PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH
A Global Journal of Clinical Research

Barriers to HIV Pre-Exposure Prophylaxis Use Among Women in the US: A Systematic Literature Review

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Abstract

Introduction: *The high acquisition rate of HIV infection among women in the United States is concerning. Despite the FDA approving the first pre-exposure prophylaxis (PrEP) drug in 2012, PrEP utilization remains significantly lower among women. This literature review aims to analyze the current body of research concerning HIV PrEP usage among women in the US.*

Methods: *A search of three medical databases was conducted. After the screening, 19 studies were selected for analysis. A risk of bias assessment was performed.*

Results: *A final set of records meeting the inclusion criteria (n=19) was included in the review for data collection and analysis. The study methodology for these research articles included interview-based designs (semi-structured and brief formats) in 1-on-1 meetings, focus groups, surveys, and retrospective data analysis. Participants' HIV risk characteristics were reported by way of sexual behavior, drug use, combined sexual behavior and drug use, and living in a high HIV rate neighborhood. Nineteen themes were identified and organized into three categories: (1) Common medication administration barriers, (2) PrEP-specific barriers, and (3) Situational barriers. The three most common themes reported by participants included a concern about side effects, low perceived risks of HIV, and lack of PrEP information. The CASP Qualitative Checklist and risk assessment summary showed acceptable validity among studies.*

Discussion: *This review identifies significant barriers hindering women's PrEP utilization, which would benefit from more prevalent stakeholder communication and education directed to at-risk populations. Inconsistently reported descriptive data on participants and the low patient populations make it difficult to generalize outcomes.*

Introduction

Pre-exposure prophylaxis (PrEP) is a novel biomedical advancement used in high-risk Human Immunodeficiency Virus (HIV) uninfected individuals for the prevention of HIV (Desai et al., 2017). PrEP can reduce the risk of acquisition of sexually transmitted HIV infection by more than 90% in HIV-negative individuals at risk of acquiring the infection (Chan et al., 2020). Although the prognosis for HIV has evolved into that of a chronic illness over the past two decades, the burdens associated with the chronic condition of HIV and its treatment effects remain significant, underscoring the heightened importance of prevention.

Women can bear a particularly difficult burden when forced to live with HIV. It has been reported that this patient population frequently encounters difficulties in navigating stigma related to gender-specific roles and identities while facing ongoing health and psychosocial hurdles. Their health histories from the time of the HIV diagnosis are often characterized by fluctuating between managing health issues and coping with the psychosocial burdens of the disease (Herron et al., 2022). Women with HIV also exhibit a greater prevalence of non-AIDS comorbidities that continue later into life, such as psychiatric illness, liver disease, dyslipidemia, bone disease, chronic kidney disease, and non-acquired immunodeficiency syndrome (AIDS) related cancer compared to those without HIV. The magnitude of disease burdens on women with HIV renders it vitally important for at-risk women to implement a PrEP treatment for prevention (Collins et al., 2021).

*Corresponding author: alenemathurin@gmail.com
Received: September 28, 2023 **Accepted:** February 20, 2024
Published: April 16, 2024
Editor: Felipe Fregni
Reviewers: Giovani Farina, Viviana Ugenti
Keywords: pre-exposure prophylaxis, women, HIV prevention, barriers
DOI: http://dx.doi.org/10.21801/ppcrj.2024.101.4

Although there is significant potential for reducing the risk of HIV infection, the adoption of PrEP among women in the US remains substantially lower compared to men (Goparaju et al., 2017).

The burden of HIV on women is not restricted to any specific race or ethnicity. Data from 2018 concerning the race/ethnicity concerning female PrEP users reveals that 25.9% were Black, 48.3% were White, and 17.5% were Hispanic (Huang et al., 2018). Among females diagnosed with HIV, Black women constituted 58% of the HIV diagnoses, while White women accounted for 21% and Hispanics 17%. These findings indicate that Black women represent the largest proportion of HIV diagnoses, yet their utilization of PrEP lags behind that of White women (Centers for Disease Control and Prevention, 2018). According to the same 2018 Centers for Disease Control and Prevention HIV surveillance report, it was observed that the Southern region of the United States reported the highest number of HIV infection diagnoses among female adults and adolescents, with a total of 3,988 cases (Centers for Disease Control and Prevention, 2018). The rates of HIV infection diagnoses were particularly elevated among Black/African American females in the South, with a rate of 24.6 per 100,000 population. The data analysis from the same report revealed that White females in the Southern region also accounted for a significantly higher rate of HIV infection diagnoses compared to other regions (Centers for Disease Control and Prevention, 2018).

The diverse burden of HIV infection among females in the United States, coupled with the low uptake of PrEP treatment, calls for a better understanding of themes surrounding the barriers to PrEP uptake. This systematic review aims to identify, organize, and analyze the current body of research designed to identify themes and barriers to PrEP use among women in the US.

Materials and Methods

Despite the fact that this was not a full Systematic Review and Meta-Analysis, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to guide this literature review process (Page et al., 2021). A search of literature databases included PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Cochrane, which covered studies published from 2018 to February 2024. A combination of thesaurus and MeSH terms relating to the three primary concepts of the research (thematic barriers to adherence or implementation of a medication, PrEP treatment for HIV prevention, and women) were developed to identify relevant articles. The following research question was generated to serve as the reference for search syntax development and primary analysis: What are the (1) thematic barriers to (2) PrEP use among (3) women in the United States?

The primary aim of this study was to investigate themes and barriers impeding the utilization of Pre-Exposure Prophylaxis (PrEP) among women. To achieve this, the research relied on peer-reviewed publications reporting on studies investigating barriers to PrEP use authored by independent researchers. Descriptive statistics and data specific to the research question were systematically identified and organized from these peer-reviewed studies in a process that best aligned with relevant guidelines outlined in the (PRISMA) framework (Page et al., 2021). A protocol for this review was not registered with PROSPERO.

Eligibility Criteria

Full-text English language qualitative studies in the form of one-on-one structured interviews, focus groups, or surveys with participant populations of 10 subjects or more were included in this review. Eligible studies included articles published in the United States between 2018 and February 5, 2024. Articles investigating thematic barriers to either initial or continued use of PrEP for adults, age 18 years or older, and females assigned at birth population were the primary focus for inclusion during the title and abstract review process. Studies reporting on populations relating to men or transgender women or investigating populations outside the United States were excluded from the review. Studies reporting mixed populations of women, men, transgender women, or ages less than 18 were excluded if the results did not delineate outcomes from the group included in this research. Studies with a mixed method approach to reporting barriers were included only if methods and results reported focused on participant data derived from the intended or actual PrEP user. This research did not include assumptions or perspectives of stakeholders, including interviewers, health care providers, or social workers.

Search Strategy and Study Selection

Health sciences literature databases, including PubMed, CINAHL, and Cochrane, were searched for studies that met the eligibility criteria. Search syntax included a combination of Medical Subject Heading (MeSH) Terms and keywords that defined PrEP, the patient population, and barriers. The search syntax was as follows:

1: PrEP OR pre-exposure prophylaxis OR emtricitabine-tenofovir disoproxil fumarate OR

tenofovir disoproxil fumarate OR tenofovir or TDF
2: Women or females OR ciswomen
3: Search #1 AND Search #2
4: Barriers OR motivation OR decision-making
5: Search #3 AND Search #4

Review Protocol

All identified literature meeting the predefined search criteria underwent initial processing in EndNote to eliminate duplicates, and two authors from the research team reviewed the titles and abstracts for inclusion and exclusion criteria.

Following the title and abstract screening, the authors reviewed discrepancies in the included articles as a team and agreed on a final selection of full-text articles for review. Subsequently, a comprehensive full-text review of selected studies was conducted by the three-member research team. This process aimed to assess the alignment of each study to the research topic. The data extraction for this study was organized using an Excel spreadsheet. Data related to risk factors associated with PrEP uptake were documented on study characteristics, participant characteristics, study outcomes, and risk of bias.

Data Collection

Two authors were involved in the data collection process. The first reviewed the identified articles, extracting descriptive data encompassing study characteristics, which included data on methods and descriptive data on the study parameters, participant demographics, and barriers to PrEP utilization—the second validated the data collected after the completion of data extracted. The data was categorized into four tables: Study Characteristics, Participant Characteristics, and Barriers to PrEP. This was designed to ensure a cross-verification process was conducted to enhance accuracy and reliability.

Data Analysis

Once the standardized data set was collected from each study, including authors, title, year of publication, region, location, study design, study description methods, patient characteristics (total number of patients, average age, diversity of study participants, and the ethnicity of study participants). A descriptive analysis of the findings was conducted. Key findings were related to the identification of barriers to PrEP use.

Risk of Bias

The identified studies were analyzed according to their quality standards by nine questions in the Critical Appraisal Skills Programme (CASP) qualitative checklist (Ma et al., 2020). One author answered each of the questions for each article independently and recorded answers in an Excel table as either "N" (No), "Y" (Yes), "M" (Maybe/unclear), or "NA" (not applicable). Two authors reviewed responses and reported inconsistencies, which were resolved through a discussion with the three authors reviewing the responses.

Results

Search Results

The initial database search identified 911 records for title abstract review. Five duplicate articles were removed, resulting in 906 records for screening. After conducting a title and abstract screening, 860 records were excluded from the initial search. The remaining 46 records were sought for full-text retrieval to be assessed for eligibility. An additional 27 articles were excluded due to access limitations or inability to meet inclusion criteria. A final set of records meeting the inclusion criteria (n=19) was included in this systematic review for data collection and analysis to answer the research question (Figure 1 for PRISMA Flow Diagram).

Study Characteristics

Eligible articles (n=19) included 18 studies with 1754 participants across 11 different states; 2 studies noted it was online without any states involved, and 1 study denotes the New England region. Two of the 19 studies were collected as independent records. However, their data were merged and reported as one because they were articles that reported results from the same research and participant population but reported responses that occurred six months apart. (Nydegger, 2021a; Nydegger, 2021b). For this reason, the total count of studies is 18, while the records identified are 19.

Methodologies across studies included interview-based designs such as semi-structured and brief formats in either 1-on-1 meetings and focus group settings (n=14), surveys (n=3, and retrospective data (n=2). The mixed method study included a semi-structured interview and a survey, both in the individual counts (Amico et al., 2019). Semi-structured interview timeframes (n=10) ranged from 30-120 minutes, whereas the brief format interview (n=1) lasted 5-10 minutes. The interview-based designs were reported to be implemented between

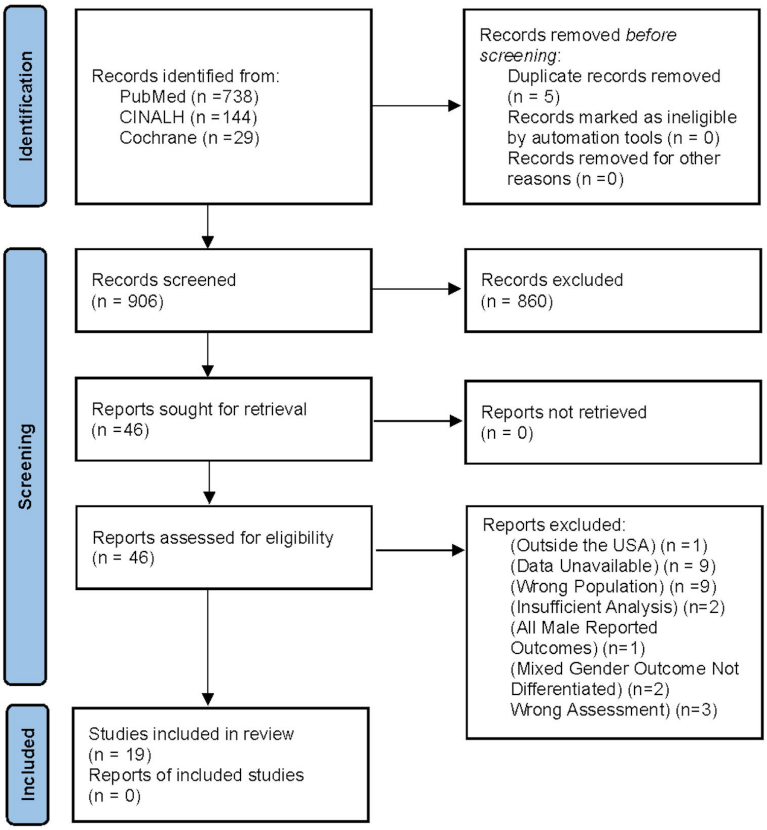

Figure 1: *PRISMA Flowchart of the article selection process.*

2013 and 2019. Survey, interview, and focus group participants were recruited from high-risk community-based organizations (n=6); family planning clinics (n=2), drug treatment centers (n=2), judicial programs (n=2), intimate partner violence organizations (n=2), and previous PrEP research participants (n=2). The retrospective data research was found through a national survey (n=1) and Facebook comments data (n=1), (Table 1 - Study Characteristics).

Participant Characteristics

Participant characteristics were generally inconsistent across studies. All studies included a female assigned at birth-only population (n=19). While various descriptive statistics on participants were listed in a percentage of the studies, none were represented. Participant characteristics included categories such as Age Range (n=13), Age Average (n=15), ethnicity (Hispanic/Latino, Non-Hispanic) (n=12), Race (Black, White, Asian, Native American) (n=14), Educational Status (n=10), HIV Risk Factor (n=18), and PrEP uptake or prescription status (n=16). One study included mixed methods, using both a survey and semi-structured interviews. Data reported from this study was inconsistent, where descriptive statistics excluded 3 of the 133 participants because they only participated in the interviews and not the surveys (Amico et al., 2019), (Table 2 - Participant Characteristics).

All participants were 18 and older across studies reporting age range. Two reported studies focused on younger women, requiring an age limit of 26 years old for inclusion (Bond et al., 2022; Pratt et al., 2022). The average age across studies reporting this statistic was as young as 22 and as old as 44. Ethnicity was reported in 12 studies, where a Hispanic/Latino population was represented in 8 of them. Of the 14 studies reporting on race, Blacks were represented in 100% of them (n=14); Whites were represented in 50% (n=7); Multiracial groups were represented in 28.5% (n=4); Native Americans and Asians were represented in 21.4% (n=3) for both; the category for "other" was represented in 28.5% (n=4). Studies reporting educational backgrounds (n9) for the participants include categories such as less than high school, high school graduate, some college, bachelor's, or graduate degree.

Participants HIV risk characteristics were included in studies (n=18) by way of sexual behavior alone (n=9), drug use alone (n=2), both sexual behavior and drug use (n=3), and high HIV rate neighborhood (n=3). PrEP uptake status was reported in studies

Author	Year	Study type - Main data collection methods	Data extracted or participants recruited from	City or state	# Participants	Lenght of study	Interview (minutes)	Trained interviewer
		Mixed Methods	Previous Research Study	Nationwide	n=133		NA	N/A
Amico [1]	2019	Survey		NJ, NY, NC	130	2013-2015	90	Yes
		Semi Structured Interview			26			
Bond	2022	Focus Group Interview	At Risk Community based Outreach	NY City	26	2016-2017	120	Yes
Braksmajer	2019	Semi Structured Interview	Intimate Partner Violence Program	NY State	26	2015-2016	32-110	Yes
Calabrese	2018	Survey	Family Planning Clinic	Connecticut	597	2017	NA[2]	NA
Felsher	2021	Semi Structured Interview	Drug Clinic	Philadelphia	23	2018-2019	60	Unclear
Hill	2021	Brief Interview	At Risk Community Based Outreach	N. Carolina	53	2018	5 to 10	Unclear
Hill	2018	Retrospective Data	Facebook Comments	Online	131	2015	NA	NA
Johnson	2020	Survey	Family Planning Clinic	Chicago	109	2018	NA	NA
Nydegger[3]	2021	Semi Structured Interview	At Risk Community Based Outreach	Milwaukee	30	2016-2018	30-120	Yes
Nydegger	2021							
Ojikuto	2020	Retrospective Data	NSHBC -National Survey on HIV in the Black (	Online	347	2016	NA	NA
Pratt	2022	Semi Structured Interview	At Risk Community Based Outreach	Alabama	12	unclear	60	Yes
Pryzbyla	2020	Semi Structured Interview	Judicial System	Buffalo, NY	31	2019	Unclear	Unclear
Pyra	2022	Semi Structured Interview	At Risk Community Based Outreach	Chicago	112	2015-2019	NA	NA
Qin	2020	Semi Structured Interview	Drug Clinic	New England	20	unclear	60	Yes
Ramsey	2021	Semi Structured Interview	Judicial System	Rhode Island	21	2017-2018	60-90	Yes
Troutman	2023	Focus Group Interview	Previous Research Study	S. Carolina	27	unclear	90	Yes
Willie	2020	Semi Structured Interview	Intimate Partner Violence Program	Connecticut	19	2018	30-90	Unclear
Willie	2022	Focus Group Interview	At Risk Community Based Outreach	Mississippi	37	2019	Unclear	Yes

[1] Amico study participants in the surveys and interviews overlap. 23 of the 26 interview participants also completed the survey. The 3 remaining participants for the interviews did not complete the survey because the because the dropped out of the PrEP interventional study. See participant# column (n=133)

[2] NA=Not Applicable to this study design.

[3] Nydegger articles cover the same 6-month longitudinal study with the same study population and same methods. The first article covers early interviews, and the 2nd Article covers later interviews. Results are merged.

Table 1: *Study Characteristics.*

(n=16) between 2 categories: those who have taken or been prescribed PrEP (n=3) and those who have not taken or been prescribed PrEP (n=13).

Study Outcomes

Study outcomes focused on two approaches to understanding barriers to PrEP: themes relating to perceived barriers by potential PrEP users (n=15) and actual barriers for PrEP users (n=3). Nineteen different "barrier to PrEP" themes were identified and organized into three categories: (1) Common medication administration barrier themes (n=5), (2) PrEP-specific barrier themes (n=7), and (3) Situational barrier themes (n=7). Common medication administration barriers focus on barriers consistent with common medication administration (cost of medication/no insurance, side effects, competing demands, lack of established routine, and missed dosing); PrEP-specific barriers relate to circumstances that connect to either HIV or the risk factors that would lead to uptake (low perceived risk of HIV, uncertainty about access and efficacy of PrEP, stigma, lack of PrEP information or awareness, medical mistrust, fear of partner rejection, and HIV, not a priority). Finally, situational barriers address the personal experiences of the participant that may affect PrEP uptake (Drug addiction needs, homelessness, need for money, lack of institutional support, a belief in untested alternative treatments, actual peer influence, and community violence).

Nearly all the studies in this review provided limited data from the semi-structured interviews. Alternatively, they opted to list barriers identified and quotes from the interviews to support such barriers. For this reason, barrier counts were reported if the barrier was identified in a study. The count is not related to how many participants identified the barrier within the study. PrEP-specific barriers were the category with the most barriers identified across studies (n=35). Common medication administration barriers ranked second in identification across studies (n=23). Situational barriers rank last in barrier identification (n=13). The three most common themes reported by participants included a concern about side effects (n=9), low perceived risks of HIV (n=8), and lack of PrEP information (n=7). Approximately 27% of the studies reported the following barriers: stigma (n=5,), medical mistrust (n=5), missed dosing (n=5), and fear of partner rejection (n=5). Less than 25% of the studies reported the following barriers: (1) Lack of institutional support by either drug clinic, health clinic, or jail (n=4, 22.2%); (2) Drug addiction needs (n=3, 16.6%); (3) Uncertainty about PrEP access and efficacy (n=3, 16.6%); (4) Competing demands (n=2, 11.1%). The remaining themes represented 11% or less of the studies (Table 3 - Study Outcomes).

Risk of Bias

The Critical Appraisal Skills Program (CASP) Checklist was used to assess the validity of the qualitative methods among the included studies. Studies were evaluated against the ten questions identified from the CASP checklist. Responses to 9 of the 10 questions were evaluated as yes - "Y," no - "N," maybe(uncertain) - "M," or not applicable – "NA." All but 2 studies had at least 6 of the 10 questions on the checklist answered in the affirmative "Y" showing

Author	Year	Age Range	Age Average (rounded to nearest whole number)	Hispanic/Latino	Black	Multiracial	Native America	White	Asian	Other	<HS degree	HS or Vocational School	Some College	BS, MS or PhD Degree	HIV Risk Factor	Prescribed or Taking PrEP (Y/N)
		Age		Ethnicity and Race							Educational Status				PrEP Related Statistics	
Amico[4]	2019	18-61	39	17	83	2	1	34	NA	13	18	54	34	24	Sex	Y
Bond	2022	18-25	22	0	26	NA	NA	0	NA	0	NA	NA	NA	NA	Sex and Drugs	N
Braksmajer	2019	18-65	40	3	21	NA	NA	2	NA	NA	14	8	4	NA	Sex	N
Calabrese	2018	18-65	unclear	144	235	NA	NA	250	13	98				163	Neighborhood	N
Felsher	2021	>18	36	4	3	NA	NA	16	NA	0	NA	NA	NA	NA	Drugs	Y
Hill	2021	18-63	32	0	53	NA	NA	NA	NA	NA	NA	NA	NA	NA	Neighborhood	N
Hill	2018	unclear	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Johnson	2020	>18	28.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Neighborhood	N
Nydegger	2021	18-57	32	NA	25	5	NA	NA	NA	NA	NA	NA	NA	NA	Sex	N
Nydegger	2021															
Ojikuto	2020	unclear	34	14	282	51	NA	NA	NA	NA	24	76	247	0	Sex	NA
Pratt	2022	19-24	20	0	12	0	0	0	0	0	0	1	8	3	Sex	N
Przybyla	2020	unclear	31	3	NA	NA	NA	NA	NA	NA	21	10	0	0	Sex and Drugs	N
Pyra	2022	>18	unclear	NA	112	NA	NA	NA	NA	NA	NA	NA	NA	NA	Sex	Y
Qin	2020	25-62	44	3	2	NA	NA	12	NA	3	7	5	6	NA	Drugs	N
Ramsey	2021	19-55	34	0	4	1	1	15	0	0	7	10	4	0	Sex and Drugs	N
Troutman	2023	20-67	39	NA	NA	NA	NA	NA	NA	NA		2	9	11	Sex	N
Willie	2020	unclear	27	3	10	NA	NA	3	NA	3	13 < BS Degree			6	Sex	N
Willie	2022	unclear	32	NA	37	NA	NA	NA	NA	NA	NA	NA	NA	NA	Sex	N

[4] Descriptive statistics exclude the 3 participants that dropped out of the Amico interventional trial and survey but participated in the semi structured interviews.

Table 2: *Participant Characteristics.*

Author	Perceived or Actual experience with PrEP	Cost of Medication/No Insurance	Side effects	Competing Demands	Lack of Established Routine (no time or transportation)	Missed dosing	Low Perceived Risk of HIV	Uncertainty about PrEP access and efficacy	Stigma	Lack of PrEP Information/Awareness	Medical Mistrust	Fear of Partner Rejection, Interference, or Violence	HIV not a Priority	Drug Addiction needs	Homelessness	Need for money-sell PrEP	Lack of Institutional Support / Jail or Rehab o Clinic	Untested Alternatives treatments to PrEP	Actual Peer Influence / Embarrassment	Community Violence
		Common Medication Administration Barriers					PrEP Specific Barriers							Situational Barriers						
Amico	Actual	0	X	X	X	X	X	X	X	0	0	0	0	0	0	0	0	0	0	0
Bond	Perceived	X	X	0	0	X	X	0	X	X	X	X	0	0	0	0	0	0	0	0
Braksmajer	Perceived	0	X	0	0	0	X	0	0	0	0	X	X	0	0	0	0	0	0	0
Calabrese	Perceived	0	0	0	0	0	0	0	X	0	0	X	0	0	0	0	0	0	0	0
Felsher	Actual	X	0	X	0	0	X	0	0	0	0	0	X	X	X	X	X	0	0	0
Hill	Perceived	0	X	0	0	0	0	0	0	0	X	0	0	0	0	0	0	X	0	0
Hill	Perceived	0	X	0	0	0	X	0	0	0	0	0	0	0	0	0	0	0	0	0
Johnson	Perceived	X	X	0	0	0	0	X	0	X	0	0	0	0	0	0	0	0	0	0
Nydegger Nydegger	Perceived	0	0	0	X	X	X	0	0	0	X	X	0	X	0	0	X	0	X	X
Ojikuto	Perceived	0	0	0	0	0	0	0	0	0	X	0	0	0	0	0	0	0	0	0
Pratt	Perceived	0	0	0	0	0	0	0	X	X	0	0	0	0	0	0	X	0	X	0
Pryzbyla	Perceived	0	X	0	0	X	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pyra	Actual	0	X	0	0	0	0	0	0	X	0	0	0	0	0	0	0	0	0	0
Qin	Perceived	0	0	0	0	0	0	0	X	X	0	0	0	0	0	0	0	0	0	0
Ramsey	Perceived	X	0	0	0	X	0	X	0	0	0	0	0	X	0	0	0	0	0	0
Troutman	Perceived	0	0	0	0	0	0	0	0	X	0	0	0	0	0	0	X	0	0	0
Willie	Perceived	0	0	0	0	0	X	0	0	0	0	X	0	0	0	0	0	0	0	0
Willie	Perceived	X	X	0	0	0	X	0	0	X	X	0	0	0	0	0	0	0	0	0
Total	3 Actual	5	9	2	2	5	8	3	5	7	5	5	2	3	1	1	4	1	2	1

[5] Barrier counts were reported with "X" if the barrier was identified in a study.

Table 3: *Study Outcomes: Barriers to PrEp Identified Across Studies.*

	Amico (2019)	Bond (2022)	Braksmajer (2019)	Calabrese (2018)	Felsher (2021)	Hill (2018)	Hill (2021)	Johnson (2020)	Nydegger (2021)	Nydegger (2021)	Ojikuto (2020)	Pratt (2022)	Przybyla (2020)	Pyra (2022)	Qin (2020)	Ramsey (2021)	Troutman (2023)	Willie (2022)	Willie (2020)
Was there a clear statement of the aims of the research?	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y
Is a qualitative methodology appropriate?	Y	Y	Y	Y	Y	Y	N	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the research design appropriate to address the aims of the research?	Y	Y	Y	Y	Y	Y	N	Y	Y		M	Y	Y	Y	Y	Y	Y	Y	Y
Was the recruitment strategy appropriate to the aims of the research?	N	Y	Y	Y	Y	Y	M	Y	Y		Y	Y	Y	Y	Y	M	Y	Y	Y
Was the data collected in a way that addressed the research issue?	N	N	Y	Y	Y	Y	N	Y	Y		M	Y	Y	M	Y	Y	M	Y	Y
Has the relationship between researcher and participants been adequately considered?	Y	Y	Y	NA	Y	NA	N	NA	Y		NA	Y	Y	Y	Y	M	Y	Y	Y
Have ethical issues been taken into consideration?	Y	Y	Y	Y	Y	Y	N	Y	Y		Y	Y	Y	Y	Y	N	Y	Y	Y
Was the data analysis sufficiently rigorous?	Y	M	M	Y	Y	N	N	N	M		Y	Y	Y	Y	Y	Y	N	Y	N
Is there a clear statement of findings?	Y	N	M	Y	Y	Y	Y	Y	Y		M	Y	Y	Y	Y	Y	M	Y	N
How valuable is the research? (L=local; G=generalizable)	L	L	L	L	L	L	L	L	L		L	L	L	L	L	L	L	L	L

Table 4: *Risk of Bias - Critical Appraisal Skills Programme - CASP Checklist for Qualitative Research.*

acceptable validity for the methods. Five of the 18 studies showed high quality, with all questions answered "Y". The remaining studies had at least one or more questions answered with "N" or "M". Three studies (Hill et al., 2018; Amico et al., 2019; Willie et al., 2020) had more than 1 question answered in the negative. The final question evaluated the value of the results as either local or generalizable. It was determined that study outcomes across all studies had local value rather than generalizable. Validity of methods was generally observed across studies. The question challenging the validity of the studies by way of a negative "N" or uncertain response "M" was: "Was the data analysis sufficiently rigorous?". Since most studies focused on small groups of participants looking to identify themes, the data reported was generally descriptive and included participant quotes (Table 4 - Risk of Bias).

Discussion

It is important to note that the common objective of these studies was to conduct interviews among small participant populations to identify themes for barriers to PrEP use. While the research allows us to understand and descriptively identify common barriers to PrEP use, it limits a more comprehensive statistical approach regarding presenting results.

The study findings unveiled various barriers to PrEP uptake, contributing to participants' hindrances. The fact that 2 of the 3 the study outcomes categories fell into common medication administration barriers or situational barriers and had nothing to do with the specifics of PrEP indicates that uptake may be improved with a general focus on medication adherence strategies. PrEP-specific barriers require an improved outreach that should focus on destigmatizing this intervention and providing informational sessions that emphasize higher HIV risk behaviors rather than relationship status or gender identity. Such approaches could address the analysis of the consistently identified side effects, low perceived risk of HIV, and lack of PrEP awareness as the top three risk factors across studies for low PrEP utilization.

Side Effects

Patients often base their decisions about taking medication on how they feel about possible side effects. Many patients who do not adhere to their medication regimens report a concern about side effects. This research shows that a concern for side effects is a prevalent barrier to PrEP uptake for those at risk not yet taking it (n=8) and PrEP adherence for those prescribed or already taking it (n=2). The implication of side effects as a significant barrier to PrEP suggests it could be helpful for healthcare providers or social workers to prepare patients for side effects when recommending or prescribing PrEP (Brown et al., 2011).

Low Perceived Risk for HIV Infection

HIV infections continue to affect individuals across all adult and adolescent age groups, regardless of marital status, gender orientation, sex, or sexual

orientation. Risk factors for HIV transmission include engaging in unprotected vaginal or anal sex within the past 6 months, remarkably when unaware of the HIV status of sexual partners. Individuals using drugs can lead to behaviors that put them at risk for HIV infection. Individuals with a diagnosis of a bacterial sexually transmitted infection such as chlamydia, syphilis, or gonorrhea within 6 months suggest participation in behaviors that put them at risk for HIV infection. When these behaviors are reported in individuals living in communities with high rates of HIV, they have an increased risk than those with the same behaviors in a community with a low rate of HIV (Centers for Disease Control and Prevention, 2021). Nearly all the studies (n=17) recruited individuals because of their higher HIV risk behavior (n=14) or because they live in a higher HIV risk environment (n=3). However, the perception that participants were at low risk for HIV infection was identified as a barrier in nearly half of the studies (n=8). The decision to identify barriers to PrEP for only women assigned female at birth also revealed through the structured interviews that some of this population only considered men having sex with men or the transgender identity as a risk factor for HIV rather than actual HIV-at-risk behavior (Pyra et al., 2022; Willie et al. 2022). This suggests there may be a disconnect with understanding HIV risk factors. The most likely pathway to overcome this barrier would be through education.

Lack of PrEP information

Similar to concerns about side effects, a lack of information about PrEP emerged as a significant barrier (n=7) to its uptake and adherence in this research. Among the studies identified, a lack of awareness or understanding about PrEP was reported as the third most prevalent barrier but plays a role in both "side effects" and "low perceived risk of HIV infection." This finding underscores the importance of healthcare providers or social workers in presenting comprehensive education about PrEP, including its purpose, effectiveness, potential side effects, and how to access it. By addressing this knowledge gap, healthcare professionals can empower individuals to make informed decisions about PrEP and overcome barriers to its use.

Remaining Barriers

Further analysis of the studies revealed that among the common medication administration barriers, the sub-categories of side effects, followed by the cost of medication and missed doses, were the prominent barriers, while in the PrEP-specific barriers, low perceived risk of HIV, followed by lack of PrEP awareness, stigma, and medical mistrust were most prevalent. Within the situational barriers, lack of institutional support and drug addiction surfaced as the most relevant.

The data from the studies could not demonstrate that these risk factors are influenced by various patient characteristics such as race and ethnicity. The existing analytical approach highlights the necessity of presenting research that includes increased patient populations and detailed sub-categories. Disaggregated data may improve the understanding of race, age, and ethnicity in such findings.

Considering the multi-layered risk factors associated with PrEP use and the disproportionately higher lifetime risk of HIV infection among black women compared to other racial/ethnic groups (Centers for Disease Control and Prevention, 2018), it is important to include the data related to race and ethnicity in the analysis.

In addition to focusing on race and ethnicity, the presence of empirical evidence pointing to elevated rates of HIV acquisition among Southern women, in comparison to other regions within the United States, underscores the need to address geographical disparity as well (Centers for Disease Control and Prevention, 2018). The studies in this paper were predominately focused in the Northeast (n=9), with limited studies in the needed South (n=2) and Southeast (n=2). The unequal distribution of regional research attention has the potential to inadvertently perpetuate health disparities, hindering the creation of effective interventions for those most affected.

Conclusion

This review identifies significant barriers hindering women's PrEP utilization. Addressing these challenges through further research will enable the development of targeted interventions for equitable PrEP access, particularly for underrepresented populations. To ensure a comprehensive understanding and to capture the nuances associated with diverse populations, future research should address these factors of PrEP uptake as they relate to race and ethnicity. This approach will enable the development of more tailored interventions that acknowledge the multifaceted nature of PrEP uptake barriers and their potential disparities across different racial and ethnic groups.

Funding

This research received no external funding.

Acknowledgments

We thank the authors of the included studies. We also thank two individuals at Rutgers, The State University of New Jersey, Lisa Palladino Kim, Lecturer and Program Director of the MS Clinical Research Management Program, School of Health Professions, and Yinting Zhang, Research Services Librarian at the Robert Wood Johnson Library of the Health Sciences, for her assistance in her initial mentoring of the scholarly work and her assistance in the systematic review search strategy, respectively.

This work was supported by the NIH National Center for Advancing Translational Science as part of The New Jersey Alliance for Clinical and Translational Science Grant UL1TR003017. Authors have no competing interests.

Conflicts of Interest

The authors declare no conflict of interest.

References

- Amico, K. R., Ramirez, C., Caplan, M. R., Montgomery, B. E., Stewart, J., Hodder, S., Swaminathan, S., Wang, J., Darden-Tabb, N. Y., McCauley, M., Mayer, K. H., Wilkin, T., Landovitz, R. J., Gulick, R., & Adimora, A. A. (2019). Perspectives of US women participating in a candidate PrEP study: Adherence, acceptability, and future use intentions. Journal of the International AIDS Society, 22(3), Article e25247. https://doi.org/10.1002/jia2.25247
- Bond, K. T., Gunn, A., Williams, P., & Leonard, N. R. (2022). Using an intersectional framework to understand the challenges of adopting pre-exposure prophylaxis (PrEP) among young adult Black women. Sexuality Research & Social Policy, 19(1), 180-193. https://doi.org/10.1007/s13178-021-00533-6
- Braksmajer, A., Leblanc, N. M., El-Bassel, N., Urban, M. A., & McMahon, J. M. (2019). Feasibility and acceptability of pre-exposure prophylaxis use among women in violent relationships. AIDS Care, 31(4), 475-480. https://doi.org/10.1080/09540121.2018.1503634
- Brown, M. T., & Bussell, J. K. (2011). Medication adherence: WHO cares? Mayo Clinic Proceedings, 86(4), 304-314. https://doi.org/10.4065/mcp.2010.0575
- Calabrese, S. K., Dovidio, J. F., Tekeste, M., Taggart, T., Galvao, R. W., Safon, C. B., Willie, T. C., Caldwell, A., Kaplan, C., & Kershaw, T. S. (2018). HIV pre-exposure prophylaxis stigma as a multidimensional barrier to uptake among women who attend Planned Parenthood. Journal of Acquired Immune Deficiency Syndromes, 79(1), 46-53. https://doi.org/10.1097/QAI.0000000000001762
- Centers for Disease Control and Prevention. (2018). HIV surveillance report: Diagnosis of HIV infection in the United States and dependent areas. Retrieved from https://www.cdc.gov/hiv/library/reports/hiv-surveillance/vol-31/content/women.html
- Centers for Disease Control and Prevention. (2021). US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 update: A clinical practice guideline. Retrieved from https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
- Chan, S. S., Chappel, A. R., Maddox, K. E. J., Hoover, K. W., Huang, Y. A., Zhu, W., Cohen, S. M., Klein, P. W., & De Lew, N. (2020). Pre-exposure prophylaxis for preventing acquisition of HIV: A cross-sectional study of patients, prescribers, uptake, and spending in the United States, 2015-2016. PLOS Medicine, 17(4), e1003072. https://doi.org/10.1371/journal.pmed.1003072
- Collins, L. F., Sheth, A. N., Mehta, C. C., Naggie, S., Golub, E. T., Anastos, K., French, A. L., Kassaye, S., Taylor, T., Fischl, M. A., Adimora, A. A., Kempf, M. C., Palella, F. J., Tien, P. C., & Ofotokun, I. (2021). The prevalence and burden of non-AIDS comorbidities among women living with or at risk for human immunodeficiency virus infection in the United States. Clinical Infectious Diseases, 72(8), 1301-1311. https://doi.org/10.1093/cid/ciaa204
- Desai, M., Field, N., Grant, R., & McCormack, S. (2017). Recent advances in pre-exposure prophylaxis for HIV. BMJ, 359, j5011. https://doi.org/10.1136/bmj.j5011
- Felsher, M., Ziegler, E., Amico, K. R., Carrico, A., Coleman, J., & Roth, A. M. (2021). "PrEP just isn't my priority": Adherence challenges among women who inject drugs participating in a pre-exposure prophylaxis (PrEP) demonstration project in Philadelphia, PA USA. Social Science & Medicine, 275, 113809. https://doi.org/10.1016/j.socscimed.2021.113809
- Goparaju, L., Praschan, N. C., Warren-Jeanpiere, L., Experton, L. S., Young, M. A., & Kassaye, S. (2017). Stigma, partners, providers and costs: Potential barriers to PrEP uptake among US women. Journal of AIDS & Clinical Research, 8(9), 730. https://doi.org/10.4172/2155-6113.1000730

- Herron, L. M., Mutch, A., Mugamu, M., Howard, C., & Fitzgerald, L. (2022). 'The spiral just keeps on going': Cascading health and social issues for women living and aging with HIV. Women's Health, 18, 17455065221074882. https://doi.org/10.1177/17455065221074882
- Hess, K. L., Hu, X., Lansky, A., Mermin, J., & Hall, H. I. (2017). Lifetime risk of a diagnosis of HIV infection in the United States. Annals of Epidemiology, 27(4), 238-243. https://doi.org/10.1016/j.annepidem.2017.02.003
- Hill, B. S., Patel, V. V., Haughton, L. J., Blackstock, O. J. (2018). Leveraging social media to explore Black women's perspectives on HIV pre-exposure prophylaxis. Journal of the Association of Nurses in AIDS Care, 29(1), 107-114. https://doi.org/10.1016/j.jana.2017.06.010
- Hill, L. M., Lightfoot, A. F., Riggins, L., & Golin, C. E. (2020). Awareness of and attitudes toward pre-exposure prophylaxis among African American women living in low-income neighborhoods in a Southeastern city. AIDS Care, 33(2), 1-5. https://doi.org/10.1080/09540121.2020.1769834
- Huang, Y. A., Zhu, W., Smith, D. K., Harris, N., & Hoover, K. W. (2018). HIV preexposure prophylaxis, by race and ethnicity — United States, 2014–2016. MMWR. Morbidity and Mortality Weekly Report, 67(41), 1147-1150. https://doi.org/10.15585/mmwr.mm6741a3
- Johnson, A. K., Fletcher, F. E., Ott, E., Wishart, M., Friedman, E. E., Terlikowski, J., & Haider, S. (2020). Awareness and intent to use pre-exposure prophylaxis (PrEP) among African American women in a family planning clinic. Journal of Racial and Ethnic Health Disparities, 7(3), 550-554. https://doi.org/10.1007/s40615-019-00683-9
- Ma, L. L., Wang, Y. Y., Yang, Z. H., Huang, D., Weng, H., & Zeng, X. T. (2020). Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: What are they and which is better? Military Medical Research, 7(1), 7. https://doi.org/10.1186/s40779-020-00238-8
- Nydegger, L. A., Dickson-Gomez, J., & Ko, T. K. (2021). A longitudinal, qualitative exploration of perceived HIV risk, healthcare experiences, and social support as facilitators and barriers to PrEP adoption among Black women. AIDS and Behavior, 25(2), 582-591. https://doi.org/10.1007/s10461-020-03015-9
- Nydegger, L. A., Dickson-Gomez, J., & Ko, T. K. (2021). Structural and syndemic barriers to PrEP adoption among Black women at high risk for HIV: A qualitative exploration. Culture, Health & Sexuality, 23(5), 659-673. https://doi.org/10.1080/13691058.2020.1720297
- Ojikutu, B. O., Amutah-Onukagha, N., Mahoney, T. F., Tibbitt, C., Dale, S. D., Mayer, K. H., & Bogart, L. M. (2020). HIV-related mistrust (or HIV conspiracy theories) and willingness to use PrEP among Black women in the United States. AIDS and Behavior, 24(10), 2927-2934. https://doi.org/10.1007/s10461-020-02843-z
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., ... Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 372, n71. https://doi.org/10.1136/bmj.n71
- Pratt, M. C., Jeffcoat, S., Hill, S. V., Gill, E., Elopre, L., Simpson, T., Lanzi, R., Matthews, L. T. (2022). "We feel like everybody's going to judge us": Black adolescent girls' and young women's perspectives on barriers to and opportunities for improving sexual health care, including PrEP, in the Southern U.S. Journal of the International Association of Providers of AIDS Care, 2022 Jan-Dec;21: 23259582221107327. https://doi.org/10.1177/23259582221107327
- Przybyla, S. M., Cerulli, C., Bleasdale, J., Wilson, K., Hordes, M., Nabila El-Bassel, & Morse, D. S. (2020). "I think everybody should take it if they're doing drugs, doing heroin, or having sex for money": A qualitative study exploring perceptions of pre-exposure prophylaxis among female participants in an opioid intervention court program. Substance Abuse Treatment, Prevention, and Policy, 15(1). https://doi.org/10.1186/s13011-020-00331-0
- Pyra, M., Johnson, A. K., Devlin, S., Uvin, A. Z., Irby, S., Stewart, E., Blum, C., Green, M., Haider, S., Hirschhorn, L. R., & Ridgway, J. P. (2022). HIV pre-exposure prophylaxis use and persistence among Black ciswomen: "Women need to protect themselves, period." Journal of Racial and Ethnic Health Disparities, 9(3), 820-829. https://doi.org/10.1007/s40615-021-01020-9
- Qin, Y., Price, C., Rutledge, R., Puglisi, L., Madden, L. M., & Meyer, J. P. (2020). Women's decision-making about PrEP for HIV prevention in drug treatment contexts. Journal of the International Association of Providers of AIDS Care, 19, 2325958219900091. https://doi.org/10.1177/2325958219900091

- Ramsey, S. E., Ames, E. G., Uber, J., Habib, S., Hunt, L., Brinkley-Rubinstein, L., Teitelman, A. M., Clarke, J. G., Kaplan, C., Phillips, N., & Murphy, M. (2021). Linking women experiencing incarceration to community-based HIV pre-exposure prophylaxis care: A qualitative study. Aids Education and Prevention, 33(3), 216-233. https://doi.org/10.1521/aeap.2021.33.3.216
- Troutman, J., Robillard, A., Ingram, L. A., Qiao, S., Gaddist, B., & Segosebe, K. (2023). Individual, social, and structural vulnerability for Black women in the South: Implications for PrEP. AIDS Education and Prevention, 35(4), 290-308. https://doi.org/10.1521/aeap.2023.35.4.290
- Willie, T. C., Keene, D. E., Kershaw, T., & Stockman, J. K. (2020). "You never know what could happen": Women's perspectives of pre-exposure prophylaxis in the context of recent intimate partner violence. Women's Health Issues, 30(1), 41-48. https://doi.org/10.1016/j.whi.2019.08.001
- Willie, T. C., Knight, D., Baral, S. D., Chan, P. A., Kershaw, T., Mayer, K. H., Stockman, J. K., Adimora, A. A., Monger, M., Mena, L. A., & Phillips, K. A. (2022). Where's the "Everyday Black Woman"? An intersectional qualitative analysis of Black women's decision-making regarding HIV pre-exposure prophylaxis (PrEP) in Mississippi. BMC Public Health, 22(1), 1604. https://doi.org/10.1186/s12889-022-13999-9