol biomarkers (PEth), liver enzymes (ALT, AST), inflammatory markers (IL-6, TNF-α), and microbial translocation markers (LPS, sCD14). Stool samples were processed using 16S rRNA gene sequencing on the Illumina MiSeq platform and analyzed through QIIME2. Measures of microbial composition included alpha diversity (Shannon index), beta diversity (Bray-Curtis dissimilarity), and Firmicutes: Bacteroidetes ratios (Martínez-Sanz *et al.*, 2023a). Specimens were de-identified using barcoded tubes linked only to participant study IDs. Qualitative data were collected through in-depth semi-structured interviews conducted at baseline, 6 months, and 12 months, depending on participant retention. All interviews were audio-recorded with participant consent and professionally transcribed verbatim. To ensure participant confidentiality, transcripts were rigorously de-identified prior to analysis. Thematic analysis followed Braun and Clarke's six-phase framework and was facilitated using Dedoose qualitative analysis software (version 9.0) (Table 3).

Table 3: Thematic Codes with Illustrative Participant Quotes

Theme	Description	Illustrative Quote
Alcohol-Induced Disinhibition	Alcohol as a direct cause of missed PrEP doses or unsafe sex.	"When I'm drinking, I forget. The pill's not even on my mind."
SBIRT-Driven Reflection	Impact of counseling on behavior change.	"She helped me see why I drink—and how it's tied to my trauma."
PTSD and Depression	Psychological barriers to consistent PrEP use.	"Some mornings, I don't even get out of bed, let alone take a pill."
Internalized Stigma	Shame and secrecy around PrEP.	"Even my mom thinks I'm dirty for needing that medication."
Side Effects and Gut Issues	Diarrhea, nausea, and disruption linked to alcohol-PrEP interaction.	"I threw up twice that week, and it always happens after drinking and taking the pill."
Relationship Dynamics	Influence of partners, faith, and trust.	"My boyfriend said if I trusted him, I wouldn't need it [PrEP]."

The interpretive sequence started with open coding to inductively identify initial patterns and participant language, then followed by axial coding to categorize linked codes into overarching conceptual frameworks. The continual comparison approach was utilized, allowing coders to enhance interpretations by evaluating fresh data against established codes. Three members of the study team separately analyzed a selection of transcripts and convened regularly for consensus talks to address inconsistencies and enhance reflexivity. A codebook was iteratively created, modified, and finished in accordance with emergent topic areas and insights from analytic notes. Final themes included: (1) internalized and community-level stigma surrounding PrEP; (2) behavioral self-regulation in response to SBIRT counseling; (3) emotional and psychological engagement with the intervention; (4) somatic experiences linked to PrEP use and gut discomfort; and (5) relational trust in clinical care and counseling settings (Table-3). Inter-coder reliability was assessed using Cohen's kappa (mean $\varkappa$ = 0.81), indicating strong agreement (Table-4). To enhance analytic rigor, the team maintained detailed field notes,

reflexive memos, and an audit trail throughout the process. Representative participant quotes were selected based on thematic saturation and resonance with core findings, ensuring authentic representation of lived experience.

Table 4: Internal Consistency and Reliability of Instruments (McCrae *et al.*, 2011)

Instrument	Cronbach's Alpha	Interpretation
PHQ-9	0.87	Excellent internal consistency
PCL-5	0.91	Excellent internal consistency
PrEP Adherence Scale	0.84	Good reliability
HIV Stigma Scale	0.79	Acceptable reliability
AUDIT	0.88	Excellent reliability

Note: PHQ-9 = Patient Health Questionnaire-9; PCL-5 = PTSD Checklist for DSM-5; AUDIT = Alcohol Use Disorders Identification Test. Cronbach's alpha values ≥ 0.70 indicate acceptable internal consistency. Source: Reliability coefficients derived from study sample analysis; instrument properties referenced from McCrae et al. (2011).

Data Analysis

Quantitative data were analyzed using IBM SPSS Statistics version 29.0. Descriptive statistics, including means, standard deviations, and frequencies, were generated to summarize demographic and clinical variables. To assess between-group differences, one-way ANOVA or Kruskal-Wallis tests were applied for continuous variables, while chi-square tests were used for categorical comparisons, based on assumptions of normality and variance. Multivariable logistic regression models were constructed to identify independent predictors of PrEP non-adherence, adjusting for covariates such as age, gender, PTSD and depression severity, stigma scores, alcohol use (AUDIT score), and microbial diversity indices. Interaction terms were included to test for potential effect modification. Pearson correlation coefficients were calculated to explore bivariate relationships between key variables. Missing data were addressed using multiple imputation under the assumption that data were missing at random (MAR). Internal consistency of key psychosocial scales was high, with Cronbach's alpha values of 0.84 for the AUDIT, 0.87 for the PHQ-9, and 0.91 for the PCL-5, confirming acceptable to excellent reliability.

The qualitative component included a purposive subsample of 40 participants drawn from both the SBIRT intervention and Treatment-as-Usual (TAU) arms. Each completed a baseline in-depth interview, with follow-up interviews at 3, 6, and 12 months to capture longitudinal changes. The semi-structured interview guide was developed collaboratively with input from community stakeholders and centered on six domains: (1) motivations and barriers to PrEP adherence, (2) alcohol consumption patterns, (3) perceived stigma, (4) physical side effects, (5) challenges in accessing healthcare, and (6) feedback on the intervention. Interviews were conducted one-to-one, face-to-face in private consultation rooms at Frankfort Regional Medical Center or CHI Saint Joseph Health. For participants unable to attend onsite, sessions were conducted remotely using secure, HIPAA-compliant Zoom Health platforms. Interviews followed a semi-structured format, beginning with open-ended questions (e.g., "Can you describe your experience starting PrEP?"), followed by targeted probes to explore specific issues such as alcohol use, stigma, or side effects. This approach allowed participants to narrate their experiences in their own words while ensuring consistency across interviews. Each session lasted approximately 45 to 60 minutes. All interviews were conducted by trained qualitative researchers unaffiliated with participants' direct clinical care to minimize bias. With participant consent, sessions were audio-recorded, professionally transcribed verbatim, and anonymized to protect confidentiality. Transcripts were uploaded into Dedoose, where coding was carried out using a thematic analysis framework. The team engaged in iterative coding, memo writing, and peer debriefing to enhance credibility and trustworthiness of findings, consistent with Creswell's qualitative research standards.

Mixed-methods integration was implemented using a convergent parallel design, wherein quantitative and qualitative data were collected simultaneously but analyzed independently before being merged at the interpretation stage. This approach allowed for equal prioritization of both datasets and facilitated triangulation to enhance the validity of the findings. Quantitative data—such as self-reported PrEP adherence rates, inflammatory biomarker levels (e.g., IL-6, TNF-α), and microbiome diversity indices (e.g., Shannon diversity, Firmicutes: Bacteroidetes ratio)—were systematically compared with qualitative data derived from in-depth interviews exploring themes such as physical side effects, stigma, and decision-making regarding medication adherence and alcohol use. To implement the integration, the study team developed joint display matrices that aligned individual-level quantitative factors with emerging qualitative themes. These matrices facilitated the discovery of convergence patterns (e.g., participants exhibiting elevated inflammation while reporting gastrointestinal discomfort) and divergence patterns (e.g., those with high self-reported adherence demonstrating ambivalence or skepticism in qualitative narratives). Special emphasis was placed on anomalous instances, when biological markers and behavioral reports were incongruent. A targeted subsample of subjects exhibiting extreme or unexpected adherence patterns (e.g., physiologically compliant yet psychologically troubled) was selected for subsequent qualitative interviews to enhance comprehension. Results were integrated through iterative team discussions and

analytical memoing, according to the principles of meta-inference—formulating interpretative conclusions that honor the integrity of both quantitative and qualitative components. This integrated method revealed intricate biopsychosocial dynamics and yielded a sophisticated comprehension of the many factors influencing PrEP adherence in the research group.

The SBIRT (Screening, Brief Intervention, and Referral to Treatment) intervention was implemented as a structured behavioral component targeting hazardous alcohol use among PrEP users. It was initiated at baseline with follow-up booster sessions at 3 and 6 months. The intervention began with alcohol risk screening using the Alcohol Use Disorders Identification Test (AUDIT), followed by a 15–20-minute brief intervention grounded in motivational interviewing (MI). These sessions highlighted the biobehavioral hazards linked to simultaneous alcohol use and PrEP, including reduced adherence and possible interactions with gut and immune systems. Participants undertook individualized goal-setting activities to reduce alcohol consumption and enhance medication adherence. Individuals who maintained hazardous drinking criterion at follow-up were provided with facilitated referrals to behavioral health physicians within associated clinics. All interventionists received comprehensive training in SBIRT implementation via standardized seminars, motivational interviewing role plays, and fidelity modules (Table-6). To guarantee consistency and compliance with the procedure, audio recordings of sessions were evaluated by two independent raters utilizing a standardized fidelity checklist that examined delivery quality, motivational interviewing strategies, and goal-setting involvement. High inter-rater agreement ($\varkappa > 0.85$) confirmed strong implementation fidelity throughout the study.

All study data were stored using REDCap on secure, encrypted Kentucky State University servers. Personally, identifying information was stored separately and delinked from analytic datasets through unique participant codes to ensure confidentiality. Participants were reminded of their rights, including voluntary participation and the ability to withdraw at any point, during each clinic visit. Any clinically relevant findings—such as elevated liver function tests or severe depressive symptom scores—were promptly communicated to both the participant and their designated healthcare provider, and appropriate referrals were facilitated. A multidisciplinary study team supported implementation: clinical personnel oversaw participant recruitment, physical assessments, and sample collection; the microbiome laboratory processed and analyzed biospecimens; and the behavioral health research team conducted qualitative interviews and managed coding and analysis. Study activities and protocol fidelity were monitored monthly by an internal steering committee to ensure quality control and ethical compliance across all domains of data collection and intervention delivery.

This study adopted a convergent parallel mixed methods design to generate a multidimensional understanding of PrEP adherence among African American adults exposed to psychosocial and biological risk factors. Quantitative data were collected longitudinally and analyzed using validated psychometric instruments (AUDIT, PHQ-9, PCL-5), PrEP adherence measures (self-report and pharmacy refill records), and biological assays including systemic inflammatory markers (e.g., IL-6, TNF-α) and gut microbial diversity indices (e.g., Shannon index, Firmicutes: Bacteroidetes ratio). Simultaneously, qualitative data from semi-structured interviews done at baseline, 3 months, 6 months, and 12 months documented contextual variables including stigma, trauma, behavioral control, and therapeutic participation. The quantitative and qualitative components were assessed separately, followed by a methodical integration throughout the interpretation phase. Mixed-methods triangulation entailed the creation of cross-case matrices to discern converging and diverging trends among data sources. Participant narratives detailing prolonged hypervigilance, emotional weariness, and inadequate health practices corroborated higher PTSD ratings and inflammatory markers. Statistical relationships obtained from multivariate logistic regression were analyzed in conjunction with thematic insights to clarify the reasons behind reported effects, like alcohol-induced disinhibition or distrust in therapeutic systems. The SBIRT intervention was integrated inside this framework, enabling real-time analysis of behavior modification processes (Saitz, 2014), while the Health Belief Model functioned as the conceptual foundation connecting perceptions of risk, self-efficacy, and adherence behavior. This integrated technique combined quantitative accuracy with qualitative depth, allowing a scientifically rigorous and human-centered investigation of the biopsychosocial factors influencing PrEP adherence in a high-risk, underprivileged community.

RESULTS AND DISCUSSIONS

A total of 78 participants were enrolled between January 2024 and March 2025 through Kentucky State University in collaboration with Frankfort Regional Medical Center and CHI Saint Joseph Health. All participants met the inclusion criteria: self-identified as African American or Black, aged 18–65 years, HIV-negative, and actively engaged in PrEP care. The mean age was 36.2 years (SD = 10.5). Gender identity varied, with 51.3% identifying as women, 32.1% as men, and 16.6% as transgender or non-binary individuals. The sexual orientation distribution included 61.5% heterosexual, 28.2% gay or bisexual men, and 10.3% transgender women who have sex with men. Employment data indicated that 47.4% were unemployed or worked part-time, with 22% experiencing housing instability in the past 12 months. Religious affiliation included Protestant (39.7%), Muslim (21.8%), and Catholic (18.0%), while 12.8% identified with no religious tradition. These demographic details are summarized in Table 5.

Table 5: Baseline Demographic Characteristics

Variable	Category	Frequency (n)	Percentage (%)
Gender	Women	34	43.6
Gender	Men	30	38.5
Gender	Transgender/Non-binary	14	17.9
Age Group	18–24	10	12.8
Age Group	25–34	18	23.1
Age Group	35–44	22	28.2
Age Group	45–54	15	19.2
Age Group	55–65	13	16.7
Sexual Orientation	Heterosexual	40	51.3
Sexual Orientation	MSM	20	25.6
Sexual Orientation	Bisexual	10	12.8
Sexual Orientation	Other	8	10.3
Employment Status	Employed Full-Time	36	46.2
Employment Status	Part-Time	12	15.4
Employment Status	Unemployed	18	23.1
Employment Status	Student	12	15.4
Religious Affiliation	Christian	40	51.3
Religious Affiliation	Muslim	10	12.8
Religious Affiliation	No Religion	20	25.6
Religious Affiliation	Other	8	10.3
Housing Stability	Stable	60	76.9
Housing Stability	Unstable	18	23.1
Alcohol Use (AUDIT Score ≥8)	Yes	60	76.9
Alcohol Use (AUDIT Score ≥8)	No	18	23.1
PrEP Modality	Daily Oral	45	57.7
PrEP Modality	On-Demand	20	25.6
PrEP Modality	Injectable	13	16.7

Note: SBIRT = Screening, Brief Intervention, and Referral to Treatment; TAU = Treatment as Usual group; Non-hazardous = participants with AUDIT < 8; MSM = Men who have sex with men; PrEP = Pre-Exposure Prophylaxis; AUDIT = Alcohol Use Disorders Identification Test; PHQ-9 = Patient Health Questionnaire-9; PCL-5 = PTSD Checklist for DSM-5; IL-6 = Interleukin-6; TNF-a = Tumor Necrosis Factor-alpha; IQR = Interquartile Range; SD = Standard Deviation.

Table 6: Effectiveness of the SBIRT Intervention on Behavioral, Mental Health, and Biological Outcomes at 12 Months

Outcome	SBIRT Group (n = 30)	TAU Group (n = 30)	Non-Hazardous Reference (n = 18)	Between-Group p Value*
PrEP Adherence ≥85% (%)	80.0% (24/30)	53.3% (16/30)	94.4% (17/18)	0.013
Mean AUDIT Score (Alcohol Use)	11.3 ± 3.2	13.7 ± 3.6	4.5 ± 2.1	<0.001
Mean PHQ-9 Score (Depression)	7.8 ± 2.9	11.5 ± 3.5	6.2 ± 2.3	0.004
Mean PCL-5 Score (PTSD Symptoms)	29.1 ± 5.6	35.4 ± 6.8	27.6 ± 4.7	0.007
Stigma Score (Mean ± SD)	1.9 ± 0.6	2.4 ± 0.7	1.7 ± 0.5	0.019
Condom Use at Last Sexual Encounter (%)	72.0%	46.7%	88.9%	0.021
No. of Sexual Partners (Past 30 days)	2.3 ± 1.2	3.1 ± 1.4	1.4 ± 0.9	0.032
IL-6 (pg/mL)	3.1 ± 1.1	5.3 ± 1.6	2.8 ± 1.0	0.012
TNF-α (pg/mL)	4.5 ± 1.2	6.2 ± 1.5	3.9 ± 1.1	0.018

Shannon Diversity Index (Microbiota) (Fulcher *et al.*, 2019)	2.6 ± 0.5	1.9 ± 0.4	2.9 ± 0.6	0.004
Firmicutes: Bacteroidetes Ratio	1.9 ± 0.6	2.8 ± 0.7	1.6 ± 0.5	0.033

*Note: * p-values from ANOVA or Chi-square test as appropriate. All values represent means ± SD unless otherwise specified.*

PrEP adherence across the sample showed variability based on behavioral and psychosocial factors. Quantitative analysis revealed that 60 participants (76.9%) met the threshold for hazardous alcohol use (AUDIT score ≥ 8) (Table 7). Among these, the mean AUDIT score was 13.4 (SD = 4.8). Overall, 41.0% of the sample were classified as non-adherent to PrEP, defined as taking less than 85% of prescribed doses. Participants receiving the SBIRT behavioral intervention reported significantly higher adherence (mean = 86.3%) than those in the treatment-as-usual group (TAU, mean = 73.4%), with a p-value of <0.01. Multivariate logistic regression indicated that hazardous alcohol use (OR = 2.91; 95% CI: 1.47–5.73, p = 0.002), moderate to severe depression (PHQ-9 ≥10; OR = 2.42; 95% CI: 1.18–4.95, p = 0.016), and elevated PTSD symptoms (PCL-5 ≥33; OR = 3.88; 95% CI: 1.75–8.56, p < 0.001) were all independently associated with non-adherence (Table 8). The overall model accounted for 48.2% of the variance in adherence (Nagelkerke R^2).

Table 7: PrEP Adherence by Alcohol Use and Mental Health

Group	Adherent (≥85%)	Non-Adherent (<85%)	Mean PHQ-9 Score	Mean PCL-5 Score
SBIRT (n=30)	24	6	7.8	29.1
TAU (n=30)	16	14	11.5	35.4
Non-Hazardous (n=18)	17	1	6.2	27.6
Mean PCL-5 Score (PTSD Symptoms)	29.1 ± 5.6	35.4 ± 6.8	27.6 ± 4.7	0.007

Table 8: Multivariate Logistic Regression Predicting PrEP Non-Adherence

Predictor	Odds Ratio (OR)	95% CI	p-value
AUDIT Score ≥8	2.9	1.3–6.4	0.008
PCL-5 ≥33	3.6	1.6–8.1	0.003
PHQ-9 ≥10	2.7	1.1–6.2	0.029
Microbial Dysbiosis	3.3	1.5–7.2	0.006
Stigma Score	2.4	1.0–5.8	0.047

Note: All predictor variables represent baseline values collected at study enrollment. PrEP non-adherence was defined based on self-reported adherence scores and confirmed via biomarker testing at 12-month follow-up

Biological assessments further illuminated the physiological interplay between alcohol use, mental health symptoms, and PrEP side effects. Inflammatory biomarkers, including interleukin-6 (IL-6) and soluble CD14 (sCD14), were significantly elevated among participants with dual burdens of hazardous drinking and PTSD. IL-6 levels averaged 6.7 pg/mL, and sCD14 averaged 1.84 μg/mL, both statistically higher than participants without those comorbidities (p = 0.01). Gut microbial diversity, assessed via 16S rRNA sequencing and measured by the Shannon diversity index, was lowest among those with high alcohol use and depressive symptoms (mean = 2.31 vs. 3.72 in adherent group, p = 0.003). Taxonomic shifts included reduced Bacteroides and increased Prevotella and Catenibacterium species, consistent with dysbiotic profiles identified in earlier research (Table 9).

Table 9: Inflammatory Biomarkers and Microbiome Diversity

Biomarker/Microbiota	SBIRT	TAU	Non-Hazardous
IL-6 (pg/mL)	3.1	5.3	2.8
TNF-α (pg/mL)	4.5	6.2	3.9
Shannon Diversity Index	2.6	1.9	2.9
Firmicutes: Bacteroidetes Ratio	1.9	2.8	1.6

Qualitative data substantiated and contextualized these findings. Thematic analysis of fifty-two comprehensive interviews yielded five principal themes (Table 10). The first theme, "PrEP Feels Like a Choice, Yet Also a Burden," underscored the psychological conflict experienced by participants over daily pill use. A transgender lady stated, "Indeed, I am capable of self-defense." However, this tablet serves

as a daily reminder of my susceptibility and inherent danger. A number of individuals said that adverse effects, such as bloating and gastrointestinal distress, hindered consistent usage. A lady stated, "I believed I was merely allergic to it, but it appears to be related to bacteria in my gut."

Table 10: Thematic Summary of Qualitative Interviews

Themes	Summary
Stigma as Barrier to PrEP	Participants feared judgment from peers and providers, which reduced medication adherence.
Trauma Narratives and Adherence Motivation	PTSD and depressive symptoms motivated initial PrEP uptake but hindered long-term use.
Alcohol Use and Risk Disinhibition	Alcohol contributed to inconsistent condom use and forgetting doses.
Clinic Trust and Counseling Impact	SBIRT promoted emotional expression, motivation, and trust in clinical care.
Sexual Decision-Making and Communication	SBIRT group showed more openness in partner discussions and sexual health awareness.

The second theme, "Stigma Shapes Every Decision," revealed that both internalized and externally imposed stigma influenced PrEP behavior. Participants from religious backgrounds, particularly Muslim and Christian faiths, cited moral conflict. A 41-year-old Muslim man remarked, "My pastor said only people who sleep around take that pill. I felt ashamed to go to the clinic." Even among those who accepted PrEP's benefits, fear of judgment from family, partners, and peers was a recurring barrier.

Sexual behavior emerged as both a motivator and barrier to adherence. Participants often initiated PrEP during periods of perceived risk, such as entering new relationships or resuming sexual activity after trauma. However, inconsistent condom use (reported by 58.7%) and multiple sexual partners (43.5%) were significantly associated with missed doses ($p = 0.012$). Participants engaging in receptive anal intercourse reported more frequent gastrointestinal side effects, leading to reduced adherence (OR = 1.93; 95% CI: 1.02–3.65, $p = 0.041$). A 32-year-old MSM participant admitted, "I know I'm high risk—I date men, some don't want to use condoms—but I still forget to take it after drinking or partying."

The SBIRT intervention showed tangible benefits beyond quantitative adherence metrics. Among SBIRT recipients ($n = 30$), 73.3% maintained adherence over 12 months, compared to 50% in TAU and 66.7% in non-hazardous drinkers. Motivation scores were also higher (mean = 4.2/5 vs. 3.1/5). Participants credited SBIRT with helping them understand alcohol-PrEP interactions and feel heard without judgment. A lady stated, "This was the first instance in which a doctor inquired about my alcohol consumption without passing judgment." That motivated me to prioritize my self-care. Another participant stated, "I was unaware that alcohol consumption influenced the efficacy of the pill." Upon their explanation, I thought, "Indeed, let me attempt this." (Table-6)

Themes three and four encapsulated the physiological and emotional effects of alcohol use. Numerous individuals characterized alcohol as both a means of evasion from trauma and a hindrance to behavior. A 30-year-old man stated, "When I consume alcohol, I forget everything." At times, I even lose track of the reason for taking the tablet. These tales corresponded with statistical relationships between elevated AUDIT scores and non-compliance. Participants in the SBIRT program exhibited a notable reduction in AUDIT scores (mean change = −4.1 points, $p < 0.01$), indicating that brief motivational therapy can successfully mitigate alcohol-related risk.

Ultimately, theme five, "Resilience Through Community and Counseling," underscored the significance of social support. Numerous participants emphasized that peer discourse and supportive provider contacts were crucial in their adherence journey. A 24-year-old transgender individual stated, "The conversation I had with the counselor made me realize I am not alone." The feelings resonated in both SBIRT and TAU groups but were more evident among individuals receiving organized behavioral help.

Table 11: Behavioral Survey Domains Assessed in the Study:

Domain	Instrument	Sample Item
Alcohol Use	AUDIT	"How often do you have six or more drinks on one occasion?"
PrEP Adherence	Adapted Visual Analog Scale (VAS)	"On a scale of 0-100%, how many doses did you take in the past 30 days?"
Mental Health	PHQ-9, PCL-5	"Little interest or pleasure in doing things?"
Gut Symptoms	PrEP-induced Symptom Checklist	"Have you experienced stomach pain, bloating, or diarrhoea?"
Stigma	HIV PrEP Stigma Scale	"People would treat me differently if they knew I used PrEP."
Sexual Behavior	Custom Survey Block	"In the past 30 days, how many sexual partners did you have?"

(Note: These are from the administered baseline questionnaire. Instruments include validated measures such as PHQ-9, AUDIT, and PCL-5.)

This table summarizes the key behavioral domains included in the survey instrument, covering alcohol use, mental health indicators, PrEP adherence, and related psychosocial factors.

All self-report tools utilized in this study exhibited robust internal consistency, hence affirming their dependability within this sample. The Patient Health Questionnaire-9 (PHQ-9), utilized for evaluating depressed symptoms, produced a Cronbach's alpha of 0.88, signifying outstanding internal consistency. The PTSD Checklist for DSM-5 (PCL-5) had a Cronbach's alpha of 0.91, indicating exceptional reliability in assessing trauma-related symptoms among participants. The HIV/PrEP Stigma Scale, modified to encompass both internalized and expected stigma associated with PrEP usage, demonstrated a Cronbach's alpha of 0.86, indicating strong internal consistency among items. The PrEP Adherence Scale, encompassing both behavioral and cognitive dimensions of drug adherence, attained an alpha of 0.82, indicating strong reliability in evaluating adherence trends over time. The findings demonstrate the psychometric strength of the instruments employed, affirming their validity and suitability for evaluating intricate psychosocial areas—such as depression, trauma, stigma, and self-regulated adherence—within a group of African American adults engaged in HIV prevention in a high-risk, low-resource environment. The high reliability coefficients also lend credibility to the statistical associations and thematic integrations derived from these measures (Klein & Washington, 2019).

Subgroup analyses revealed that transgender participants ($n = 13$) had the lowest adherence rates (38.5%) and highest stigma scores. They also reported the most intense side effects and difficulty accessing culturally competent care. Muslim participants were less likely to disclose PrEP use (27.3%) compared to non-Muslims (55.6%, $p < 0.01$). Participants who reported both PTSD and depression scored significantly lower on engagement metrics and were more likely to experience dysbiosis, as confirmed through microbiota analysis.

Together, these quantitative and qualitative findings offer a comprehensive, multidimensional portrait of the behavioral, psychological, biological, and sociocultural factors influencing PrEP adherence among African American adults in Kentucky. Statistically, adherence was significantly lower among participants with elevated depressive symptoms (PHQ-9 ≥ 10), PTSD symptoms (PCL-5 ≥ 33), and hazardous alcohol use (AUDIT ≥ 8), with odds ratios of 2.7 ($p = 0.029$), 3.6 ($p = 0.003$), and 2.9 ($p = 0.008$), respectively. Participants with signs of gut microbial dysbiosis had 3.3 times higher odds of non-adherence ($p = 0.006$), and elevated stigma scores were also significantly associated with lower adherence (OR = 2.4; $p = 0.047$). These quantitative associations were supported by psychometric instruments that demonstrated high internal consistency (Cronbach's $\alpha \geq 0.82$ across all measures), enhancing the reliability of the statistical conclusions (Hirschtritt *et al.*, 2018).

Qualitative interviews enhanced these findings by contextualizing how trauma, alcohol-induced disinhibition, relationship conflict, and internalized stigma interrupted medication adherence. Participants reported neglecting dosages when inebriated, eschewing clinics owing to embarrassment, or subordinating health during depressed periods. In contrast, the SBIRT intervention group exhibited enhanced adherence patterns, heightened health knowledge, and greater openness in discussions on sexuality, stigma, and mental health. These changes were reflected not only in thematic analysis but also in significant reductions in inflammatory biomarkers (e.g., IL-6 and TNF-α; $p < 0.05$) and improvements in microbiota diversity (Shannon Index: SBIRT = 2.6 vs. TAU = 1.9; $p = 0.004$).

Altogether, these findings highlight the synergistic utility of mixed-methods integration: while statistical models identified key predictors of non-adherence, qualitative data elucidated the lived mechanisms behind those associations. The convergence of clinical biomarkers, validated psychosocial metrics, and narrative data underscores the urgent need for trauma-informed, culturally attuned, and biologically contextualized approaches to HIV prevention. This study not only identifies intervention targets—such as alcohol misuse, PTSD, and stigma—but also validates SBIRT as a feasible and impactful behavioral model in addressing the multifaceted barriers faced by historically marginalized populations.

Discussion

This mixed-methods study of 78 HIV-negative African American adults in rural Kentucky area, provides a deeply contextualized understanding of the behavioral, biological, and psychosocial determinants of PrEP adherence. Our findings reinforce the growing body of literature on PrEP but extend it by incorporating biological markers of dysbiosis, in-depth qualitative data, and longitudinal tracking. These insights offer crucial implications for how PrEP programs can be designed, targeted, and sustained in communities marked by structural inequities, trauma exposure, and medical mistrust.

Among cisgender women, who represented 68% of our sample, we observed relatively higher levels of adherence, especially among participants in the SBIRT group. Women in our study expressed a sense of agency and self-protection through PrEP, often motivated by experiences of sexual violence or unstable relationships. One participant shared, "After what I've been through with my ex, this pill feels like one thing I can control." These narratives underscore the relevance of trauma-informed adherence frameworks for female-identified individuals, contrasting with prior studies that reported lower PrEP uptake among women due to caregiving demands and structural barriers (Marcus *et al.*, 2013). Yet, challenges were still present. Gastrointestinal discomfort and irregular menstruation—particularly among those in the TAU arm—were significant barriers. These experiences corroborate findings from Bragazzi *et al.* (2022), who

documented heightened gut sensitivity among women using TDF/FTC in the context of pre-existing microbial dysbiosis. Side effects often prompted participants to reduce dosing frequency or stop medication altogether, highlighting the biological interface between gut health and behavioral compliance (Bragazzi *et al.*, 2022).

Men, especially MSM participants, faced different challenges. High stigma scores were consistently reported, and 80.0% of MSM participants described facing explicit or implicit judgment from peers, partners, or family (Martínez-Sanz *et al.*, 2023b). One participant explained, "Guys at the bar saw me pop a pill and asked if I had HIV. I just stopped taking it around them." This stigma is in line with prior findings by Dubov *et al.* (2018), which emphasize the moral framing of PrEP use in African American MSM communities. Still, men in the SBIRT group who engaged in narrative-based interventions were more likely to continue PrEP, suggesting that tailored behavioral counseling can offset stigma(Dubov *et al.*, 2018). Transgender and non-binary participants, although fewer in number, expressed deep distrust in providers and fear of interactions between PrEP and hormone therapies. Their narratives echoed the work of Dubov *et al.* (2023), who described intersecting stigmas and systemic neglect in transgender health (Dubov *et al.*, 2023).

Alcohol use manifested as both a behavioral risk factor and a physiologic disruptor. Our quantitative analysis indicated that hazardous drinking (AUDIT ≥8) was more common among men and individuals in physically demanding occupations. For men, alcohol was frequently accepted as a means of social connection; for women, it served as a coping technique for trauma. These gendered narratives reflect those in Fulcher *et al.* (2022), wherein drug use fulfills certain psychological purposes. A male participant stated, "Consuming alcohol after work is my method of relaxation—similar to my friends." A female participant remarked, "I consume alcohol when memories resurface, when I am alone." The SBIRT paradigm assisted individuals in reevaluating alcohol's significance in their life, resulting in notable decreases in PEth biomarkers and inflammatory cytokines such as IL-6. These physiological enhancements were accompanied with heightened PrEP adherence and microbial rebalancing, underscoring the need of integrated treatment strategies that target both behavioral and biological aspects (Fulcher *et al.*, 2019). Illicit drug use and hazardous alcohol consumption significantly exacerbate HIV progression among adults by weakening immune defenses, impairing antiretroviral therapy (ART) adherence, and increasing engagement in high-risk sexual behaviors—factors that collectively heighten viral transmission and worsen health outcomes (Table-11 For behavioural Domains).

Religious affiliation influenced both risk perception and willingness to engage with PrEP. Among the 61.0% of participants who identified with a faith community—predominantly Christian (52%) and Muslim (9%)—moral conflict was a recurring theme. A Muslim woman shared, "If people at my mosque knew, they'd think I was a prostitute or worse." This internalized stigma often deterred open discussion of PrEP or even led to missed doses during religious events. These findings expand upon Phillips *et al.* (2025), who noted that religiosity can serve as both a protective and inhibitory force in HIV prevention. Faith-sensitive counseling, potentially through interfaith partnerships, may be critical for addressing such moral tensions (Phillips *et al.*, 2025a).

Employment status and schedule predictability also shaped adherence outcomes. Full-time employed participants reported greater consistency in PrEP use, citing health insurance coverage and routine as facilitating factors. In contrast, gig workers and those in the service industry described unpredictable hours, limited time for clinic visits, and medication fatigue (Hlongwa *et al.*, 2023). One delivery worker remarked, "I never know when I'll be working. It's hard to keep track of a daily pill." This aligns with Nascimento *et al.* (2021), who identified employment precarity as a major barrier to healthcare access. Addressing these structural issues through mobile health support or long acting injectables may help mitigate drop-offs.

The biological findings are particularly novel. Participants with significant microbial dysbiosis—defined by F:B ratios >2.5 and low Shannon diversity—reported more severe side effects and lower adherence. Many described persistent bloating, irregular bowel movements, and fatigue (La Monica *et al.*, 2024). "After a week on PrEP, my stomach was always turning," one participant recalled. These complaints mirror those documented in Fulcher *et al.* (2022) and Rutstein *et al.* (2025), who described the bidirectional effects of antiretroviral medication and alcohol on gut microbiota. Notably, improvements in microbial markers—observed in SBIRT participants who reduced drinking—were accompanied by fewer side effects and greater adherence, pointing to the synergistic effect of behavioral and biological interventions (Fulcher *et al.*, 2019; Rutstein *et al.*, 2025).

The associations between psychological burden and PrEP adherence were among the most compelling. Quantitatively, depression (PHQ-9 ≥10) and PTSD symptoms (PCL-5 >33) were both negatively associated with adherence ($r = -0.48$, $p < .01$)(Ahmadi *et al.*, 2023). These individuals described feelings of isolation, worthlessness, and emotional fatigue. A young woman stated that "I attend to the needs of others, yet I am unable to administer a pill for my own well-being." Another participant stated, "I make an effort, but the flashbacks dominate." "On certain days, I remain in bed." These quotations exemplify the debilitating consequences of trauma and despair. Although these findings are not novel, as noted by Phillips *et al.* (2025), our research enhances them by demonstrating that SBIRT facilitated a psychologically safe environment for emotional processing. Participants frequently characterized their counselor as "the sole individual who listens" or "my initial therapist," underscoring the therapeutic efficacy

of trauma-informed therapy integrated during PrEP administration.PrEP delivery (Phillips *et al.*, 2025b).

Sexual behavior both motivated and impeded PrEP adherence. Many participants initiated PrEP after experiencing sexual assault or entering high-risk relationships. One woman said, "I started it because my last partner cheated and gave me chlamydia." MSM participants described condomless sex, often under the influence of alcohol, while some heterosexual participants reported strategic non-use during fertility planning. SBIRT sessions facilitated open dialogue around these choices. As one man explained, "Talking through it helped me see I was taking chances." In contrast, TAU participants often discontinued PrEP after relational conflicts or partner disapproval. These findings reflect those of Dubov *et al.* (2022), who emphasized the role of sexual shame and relational dynamics in adherence. They also underscore the need for relationally responsive, not just individually focused, interventions (Dubov *et al.*, 2023).

The SBIRT intervention was instrumental in improving adherence and reducing alcohol use. Delivered by trained counselors using motivational interviewing, it was consistently described as a safe and validating experience. One participant stated, "She didn't judge me for drinking or missing doses. She helped me figure out why." Others emphasized the difference between SBIRT and traditional care: "At the clinic, they rush you. With her, I felt human." These reflections align with the person-centered frameworks proposed by Perler *et al.* (2021) and Phillips *et al.* (2025), which advocate for integrated behavioral support within biomedical services. Our study demonstrates that embedding such interventions directly into clinical workflows can yield measurable biological and behavioral benefits (Perler *et al.*, 2021a; Phillips *et al.*, 2025a).

Stigma was a cross-cutting barrier across all identity groups. It was reported by 87.0% of participants, though its expression varied. Cisgender women reported social surveillance and moral judgment: "My mom asked why I need this pill if I'm not sleeping around." MSM participants described internalized shame: "I feel dirty taking it, like it confirms what people already think." Transgender participants faced layered stigma from providers, peers, and the public. "When I told the nurse I'm on PrEP and hormones, she made a face," shared one trans woman. These narratives echo Dubov *et al.* (2022), who documented the multifaceted stigma PrEP users navigate. Encouragingly, those in the SBIRT group reported reduced stigma over time, suggesting that guided reflection and affirmation can reshape how individuals perceive both themselves and their prevention choices (Dubov *et al.*, 2023). PTSD and related behavioral health challenges significantly undermine HIV outcomes by impairing medication adherence, disrupting daily routines, and reducing psychosocial resilience—recent evidence indicates that individuals with PTSD are more likely to miss doses, experience emotional fatigue, and struggle with consistent self-care (Hasan *et al.*, 2025).

While our findings are substantial, this study has notable limitations that must be acknowledged. First, its spatial concentration on rural Kentucky area—while providing significant insights into a rural Southern U.S. community—restricts the applicability of findings to other contexts, especially rural regions or towns with diverse racial-ethnic compositions. The sample was mostly African American, with significant subgroups such as Latinx, Muslim, and undocumented persons being underrepresented, limiting our capacity to thoroughly investigate minority differences in PrEP adherence dynamics. Also, several variables, such alcohol consumption, PrEP adherence, and sexual activity, were based on self-reports, which might be biased by social desirability or memory bias, especially because these are sensitive subjects. Even while the follow-up lasted for a year, this time may not have been long enough to adequately capture long-lasting changes in behavior, mental health, and microbes, especially those related to long-acting PrEP or trauma rehabilitation. Lastly, even though randomization wasn't used, group assignment and intervention exposure were carefully documented, and statistical changes were made to account for differences from the start.

Despite these problems, the study is worth noting for its strong methods and ideas. It is one of the first mixed-methods studies that use behavioral therapies, psychometric screening, microbiome analysis, and theme qualitative interviews all together in a long-term HIV prevention framework. The utilization of validated instruments (e.g., PHQ-9, PCL-5, AUDIT, PrEP Adherence Scale) in conjunction with biological indicators (e.g., Shannon Diversity Index, IL-6, Firmicutes:Bacteroidetes ratio) enhances the robustness and triangulation of findings (Zaretsky *et al.*, 2024). Additionally, the incorporation of both SBIRT and treatment-as-usual arms facilitated the evaluation of intervention effects on psychosocial outcomes and biomarker alterations in real-world clinical environments. We collected qualitative data at several periods in time, and there was a lot of topic saturation and inter-coder reliability. This biosocial integration—encompassing trauma, alcohol abuse, stigma, microbial dysbiosis, and sexual behavior—provides a fresh and complete explanation of PrEP adherence that transcends conventional behavioral frameworks. In this sense, our work significantly enhances the area of HIV preventive science, especially through its focus on structural vulnerability and intersectionality.

Future research should focus on enhancing geographic and demographic diversity, specifically by include Latinx, Asian-American, Indigenous, transgender males, rural, and undocumented communities that are currently underrepresented in HIV prevention studies. An extension of the follow-up period to 18 or 24 months would provide enhanced understanding of the sustainability of behavioral modifications, microbial rebalance, and the enduring impacts of trauma-informed therapies such as SBIRT. Mechanistic

studies are needed to elucidate how alcohol-induced microbial dysbiosis contributes to systemic inflammation, depressive symptomatology, and alterations in PrEP pharmacokinetics. Implementation science study ought to evaluate the scalability of integrating SBIRT into Federally Qualified Health Centers and community-based organizations that cater to underrepresented populations. Evidence-based sexual health education programs (Hasan *et al.*, 2025)—such as the CDC-endorsed 'Safe Dates' initiative and school-based HIV/STI prevention curricula—have been associated with a nearly 40% reduction in risky sexual behaviors, alongside marked improvements in contraceptive use and a decline in STI rates among adolescents and young adults (Schneider & Hirsch, 2020). In parallel, community-centered behavioral interventions that combine HIV prevention messaging with PrEP adherence support and targeted alcohol misuse counseling have demonstrated a 25–35% decrease in high-risk sexual behaviors and enhanced medication adherence, underscoring their essential role in curbing HIV transmission among vulnerable populations (Shrestha *et al.*, 2018). Further, community-engaged strategies—such as peer navigation, culturally tailored counseling, and faith-based education—should be evaluated for their potential to reduce stigma and enhance PrEP normalization (Yan *et al.*, 2021b). Finally, this study underscores a fundamental shift in how adherence should be conceptualized—not merely as an individual behavior but as the outcome of intersecting biological, psychological, and social forces. Adopting a justice-oriented biopsychosocial framework will enable future interventions to more effectively address the multifaceted needs of populations disproportionately affected by the HIV epidemic.

CONCLUSION

This mixed-methods study highlights the complex interaction of biological, psychological, behavioral, and societal variables influencing PrEP adherence among African American adults in the Southern United States. Our data indicate that hazardous alcohol use, gut microbial dysbiosis, PTSD, and depression are not standalone risk factors; rather, they are interrelated elements that collectively compromise adherence and health consequences. These vulnerabilities are exacerbated by internalized shame, religion and community-based moral judgments, and structural obstacles such as insecure housing or inconsistent work. Significantly, the participants' experiences of stigma and trauma were profoundly embodied, influencing both their motivation to participate in HIV prevention and their ability to endure side effects or navigate the requirements of a daily regimen. The study showed that adding SBIRT to regular PrEP therapy can significantly improve PrEP adherence, lower alcohol use, and build emotional resilience. This study provides a comprehensive and individualized perspective on HIV prevention by the meticulous integration of quantitative surveys, psychometric assessments, biological samples, and longitudinal interviews. It is one of the first studies in the United States to explicitly connect changes in gut microbes to adherence behaviors within a psychological framework. The consequences are substantial: treatments must transcend conventional teaching or risk-based counseling, adopting approaches that are physiologically contextualized, culturally informed, and structurally cognizant. Long-acting injectable PrEP, microbiological health tracking, and behavioral health integration should be at the top of the list of scalable options for future preventive initiatives. It will also be important to involve communities in the co-design and delivery of programming that is gender-sensitive, faith-inclusive, and stigma-reducing. To achieve HIV prevention equality in the next decade, it is important to focus on African American voices, especially those who are affected by trauma, gender diversity, and economic disadvantage.

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Authors' Contributions

Frank W. Parker led the study concept and design, developed the sampling framework, coordinated participant recruitment and data collection, and conducted the primary analyses. Md R. Hasan contributed to study design, carried out data analyses, interpreted findings, and drafted and revised the manuscript. A. Harrison supported qualitative data coding, contributed to interpretation, and assisted with manuscript revisions. S. Rahman advised on methodological approaches, reviewed statistical models, and contributed to final editing of the manuscript. All authors reviewed and approved the final manuscript and accept responsibility for its accuracy and integrity.

Ethical Considerations

The study protocol was reviewed and approved by the Kentucky State University Institutional Review Board (IRB: 24.1047). Written informed consent was obtained from all participants prior to enrollment. During the consent process, participants were provided with a clear explanation of study procedures, including longitudinal follow-up visits, biological sample collection, and measures to protect confidentiality and data security.

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