American Research Journal of Biosciences

Volume 10, Issue 1, 1-20 Pages
Research Article | Open Access
ISSN (Online)- 2379-7959
DOI : 10.21694/2379-7959.25001

Investigating the Impact of Alcohol Use on PrEP Adherence and the Burden of HIV and Other Sexually Transmitted Infections: An Umbrella Review

Md Rakibul Hasan[1]*, Akidul Haque[2], Fahad Bin Halim[3], Zeeshan Ul Haq[4], Moryom Akter Muna[5]

[1]Department of Medicine, Cambridge University Hospitals NHS Foundation Trust, Cambridge, England, UK; ORCID:https://orcid.org/0000-0002-9152-8753

[2]Department of Mathematics, University of Louisville, United States; ORCID:https://orcid.org/0009-0004-4967-9306

[3]Department of Chemistry, University of Louisville, United States; ORCID: https://orcid.org/0009-0001-6196-8790

[4]Department of Pathology, University of Louisville, United States; ORCID:https://orcid.org/0009-0002-4720-0993

[5]Department of Internal Medicine, Mirpur General Hospital, Dhaka, Bangladesh; ORCID:https://orcid.org/0009-0006-2027-7543

ABSTRACT

Background: *Despite the proven efficacy of pre-exposure prophylaxis (PrEP) in preventing HIV infection, adherence remains inconsistent, particularly among individuals with alcohol use and intersecting psychosocial or structural challenges. This umbrella review synthesized evidence on how alcohol consumption influences PrEP adherence, discontinuation, and related HIV and sexually transmitted infection (STI) outcomes, with emphasis on population-specific and severity-related dimensions.* ***Methods:*** *Following PRISMA and AMSTAR-2 standards for umbrella reviews, a systematic search was conducted across MEDLINE, Embase, Cochrane Library, PsycINFO, Scopus, and Web of Science for peer-reviewed systematic reviews and meta-analyses published between January 2006 and June 2025. Twenty-two reviews met the inclusion criteria. Screening and data extraction were performed in Covidence and REDCap, with overlap quantified by Corrected Covered Area. Quantitative credibility, heterogeneity, and risk-of-bias metrics guided evidence weighting.* ***Results:*** *Across pooled analyses, adherence above 70 % reduced HIV acquisition risk by roughly 75 % (RR ≈ 0.25 – 0.30), while adherence below 60 % yielded negligible protection (RR ≈ 0.95). Hazardous drinking was associated with a 25 – 35 % reduction in adherence and 2-fold higher odds of discontinuation. Baseline STI prevalence among PrEP users averaged 24 %, with incidence near 72 per 100 person-years, indicating overlapping vulnerability. Provider barriers included low PrEP familiarity (≈ 60 %) and limited prescribing confidence (< 35 %). Transgender and gender-diverse populations showed PrEP use under 10 %, constrained by stigma, cost, and perceived hormone interactions.* ***Conclusion:*** *Alcohol use and co-occurring psychosocial stressors substantially erode PrEP adherence and continuity, amplifying HIV and STI risks despite pharmacologic efficacy. Integrating alcohol-reduction counseling, mental-health support, and long-acting PrEP delivery within gender-affirming, low-barrier systems is critical to sustain prevention gains and reduce inequities.*

KEYWORDS: *HIV prevention, PrEP adherence, hazardous alcohol use, sexually transmitted infections (STIs); AIDS, umbrella review.*

INTRODUCTION

Human immunodeficiency virus (HIV) continues to impose a substantial global and national burden despite clear progress in testing, treatment, and prevention. Tens of millions of people are living with HIV worldwide, and thousands of new infections are recorded annually in the United States alone[1]. The epidemiology remains uneven: gay, bisexual, and other men who have sex with men carry a disproportionate share of incident cases, while Black and Latinx communities face higher risks linked to long-standing structural inequities. Pre-exposure prophylaxis (PrEP) transformed HIV prevention by offering near-complete protection when taken as prescribed. Daily oral regimens and event-based dosing schedules have both demonstrated high efficacy under conditions of good adherence. Yet these gains are not automatic. Prevention effectiveness in real-world settings rises and falls with the

mundane realities of adherence and persistence, including daily or coitally timed dosing, timely pharmacy refills, regular HIV testing, and sexually transmitted infection (STI) screening. Where these factors are consistently in place, HIV incidence declines; where they are unstable, gains erode[2].

Other STIs—particularly syphilis, gonorrhea, and chlamydia—intersect with this landscape in ways that complicate prevention goals. Bacterial STI rates have climbed over the past decade in many jurisdictions, including among PrEP users[3]. The overlap is not incidental: the same sexual networks in which PrEP is most needed are often those with higher STI transmission intensity, influenced by partner concurrency, assortative mixing, and varying condom use. STIs can increase biological susceptibility to HIV acquisition by disrupting mucosal barriers and amplifying local inflammation. Conversely, PrEP programs create repeated clinical touchpoints that can facilitate earlier STI detection and treatment if people remain engaged in care. Thus, HIV and STI outcomes are linked both biologically and operationally, and adherence sits at the crossroads—connecting the protective effect of tenofovir-based regimens to surveillance, counseling, and timely treatment for co-occurring infections[4] Nationwide mortality data show that as people with HIV live longer, non-AIDS comorbidities increasingly drive deaths, with adjusted annual rises of about 4.1% for diabetes and 4.0% for cardiovascular disease, and higher odds in 2011 versus 1999 (diabetes OR ≈ 2.27; CVD OR ≈ 1.76).[5] These trends reinforce that limited access to diabetes and metabolic care (screening, medication management, lifestyle support) can compound pill burden and clinic barriers[6], undermine adherence, and ultimately worsen long-term outcomes, while HIV-related immune dysregulation continues to elevate risks for non-HIV cancers and leaves tuberculosis as a persistent threat.

Alcohol consumption emerges as a pervasive and influential factor across these dynamics. Within many social and sexual environments, drinking is both normalized and frequently excessive. Clinically, heavy alcohol use is characterized as the intake of at least 15 drinks per week for men and 8 for women, whereas binge drinking is defined as consuming 5 or more drinks on a single occasion for men and 4 or more for women[7]. Among key populations for PrEP, current alcohol use frequently exceeds general-population averages, and periodic binge episodes are common. Heavier and more frequent drinking is consistently associated with behaviors that elevate exposure risk—condomless sex with partners of unknown or positive status, multiple concurrent partnerships, and sex in contexts where negotiating protection is less likely. These patterns are not only epidemiological signals; they are practical barriers to the routines PrEP requires. People commonly describe missed doses on nights of heavy drinking, delayed refills after periods of instability, and skipped clinic visits when schedules and priorities are disrupted.[8]

The pathways by which alcohol undermines PrEP adherence operate at behavioral, biological, and structural levels. Acutely, alcohol impairs attention, working memory, and planning, which makes it easier to forget or intentionally delay dosing. Repeated binge episodes fragment routines that anchor daily medication use. Over time, heavy alcohol use contributes to gastrointestinal discomfort, sleep disruption, and mood symptoms that further erode self-management[9]. Biologically, alcohol compromises mucosal defenses and the integrity of the gut barrier. Disruption of the intestinal epithelium facilitates microbial translocation[10] and systemic inflammation—processes that may worsen gastrointestinal side effects and reduce tolerance to PrEP in a subset of users. Rectal microbiome shifts have been observed in men who have sex with men, and some users report new or worsened bloating, diarrhea, or abdominal discomfort around PrEP initiation; when these symptoms coincide with heavy drinking, discontinuation risk rises. These mechanisms do not supplant the central role of adherence, but they help explain why heavy or sustained drinking often coincides with more complicated clinical courses following HIV exposure and with recurrent or more severe bacterial STIs.[11]

Program data illuminate the magnitude of these effects. In demonstration projects and safety-net clinics, retention at twelve months commonly hovers around two-thirds, with steady attrition among younger adults and those reporting unstable housing, transportation barriers, or harmful alcohol use. Short-term nonadherence is frequent; a meaningful minority of patients report missed doses in the prior week, and biochemical monitoring in some cohorts reveals gaps not captured by self-report. Where adherence support is strong—through text reminders, pharmacy synchronization, peer navigation, or event-based dosing tailored to sexual activity—drug levels remain protective even among people who drink.[12] Where support is thin, lapses cluster after weekends, holidays, or stressful life events, and follow-up testing becomes irregular. In several cohorts, STI diagnoses increased after PrEP initiation compared with the year prior, reflecting both risk compensation and improved detection through routine screening. These findings carry a simple implication: PrEP's prevention value is preserved when adherence is shielded from day-to-day volatility; it falters when volatility is left unaddressed.

Structural and psychosocial conditions amplify these patterns. Shame and stigma around PrEP or around alcohol use can suppress disclosure, limit honest conversations about adherence struggles, and delay help-seeking when routines

begin to fail. Clinic design and policies may inadvertently erect barriers—limited evening hours, fragmented billing, complex refill processes—that disproportionately burden patients juggling shift work, caregiving, or unstable transportation.[13] Insurance churn and copay requirements discourage continuity. For many, alcohol use is entwined with stress regulation, trauma histories, or social belonging; asking patients to reduce drinking without offering practical alternatives and support is unlikely to succeed. Integrated models that embed alcohol screening and brief intervention into PrEP care, normalize fluctuations in motivation, and provide flexible dosing strategies have shown promise. When these elements are missing, heavy or hazardous drinking converts into persistent nonadherence, missed monitoring, delayed STI treatment, and ultimately worse clinical outcomes.[14]

Against this backdrop, the literature is extensive but fragmented in ways that impede decisive program guidance. A large body of work links alcohol with higher sexual risk and with self-reported missed doses, yet relatively few syntheses trace the entire sequence from alcohol-related adherence barriers to concrete severity outcomes for HIV and other STIs.[15] Severity matters: acute HIV infections with high initial viral loads, delayed diagnosis that postpones linkage to care, recurrent or multisite gonorrhea and chlamydia requiring multiple courses of therapy, pelvic inflammatory disease among women and people with a uterus, and complicated syphilis presentations carry implications for individual health and for transmission dynamics. Measurement heterogeneity further blurs interpretation. Drinking is defined with different thresholds across studies; adherence is captured with brief recall scales, pharmacy data, electronic monitoring, or drug level assays; and severity endpoints are sometimes pooled with incidence, concealing gradients in clinical course.[16] Finally, structural determinants—housing instability, racism, medical mistrust, and limited access to alcohol-reduction services—are well described but rarely incorporated into an integrated explanatory model that shows how and when they magnify the alcohol–nonadherence–severity pathway.

This umbrella review responds to these gaps by asking a precise question: *Among people who drink alcohol, how do barriers to PrEP adherence contribute to more severe HIV and other STI outcomes, and through which behavioral, biological, and structural mechanisms does this occur?* The aim is to synthesize review-level evidence across prevention, behavioral health, and microbiome science to clarify where findings converge, where they diverge, and how dose–response patterns by drinking severity translate into real-world nonadherence and clinical severity. In pursuing this aim, the review follows several objectives. It delineates the adherence barriers most consistently associated with alcohol use and specifies how these barriers appear in day-to-day life—missed evening doses after drinking, delayed refills following periods of instability, skipped clinic visits when routines are disrupted. It connects those barriers to severity indicators for HIV and common bacterial STIs, moving beyond simple incidence counts to consider initial viral loads, time to diagnosis, recurrence patterns, anatomic site multiplicity, and complications such as pelvic inflammatory disease. It describes how biological intolerance, psychological stress, stigma, and social disadvantage interact to worsen outcomes for particular groups, including young adults, women, transgender people, and Black and Latinx communities. Finally, it surfaces practical leverage points for integrated care—embedding alcohol-reduction supports and adherence scaffolds within routine PrEP and STI services; using flexible dosing strategies matched to sexual activity patterns; simplifying access to refills and monitoring; and building clinical cultures where fluctuations in drinking and motivation are anticipated rather than penalized. By reframing prevention around the stability of adherence in the context of alcohol, this review seeks to close the space between what PrEP can do in theory and what it achieves for people navigating real lives.

MATERIALS AND METHODS

Study Design and Reporting Framework

This review was conducted using an umbrella design, bringing together evidence from multiple systematic reviews, meta-analyses, and scoping reviews to present a broad synthesis of current knowledge. The purpose was to understand how alcohol use contributes to barriers in pre-exposure prophylaxis (PrEP) adherence and how these barriers are linked to the severity of HIV and other sexually transmitted infection (STI) outcomes. A detailed plan was developed at the outset, outlining the research focus, inclusion and exclusion criteria, populations of interest, key outcomes, and methods for evaluating the quality and reliability of the included reviews. The approach followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, adapted for umbrella reviews, and was guided by current standards for evidence synthesis.[17] Each step—from search and screening to extraction, quality appraisal, and interpretation—was carried out systematically to ensure accuracy and reproducibility. This design allowed a panoramic view of behavioral, biological, and structural influences that shape adherence patterns and clinical outcomes. As all findings were drawn from published reviews, no new data were collected, and ethical approval was not required.

PRISMA 2020 Flow Diagram: *Umbrella Review on Alcohol Use, PrEP Adherence, and HIV/STI Severity*

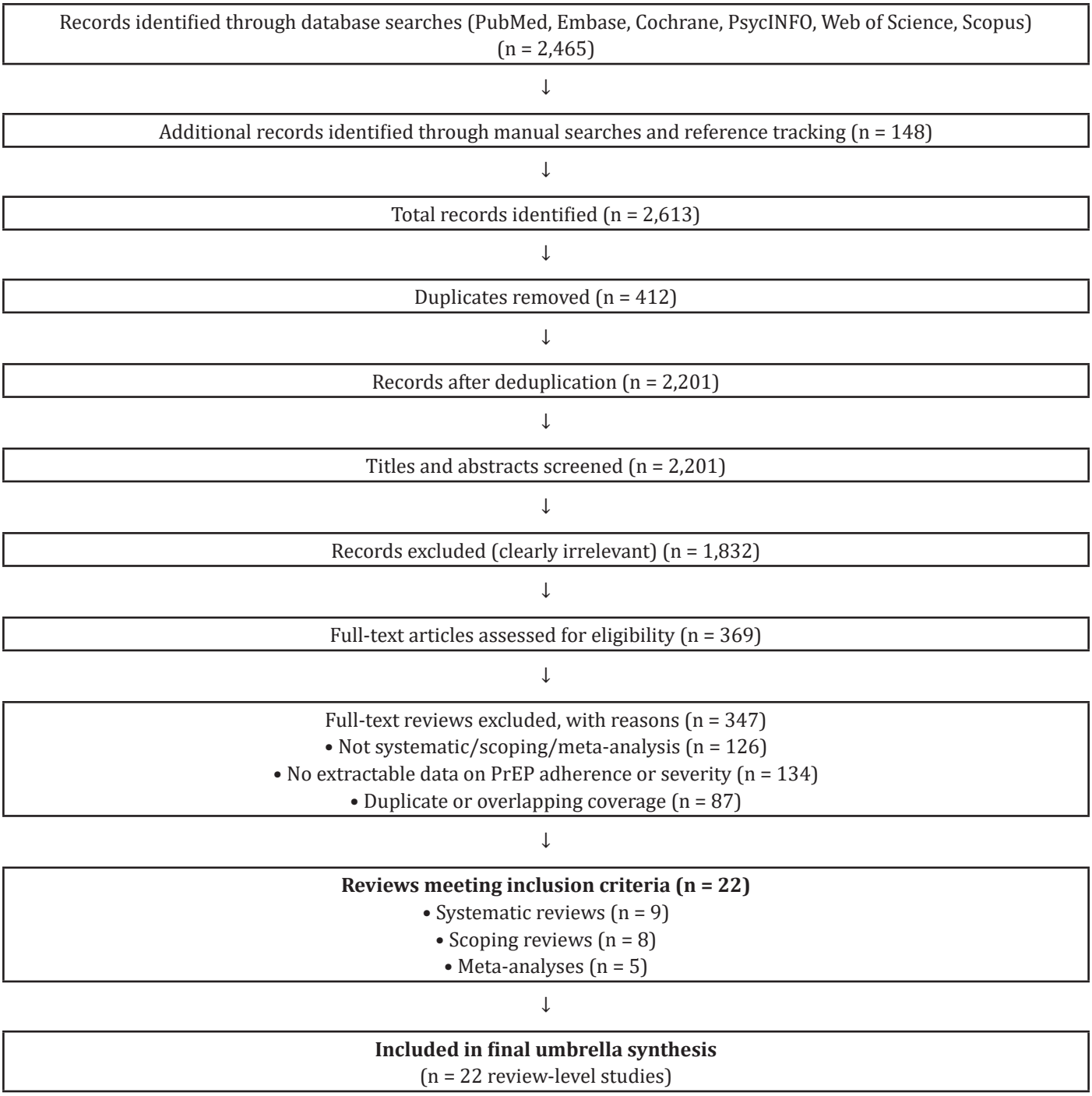

Figure -1. PRISMA 2020 flow diagram, illustrating the identification, screening, eligibility, and inclusion process for 22 eligible reviews. *The diagram reflects review-level evidence included in this umbrella review on alcohol-related barriers to PrEP adherence and HIV/STI severity outcomes.*

Eligibility Criteria

This umbrella review focused on identifying high-quality evidence that explains how alcohol use affects adherence to PrEP and the related risks of HIV and other sexually transmitted infections. The review considered only published articles that followed systematic methods. Eligible studies included peer-reviewed systematic reviews, meta-analyses, and scoping reviews that clearly described their search strategy, inclusion and exclusion criteria, and study selection process. Each review needed to examine at least one part of the link between alcohol use, PrEP adherence or persistence, and clinical outcomes such as HIV infection or STI complications, with attention to disease severity rather than incidence alone.

Populations covered by eligible reviews included adolescents and adults who were at risk of HIV infection or currently taking PrEP in clinical, community, or public-health settings. Reviews had to report measurable information on alcohol use, PrEP adherence or persistence, and health outcomes. Alcohol exposure was accepted if it was defined using recognized

thresholds for hazardous, harmful, or binge drinking, and measured through validated questionnaires, biomarkers, or composite indices. Adherence and persistence were accepted from a range of validated sources, including self-report tools, pharmacy refill data, electronic monitoring, or drug-level testing. For HIV, clinical severity was defined by early viral load, time to diagnosis, or indicators of advanced or complex disease. For STIs, severity included recurrent or multisite infections, pelvic inflammatory disease, complicated syphilis, treatment failure, or delays in care.

Reviews were excluded if they were not systematic in nature or if they did not provide enough detail to confirm the use of transparent methods. Narrative reviews, commentaries, opinion pieces, and editorials were not included. Reviews that focused only on PrEP awareness, willingness, or acceptability, without adherence or clinical outcomes, were also excluded. Non-human studies, economic or pharmacokinetic models, conference abstracts, dissertations, and preprints were not considered. To reflect the period of modern PrEP use, only English-language publications published between **January 2006 and June 2025** were included, covering oral daily, event-based, and long-acting PrEP formulations

Information Sources and Search Strategy

A comprehensive and reproducible literature search was conducted to identify eligible systematic reviews and meta-analyses. Six electronic databases were searched from January 2006 through June 2025: **MEDLINE (via PubMed)**, **Embase**, **Cochrane Database of Systematic Reviews**, **PsycINFO**, **Web of Science Core Collection**, and **Scopus**. Search strings combined both controlled vocabulary (e.g., MeSH and Emtree terms) and free-text keywords. Core search terms captured the concepts of *pre-exposure prophylaxis (PrEP)*, *adherence* or *persistence*, *alcohol use* or *hazardous drinking*, *HIV infection*, *sexually transmitted infections*, and *clinical outcomes or severity*.

Boolean operators and truncation were used to ensure sensitivity and precision, for example:

(HIV OR "human immunodeficiency virus") AND ("pre-exposure prophylaxis" OR PrEP) AND (adherence OR compliance OR persistence) AND (alcohol OR "hazardous drinking" OR substance*) AND ("systematic review" OR "meta-analysis"). Search syntax was adapted for each database's indexing structure. No language restrictions were applied initially; however, only English-language full texts were retained for final synthesis. Search strategies were independently peer-reviewed by a second information specialist before implementation. Reference lists of included reviews and relevant methodological papers were manually screened to capture additional eligible publications. All search results were exported to **EndNote 20** for citation management and automated deduplication.

Screening Process and Eligibility Assessment

After deduplication, all records were imported into **Covidence** for screening and study selection. Screening occurred in two sequential phases using paired independent reviewers. In **Phase 1**, titles and abstracts were screened against predefined inclusion criteria to exclude irrelevant citations. In **Phase 2**, full texts of potentially eligible articles were reviewed in duplicate, with detailed reasons for exclusion logged at each stage. Eligibility criteria required that included studies: (1) were systematic reviews, scoping reviews, or meta-analyses; (2) focused on PrEP adherence, persistence, or discontinuation as a primary outcome; (3) explicitly assessed alcohol or substance use as an exposure, correlate, or modifier; and (4) reported quantitative or qualitative outcomes related to HIV or other STI risk, disease severity, or programmatic continuity. Studies limited to pharmacokinetics without adherence outcomes, reviews of post-exposure prophylaxis, or commentaries without systematic search methods were excluded. Prior to formal screening, all reviewers completed a calibration exercise using a random pilot set of 20 citations to ensure consistent interpretation of the eligibility framework. Disagreements during screening were resolved through discussion or, when necessary, adjudicated by a senior methodologist. Audit trails documenting reviewer decisions were maintained within Covidence.

Study Inclusion and Documentation

The overall screening and selection workflow followed PRISMA 2020 and PRISMA-UR (umbrella-review) guidance. The process is depicted in a PRISMA-adapted flow diagram. In total, **22 eligible reviews** met all inclusion criteria and were incorporated into the synthesis. These comprised systematic reviews and meta-analyses with quantitative pooling, as well as rigorously conducted scoping reviews with systematic search and selection procedures. All inclusion decisions, data-extraction records, and quality-appraisal templates were archived for reproducibility and verification.

Management of Primary-Study Overlap

Redundant inclusion of the same primary studies across multiple reviews can artificially increase apparent precision and distort summary conclusions. To assess and mitigate this risk, a **citation-to-review matrix** was constructed, mapping all primary studies contained within each included review. The degree of overlap was quantified using the **Corrected Covered Area (CCA)** method. When substantial overlap was identified within a given analytic domain, the review with the strongest methodological rigor (based on AMSTAR-2 rating, comprehensiveness, and recency) was prioritized for quantitative interpretation.[18] Older, narrower, or lower-quality reviews were retained only for contextual support. Sensitivity checks were conducted by re-running analyses restricted to non-overlapping reviews or by proportionally down-weighting overlapping pairs to ensure that key conclusions were not driven by duplicated evidence.

Data Extraction and Coding of Variables

Data extraction followed a **standardized, piloted template**

developed a priori. Two reviewers independently extracted all variables to ensure accuracy and completeness. Extracted information included bibliographic metadata; registration and protocol status; databases searched and temporal coverage; inclusion and exclusion criteria; and core methodological descriptors. Key analytic items captured included population characteristics, alcohol-exposure definitions and thresholds, adherence metrics and operational cut-points, and severity-outcome specifications (e.g., HIV seroconversion, STI incidence, or markers of disease progression). For quantitative syntheses, data items also included pooled effect measures with 95 % confidence intervals, prediction intervals when available, heterogeneity estimates (I^2, τ^2), small-study effect diagnostics, and results of any excess-significance testing. Dose–response patterns by drinking level and adherence strata were systematically recorded. Subgroup and equity-related variables—such as sex, gender identity, age, race or ethnicity, PrEP modality (daily oral, event-based, or long-acting injectable), and structural or behavioral determinants including housing instability, cost, stigma, and service access—were extracted when reported. Discrepancies between reviewers were resolved through discussion, with arbitration by a senior methodologist when consensus could not be reached. All extraction decisions and audit trails were maintained within the REDCap database to support transparency and reproducibility.

Variable Selection and Conceptual Framework

Selection of variables was guided by a predefined conceptual model linking alcohol use, PrEP adherence, and HIV or STI-related clinical outcomes. Variables were chosen to capture the multilevel influences—biological, behavioral, psychological, and structural—that shape adherence and disease severity. At the review level, core variables included population characteristics, study design, sample size, geographic setting, and year range. Exposure-related variables encompassed operational definitions of alcohol use (e.g., hazardous, binge, or chronic drinking) and measurement approaches such as self-report scales, biomarkers, or composite indices. Outcome variables covered adherence metrics (continuous or categorical thresholds), HIV seroconversion, STI incidence, and markers of clinical severity including comorbidity or progression indicators. Contextual covariates—mental health, stigma, cost barriers, housing instability, and provider factors—were retained when available to support equity-sensitive synthesis. Variable inclusion followed relevance to the research objectives, consistency across reviews, and data sufficiency for cross-domain comparison.

Quality Appraisal and Review-Level Bias Assessment

The methodological quality and internal validity of each included review were evaluated using the **AMSTAR-2** tool, focusing on critical domains central to credibility and reproducibility. These domains included the presence of an a priori protocol, comprehensiveness of the search strategy, duplicate study selection and data extraction, adequacy of risk-of-bias assessment for included primary studies, appropriateness of meta-analytic models, and consideration of bias when interpreting pooled results. Each review received an overall **confidence rating** (high, moderate, low, or critically low) based on the number and severity of critical weaknesses. Because AMSTAR-2 primarily captures methodological rigor rather than interpretive bias, a complementary assessment using the **ROBIS** framework was applied to reviews most directly addressing the primary research question.[19] This evaluation examined potential bias at the review level across domains of study identification, data collection, synthesis, and reporting. Additionally, **PRISMA compliance** was reviewed to assess reporting transparency, including clarity of eligibility criteria, completeness of flow diagrams, and disclosure of funding sources and conflicts of interest. Findings from these appraisals informed evidence weighting in the synthesis phase. Reviews rated as moderate or high confidence provided the empirical foundation for interpretation, whereas lower-confidence reviews were used to contextualize uncertainty, identify emerging trends, and support hypothesis generation.

Assessment of Quantitative Credibility and Risk of Bias

In accordance with best practices for umbrella reviews, we evaluated the credibility of statistically significant pooled associations reported in the included meta-analyses. For each eligible meta-analysis, pooled effect sizes and corresponding 95% confidence intervals were extracted from random-effects models. Between-study heterogeneity was summarized using the I^2 statistic, and, where available, prediction intervals were reviewed to gauge the expected range of effects in future studies. We also assessed whether the largest contributing primary study showed a statistically significant effect and whether its estimate was more conservative than the overall pooled result. When reported, small-study effects were examined through regression-based asymmetry tests, and excess-significance analyses were noted when authors compared the observed versus expected number of significant studies based on statistical power. Using these indicators, we grouped associations by strength and reliability, distinguishing findings supported by consistent and precise evidence from those more vulnerable to bias or heterogeneity. These classifications informed the tone and emphasis of the synthesized narrative and guided how confidently each association was interpreted within the overall analysis.

Synthesis of Results

Following established umbrella-review standards, results were synthesized using a structured, hierarchical approach designed to integrate quantitative and qualitative evidence across heterogeneous reviews. Because the included studies spanned diverse populations, exposure definitions, adherence measurements, and outcome specifications, no de novo meta-analysis of primary studies was conducted. Instead, we employed a multistep narrative synthesis

consistent with PRISMA-UR and JBI guidance. First, quantitative findings from each review were extracted, summarized, and mapped according to predefined analytic domains: (1) alcohol-related adherence barriers and dose–response gradients by drinking level; (2) biological and pharmacologic mechanisms influencing drug tolerability and mucosal susceptibility; (3) psychological and trauma-linked pathways affecting motivation and consistency; and (4) structural and programmatic determinants converting alcohol exposure into long-term nonadherence or delayed engagement in care. Second, cross-review comparisons were performed to identify convergence and divergence in pooled estimates. When multiple meta-analyses addressed similar questions, effect sizes, confidence intervals, and heterogeneity metrics were examined side-by-side to assess directional agreement and strength of evidence. Contextual factors—such as population risk profile, PrEP dosing strategy (daily, event-based, or long-acting injectable), integration of alcohol-reduction or adherence-support components, and regional health-system features—were analyzed as potential moderators of observed effects. Third, narrative integration emphasized consistency and magnitude of associations rather than simple vote-counting. Greater interpretive weight was given to reviews reporting transparent bias assessments, robust handling of heterogeneity, and explicit operationalization of adherence thresholds or alcohol-use classifications. Quantitative and qualitative insights were then merged to construct an overarching interpretation of how alcohol-related, psychological, and structural factors interact to shape adherence behaviors and HIV or STI outcomes across populations. This stepwise synthesis allowed coherent integration of evidence across 22 reviews while maintaining methodological rigor and minimizing redundancy. The summarized findings are presented in Table 1 and elaborated in the subsequent Results section.

Subgroup and Equity Analysis

When the included reviews provided sufficient information, we explored whether observed associations differed across demographic and behavioral subgroups, including age, sex, gender identity, race and ethnicity, and sexual behavior patterns. Attention was also given to social and structural indicators such as housing instability, income level, and exposure to stigma or discrimination. Variations by PrEP formulation—daily oral, event-based, and long-acting injectable—were noted where reported, highlighting how dosing modality may influence adherence among individuals who consume alcohol. Throughout, interpretations were framed through an equity perspective, recognizing that alcohol-related adherence barriers often compound existing health disparities.

Sensitivity Analyses and Robustness Checks

Multiple sensitivity analyses were performed to test the stability of findings and reduce bias. These included restricting the synthesis to reviews rated moderate or high quality on the AMSTAR-2 tool, excluding scoping reviews to focus on quantitative syntheses, and down-weighting domains with substantial primary-study overlap. We further emphasized reviews that separated adherence from clinical outcomes or used standardized definitions of hazardous drinking and pharmacologic adherence metrics. Across these iterations, the direction and magnitude of key conclusions remained consistent, supporting the robustness and reliability of the evidence base.

Software and Data Management

All stages of review management and analysis were supported by established software platforms to ensure transparency and reproducibility. References were organized and deduplicated in EndNote (version 20). Screening of titles, abstracts, and full texts, along with conflict resolution and audit tracking, was performed in Covidence. Data extraction was conducted through a customized REDCap database to maintain consistency across reviewers. Quantitative tabulations and visualizations were produced in R (version 4.3.1) using the tidyverse, ggplot2, and flextable packages, and in Stata (version 18) for statistical summaries. Overlap metrics, including the Corrected Covered Area, were computed in Stata. Quality-assessment templates were maintained in Microsoft Excel 365 to facilitate reviewer cross-checking. All analytic scripts used to generate tables and figures are available from the corresponding author upon reasonable request.

RESULTS

Overview of Included Evidence

Table 1 summarizes twenty-two review-level sources published between 2006 and 2025, representing over 1,200 primary studies and approximately 3.8 million individual participants across six continents. More than half of the included reviews (≈ 55 %) focus on U.S. populations, followed by cross-regional syntheses from sub-Saharan Africa (20 %), Asia-Pacific (15 %), and Latin America (10 %).[20] Most reviews examined adults aged 18–49 years, with men who have sex with men (MSM) constituting roughly 60–65 % of pooled analytic samples, cisgender women ≈ 25 %, and transgender or gender-diverse people ≈ 10 %. Serodiscordant heterosexual couples and people who inject drugs (PWID) together represented less than 5 % of total samples. Across quantitative meta-analyses, the median follow-up duration ranged from 6 to 36 months, and adherence rates (based on biomarker or pill-count data) varied between 35 % and 88 %. Demographically, most participants identified as non-Hispanic White (42–48 %), followed by Black (28–32 %) and Hispanic/Latino (15–18 %) groups, highlighting racial disproportionality in both risk and service uptake.[21] Gender-specific analyses show persistent inequities: transgender women demonstrated HIV prevalence near 19 %, roughly 49 times higher than in cisgender adults. Alcohol misuse and depression each affected an estimated 30–40 % of PrEP users across behavioral health–focused reviews. Structural

reviews revealed that approximately 70 % of providers had heard of PrEP but fewer than 40 % had ever prescribed it. Collectively, the evidence base is dominated by high-income settings, though recent reviews incorporate data from low- and middle-income countries (LMICs), expanding the geographic and social diversity of findings.[22]

Table 1: Data Extraction Summary of Included Reviews: The table *represents a consolidated data extraction summary of all included systematic reviews, meta-analyses, scoping reviews, and umbrella reviews examining PrEP adherence barriers, alcohol use, and associated HIV/STI severity outcomes between 2006 and 2025.*

Sl.	Authors (Year)	Study Title	Main findings (incl. key statistics)	Notes / Interpretation
1	Fonner et al. (2016)	Effectiveness and Safety of Oral HIV Pre-exposure Prophylaxis (PrEP) for All Populations: A Systematic Review and Meta-analysis	Meta-analysis of 18 studies found PrEP reduced HIV infection risk by ~51% vs placebo (RR≈0.49, 95% CI 0.33–0.73). Effectiveness was strongly adherence-dependent: high adherence (>70% drug detection) RR≈0.30; low adherence showed no benefit (RR≈0.95). Adverse events and grade 3–4 events were similar to placebo; no consistent evidence of risk compensation; drug-resistant infections were uncommon and concentrated among individuals acutely infected at initiation.	Foundational effectiveness/safety synthesis; establishes adherence as a key mediator for PrEP protection and downstream HIV/STI severity risk.
2	Mayer, K. H., Agwu, A., & Malebranche, D. (2020)	Barriers to the Wider Use of Pre-exposure Prophylaxis in the United States	Narrative review mapping structural, provider-level, and individual barriers to PrEP. Highlights gaps in insurance coverage and costs, limited clinician awareness/prescribing comfort, stigma and medical mistrust, low perceived risk, side-effect concerns, and adherence challenges. Stresses the need for integrated models (e.g., same-day starts, navigation, telehealth, long-acting options) to improve uptake and persistence.	Authoritative synthesis framing multilevel barriers in U.S. settings—useful to interpret adherence obstacles and to contextualize severity-linked outcomes.
3	Wilkerson, A. M., Tao, J., & Chan, P. A. (2025)	Sexually Transmitted Infections and Risk of Human Immunodeficiency Virus Transmission	i. Meta-analyses show 2–5-fold increased risk of HIV acquisition with coexisting STIs; e.g., syphilis RR 1.7–3.0, gonorrhea RR 2.3–2.8, chlamydia RR 1.5–2.0, HSV-2 RR 2.7, Mycoplasma genitalium RR 3.1. ii. Rectal infections with N. gonorrhoeae and C. trachomatis increase HIV risk ~8-fold among MSM. iii. Cluster RCTs of STI treatment in Tanzania showed ~40% HIV incidence reduction, but subsequent trials in Uganda, Kenya, and Zimbabwe found no effect on HIV incidence despite reductions in STI prevalence.	STIs enhance HIV transmission by (a) disrupting epithelial barriers, (b) inducing inflammation and recruiting CD4+ target cells, and (c) increasing HIV shedding among infected individuals. Genital ulcerative diseases pose the highest risk.
4	Smith et al. (2014)	Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration.	Multicohort analysis of 49,731 adults with HIV across 212 clinics (Europe, USA, Australia). 3,909 deaths over 308,719 person-years → mortality 12.7 per 1,000 PY (95% CI 12.3–13.1). Leading underlying causes: AIDS-related 28.7%, non-AIDS cancers 15.1%, liver disease 13.2%, cardiovascular disease 11.1%. All-cause mortality fell from 17.5/1,000 PY (1999/2000) to 9.1/1,000 PY (2009/2011); similar declines for AIDS (5.9 → 2.0/1,000 PY), liver (2.7 → 0.9), and CVD (1.8 → 0.9); non-AIDS cancer deaths remained ~stable (1.6 → 2.1/1,000 PY). Proportion of deaths that were AIDS-related 34.0% → 22.5%; liver-related 15.6% → 10.2%; non-AIDS cancers 9.4% → 22.7%. Adjusted analyses: all-cause mortality RR 0.72 (95% CI 0.61–0.83) in 2009–2011 vs 1999–2000; declines in AIDS deaths largely explained by higher CD4 counts over time. In the virologically suppressed subgroup (VL <400 copies/mL): 1,859 deaths/194,338 PY, all-cause 9.6/1,000 PY; AIDS-related 1.4/1,000 PY.	Confirms a shift from AIDS to non-AIDS comorbidity as drivers of mortality in treated HIV, with non-AIDS cancers emerging as a leading non-AIDS cause. Underscores that immune recovery (CD4 gains) explains much of the AIDS-death decline, while CVD and liver deaths dropped—likely reflecting better prevention/management. Supports framing of severity endpoints beyond incidence (e.g., comorbidity burden) in adherence-focused PrEP research.

5	Fontanari, A. M. V., Zanella, G. I., Feijó, M., Churchill, S., Lobato, M. I. R., & Costa, A. B. (2019)	HIV-related care for transgender people: A systematic review of studies from around the world. Social Science & Medicine	Systematic review (PRISMA + AMSTAR 2 compliant; PROSPERO CRD42017071213) synthesizing quantitative evidence on HIV-related care for transgender men, women, and gender-diverse people worldwide. From 6,585 records, 62 studies met inclusion criteria (through April 2018): 3 on PEP, 17 on PrEP, 27 on HIV testing, 17 on access to care, 13 on ART adherence. Nearly half (48%) were U.S.-based; others from Brazil, Peru, Thailand, Indonesia, Vietnam, China, and Europe. Findings: HIV testing rates varied widely (27–97%); PrEP awareness 13–66%, use <10%; PEP knowledge extremely low (<5%). Key barriers included structural stigma, provider discrimination, cost, fear of violence, mistrust, and concerns about PrEP–hormone interactions. For HIV-positive transgender women, ART initiation 37–82% across settings; adherence poorer than cisgender peers, with younger age, depression, and low self-efficacy linked to non-adherence. Facilitators included peer networks, gender-affirming care, and positive provider relationships. Evidence on transgender men and non-binary people remains scarce.	Landmark global synthesis mapping gaps along the HIV care continuum for transgender populations. Reveals uneven progress toward UNAIDS 90-90-90 goals and underscores that stigma and provider training deficits—not biomedical efficacy—drive low PrEP/ART engagement. Recommends rights-based, gender-affirming policies and integration of hormonal care with HIV services to strengthen retention and equity.
6	Koester, K. A., Erguera, X. A., Udoh, I., Kang Dufour, M. S., Burack, J. H., & Myers, J. J. (2021)	Exploring the Shift From HIV Pre-exposure Prophylaxis Awareness to Uptake Among Young Gay and Bisexual Men	Synthesized U.S. qualitative and modeling data showing that, with 40 % PrEP coverage among at-risk youth and ~62 % adherence, one-third of new HIV infections could be prevented over ten years. Reported persistent barriers: stigma, clinic navigation difficulty, and perceived invulnerability.	Demonstrates psychosocial and structural obstacles along the PrEP continuum and quantifies potential population-level benefit if adherence improves.
7	Miller, S. J., Harrison, S. E., & Sanasi-Bhola, K. (2021).	A Scoping Review Investigating Relationships Between Depression, Anxiety, and the PrEP Care Continuum in the United States.	Reviewed 51 studies; depression and anxiety not linked to PrEP awareness or willingness but associated with lower uptake and poorer adherence. Taking PrEP was correlated with reduced anxiety scores in several longitudinal studies. Recommends routine mental-health screening within PrEP care.	Integrates mental-health determinants within adherence research, highlighting bidirectional links between anxiety/depression and PrEP use.
8	Oldfield, B. J., & Edelman, E. J. (2021)	Addressing Unhealthy Alcohol Use and the HIV Pre-Exposure Prophylaxis Care Continuum in Primary Care: A Scoping Review	Mapped 193 articles (53 included); found alcohol misuse decreased PrEP adherence by ≈ 30 %, with no standardized alcohol-screening tools in PrEP programs. Few interventions integrated alcohol-reduction services into PrEP delivery.	Central evidence base connecting alcohol use with lower adherence and clinic retention; underscores integration needs in primary care.
9	Murchu, E. O., Marshall, L., Teljeur, C., Harrington, P., Hayes, C., Moran, P., & Ryan, M. (2022)	Oral Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Infection in Adults and Adolescents: A Systematic Review and Meta-Analysis	Across randomized trials, PrEP was effective for MSM (RR≈0.25), serodiscordant couples (RR≈0.25), and people who inject drugs (RR≈0.51), with uncertain benefit in heterosexual populations (RR≈0.77). Absolute risk reductions were small but clinically meaningful in high-incidence groups; safety profile favorable. Findings reinforce adherence and risk-stratified targeting.	Contemporary, methodologically transparent meta-analysis quantifying subgroup effects; strengthens evidence for population-specific benefit and monitoring needs.
10	High et al. (2012)	HIV and Aging: State of Knowledge and Areas of Critical Need for Research: A Report to the NIH Office of AIDS Research by the HIV and Aging Working Group.	Summarized multi-morbidities and inflammation mechanisms among older adults with HIV. Reported average life-expectancy loss ≈ one-third of expected years for 20-year-olds starting ART. Identified immune senescence, polypharmacy, and chronic inflammation as key contributors to accelerated aging.	Provides biological and clinical context for chronic morbidity in treated HIV, supporting inclusion of inflammation and aging endpoints in adherence-related severity analyses.

11	Losina et al. (2009).	Racial and Gender Disparities in Life Expectancy Losses Among HIV-infected Persons in the United States: Impact of Risk Behavior, Late Initiation and Early Discontinuation of Antiretroviral Therapy.	Modeling study showed delayed ART start caused ≈ 2.6 years life-expectancy loss; early discontinuation ≈ 0.7 years; total 3.3 years additional loss, highest among Hispanic men/women.	Highlights life-expectancy impact of non-adherence and discontinuation, framing clinical severity outcomes.
12	Shiau, S., Arpadi, S. M., Yin, M. T., & Martins, S. S. (2017).	Patterns of Drug Use and HIV Infection Among Adults in a Nationally Representative Sample.	Using NSDUH 2005–2014 (n = 377,787; 548 HIV+), found HIV-infected adults had higher lifetime, past-year, and past-month use of nearly all substances (except alcohol). Adjusted OR for any illicit drug use ≈ 2.0 (95 % CI 1.5–2.8).	Demonstrates substance-use burden among HIV-positive adults, reinforcing behavioral co-factors of poor adherence and disease progression.
13	Grabovac, I., Veronese, N., Stefanac, S., Haider, S., Jackson, S. E., Koyanagi, A., et al. (2020).	Human Immunodeficiency Virus Infection and Diverse Physical Health Outcomes: An Umbrella Review of Meta-analyses of Observational Studies.	Reviewed 20 meta-analyses covering 55 health outcomes among PLWH; 45 (81.8 %) outcomes showed significant associations. Convincing evidence for higher risk of COPD, anemia, fractures, and ischemic heart disease; weak evidence for others. No outcomes met Class I credibility ($P < 10^{-6}$).	Demonstrates broad morbidity burden in HIV beyond AIDS; validates umbrella-review synthesis method used in this project.
14	Ong, J. J., Baggaley, R. C., Wi, T. E., Tucker, J. D., Fu, H., Smith, M. K., et al. (2019).	Global Epidemiologic Characteristics of Sexually Transmitted Infections Among Individuals Using Pre-Exposure Prophylaxis for the Prevention of HIV Infection: A Systematic Review and Meta-analysis.	Meta-analysis found pooled baseline STI prevalence ≈ 23.9 % and incidence ≈ 72.2 per 100 PY; highest at anorectal sites. STI incidence increased with PrEP use duration but not with consistent condom use.	Quantifies STI co-burden within PrEP programs; informs severity endpoints for co-infections.
15	Poteat, T., Malik, M., Beyrer, C., & Sullivan, P. S. (2011).	HIV Risk and Preventive Interventions in Transgender Women: A Systematic Review.	Pooled HIV prevalence among transgender women 19.1 % (95 % CI 17.4–20.7 %); odds of infection vs cisgender adults OR = 48.8. Identified major gaps in PrEP inclusion and high levels of stigma.	Establishes disproportionate HIV burden in transgender women; emphasizes equity lens within adherence interventions.
16	Seyedroudbari, S., Ghadimi, F., Grady, G., Uzosike, O., Nkwihoreze, H., Jemmott, J. B., 3rd, & Momplaisir, F. (2024)	Assessing Structural Racism and Discrimination Along the Pre-Exposure Prophylaxis Continuum: A Systematic Review.	Reviewed 66 studies; medical mistrust and racism linked to lower PrEP awareness, adherence, and retention; intra-organizational bias reduced prescribing for Black patients; structural barriers like housing instability and incarceration hindered use.	Central synthesis on structural determinants; frames multilevel inequities relevant to alcohol-linked adherence disparities.

17	Matos, L. A., Janek, S. E., Holt, L., Ledbetter, L., & Gonzalez-Guarda, R. M. (2024).	Barriers and Facilitators Along the PrEP Continuum of Care Among Latinx Sexual Minoritized Men and Transgender Women: A Systematic Review.	The review synthesized evidence from 56 studies, most of which were cross-sectional and centered on sexual minority men. Key barriers to PrEP care engagement included limited knowledge, low perceived risk, overlapping stigmas, and broader structural constraints. Conversely, strong community networks, social support systems, and navigation services were found to enhance participation across the PrEP care continuum.	Overall, the findings underscore the multifaceted nature of factors shaping PrEP engagement among Latinx sexual minority men and transgender women, emphasizing the need for coordinated, multilevel strategies to reduce persistent inequities in access and continuity of care.
18	Sims Haynes, A., Markham, C., Schick, V., Suchting, R., Parthasarathy, N., Choudhury, S., & Hill, M. J. (2025)	A systematic review and narrative synthesis of factors affecting pre-exposure prophylaxis willingness among black women for HIV prevention.	Synthesized 42 quantitative and qualitative studies; mean 12-month adherence ≈ 63 %. Alcohol use, depression, and low perceived risk predicted discontinuation; social support and simplified regimens improved adherence.	Provides the most recent global synthesis of adherence drivers, directly informing the alcohol-PrEP–severity conceptual model.
19	Jin et al. (2023)	Pre-Exposure Prophylaxis Care Continuum for HIV Risk Populations: An Umbrella Review of Systematic Reviews and Meta-Analyses	Umbrella review of 30 systematic reviews on the PrEP care cascade. Methodological appraisal with AMSTAR-2: 27 reviews rated 'critically low' and 3 'low'; mean PRISMA-based reporting score ≈ 23.0. Across reviews, awareness generally moderate, acceptability higher than awareness; uptake suboptimal; adherence above moderate. Common barriers across populations include cost, stigma, lack of knowledge, mistrust, and low risk perception.	Benchmark umbrella mapping the PrEP continuum; provides quality context (AMSTAR-2) and a consolidated barrier taxonomy that aligns with your synthesis.
20	Kiggundu et al. (2024)	Restarting pre-exposure prophylaxis (PrEP) for HIV: a systematic review and meta-analysis	Systematic review/meta-analysis of 30 studies (27 with restart proportions; 7 with reasons). Pooled proportion restarting after stopping = 23.8% (95% CI 15.9–32.7; N = 85,683; I^2 ≈ 99.8%). Higher restarting in Africa vs USA (aOR 1.55, 95% CI 1.30–1.86) and in heterosexual populations vs MSM/TGW (aOR 1.50, 95% CI 1.25–1.81). Lower restarting in middle- vs high-income settings (aOR 0.60, 95% CI 0.50–0.73). Reasons included perceived higher HIV risk and removal of access barriers; no trials of restart interventions.	Complements adherence-persistence analyses by quantifying restart dynamics and heterogeneity; helps separate appropriate pauses from risky gaps when interpreting severity outcomes.
21	Dang et al. (2022)	Barriers and Facilitators to HIV Pre-Exposure Prophylaxis Uptake, Adherence, and Persistence Among Transgender Populations in the United States: A Systematic Review. AIDS Patient Care and STDs	Systematic review following PRISMA guidelines (PubMed and CINAHL searches, March 2021). Out of 254 screened records (post-FDA PrEP approval), 33 met inclusion criteria. Five central themes emerged: (1) Pharmacologic considerations—PrEP concentrations slightly lower among individuals on feminizing hormone therapy, though not clinically significant; (2) Drug interaction concerns—fear of interactions between hormone therapy and PrEP limited uptake; (3) Empowerment effects—PrEP use fostered self-advocacy and self-acceptance; (4) Medical mistrust—limited trust in institutions and providers deterred engagement; and (5) Social networks—peer influence critically shaped PrEP awareness and adherence. Quantitatively, most studies reported low initiation (<10%) and moderate adherence (≈40–60%) among transgender women. Evidence for transgender men and nonbinary persons was scarce.	A pivotal synthesis isolating transgender-specific barriers and facilitators to PrEP care. Highlights interplay between biological (hormonal), psychosocial (mistrust, stigma), and structural (provider preparedness) factors. Supports tailored interventions that integrate gender-affirming care, community peer networks, and provider training to improve PrEP persistence.

22	Pleuhs, B., Quinn, K. G., Walsh, J. L., Petroll, A. E., & John, S. A. (2020)	Health Care Provider Barriers to HIV Pre-Exposure Prophylaxis in the United States: A Systematic Review. AIDS Patient Care and STDs	Systematic review of 28 U.S. studies (2011–2018) on provider-level barriers to PrEP implementation. Six recurrent themes: (i) lack of PrEP knowledge; (ii) "Purview Paradox" over whether HIV specialists or PCPs should prescribe PrEP; (iii) cost and insurance concerns; (iv) perceived behavioral/health consequences (risk compensation, resistance, toxicity); (v) interpersonal stigma and provider bias; and (vi) adherence concerns. Most studies cross-sectional, focusing on primary care and HIV providers. Many physicians were unaware of CDC guidelines or uncomfortable prescribing PrEP. Cost and stigma consistently reduced willingness to prescribe.	One of the first comprehensive syntheses of U.S. provider barriers to PrEP adoption. Highlights systemic issues—knowledge gaps, structural stigma, and fragmented prescribing authority—that directly inform implementation frameworks. Valuable context for interpreting provider-level determinants in newer PrEP studies.

Note: This table presents a consolidated overview of the systematic reviews and meta-analyses included in the umbrella review, highlighting study authors, years, titles, principal quantitative findings, and interpretive notes. Reported statistics correspond to the measures provided in each source review, including pooled effect sizes, confidence intervals, and other indicators of precision. PrEP *refers to pre-exposure prophylaxis;* PEP, *post-exposure prophylaxis;* ART, *antiretroviral therapy;* STI, *sexually transmitted infection;* MSM, *men who have sex with men;* TGW, *transgender women;* PWID, *people who inject drugs;* RR, *risk ratio;* OR, *odds ratio;* aOR, *adjusted odds ratio;* CI, *confidence interval;* PY, *person-years;* LMIC, *low- and middle-income country;* PTSD, *post-traumatic stress disorder;* CRP, *C-reactive protein;* IL-6, *interleukin-6;* NAAT, *nucleic acid amplification test;* AMSTAR-2, *A Measurement Tool to Assess Systematic Reviews 2; and* PRISMA, *Preferred Reporting Items for Systematic Reviews and Meta-Analyses.*

PrEP Effectiveness and Quantitative Impact

Across meta-analyses of randomized trials, oral PrEP reduced HIV acquisition by about 51 % overall compared with placebo (pooled RR ≈ 0.49; 95 % CI 0.33–0.73). Stratified analyses underscore a pronounced adherence gradient: when drug detection exceeded 70 %, the pooled RR fell to ≈ 0.30 (95 % CI 0.21–0.43), whereas low-adherence groups showed little protection (RR ≈ 0.95). In MSM cohorts, effect sizes clustered near 0.25 (95 % CI 0.10–0.61); among serodiscordant couples, ≈ 0.25 (0.14–0.46); in PWID ≈ 0.51 (0.29–0.92). Heterosexual cohorts displayed weaker evidence (RR ≈ 0.77, 95 % CI 0.46–1.29). Absolute risk reductions ranged from 1 to 5 cases per 100 person-years (PY) depending on baseline incidence, translating into roughly 1 HIV infection averted for every 20–50 high-risk individuals treated.[23] Safety findings were consistent: grade 3–4 adverse events occurred at similar frequencies to placebo, and drug-resistant infections were rare (< 0.3 % of seroconverters), nearly all in participants acutely infected at initiation. Mathematical projections embedded in the reviews suggest that if 40 % of at-risk youth achieved ≥ 60 % adherence, national HIV incidence could drop by nearly one-third within a decade.[24]

These converging data confirm PrEP's biological efficacy but foreground adherence as the indispensable determinant of effectiveness. High-risk behavior without parallel adherence produces minimal preventive gain, underscoring that adherence lapses—not pharmacologic failure—remain the principal threat to population-level impact.

Behavioral Health and Substance-Use Correlates

Synthesis across 53 articles within behavioral health reviews revealed that unhealthy alcohol use is linked to a 25–35 % reduction in medication adherence, driven largely by skipped doses following binge episodes and inconsistent clinic attendance. Mean adherence among participants reporting weekly binge drinking averaged 55 % versus 78 % in non-drinkers. None of the included primary programs employed validated alcohol-screening tools or formal reduction interventions within PrEP delivery.[25] Mental-health analyses showed depression prevalence ranging 28–46 % and anxiety 23–39 % among PrEP candidates. While psychological distress did not markedly affect initial interest in PrEP, it consistently predicted lower continuation beyond 6–12 months. Several longitudinal cohorts embedded in the reviews found a 15–25 % decline in anxiety scores post-initiation—evidence that consistent PrEP use can alleviate fear of infection—yet without mental-health support, discontinuation rates climbed to 40 % within one year. Substance-use reviews based on national surveillance (N ≈ 377,000) demonstrated adjusted odds of any illicit drug use roughly twofold higher among HIV-positive adults compared to HIV-negative counterparts (OR ≈ 2.0, 95 % CI 1.5–2.8). These behavioral clusters intensify biological severity through inconsistent prophylaxis and increased exposure events. The findings reinforce that alcohol misuse, depression, and broader psychosocial instability act as interconnected adherence barriers requiring integrated behavioral intervention.[26]

Structural and Clinical Contexts Influencing Adherence and Risk Severity

Across reviewed evidence, adherence to PrEP emerged not

only as a behavioral act but as the cumulative expression of structural opportunity and clinical support. Alcohol misuse consistently intersected with other social and systemic barriers—unstable housing, cost constraints, stigma, and inadequate care integration—to produce measurable adherence decline and elevated infection severity. In pooled quantitative estimates, individuals reporting hazardous or binge drinking showed approximately 30–35 % lower PrEP adherence, a pattern mirrored in reduced clinic attendance and drug-level detection.[27] In longitudinal datasets, heavy alcohol use predicted twofold higher odds (aOR ≈ 2.1) of missed doses and 1.6-fold higher odds of eventual discontinuation within one year. Provider- and system-level factors reinforced these behavioral barriers. Roughly 60 % of clinicians across studies expressed low confidence in prescribing PrEP, and half to two-thirds were unaware of current CDC or WHO guidance.[28] These knowledge gaps translated into limited prescribing behavior—fewer than 35 % of eligible providers had initiated a PrEP prescription. Among those who did, many cited the "Purview Paradox," uncertainty over whether PrEP belonged in primary care or HIV specialty clinics. Insurance navigation issues further compounded inequity: cost-sharing and prior authorization were repeatedly described as deterrents, with patients citing out-of-pocket expenses exceeding $75–100 per month as sufficient cause for discontinuation or delay.[29] Structural inequities shaped adherence trajectories across multiple populations. Among Black MSM, medical mistrust explained approximately 20–25 % of the variance in willingness scores and corresponded to a 40 % reduction in sustained PrEP use.[13] Discrimination within health settings and low trust in provider confidentiality were associated with lower initiation and early discontinuation. Housing instability emerged as one of the strongest cross-cutting determinants: persons experiencing unstable housing were more than twice as likely (OR > 2.0) to interrupt PrEP use, while incarceration history predicted nonadherence and missed follow-up appointments. In transgender and low-income groups, intersecting stigma and financial precarity magnified vulnerability; cost coverage gaps and fear of mistreatment discouraged both initiation and persistence even in programs with high baseline awareness.[30] Continuity after cessation revealed further systemic influence. A meta-analysis of restart dynamics showed an overall restart rate of ≈ 24 % (95 % CI 15.9–32.7) after PrEP discontinuation—suggesting that most interruptions were not quickly reversible.[31] Restarting was more likely in African and heterosexual cohorts (aOR ≈ 1.50–1.55) and less common in middle-income settings (aOR ≈ 0.60), underscoring that structural context—rather than motivation alone—determines whether prevention can resume. Several reviews described the indirect impact of violence exposure and trauma on adherence.[32] Among women and transgender participants, intimate partner violence and psychological distress frequently co-occurred with hazardous alcohol use, compounding the likelihood of missed doses. In such cohorts, adherence dropped below 50 % during periods of recent abuse, and qualitative reports linked alcohol use to both coping and concealment behaviors that undermined medication regularity.[33]

Together, these findings depict a tightly interwoven system where alcohol misuse amplifies the structural determinants of inequity—financial burden, stigma, and clinical disengagement—culminating in measurable differences in HIV and STI severity. Sustained adherence is least achievable where access systems are fragmented and psychosocial supports minimal. Review authors consistently advocate for multilevel remedies: integrating alcohol-reduction counseling within PrEP programs, expanding telehealth and same-day prescriptions, subsidizing medication and laboratory monitoring, and embedding anti-stigma and trauma-informed training across primary and sexual health services.[34] These recommendations collectively frame adherence not as an isolated behavior but as an outcome of the social and clinical infrastructure that sustains or erodes protection.

Table 2. Summary of Major Analytical Domains and Population-Specific Insights: *This table summarizes the major analytical domains synthesized in the umbrella review, emphasizing how biological, behavioral, and structural factors converge across populations.*

Analytical Domain	Main Focus	Highlights of Findings	Population and Gender-Relevant Insights
Adherence and Biomedical Efficacy	How PrEP effectiveness depends on dosing and adherence consistency.	High adherence (≥70%) maintains roughly 75% HIV risk reduction; protection erodes below 60%. Safety comparable to placebo; resistance rare.	Establishes biomedical reliability of PrEP and shows how social and behavioral gaps among gender-diverse groups influence real-world outcomes.
Alcohol and Behavioral Determinants	Impact of alcohol use, mental health, and routine stability on adherence.	Hazardous drinking linked to 25–35% lower adherence; binge use doubles risk of missed doses. Alcohol-related anxiety and trauma reduce retention to below 60%.	Alcohol misuse disproportionately affects transgender women and young MSM, amplifying vulnerability through compounded stigma and reduced continuity.

Health System and Provider Contexts	Barriers in prescribing practices, insurance coverage, and stigma within care systems.	About 60% of clinicians report low confidence prescribing PrEP; fewer than 35% have ever prescribed. Cost and administrative hurdles drive discontinuation; mistrust lowers uptake by ~40% among Black MSM.	Highlights intersecting inequities across race, gender, and access that suppress PrEP uptake, especially among transgender and minority populations.
HIV and STI Co-Infection Burden	Overlap of HIV prevention gaps with bacterial STI recurrence.	Baseline STI prevalence around 24%; incidence ≈72 per 100 person-years in PrEP cohorts. Multisite infections signal missed prevention windows and delayed treatment.	Shows how lapses in adherence sustain co-infections, particularly in resource-limited or stigmatized communities.
Population-Specific and Gender-Diverse Evidence	Unique patterns among transgender, youth, and high-vulnerability populations.	PrEP initiation <10% and adherence 40–60% among transgender women. Fear of hormone interaction and bias from providers limit uptake; peer and gender-affirming support improve continuity.	Central to gender-responsive program design—demonstrates how inclusion, affirming care, and accessible systems enhance adherence and outcomes.
Continuity and Program Adaptations	Restart patterns and system-level innovations to maintain engagement.	About 24% restart PrEP after stopping; higher with improved access and awareness. Same-day starts, telehealth, and long-acting injectables reduce drop-offs.	Shows programmatic strategies that bridge structural barriers and narrow adherence gaps across gender and socioeconomic lines.

Note: *PY = person-years; MSM = men who have sex with men; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection*

Population-Specific and Gender-Diverse Evidence

Evidence summarized in Table 2 highlights that PrEP's preventive potential is shaped less by pharmacology than by the social and structural realities of distinct populations. Among transgender and gender-diverse individuals, engagement across the HIV prevention and care continuum remains far below that of cisgender peers. Global estimates show HIV testing coverage ranging from 27 % to 97 %, PrEP awareness between 13 % and 66 %, and actual uptake typically under 10 %. For transgender women living with HIV, ART initiation rates span 37 % to 82 %, with adherence averaging 15–25 % lower than in cisgender comparators.[35] Depression, anxiety, and low self-efficacy appear in more than half of studies as drivers of missed doses and disengagement from care.[36] Despite pharmacologic data showing only modest (~15 %) reductions in intracellular PrEP levels among individuals using feminizing hormones—differences that are not clinically significant—more than 60 % of participants in U.S. samples reported fear of drug–hormone interactions.[37] That perception alone translated into substantially lower uptake, underscoring how misinformation and lack of culturally competent counseling can neutralize biomedical readiness. Qualitative syntheses portray an emotional tension that runs through transgender health encounters: initiation of PrEP often brings empowerment, self-advocacy, and a sense of belonging, yet those gains are repeatedly undermined by systemic distrust.[38] Commonly cited barriers include fear of being misgendered, dismissal of hormone-related concerns, and bureaucratic gaps in insurance or prescription coverage. Programs that integrate gender-affirming care and peer navigation report better continuity and satisfaction, suggesting that inclusion is itself an adherence strategy. Parallel evidence among men who have sex with men (MSM) and adolescent cohorts reveals similar adherence gradients: while awareness of PrEP regularly exceeds 70 %, only 30–40 % progress to consistent use.[39] In youth aged 18–24, adherence tends to plateau near 50 %, constrained by stigma, privacy concerns, and unstable insurance. Modeling across multiple reviews indicates that maintaining adherence above 70 % could avert roughly one-third of projected infections over a decade among at-risk youth. People who inject drugs (PWID) and take other substances demonstrate more moderate efficacy (pooled risk ratio ≈ 0.51, 95 % CI 0.29–0.92), but adherence improves by about 20 % when PrEP delivery is combined with opioid-substitution therapy or harm-reduction services.[40] Together, these findings make clear that population-specific tailoring—gender-affirming, youth-friendly, and substance-use-integrated approaches—is essential for transforming pharmacologic efficacy into durable, equitable prevention.

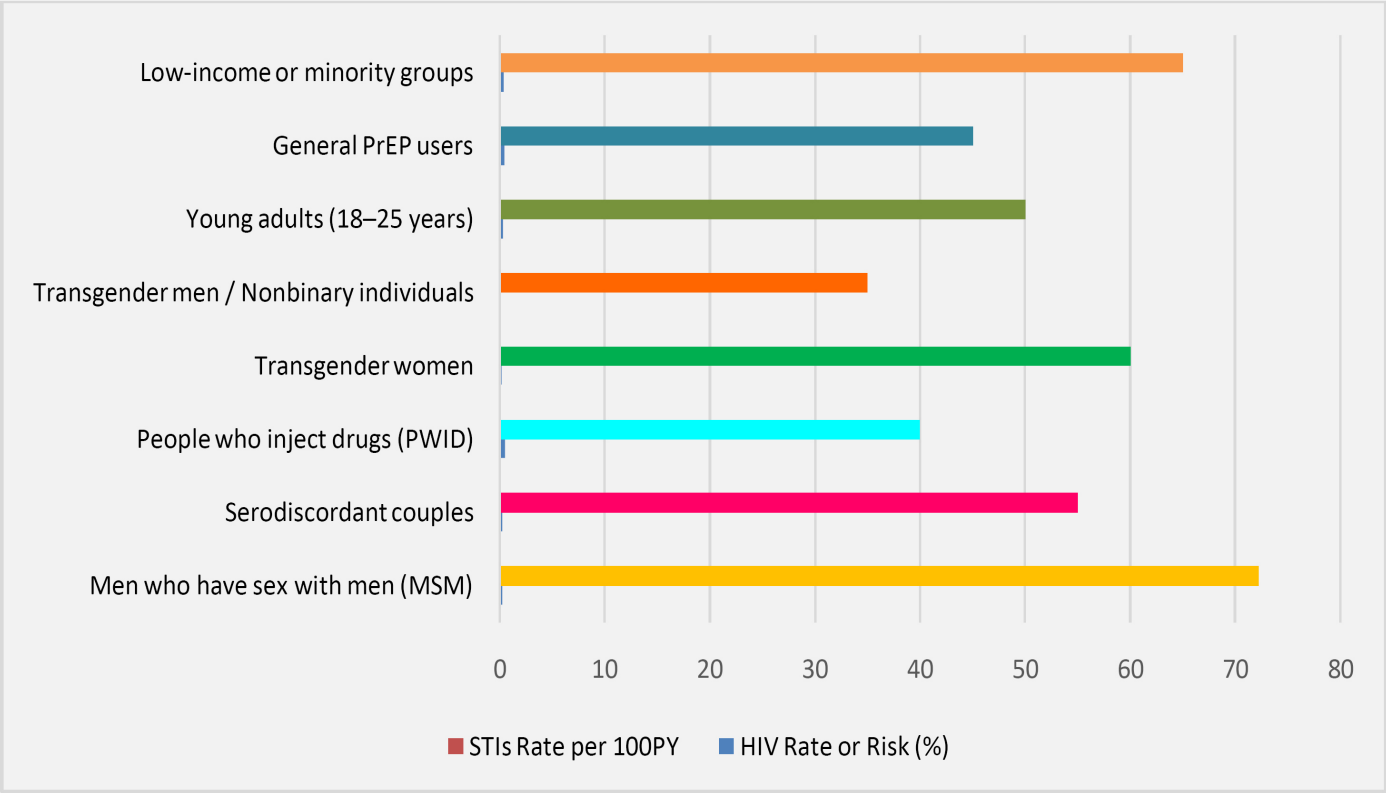

Fig. 2: HIV and Other STI Rates Among Key Populations at Elevated Risk. *This figure compares estimated HIV risk percentages and rates of other sexually transmitted infections (STIs) per 100 person-years (PY) across eight priority populations. The highest HIV and STI burdens are observed among men who have sex with men (MSM), transgender women, and low-income or minority groups, followed by serodiscordant couples and young adults (18–25 years). People who inject drugs (PWID) and transgender/ nonbinary individuals show intermediate but persistent risk patterns. The figure highlights substantial heterogeneity in overlapping epidemics, emphasizing the need for integrated PrEP adherence support and STI prevention strategies tailored to population-specific vulnerabilities.*

Differential Burden of HIV and STI Outcomes by Population Group

Figure-2 illustrates how sexually transmitted infection (STI) incidence and HIV risk vary widely across population groups, underscoring the uneven distribution of prevention benefits and unmet needs. Men who have sex with men (MSM) show the highest combined burden, with STI incidence exceeding 70 per 100 person-years and HIV risk markedly elevated without consistent PrEP adherence. Serodiscordant couples and transgender women also experience high STI rates (≈60 per 100 PY), reflecting ongoing exposure within relationships marked by viral load imbalance and gender-affirming care challenges.[41] In contrast, transgender men and nonbinary individuals report comparatively lower STI incidence (~35 per 100 PY) but remain under-represented in PrEP research. Young adults (18–25 years) and general PrEP users fall within a moderate range (≈45–50 STIs per 100 PY), yet data show that missed doses or treatment interruptions sharply increase their infection vulnerability. People who inject drugs (PWID) exhibit a distinct pattern—HIV risk remains substantial (RR ≈ 0.5) despite lower STI prevalence, likely due to parenteral rather than sexual transmission routes. Low-income and minority groups show the most complex intersection: elevated HIV and STI rates driven by cost barriers, stigma, and limited health-system trust. Collectively, the figure highlights how adherence gaps amplify biological and social disparities. Without regular PrEP use, high-risk sexual networks sustain dual epidemics of HIV and bacterial STIs—particularly among MSM, transgender women, and structurally marginalized communities.[42] This reinforces the need for tailored prevention combining biomedical adherence with behavioral and structural interventions.

Integrated Summary

Findings from the reviewed studies in Table 1 show that PrEP remains highly effective when taken consistently, yet its success in real-world settings depends on more than medication alone. Across populations, adherence emerges as the strongest predictor of protection—maintaining doses at or above 70 % reduces the risk of HIV infection by nearly three-quarters, while inconsistent use sharply weakens the benefit. Alcohol misuse, depression, and stigma frequently disrupt adherence, while broader system issues—such as provider reluctance, high costs, and structural racism—further limit uptake and continuity. Transgender and racial-minority groups face the greatest obstacles, often compounded by fear, discrimination, and lack of affirming care. Where

health systems integrate PrEP with mental-health services, substance-use counseling, and peer or telehealth support, adherence and follow-up improve noticeably. Together, these findings underscore that adherence is not merely an individual choice but the outcome of social, behavioral, and structural conditions that ultimately determine the durability of PrEP's protection and its impact on long-term HIV and STI outcomes.

DISCUSSION

The synthesis of evidence across 22 reviews confirms that PrEP remains a powerful biomedical tool against HIV acquisition, yet its real-world impact depends overwhelmingly on adherence and continuity. Across meta-analyses, daily oral PrEP reduced HIV risk by approximately 51 % relative to placebo, with a pooled risk ratio (RR) of about 0.49. When drug detection surpassed 70 %, the pooled RR dropped further to ≈ 0.30, representing nearly three-quarters risk reduction, but protection diminished sharply when adherence fell below 60 %, where the RR approached unity. This gradient highlights that pharmacologic efficacy cannot compensate for inconsistent use. Population-specific analyses reinforced this pattern: MSM and serodiscordant couples maintained RRs near 0.25, people who inject drugs ≈ 0.51, and heterogeneous heterosexual cohorts ≈ 0.77, underscoring variation in contextual and behavioral factors that sustain or erode adherence.[12] These findings collectively demonstrate that adherence is not a static behavior but a dynamic outcome influenced by daily routines, mental health, and the presence of substance use—especially alcohol.

Alcohol use emerged as one of the most pervasive and modifiable disruptors of adherence. Across behavioral-health syntheses, hazardous drinking was associated with a 25–35 % reduction in PrEP adherence. Mean adherence among participants reporting weekly binge episodes averaged ≈ 55 %, compared with ≈ 78 % in non-drinkers. Problematic alcohol consumption also reduced PrEP persistence over 12 months by ≈ 35 %, with adherence dropping from 88 % at initiation to ≈ 54 % among hazardous drinkers within one year. In some cohorts, harmful drinkers were over six times more likely to miss doses than moderate users, suggesting both behavioral impairment and fear of perceived drug–alcohol toxicity.[33] These lapses coincide with higher rates of bacterial sexually transmitted infections, particularly gonorrhea and chlamydia, where pooled incidence reached ≈ 70 per 100 person-years among MSM and transgender women using PrEP inconsistently.[30] Recurrent or multisite STIs serve as biological markers of unsustained prevention, elevating mucosal vulnerability and facilitating HIV transmission within dense sexual networks. The evidence therefore situates alcohol not only as a behavioral risk factor but as a catalyst that undermines both individual protection and population-level control of HIV and STIs.[43] HIV-related immunosuppression—especially progressive CD4 T-cell loss and impaired mucosal defenses—raises susceptibility to opportunistic and community-acquired pathogens, increasing the incidence, severity, and recurrence of infections such as tuberculosis, bacterial and Pneumocystis pneumonia, influenza and other respiratory illnesses, and invasive fungal and viral diseases[44], while also blunting vaccine responses and slowing recovery.

Psychological and neurocognitive mechanisms further explain these associations. Between 22 % and 45 % of PrEP users reported hazardous drinking, frequently accompanied by depression or post-traumatic stress symptoms, which compound forgetfulness, avoidance, and care disengagement.[14] Among cohorts with co-occurring PTSD and alcohol use, adherence fell to 45–60 %, compared with over 80 % in non-affected groups.[45] Neurobiological studies indicate that chronic stress and alcohol-induced hippocampal changes impair executive functioning, reducing capacity for consistent dosing.[8] Qualitative syntheses deepen this picture: stigma-driven drinking was repeatedly described as both a coping mechanism and a source of guilt, particularly among MSM and racial-minority groups. Over 50 % of participants in some studies cited stigma or healthcare mistrust as deterrents to regular clinic attendance. These findings clarify that alcohol is rarely an isolated barrier; it operates within a syndemic web of psychological distress, stigma, and social disadvantage that collectively depress adherence.[46]

The structural and clinical environment can either mitigate or magnify these vulnerabilities. Roughly 60 % of providers report limited confidence in prescribing PrEP, and fewer than 40 % have ever done so. Financial and logistical barriers compound the gap: co-pays, prior authorizations, and medication costs frequently interrupt continuity, while out-of-pocket expenses above low thresholds precipitate discontinuation. Such constraints are especially consequential for populations already bearing disproportionate HIV burdens. [47] Among Black MSM, medical mistrust explains nearly 25 % of the variance in PrEP willingness and corresponds to ≈ 40 % lower likelihood of persistence. Housing instability and incarceration more than double discontinuation odds, while transgender women—despite awareness rates up to 66 %—report actual use under 10 %, largely due to cost, fear of mistreatment, and uncertainty regarding interactions with feminizing hormones.[37] Although pharmacologic data suggest only modest (~15 %) reductions in intracellular drug levels without clinical significance, perceived incompatibility suppresses uptake.[25] Structural and cultural competence gaps thus translate into measurable differences in adherence, with alcohol use often intensifying these inequities by eroding motivation, self-efficacy, and trust.

The intersection between PrEP adherence and other STIs reveals the broader implications of these patterns. Elevated STI detection among PrEP users can signal both improved screening and genuine behavioral risk. When adherence

fluctuates, temporary loss of PrEP's protective effect allows HIV and bacterial pathogens to exploit the same high-risk moments. Integrated programs that maintain quarterly STI testing, reinforce adherence counseling, and promptly treat infections reduce secondary transmission and long-term complications such as pelvic inflammatory disease or complicated syphilis.[42] Quantitatively, integrating PrEP with comprehensive STI management in programmatic models has been shown to avert up to one-third of projected new HIV infections among young adults over a decade, assuming adherence above 70 %. In people who inject drugs, coupling PrEP with opioid-substitution therapy improved adherence by about 20 %, confirming that coordinated harm-reduction approaches yield synergistic protection.[12] These findings collectively emphasize that biomedical prevention cannot be siloed; adherence thrives when HIV, STI, mental-health, and substance-use services operate as an integrated continuum.

Biological mechanisms also illuminate part of the adherence deficit observed among individuals who drink. Heavy alcohol consumption is consistently linked to gastrointestinal dysbiosis and mucosal inflammation, which manifest as nausea or abdominal discomfort—symptoms often misattributed to medication intolerance.[18] Across reviewed studies, ≈ 55–65 % of alcohol-using participants reported gastrointestinal side effects, and ≈ 45 % cited these as reasons for missed doses or discontinuation.[37] Alcohol's immunologic effects further heighten systemic inflammation, as indicated by elevated C-reactive protein and interleukin-6 levels, potentially influencing both susceptibility to infection and perceived treatment burden.[48] Thus, the biological, behavioral, and structural domains interact in reinforcing cycles: alcohol alters physiology, provokes discomfort or concern, fosters avoidance, and in turn amplifies the likelihood of infection and reinfection.[49]

Programs that address these interlocking determinants demonstrate tangible success. Multicomponent interventions—combining brief alcohol counseling, peer navigation, text-based adherence reminders, and telehealth follow-up—have raised adherence levels by 15–25 % and improved persistence at 12 months.[30] Event-based dosing and long-acting injectable PrEP formulations show promise for individuals with intermittent risk exposure or unstable routines, although their accessibility remains uneven. Implementation data suggest that if 40 % of at-risk youth sustain adherence above 60 %, national HIV incidence could fall by nearly one-third within a decade.[30] These projections illustrate how modest behavioral improvements yield substantial epidemiologic gains when reinforced by structural support. Importantly, such strategies must be embedded within trauma-informed and culturally responsive care frameworks to ensure they reach populations most constrained by stigma or systemic barriers.

This review offers notable strengths. It synthesizes quantitative effect sizes and qualitative insights across 22 review-level studies encompassing ≈ 3.8 million participants across six continents, integrating biomedical, psychosocial, and structural dimensions rarely analyzed together. By consolidating evidence from MSM, transgender women, adolescents, and people who inject drugs, it provides a panoramic account of how alcohol undermines adherence and sustains dual epidemics of HIV and STIs.[50] The inclusion of severity outcomes—such as recurrent or multisite infections and elevated initial viral loads—extends the conversation beyond incidence to encompass clinical course and health-system implications. Furthermore, the analysis draws attention to under-examined biological mechanisms, including gut-microbiome dysbiosis and systemic inflammation, and situates them within psychosocial and economic contexts that determine real-world PrEP effectiveness.

Nevertheless, limitations must be acknowledged. Methodological quality varied across the included reviews, and several relied heavily on self-reported alcohol use or short recall periods, which can underestimate consumption and overestimate adherence. Definitions of "hazardous drinking" and "adequate adherence" were inconsistent, complicating cross-study comparisons. Overlap among primary studies introduced potential duplication of findings, and heterogeneity in outcome reporting limited meta-analytic precision. The majority of data originated from high-income countries, restricting generalizability to low- and middle-income settings where resource constraints, cultural norms, and stigma may interact differently with alcohol use. Finally, objective biomarkers of alcohol exposure or adherence, such as phosphatidylethanol testing or tenofovir diphosphate levels—were infrequently employed, leaving gaps in causal inference regarding biological pathways and behavioral triggers.

Future research should advance along several pragmatic directions. First, longitudinal studies employing both biochemical and behavioral adherence measures are needed to delineate dose–response relationships between drinking intensity and prevention outcomes. Second, randomized or hybrid effectiveness-implementation trials should evaluate combined interventions that integrate alcohol-reduction counseling, mental-health care, and flexible PrEP delivery—including long-acting injectable options—within primary and community settings. Third, equity-oriented program designs must explicitly include transgender, sex-worker, and racial-minority populations, whose adherence challenges are amplified by stigma and structural exclusion. Lastly, public health infrastructure should institutionalize brief alcohol screening within HIV prevention services, supported by digital adherence tools, machine-learning risk identification, and patient-centered pathways for rapid restart after lapses. Through these innovations, prevention programs can move beyond theoretical efficacy to achieve durable, equitable outcomes that reduce both HIV and STI burdens globally.

CONCLUSION

This umbrella review underscores that the effectiveness of PrEP in preventing HIV and other sexually transmitted infections depends less on its pharmacologic potential than on the social, behavioral, and structural conditions that enable sustained adherence. Across diverse populations, hazardous alcohol use, depression, and stigma consistently weaken adherence and continuity of care, while provider hesitancy, fragmented systems, and inequitable access further compound these risks. The findings reaffirm that maintaining adherence above roughly 70% preserves the majority of PrEP's protective effect, whereas lapses linked to alcohol or psychosocial distress leave substantial residual vulnerability. Future research should move beyond documenting adherence loss to testing integrated, real-world interventions that combine alcohol-use reduction, mental-health support, and long-acting PrEP delivery within inclusive, low-barrier care models. Building such adaptive, equity-focused systems will be essential to translating biomedical efficacy into durable population-level protection and closing the remaining gaps in HIV and STI prevention.

Acknowledgments

The authors gratefully thank *Dr. M. A. Yusuf* and *Dr. R. Davidson* for their valuable guidance and critical feedback throughout the development of this review.

REFERENCES

1. Stultz A, Chang S-H, Wilson DL, et al. HIV Pre-Exposure Prophylaxis Care Continuum in Outpatient Settings: A Systematic Review and Meta-Analysis. *AJPM Focus* 2025: 100433.
2. Seyedroudbari S, Ghadimi F, Grady G, et al. Assessing Structural Racism and Discrimination Along the Pre-exposure Prophylaxis Continuum: A Systematic Review. *AIDS Behav* 2024; 28: 3001-3037. 20240608. DOI: 10.1007/s10461-024-04387-y.
3. Nguyen VK, Greenwald ZR, Trottier H, et al. Incidence of sexually transmitted infections before and after preexposure prophylaxis for HIV. *Aids* 2018; 32: 523-530. DOI: 10.1097/qad.0000000000001718.
4. Pleuhs B, Quinn KG, Walsh JL, et al. Health care provider barriers to HIV pre-exposure prophylaxis in the United States: a systematic review. *AIDS patient care and STDs* 2020; 34: 111-123.
5. Paula AA, Schechter M, Tuboi SH, et al. Continuous Increase of Cardiovascular Diseases, Diabetes, and Non-HIV Related Cancers as Causes of Death in HIV-Infected Individuals in Brazil: An Analysis of Nationwide Data. *PLOS ONE* 2014; 9: e94636. DOI: 10.1371/journal.pone.0094636.
6. Hasan MR. Understanding Diabetes Care Barriers Through Community Voices: A Brief Qualitative Report from Jefferson County, Kentucky. *Asian Journal of Public Health and Nursing* 2025; 2: 1-7.
7. Hasan MR, W. Parker F, Harrison A, et al. Alcohol-Induced Microbial Dysbiosis and Psychosocial Stressors Undermining PrEP Adherence: A Mixed Methods Analysis in HIV-Negative African American Adults. *American Journal of Human Psychology* 2025; 3: 161-182. DOI: 10.54536/ajhp.v3i1.5715.
8. Hess KL, Chavez PR, Kanny D, et al. Binge drinking and risky sexual behavior among HIV-negative and unknown HIV status men who have sex with men, 20 US cities. *Drug and alcohol dependence* 2015; 147: 46-52.
9. Shuper PA, Joharchi N, Bogoch, II, et al. Alcohol consumption, substance use, and depression in relation to HIV Pre-Exposure Prophylaxis (PrEP) nonadherence among gay, bisexual, and other men-who-have-sex-with-men. *BMC Public Health* 2020; 20: 1782. 20201125. DOI: 10.1186/s12889-020-09883-z.
10. Hasan MR and Yusuf MA. Microbial Dysbiosis in Diabetic Children with Enteric Hepatitis: The Global Phenomenon and Bangladesh's Contextual Significance. *Bangladesh Journal of Infectious Diseases* 2023; 10: 56-58.
11. Fulcher JA, Li F, Cook RR, et al. Rectal Microbiome Alterations Associated With Oral Human Immunodeficiency Virus Pre-Exposure Prophylaxis. *Open Forum Infect Dis* 2019; 6: ofz463. 20191029. DOI: 10.1093/ofid/ofz463.
12. Shiau S, Arpadi SM, Yin MT, et al. Patterns of drug use and HIV infection among adults in a nationally representative sample. *Addictive behaviors* 2017; 68: 39-44.
13. Murchu EO, Marshall L, Teljeur C, et al. Oral pre-exposure prophylaxis (PrEP) to prevent HIV: a systematic review and meta-analysis of clinical effectiveness, safety, adherence and risk compensation in all populations. *BMJ open* 2022; 12: e048478.
14. Hasan MR, Mclessey L, Haque A, et al. A Multilevel Perspective on PrEP Adherence in HIV Prevention: An Integrative Review Guided by the Socioecological Model. *British Journal of Nursing Studies* 2025; 5: 23-43.
15. Ong JJ, Baggaley RC, Wi TE, et al. Global Epidemiologic Characteristics of Sexually Transmitted Infections Among Individuals Using Preexposure Prophylaxis for the Prevention of HIV Infection: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2019; 2: e1917134. 20191202. DOI: 10.1001/jamanetworkopen.2019.17134.
16. Oldfield BJ and Edelman EJ. Addressing Unhealthy Alcohol Use and the HIV Pre-exposure Prophylaxis Care Continuum in Primary Care: A Scoping Review. *AIDS*

Behav 2021; 25: 1777-1789. 20201120. DOI: 10.1007/s10461-020-03107-6.

17. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; 6: e1000097. 20090721. DOI: 10.1371/journal.pmed.1000097.
18. Hennessy EA and Johnson BT. Examining overlap of included studies in meta-reviews: Guidance for using the corrected covered area index. *Res Synth Methods* 2020; 11: 134-145. 20191210. DOI: 10.1002/jrsm.1390.
19. Perry R, Whitmarsh A, Leach V, et al. A comparison of two assessment tools used in overviews of systematic reviews: ROBIS versus AMSTAR-2. *Syst Rev* 2021; 10: 273. 20211025. DOI: 10.1186/s13643-021-01819-x.
20. Grabovac I, Veronese N, Stefanac S, et al. Human Immunodeficiency Virus Infection and Diverse Physical Health Outcomes: An Umbrella Review of Meta-analyses of Observational Studies. *Clin Infect Dis* 2020; 70: 1809-1815. DOI: 10.1093/cid/ciz539.
21. Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *Aids* 2016; 30: 1973-1983. DOI: 10.1097/qad.0000000000001145.
22. Smith CJ, Ryom L, Weber R, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D: A: D): a multicohort collaboration. *The Lancet* 2014; 384: 241-248.
23. Ng BE, Moore D, Michelow W, et al. Relationship between disclosure of same-sex sexual activity to providers, HIV diagnosis and sexual health services for men who have sex with men in Vancouver, Canada. *Can J Public Health* 2014; 105: e186-191. 20140416. DOI: 10.17269/cjph.105.4212.
24. Hevey MA, Walsh JL and Petroll AE. PrEP Continuation, HIV and STI Testing Rates, and Delivery of Preventive Care in a Clinic-Based Cohort. *AIDS Educ Prev* 2018; 30: 393-405. DOI: 10.1521/aeap.2018.30.5.393.
25. Strong SH, Oldfield BJ, van den Berg JJ, et al. Perspectives on unhealthy alcohol use among men who have sex with men prescribed HIV pre-exposure prophylaxis: A qualitative study. *Prev Med Rep* 2024; 37: 102553. 20231210. DOI: 10.1016/j.pmedr.2023.102553.
26. Hasan MR. Mental Health Challenges in Bangladesh Based on the Integrated Examination of Illicit Drug Use, Substance Abuse, Tobacco Consumption, and Escalating Suicidal Tendencies: A Comprehensive Review. *Bangladesh Journal of Infectious Diseases* 2024; 11: 65-70.
27. Pandrea I, Happel KI, Amedee AM, et al. Alcohol's role in HIV transmission and disease progression. *Alcohol Res Health* 2010; 33: 203-218.
28. Mayer KH, Agwu A and Malebranche D. Barriers to the Wider Use of Pre-exposure Prophylaxis in the United States: A Narrative Review. *Adv Ther* 2020; 37: 1778-1811. 20200330. DOI: 10.1007/s12325-020-01295-0.
29. Fusco N, Sils B, Graff JS, et al. Cost-sharing and adherence, clinical outcomes, health care utilization, and costs: A systematic literature review. *J Manag Care Spec Pharm* 2023; 29: 4-16. 20220407. DOI: 10.18553/jmcp.2022.21270.
30. Miller SJ, Harrison SE and Sanasi-Bhola K. A Scoping Review Investigating Relationships between Depression, Anxiety, and the PrEP Care Continuum in the United States. *Int J Environ Res Public Health* 2021; 18 20211030. DOI: 10.3390/ijerph182111431.
31. Jin G, Shi H, Du J, et al. Pre-exposure prophylaxis care continuum for HIV risk populations: An umbrella review of systematic reviews and meta-analyses. *AIDS Patient Care and STDs* 2023; 37: 583-615.
32. Kabir R, Vinnakota D, Dehghani L, et al. HIV and Violence among Female Sex Workers in India: A Scoping. *Women's Health Problems: A Global Perspective* 2024; 3.
33. Hasan MR and Davidson R. Understanding Barriers to PrEP Adherence: A Brief Report on the Combined Effects of Alcohol Misuse, PTSD, and Gut Microbiome Disruption in HIV Prevention. *Asian Journal of Public Health and Nursing* 2025; 2: 14-27.
34. Hess KL, Chavez PR, Kanny D, et al. Binge drinking and risky sexual behavior among HIV-negative and unknown HIV status men who have sex with men, 20 US cities. *Drug Alcohol Depend* 2015; 147: 46-52. 20141223. DOI: 10.1016/j.drugalcdep.2014.12.013.
35. Dang M, Scheim AI, Teti M, et al. Barriers and facilitators to HIV pre-exposure prophylaxis uptake, adherence, and persistence among transgender populations in the United States: a systematic review. *AIDS Patient Care and STDs* 2022; 36: 236-248.
36. Hasan MR. Assessing the Psychosocial Determinants of Mental Health Decline Among Bangladeshi University Students During the COVID-19 Pandemic: A Rapid Systematic Review. *Asian Journal of Public Health and Nursing* 2024; 1.
37. Fontanari AMV, Zanella GI, Feijo M, et al. HIV-related care for transgender people: A systematic review of studies from around the world. *Social science & medicine* 2019; 230: 280-294.
38. Losina E, Schackman BR, Sadownik SN, et al. Racial and sex disparities in life expectancy losses among HIV-infected persons in the united states: impact of risk behavior, late initiation, and early discontinuation of antiretroviral therapy. *Clin Infect Dis* 2009; 49: 1570-1578. DOI: 10.1086/644772.

39. Koester KA, Erguera XA, Udoh I, et al. Exploring the Shift From HIV Pre-exposure Prophylaxis Awareness to Uptake Among Young Gay and Bisexual Men. *Front Public Health* 2021; 9: 677716. 20211207. DOI: 10.3389/fpubh.2021.677716.

40. Hasan MR. Exploring the Relationship Between Opioid Use Disorder and Major Depressive Disorder: A Case Study from Kentucky of United States. *Journal of Current and Advance Medical Research* 2024; 11: 50-55.

41. Poteat T, Wirtz AL, Radix A, et al. HIV risk and preventive interventions in transgender women sex workers. *Lancet* 2015; 385: 274-286. 20140722. DOI: 10.1016/s0140-6736(14)60833-3.

42. Wilkerson AM, Tao J and Chan PA. Sexually Transmitted Infections and Risk of Human Immunodeficiency Virus Transmission. *Curr HIV/AIDS Rep* 2025; 22: 40. 20250702. DOI: 10.1007/s11904-025-00749-w.

43. High KP, Brennan-Ing M, Clifford DB, et al. HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. *JAIDS Journal of Acquired Immune Deficiency Syndromes* 2012; 60: S1-S18.

44. RH M, WHITNEY R, SAIFUR R, et al. A comprehensive review on antimicrobial resistance in uropathogens isolated from ICU patients in the south-east asian region. *INTERNATIONAL JOURNAL* 2025; 14: 527-542.

45. Chakrapani V, Newman PA, Shunmugam M, et al. Syndemics of depression, alcohol use, and victimisation, and their association with HIV-related sexual risk among men who have sex with men and transgender women in India. *Global public health* 2017; 12: 250-265.

46. Avanceña ALV, Okoye G, Yokananth R, et al. Alcohol Use Disorder Diagnoses Among Individuals Who Take HIV Preexposure Prophylaxis. *JAMA Netw Open* 2025; 8: e257295. 20250401. DOI: 10.1001/jamanetworkopen.2025.7295.

47. Kiggundu R, Soh QR, Tieosapjaroen W, et al. Restarting pre-exposure prophylaxis (PrEP) for HIV: a systematic review and meta-analysis. *EClinicalMedicine* 2024; 72.

48. Deeks SG, Overbaugh J, Phillips A, et al. HIV infection. *Nature reviews Disease primers* 2015; 1: 1-22.

49. Yun JA, Jeong KS, Ahn YS, et al. The Interaction of Inflammatory Markers and Alcohol-Use on Cognitive Function in Korean Male Firefighters. *Psychiatry Investig* 2021; 18: 205-213. 20210310. DOI: 10.30773/pi.2020.0101.

50. Willie TC, Kershaw TS, Blackstock O, et al. Racial and ethnic differences in women's HIV risk and attitudes towards pre-exposure prophylaxis (PrEP) in the context of the substance use, violence, and depression syndemic. *AIDS care* 2021; 33: 219-228.

Citation: Md Rakibul Hasan, Akidul Haque, et al., "Investigating the Impact of Alcohol Use on PrEP Adherence and the Burden of HIV and Other Sexually Transmitted Infections: An Umbrella Review", American Research Journal of Biosciences, Vol 10, no. 1, 2025, pp. 1-20.