

Health Care Provider Barriers to HIV Pre-Exposure Prophylaxis in the United States: A Systematic Review

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Abstract

Increasing prescription of pre-exposure prophylaxis (PrEP) is imperative to ending the HIV epidemic in the United States. The objective of this review was to identify health care provider barriers to PrEP implementation. A systematic review was conducted in February 2019 using PubMed to identify barriers to PrEP prescribing practices in the United States. Targeted search terms surrounding PrEP and providers resulted in 222 original studies, 28 of which were ultimately included in our review, with data collected between 2011 and 2018. Six themes were identified across reviewed studies: (i) a lack of PrEP knowledge, (ii) the presence of the Purview Paradox, which refers to discordance in beliefs between HIV specialists and primary care providers on who should prescribe PrEP, (iii) concerns about PrEP costs, (iv) concerns about behavioral and health consequences, (v) interpersonal stigma, and (vi) concerns about patient adherence. A majority of providers were lacking knowledge regarding PrEP, resulting in discomfort in prescribing PrEP, or limited awareness and understanding of PrEP clinical guidelines. Discrepant opinions were identified regarding whether PrEP was best managed within primary care or specialty clinics. Other barriers included concerns about cost, patient adherence, and follow-up maintenance care. Finally, concerns about risk compensation and discomfort discussing sexual activities with patients who would benefit most from PrEP were apparent. Additional work is needed to prepare providers to prescribe and manage patients on PrEP, optimize PrEP delivery, and reduce provider bias. Future research is needed to identify providers' attitudes and beliefs regarding innovations in PrEP dosing, task shifting, and novel strategies for PrEP care.

Keywords: pre-exposure prophylaxis, providers, prescription, HIV

Introduction

THE HIV EPIDEMIC is a continued problem in the United States, with ~40,000 new diagnoses consistently reported each year between 2011 and 2016.¹ The introduction of HIV pre-exposure prophylaxis (PrEP) has shown significant promise in reducing the rate of HIV incidence.^{2–15} The combination pill containing emtricitabine and tenofovir disoproxil fumarate was approved for PrEP by the United States Food and Drug Administration in 2012 and 2018 for adults and individuals <18 years of age, respectively,^{14,15} with supporting clinical guidelines for adult use issued by the Centers for Disease Control and Prevention (CDC) in 2014 and 2017.^{16,17} Although nearly 1.2 million people could benefit from PrEP, AIDS Vaccine Advocacy Coalition (AVAC) estimates that ~130,000–135,000 individuals were actively on

PrEP in late 2019—meaning <15% of individuals in need of PrEP had a current prescription.¹⁸

Health care providers have a central role in facilitating PrEP uptake among patients at risk of HIV acquisition through medication prescription, yet they may face significant barriers to prescribing PrEP for patients. They are also uniquely situated to educate patients on the risks and benefits of PrEP and have the ability to reach a large number of high-risk individuals. Two prior reviews have highlighted the substantial breadth of research on barriers to PrEP use among populations with higher rates of HIV,^{19,20} and two other reviews have incorporated health care provider barriers to PrEP service delivery,^{21,22} but a comprehensive and systematic review on provider-level barriers to PrEP prescription was needed.

The purpose of this literature review was to identify and thematically review studies on health care provider barriers

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to HIV PrEP in the United States. In light of the barriers systematically identified, we discuss areas in need of future study to expand PrEP implementation as new methods of PrEP care and management are forthcoming.

Methods

The database PubMed was used to identify published original studies focusing on PrEP prescription among health care professionals in the United States. The search terms used for this review were “Pre-Exposure Prophylaxis,” “PrEP,” “Preexposure Prophylaxis,” “providers,” and “physicians.” The exact search method used was (((“Pre-Exposure Prophylaxis”[Title] OR PrEP[Title] OR “Preexposure Prophylaxis” [Title] AND (provider* OR physician*))). Articles were extracted on February 15, 2019. Titles and abstracts were reviewed to identify articles for full text review. Studies were excluded if they took place outside of the United States or did not focus on PrEP prescription or implementation. Only published original articles were considered for this review.

Results

Based on our search terms, 222 articles were identified. Of these, 137 were excluded because they were conducted outside of the United States or were unrelated to PrEP. The remaining 85 articles’ abstracts were reviewed, and 56 articles were excluded because they did not focus on barriers to PrEP implementation at the health care provider level. This resulted in 29 articles accepted for full text review, after which 2 more articles were excluded for not meeting inclusion criteria since they did not focus on health care provider-level barriers to PrEP. In addition, article citations were reviewed to see if any articles were present that might be relevant but missed by our search, which resulted in the addition of one article. In total, 28 primary articles were identified in this systematic review (Fig. 1).

Of these 28 articles, 54% were national studies, whereas the remaining studies focused on more coastal and Southern areas of the United States. The main populations of health care providers included primary care providers (PCPs) and HIV specialists. Several studies included nurse practitioners (NPs), physicians’ assistants (PAs), and other providers able to prescribe medication. Nearly 80% of articles were cross-sectional surveys, with the remaining based on qualitative interviews (Table 1).^{23–49}

There were several overarching themes across studies, including a general lack of knowledge among health care providers about PrEP efficacy and guidelines, as well as worries about developing drug resistance, cost of the drug, and side effects of prolonged usage. Some providers revealed negative attitudes toward PrEP usage, such as worries about risk compensation. Many providers disagreed about who is more equipped to handle PrEP conversations, PCPs or HIV specialists, and were unsure which clinical setting is the most appropriate for PrEP. Finally, some research identified personal biases and stigma that affected providers’ ability and willingness to prescribe PrEP.

Lack of knowledge

Of the 28 articles included in our systematic review, 18 studies reported lack of provider knowledge as a barrier to PrEP prescription.^{24,26–28,31,32,34,38,40–47,49} PrEP awareness

among PCPs increased steadily, from 24% to 66% between 2009 and 2015.⁴⁴ However, PrEP knowledge remained low, with only 17% of providers indicating that they had read the CDC guidelines in 2014.⁴⁴

In a 2017 study, 39% of interviewed family physicians were unaware of CDC PrEP guidelines, and only 6% of interviewed family physicians were comfortable prescribing PrEP.⁴¹ In a larger study with 735 health care providers of varying specialties in Washington State, only 65% had ever heard of PrEP, and among those, approximately one-third could not determine who would benefit most from PrEP, indicating that a major barrier to PrEP implementation is lack of familiarity with CDC guidelines and difficulty determining eligibility of patients.⁴⁹

Similarly among both PCPs in North Carolina and family planning providers throughout the United States, the most frequently reported barrier to prescribing PrEP was a lack of knowledge.^{32,43} Seventy-five percent of the family planning providers and 42% of the PCPs reported they were uncomfortable prescribing PrEP due to a lack of knowledge. Notably, a majority of both PCPs and family planning providers stated that they would be willing to provide PrEP with more training.^{32,43}

In general, HIV specialists were more knowledgeable about PrEP and the CDC guidelines pertaining to its use. A study done with PCPs noted that although 75% of participants were aware that PrEP existed, only 37% stated that they were somewhat or very familiar with the guidelines for prescription, and only 17% had prescribed it.⁴⁷ Although this study did not focus on the differences between the two provider classes, a similar study done found that 98% of HIV specialists interviewed had heard of PrEP and 76% were familiar with the guidelines, whereas only 28% of PCPs were familiar with the guidelines.⁴² In addition, younger providers and MDs were more likely to have heard of PrEP compared with their older counterparts and DOs, PAs, and NPs, respectively.⁴⁹

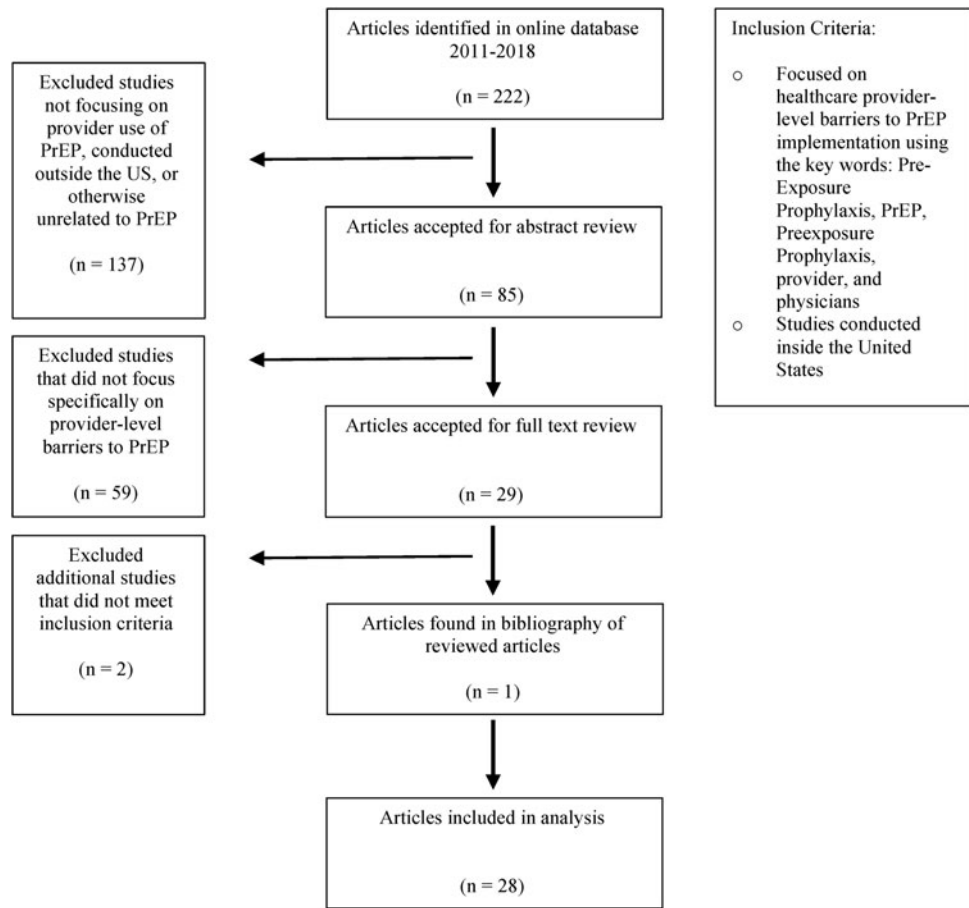
Purview paradox

Another barrier to PrEP prescription was discordance in beliefs about who should prescribe PrEP, a concept called the “Purview Paradox” by Krakower and colleagues.^{25,28,34–36,41,50} In their 2014 study, HIV specialists believed that PrEP was more suited for primary care clinics because PCPs see HIV-negative patients more often, whereas PCPs reported that PrEP should be provided in HIV clinics, since PCPs lack knowledge regarding HIV medication.³⁶ HIV specialists in two other studies stated that HIV-negative patients are seen mainly by PCPs and not in specialty clinics, whereas PCPs stated that HIV specialists are more suited to seeing PrEP patients because of their greater knowledge of the subject and better ability to provide adherence support.^{25,35} Similarly, 87% of PCPs and infectious disease specialists serving in the Air Force indicated that PrEP should be provided in infectious disease clinics, but 68% also felt it should be provided in sexually transmitted infection (STI) clinics.³⁴

Concerns about cost

Cost of PrEP was another commonly cited barrier among health care providers, with research suggesting that this might be due to a lack of awareness of options for paying for PrEP.^{28,29,32,34,37,40,42,43,45,49} In a study of Washington State

FIG. 1. Flow diagram for systematic review of the literature related to PrEP barriers, 2011–2018. PrEP, pre-exposure prophylaxis.



medical providers, 43% of participants were worried about PrEP costs to patients; however, only 25% of those had tried to access the drug assistance program in Washington.⁴⁹ Similarly, two other studies reported that providers who did not prescribe PrEP due to cost/insurance issues were unaware of insurance coverage options.^{32,42} An extension of this barrier was reported by providers with PrEP prescribing experience, where providers reported a significant amount of time spent on the phone with insurance companies and paperwork required to establish coverage.²⁹

In contrast, only 12% of HIV specialists nationwide reported cost as an issue in another study.⁴⁵ Some studies suggest that this barrier may differ based on geographic region. For example, only 36% of providers in New York, San Diego, and Los Angeles listed cost as a potential concern to PrEP.²⁸ However, one study found that lower endorsement of cost and insurance factors was associated with higher intentions to prescribe PrEP.⁴⁰

Concerns about behavioral and health consequences

Another theme we identified in the literature was the belief that being on PrEP would cause individuals to engage in more “risky” behavior, such as having sex without a condom or not inquiring about STIs before engaging in sexual activity.^{25,27–29,33,34,36,37,39,42,43,45,49,50} Although in most studies worries about risk compensation were minimal, it did emerge as a common theme across the reviewed literature. Specifically, 26% of Washington State providers believed that being on PrEP could increase engagement in risky sexual

behavior.⁴⁹ Moreover, some providers had misgivings about prescribing PrEP, stating that they thought it would lead to an increase in risky behavior and increased HIV transmission, with some providers stating that patients had disclosed increased risky behavior after starting PrEP.^{36,37} Some providers even stated that higher-risk individuals would be better off using condoms instead of PrEP.³³

Another study found that fears of risk compensation were more prominent in providers with little PrEP prescribing experience.²⁷ In addition to concerns about risk compensation, providers in another reviewed study worried about HIV resistance caused by PrEP, cited minimal concerns about side effects, but recognized the importance of monitoring patients to minimize risks.²⁵

Interpersonal stigma

Several studies found that stigma and biases were influential barriers to PrEP prescription.^{24,26,30,36,42,44,48} In one qualitative study, researchers highlighted the negative influence of providers’ race, gender, and age biases on PrEP decision-making. Physicians described how their own personal values related to sex, including discussing sexual activity with LGBTQ individuals, were barriers to PrEP prescription. They similarly noted being less likely to discuss sexual activity with older patients, which could lead to lower rates of prescription among this population. In addition, many providers were unwilling to accept that they may be vulnerable to personal biases when prescribing PrEP, even after being shown data to suggest bias.³⁰

TABLE 1. SYSTEMATIC REVIEW FINDINGS OF PROVIDER-LEVEL BARRIERS TO PRE-EXPOSURE PROPHYLAXIS IMPLEMENTATION

<i>Authors</i>	<i>Study design</i>	<i>Location</i>	<i>Year</i>	<i>Sample size</i>	<i>Provider types</i>	<i>Provider-level barriers of PrEP implementation</i>
Adams et al. ²³	Primary, survey data collection	National, United States	2018	342	HIV specialists	Lack of knowledge <ul style="list-style-type: none"> • Two-thirds of providers reported that MSM comprised 75–100% of their PrEP caseload • 47% of providers reported that serodiscordant couples, women, and PWID comprised <25% of their PrEP caseload
Adams et al. ²⁴	Primary, survey data collection	National, United States	2016	363	HIV specialists	Stigma <ul style="list-style-type: none"> • Providers were significantly more likely to prescribe PrEP to MSM with an HIV+ partner
Arnold et al. ²⁵	Primary, qualitative interviews	San Francisco, Oakland, and Los Angeles, United States	2012	22	Health care providers	Purview paradox <ul style="list-style-type: none"> • Out of the 22 providers interviewed, most felt that PrEP is best provided in a PCP clinic • Negative attitudes • While most providers stated minimal concerns about side effects, they recognized the importance of monitoring patients closely and acknowledged the burden this would place on themselves and their staff
Bacon et al. ²⁶	Primary, survey data collection	San Francisco Bay Area, United States	2017	99	PCPs, HIV specialists, NPs, and PAs	Lack of knowledge <ul style="list-style-type: none"> • Although almost all the providers had heard of PrEP, only 26% had prescribed it • Stigma • Providers with greater experience treating HIV patients were more likely and willing to prescribe PrEP
Blackstock et al. ^{27,b}	Primary, survey data collection	National, United States	2017	266	PCPs	Lack of knowledge <ul style="list-style-type: none"> • Providers with PrEP experience were more likely to describe themselves as knowledgeable Negative attitudes <ul style="list-style-type: none"> • 75% of providers were concerned about side effects • 60% of providers were worried about resistance • Providers with no PrEP experience were more likely to indicate worries about risk compensation • 58% of providers were worried about adherence
Blumenthal et al. ²⁸	Primary, survey data collection	New York, San Diego, and Los Angeles, United States	2015	233	HIV specialists and non-HIV providers	Lack of knowledge <ul style="list-style-type: none"> • Knowledge was assessed using a five-question test. The average among all respondents was 2.5 correct answers • HIV specialists averaged 2.8, whereas non-HIV providers averaged 2.2 Purview paradox <ul style="list-style-type: none"> • Scores were significantly higher for providers with PrEP prescribing experience • 35% of respondents indicated that PrEP should be provided in HIV clinics • 31% of respondents said that PrEP should be provided in non-HIV clinics Concerns about cost <ul style="list-style-type: none"> • 36% of providers indicated cost as a barrier to prescription Negative attitudes <ul style="list-style-type: none"> • 40% of respondents indicated that they were worried about resistance and/or drug toxicity • One-third of respondents said they were worried about risk compensation with increased PrEP usage • 40% of providers were worried about patient adherence

(continued)

TABLE 1. (CONTINUED)

<i>Authors</i>	<i>Study design</i>	<i>Location</i>	<i>Year</i>	<i>Sample size</i>	<i>Provider types</i>	<i>Provider-level barriers of PrEP implementation</i>
Calabrese et al. ²⁹	Primary, qualitative interviews	National, United States	2016	18	PCPs and ID specialists with PrEP prescribing experience	Stigma <ul style="list-style-type: none"> Qualitative themes of barriers to PrEP prescriptions include structural stigma (e.g., the requirement of accessing PrEP through a medical provider was identified as a deterrent among populations who have been mistreated in health care), interpersonal stigma, physician bias discussing sex, and physician bias regarding sociodemographic factors Concerns about cost <ul style="list-style-type: none"> Providers indicated that a significant barrier they encountered was the time spent on the phone with insurance to establish coverage for patients Concerns about behavioral and health consequences <ul style="list-style-type: none"> Some physicians indicated that some patients were overwhelmed by the follow-up requirements Patients who initiated PrEP conversations were more comfortable with the requirements
Calabrese et al. ³⁰	Primary, qualitative interviews	National, United States	2019	28	Variety of providers with PrEP prescribing experience	Lack of knowledge <ul style="list-style-type: none"> Providers were classed into two different categories. Class 1 found PrEP to be less effective and perceived barriers to prescription. Class 2 viewed PrEP as effective and perceived less barriers Class 1 had significantly less experience prescribing PrEP and was less likely to prescribe PrEP to patients with multiple sex partners and patients with drug use history
Castel et al. ³¹	Primary, survey data collection	Miami and Washington DC, United States	2015	142	HIV specialists	Lack of knowledge <ul style="list-style-type: none"> 45% of providers stated lack of knowledge as biggest barrier 42% of providers were uncomfortable prescribing PrEP 58% noted that they considered cost a barrier 37% noted worries about compliance Concerns about behavioral and health consequences <ul style="list-style-type: none"> One-fifth of providers were worried about developing drug resistance One-third of providers indicated that high-risk individuals are better off using condoms Providers were less likely to prescribe PrEP to PWID
Clement et al. ³²	Primary, survey data collection	North Carolina, United States	2018	115	PCPs	Lack of knowledge <ul style="list-style-type: none"> 45% of providers stated lack of knowledge as biggest barrier 42% of providers were uncomfortable prescribing PrEP 58% noted that they considered cost a barrier 37% noted worries about compliance Concerns about behavioral and health consequences <ul style="list-style-type: none"> One-fifth of providers were worried about developing drug resistance One-third of providers indicated that high-risk individuals are better off using condoms Providers were less likely to prescribe PrEP to PWID
Edelman et al. ^{33,b}	Primary, survey data collection	National, United States	2017	250	PCPs	Lack of knowledge <ul style="list-style-type: none"> Some physicians cited a lack of clear evidence as a reason they were uncomfortable prescribing PrEP Using a quiz to measure knowledge, out of a possible 10 points, only 55% (100% of IDs and 53% of PCPs) scored 7 or more points Purview paradox <ul style="list-style-type: none"> 87% of responders indicated that PrEP should be provided in ID clinics 68% indicated it should be provided in STI clinics Concerns about cost <ul style="list-style-type: none"> 48% of providers indicated issues with cost Concerns about behavioral and health consequences <ul style="list-style-type: none"> 67% of providers were worried about potential side effects None of the providers indicated time constraints to be a barrier to prescription 54% of providers were worried about patient adherence
Hakre et al. ³⁴	Primary, survey data collection	National, United States	2016	403	United States Air Force PCPs and ID specialists	Lack of knowledge <ul style="list-style-type: none"> Some physicians cited a lack of clear evidence as a reason they were uncomfortable prescribing PrEP Using a quiz to measure knowledge, out of a possible 10 points, only 55% (100% of IDs and 53% of PCPs) scored 7 or more points Purview paradox <ul style="list-style-type: none"> 87% of responders indicated that PrEP should be provided in ID clinics 68% indicated it should be provided in STI clinics Concerns about cost <ul style="list-style-type: none"> 48% of providers indicated issues with cost Concerns about behavioral and health consequences <ul style="list-style-type: none"> 67% of providers were worried about potential side effects None of the providers indicated time constraints to be a barrier to prescription 54% of providers were worried about patient adherence

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<i>Authors</i>	<i>Study design</i>	<i>Location</i>	<i>Year</i>	<i>Sample size</i>	<i>Provider types</i>	<i>Provider-level barriers of PrEP implementation</i>
Hoffman et al. ³⁵	Primary, qualitative interviews	New York City, United States	2016	30	PCPs and HIV specialists	<p>Purview paradox</p> <ul style="list-style-type: none"> • HIV specialists do not see HIV patients • “People who do not have HIV and could benefit from prophylaxis are not going to HIV providers” • “HIV providers are best positioned because of their greater knowledge of the subject” <p>Concerns about patient adherence</p> <ul style="list-style-type: none"> • PCPs described themselves as less experienced with adherence guidelines and not having the skills or the time to help
Krakower et al. ³⁶	Primary, qualitative interview and focus groups	Boston, United States	2014	39	HIV specialists	<p>Purview paradox</p> <ul style="list-style-type: none"> • Participants stated that high-risk individuals would be more likely to see a PCP before an HIV specialist • PCPs indicated that prescribing PrEP would not be feasible at their clinics because of time constraints <p>Concerns about cost</p> <ul style="list-style-type: none"> • Some providers mentioned cost as a potential issue • Concerns about behavioral and health consequences • Providers indicated misgivings about prescribing PrEP because they think it will increase risky behaviors among high-risk individuals <p>Stigma</p> <ul style="list-style-type: none"> • Providers stated that the individuals at highest risk for needing PrEP would have the most difficulty adhering to the regimen because of a prior history of poor engagement with the health care system
Krakower et al. ³⁷	Primary, survey data collection	Boston, United States	2016	32	PCPs	<p>Concerns about cost</p> <ul style="list-style-type: none"> • Nearly half of providers stated that cost was an issue for their patients <p>Concerns about behavioral and health consequences</p> <ul style="list-style-type: none"> • 42% of providers indicated that patients disclosed increased sexual risk behaviors after starting PrEP • 23% of providers indicated that patients had more sexual partners after starting PrEP • 29% of providers indicated that patients had increased sex with HIV-positive persons
Krakower et al. ⁵⁰	Primary, survey data collection	New England, United States	2015	184	Health care providers affiliated with an AIDS Education and Training Center	<p>Concerns about behavioral and health consequences</p> <ul style="list-style-type: none"> • 51 providers were worried about potential side effects of PrEP • Purview paradox • 48 providers indicated that they believe it is more feasible to provide PrEP in STI clinics than in HIV clinics
Mimiaga et al. ³⁸	Primary, survey data collection	Massachusetts, United States	2014	115	HIV specialists and non-HIV providers	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • HIV specialists were more knowledgeable than generalists about the results of two studies showing the efficacy of PrEP

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TABLE 1. (CONTINUED)

<i>Authors</i>	<i>Study design</i>	<i>Location</i>	<i>Year</i>	<i>Sample size</i>	<i>Provider types</i>	<i>Provider-level barriers of PrEP implementation</i>
Mullins et al. ³⁹	Primary, qualitative interviews	United States	2016	15	Physicians and NPs	Concerns about adherence <ul style="list-style-type: none"> • 11 providers indicated concerns about adherence and monitoring visits, including concerns about developing viral resistance due to low adherence Concerns about behavioral and health consequences <ul style="list-style-type: none"> • 8 providers indicated concerns about patients participating in riskier sexual behavior because of PrEP
Mullins et al. ⁴⁰	Primary, survey data collection	United States	2017	56	Physicians and NPs	Concerns about cost <ul style="list-style-type: none"> • Lower endorsement of cost and insurance factors was associated with higher intentions to prescribe PrEP Lack of knowledge <ul style="list-style-type: none"> • Lower knowledge of PrEP guidelines was associated with higher intention to prescribe PrEP
Ojile et al. ⁴¹	Primary, survey data collection	Kansas, United States	2017	20	Family physicians	Lack of knowledge <ul style="list-style-type: none"> • 39% unaware of CDC guidelines for PrEP Purview paradox <ul style="list-style-type: none"> • Disagreement on which domain PrEP belongs to
Petroll et al. ^{42,a}	Primary, survey data collection	National, United States	2017	525	PCPs and HIV specialists	Lack of knowledge <ul style="list-style-type: none"> • 76% of PCPs and 98% of HIV specialists had heard of PrEP • 28% of PCPs and 76% of HIV specialists were familiar with the prescribing practices Concerns about cost <ul style="list-style-type: none"> • Both PCPs and HIV specialists cited lack of insurance coverage as a major barrier Concerns about behavioral and health consequences <ul style="list-style-type: none"> • One-fifth of providers indicated worries about risk compensation • Stigma • PCPs were significantly less likely to discuss sexual activities and deliver risk reduction counseling • PCPs were significantly less likely to discuss sexual activities and deliver risk reduction counseling
Seidman et al. ⁴³	Primary, survey data collection	National, United States	2016	342	Family planning providers	Lack of knowledge <ul style="list-style-type: none"> • Two-third of potential prescribers were uncomfortable educating patients about PrEP • Three-fourth of potential prescribers were uncomfortable prescribing PrEP due to their own lack of knowledge Concerns about cost <ul style="list-style-type: none"> • 58.5% of providers were unsure about how patients would pay for PrEP Concerns about behavioral and health consequences <ul style="list-style-type: none"> • 50.9% of providers were worried about time constraints with PrEP

(continued)

TABLE 1. (CONTINUED)

<i>Authors</i>	<i>Study design</i>	<i>Location</i>	<i>Year</i>	<i>Sample size</i>	<i>Provider types</i>	<i>Provider-level barriers of PrEP implementation</i>
Smith et al. ⁴⁴	Primary, survey data collection	National, United States	2016	1500	Physicians and NPs	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • Awareness of PrEP was initially low (24% in 2009), but increased every year • 49% of providers were aware of PrEP in 2012, 51% in 2013, 61% in 2014, and 66% in 2015 • In 2014, only 17% of providers surveyed had read the CDC guidelines <p>Stigma</p> <ul style="list-style-type: none"> • Surveyed providers were most likely to give PrEP to serodiscordant couples than MSM and PWID
Tellalian et al. ⁴⁵	Primary, survey data collection	National, United States	2013	189	HIV specialists	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • Although a majority of respondents were aware of the efficacy of PrEP, only 19% had ever prescribed it • Only 13% of respondents said that PrEP was the most effective method to prevent HIV <p>Concerns about cost</p> <ul style="list-style-type: none"> • 12% of providers said cost is a potential barrier to prescription <p>Concerns about behavioral and health consequences</p> <ul style="list-style-type: none"> • 32% of providers said that they were worried about potential resistance developing • 21% were worried about risk compensation
Tripathi et al. ⁴⁶	Primary, survey data collection	South Carolina and Mississippi, United States	2012	360	Health care providers	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • Willingness to prescribe PrEP was more likely in providers with higher PrEP knowledge
Walsh et al. ^{47,a}	Primary, survey data collection	National, United States	2017	280	PCPs with zip codes from high HIV incidence	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • 37% of providers said they were somewhat or very familiar with PrEP • 17% of providers had prescribed PrEP
Weiser et al. ⁴⁸	Primary, survey data collection	National, United States	2017	1234	HIV specialists	<p>Stigma</p> <ul style="list-style-type: none"> • Male providers were more likely to prescribe PrEP • LGBT providers were more likely to prescribe PrEP • Only prescribe to MSM
Wood et al. ⁴⁹	Primary, survey data collection	Washington State, United States	2018	735	Variety of licensed medical providers	<p>Lack of knowledge</p> <ul style="list-style-type: none"> • 64.8% of providers were unaware of PrEP • Of those who indicated knowledge of PrEP, 32.6% were uncertain about who PrEP is for <p>Cost</p> <ul style="list-style-type: none"> • 42.9% were worried about costs to patients <p>Concerns about behavioral and health consequences</p> <ul style="list-style-type: none"> • 24.1% were worried about developing drug resistance • 25.6% believed that being on PrEP would increase risky behavior • 46% reported worries about adherence

^{a,b}These indicate that the studies came from the same data set.

CDC, Centers for Disease Control and Prevention; ID, infectious disease; LGBTQ, lesbian, gay, bisexual, transgender, or queer; MSM, men who have sex with men; NP, nurse practitioner; PA, physicians' assistant; PCP, primary care provider; PrEP, pre-exposure prophylaxis; PWID, people who inject drugs; STI, sexually transmitted infection.

Two of the populations with higher rates of HIV are men who have sex with men (MSM) and people who inject drugs (PWID). Meanwhile, a study with PCPs found that providers were more likely to provide PrEP to HIV-serodiscordant couples than single MSM and PWID, suggesting bias against these populations.⁴⁴ HIV specialists were more comfortable prescribing PrEP to MSM with an HIV-positive partner and less likely to prescribe PrEP to heterosexual couples or PWID in two additional studies.^{23,24}

Concerns about patient adherence

In nine reviewed studies, providers reported worries about adherence to the drug regimen and the strict follow-up requirements for daily PrEP usage.^{27,28,31,32,34–36,39,49} According to the CDC guidelines, patients on PrEP should follow up every 3 months to undergo HIV/STI testing, with tests for renal functioning twice yearly.¹⁷ This level of care can present a burden to providers and their clinics, as they may not have the staff or time necessary to assess each patient. One study done with PCPs found that they described themselves as less experienced with adherence guidelines and not having the skills or the time to help.³⁵

However, the rigid follow-up requirements also raise concerns beyond structural and logistical problems. In one study of HIV specialists, <5% of providers were likely to prescribe PrEP to patients who previously missed appointments or had a history of nonadherence.³¹ Providers in another study noted that they read studies showcasing low adherence to PrEP regimens and believed that the individuals who are at risk for HIV infection would have the highest difficulty with adherence because of poor engagement with the health care system previously.³⁶ Finally, providers in another study cited concerns about the large number of follow-up visits and how low adherence can lead to viral resistance.³⁹

Discussion

The purpose of this review was to identify perceived barriers to PrEP implementation at the health care provider level in the United States. Our review of 28 articles found several notable barriers to prescribing PrEP. First, providers largely reported insufficient knowledge of PrEP and the accompanying CDC guidelines, leading to discomfort prescribing it and insufficient levels of PrEP prescription.

This lack of knowledge and awareness of PrEP also extends to other barriers. For example, many providers mentioned cost as a major barrier to PrEP implementation, citing concerns that patients would be unable to afford the medication. However, when asked if they were aware of assistance programs or if they had tried to use these programs before, providers said that they had not tried to access these programs and were unaware of their existence.^{32,42} This can lead patients who would be able to afford PrEP to not be considered for PrEP if they are relying on provider initiation of the topic. Although awareness of PrEP is rising, with double the number of providers citing awareness of PrEP in 2015 versus 2009,⁴⁴ greater knowledge of the specific care required for PrEP patients is needed to increase PrEP implementation nationwide.

Many studies found that greater PrEP knowledge was associated with higher prescription rates, suggesting the need for interventions with educational components on PrEP, PrEP maintenance care, and providing competent care to those

who would benefit most from PrEP.^{27,32} Interventions that support providers in prescribing PrEP for the first time could be particularly impactful, since one study showed that providers with previous experience with PrEP had higher intention to prescribe it in the future.⁴⁶ Some providers also mentioned that they would feel more comfortable prescribing PrEP after an educational intervention, and providers with greater experience treating HIV patients were more likely and willing to prescribe PrEP.^{26,27,31,32,46}

Findings from our review support the need for intervention work, but we were unable to identify any published literature evaluating the impact of interventions focused on increasing PrEP prescription among health care providers in the United States during our article extraction. Two articles newly published have since emerged. In one Atlanta-based intervention, 28 providers received 1.5 h of PrEP training, after which the researchers found a significant increase in PrEP knowledge and confidence.⁵¹ Another intervention was done with 34 internal medicine residents where they received training on how to improve sexual history taking and HIV prevention care, leading to a significant increase in confidence with discussing PrEP.⁵²

Although excluded from our literature review because of our geographical inclusion criteria, we are aware of an international intervention where researchers found that an intervention helped providers stay current on PrEP guidelines, improved knowledge, and increased likelihood to prescribe PrEP.⁵³ Nonetheless, research is ongoing, and several intervention models have shown significant promise in pilot study, such as the PrEP provider champion model as a social network intervention led by members of our authorship team.

Another significant barrier that presents a problem to PrEP prescription is the Purview Paradox. Neither PCPs nor HIV specialists believe that they are responsible for PrEP prescription. The argument from HIV specialists is that they do not see (or do not have the capacity to see) HIV-negative patients; meanwhile, PCPs state they do not have the knowledge required to adequately educate patients on the efficacy and benefits of PrEP. Notably, a newer study completed in 2017 by Krakower et al. found that PCPs view PrEP as being in their purview, indicating that the Purview Paradox could be diminishing over time.⁵⁴ However, each have a unique role in promoting PrEP. For HIV specialists, interventions focused on the promotion of PrEP use to the partners of their patients living with HIV would be a method of broader HIV prevention within the communities they serve, in addition to focusing on treatment as prevention.

Alternatively, interventions are needed aimed at helping PCPs recognize individuals who might benefit from PrEP and initiating conversations about PrEP, as well as increasing comfort with sexual history taking. In addition, the use of referrals could be a useful method of intervention, where HIV specialists can help patients begin PrEP—based on the greater experience with HIV testing and antiretroviral medications—and PCPs can provide the subsequent PrEP maintenance care. Moreover, establishing community-based clinics with trusted providers providing affordable care and providers experienced with LGBTQ populations and racial minorities could help address both the purview paradox and provider bias barriers.

One method that could improve PrEP implementation within the United States is task shifting. Task shifting refers

to the process whereby roles are shifted between health care workers with different types of training to use resources more efficiently.⁵⁵ In our reviewed studies, providers were worried about the time required to establish insurance coverage and the burden of follow-up requirements with each patient on PrEP. Optimizing PrEP care delivery by using existing resources, such as expanding the roles of HIV test counselors, PrEP navigators, nurses, and pharmacists could be an avenue to streamline PrEP care delivery and reduce the burden on prescribing physicians and other specialists. Nonetheless, no studies have tested the impact of task shifting on PrEP care delivery—a high priority area for future research.

Another area of future research relates to barriers to PrEP provision for women and transgender populations. Only one study in our review mentioned a barrier to PrEP implementation for women, and none of the studies we reviewed focused on barriers to prescribing PrEP to transgender populations.³⁰ Providers in this study described a selective approach to PrEP counseling, preferentially educating MSM about PrEP and keeping the onus on women to bring up PrEP during their visits instead of proactively discussing PrEP. However, this presents an issue, as a study done in 2015 among women at a family planning obstetrics/gynecology clinic found that only 27% of the 389 participants were aware that a PrEP regimen existed, and only 64% felt comfortable discussing the subject with their doctor.⁵⁶

Transgender populations are also disproportionately affected by the HIV epidemic and can benefit greatly from PrEP.^{57,58} One study by Harper et al. conducted 66 in-depth interviews with transgender and other gender-diverse youth in 14 cities across the United States to identify potential barriers to accessing HIV care.⁵⁹ A prominent finding was consistent negative health care and social service provider interactions, where participants perceived a lack of respect for patient autonomy and stated health concerns.⁵⁹ This is a significant barrier to PrEP access for these patients, and further research is needed to better prepare providers to competently prescribe PrEP to cis- and transgender women, as well as transgender men, who are frequently overlooked in HIV prevention efforts.

Our review identified a lack of research on several other important topics, mainly innovations in PrEP dosing and forthcoming long-acting injectables. On-demand PrEP—also referred to as event-driven and 2-1-1 PrEP—was found to be highly effective in the prevention of HIV,⁶⁰ which could be beneficial to patients with more episodic patterns of condomless sex. However, research is limited on providers' opinions about on-demand PrEP. In addition, PrEP effectiveness is robust among male patients, where four out of seven PrEP doses provide adequate protection against HIV with anal sex.⁶¹ It is plausible that providers could have fewer concerns about daily PrEP adherence if aware of the robust protection provided, even with periodic missed doses among their male patients.

Long-acting injectable formulations of PrEP could soon be available with promising evidence^{62,63} and ongoing clinical trials, but little is known about barriers and facilitators to integrating this method of PrEP into care delivery. Since the demand for long-acting PrEP could be significant,^{64–68} greater attention to providers' opinions before implementation could help anticipate barriers and facilitate timely intervention upon approval for consumer use.

Finally, research is needed to identify providers' attitudes, beliefs, and potential adoption of novel methods of care delivery, such as using home-based strategies for PrEP maintenance care with at-home testing kits^{69,70} and using community-based pharmacists to support PrEP prescription and care,^{71,72} among other methods. In addition to long-acting injectables, there are several other forthcoming alternative PrEP modalities. Vaginal rings, implants, and topical gels have all shown promise and can help alleviate provider concerns about adherence and barriers to PrEP implementation.⁷³ These types of structural interventions could directly overcome some provider-identified barriers to PrEP implementation, including concerns about missed appointments and adherence to follow-up PrEP maintenance care. Addressing structural-level barriers to PrEP implementation could also help improve efficiency of PrEP care delivery as prescription rates increase, but further research is needed.

Limitations

Our literature review is not without limitation. First, we focused on thematically reviewing the literature, but we did not assess rigor of the studies identified in our review. Second, we may have inadvertently missed publications that could merit inclusion in our review; however, our review included a rigorous method of data extraction with bibliography review of selected articles to minimize this risk. Third, we focused only on studies in the United States, and so our results may not be generalizable to other countries, especially countries that lack the resources the United States has in regard to medical and PrEP care. Finally, the rapidly changing landscape of PrEP means that the barriers we identified are also rapidly changing. Barriers identified in 2012–2014 may not be as relevant today as at the time of the study, suggesting the need for continued research to monitor trends in barriers to PrEP implementation among health care providers in the United States.

In this study, we systematically reviewed the literature on barriers to PrEP prescription in the United States and identified six themes across 28 studies: (i) a lack of knowledge about PrEP, (ii) the presence of the Purview Paradox, (iii) concerns about PrEP costs, (iv) concerns about behavioral and health consequences, (v) interpersonal stigma, and (vi) concerns about patient adherence. Additional work is needed to better prepare health care providers to prescribe and manage patients on PrEP, optimize PrEP delivery, and reduce provider bias. Future research is needed to identify providers' attitudes and beliefs regarding innovations in PrEP dosing, long-acting formulations, task shifting, and novel strategies for PrEP prescription and maintenance care.

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