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Understanding HIV Pre-Exposure Prophylaxis Questions of U.S. Health Care Providers: Unique Perspectives from the PrEPline Clinical Teleconsultation Service

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Abstract

Introduction: *Fewer than a quarter of people considered to have factors associated with HIV acquisition are prescribed pre-exposure prophylaxis (PrEP) in the United States. Prior studies demonstrate disparities in provider comfort and knowledge regarding PrEP, suggesting a need for provider capacity building to support widespread PrEP availability. This study examined real-world PrEP clinical questions/cases from providers to a teleconsultation service to identify knowledge gaps and improve PrEP-related training materials and clinical guidelines.*

Methods: *The National Clinician Consultation Center (NCCC) PrEPline provides educational teleconsultation services on clinical decision-making related to PrEP for U.S. health care providers. The NCCC PrEP consultation data collected between 2017 and 2020 were reviewed and systematically categorized by clinical topics, subtopics, and complexity levels (low, moderate, and high).*

Results: *Within the study period, the PrEPline provided 1,754 teleconsultations. More than three quarters came from advanced practice nurses and physicians. The topics of questions commonly focused on medication-based HIV prevention strategies (22.7%), PrEP laboratory ordering/monitoring (17.4%), and side effects and contraindications (14.6%). The majority of teleconsultations (57.9%) involved sharing information that was directly available/addressed in the Centers for Disease Control and Prevention (CDC) 2017 PrEP Guidelines (i.e., low complexity).*

Discussion: *The low frequency of consultations from non-physician and non-nurse practitioner providers may suggest a need for increased training and collaborative opportunities for other types of providers. The high percentage of low-complexity inquiries may reveal a desire for capacity-building materials specifically designed for practicing providers (e.g., abridged versions of guidelines). This study may inform future research, best clinical practices, and aid in the development of training materials to increase providers' HIV prevention comfort and knowledge.*

Keywords: *HIV pre-exposure prophylaxis, PrEP, health care provider, clinical consultation, teleconsultation*

Introduction

Despite a 56% increase in HIV pre-exposure prophylaxis (PrEP) uptake from 2012 to 2017 in the United States,[1] of the nearly 1.2 million individuals at substantial likelihood of HIV infection, only 23% were prescribed PrEP in 2019.[2,3] There are considerable disparities in PrEP use across demographic groups and U.S. geographic regions.[4] Health care providers' lack of PrEP knowledge, willingness to prescribe PrEP, and provision of PrEP prescriptions have repeatedly been shown to be key barriers to PrEP implementation.[5–14]

In 2019, a comprehensive systematic review of published studies showed that among 18,265 providers, 68% had heard

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of PrEP and 66% were willing to prescribe PrEP; however, 37% had ever provided a PrEP consultation to a patient and only 24% had ever prescribed PrEP.[12] Therefore, there is evident need for capacity-building among providers to strengthen the upstream drivers of the PrEP care continuum[15] (i.e., supporting providers to increase PrEP knowledge and comfort in prescribing PrEP) to influence downstream factors of PrEP uptake and persistence at the patient level.

Clinical consultation services, particularly teleconsultation services, staffed by HIV subject matter experts play a unique and important role and complement other HIV education and training activities. In addition to helping mitigate disparities in resource-limited settings and locations lacking or with limited availability/accessibility of clinical experts, such services may improve concordance of provider practices with evolving and evidence-based HIV care delivery, and potentially improve clinical outcomes for people living with HIV or with factors associated with HIV acquisition. National teleconsultation services may be of particular importance for clinics or health care systems without in-house access to clinical experts. Additionally, clinical consultants can identify knowledge gaps and provide innovative and/or pragmatic options to address clinical questions that are not yet addressed in national guidelines due to lack of data or lack of expert consensus.

By examining real-world clinical questions posed by health care providers, clinical consultants in turn have an opportunity to better understand the needs of providers—the gatekeepers of widespread PrEP provision—to improve their PrEP knowledge and comfort and identify specific PrEP-related issues for which research or guidelines are needed. Therefore, with the ultimate goal of improving PrEP provision, the objective of this research was to develop a collection of key PrEP-related topics by reviewing questions posed by real-world providers and teleconsultations provided by the National Clinician Consultation Center (NCCC) PrEPline (described below).

Methods

The NCCC is the first and longest running national teleconsultation service of its kind, which operates under the University of California, San Francisco's (UCSF) Department of Family and Community Medicine, and is supported by the U.S. Health Resources and Services Administration (HRSA) and the Centers for Disease Control and Prevention (CDC). The NCCC is a unique component of the national AIDS Education and Training Centers program and operates multiple national teleconsultation services for U.S.-based providers, including the HIV Warmline,[16] Perinatal HIV Hotline,[17] PrEPline, Postexposure Prophylaxis Hotline (PEPline), Substance Use Warmline, and Hepatitis C Warmline.

The NCCC principal objective is to promote health equity by facilitating free, timely, evidenced-informed, and person-centered access to clinical subject matter experts through a model of direct clinician-to-clinician telephone- and web-based consultations and education. Since its inception in 1991, the NCCC has provided more than 300,000 on-demand clinical teleconsultations to individuals with a variety of health professional backgrounds and HIV experience levels. The NCCC consultants include multiprofessional medical, nursing, and pharmacy subject matter experts. Consultations are conducted in real time and documented by the NCCC consultants by entering de-identified data directly into the database either during or shortly after the call. Documented data include fixed data fields (e.g., caller name, profession, contact information) and open text fields including description of the case, caller's question(s), and consultant's response(s). The discussions are organized by the caller profile in the NCCC consultation database.

In the wake of the Food and Drug Administration's 2012 approval of the first PrEP regimen, the NCCC PrEPline was introduced in 2014 to offer clinicians access to an educational resource staffed by clinical subject matter experts who could respond to a wide variety of PrEP-related questions. The PrEPline receives questions related to PrEP eligibility, PrEP regimen selection and dosing strategies, PrEP initiation, baseline and follow-up laboratory testing, special circumstances (e.g., kidney or bone disease, pregnancy), and specific populations (e.g., transgender individuals and adolescents).

The NCCC consultation data are collected and stored in a secure, cloud-based customer relationship management platform. No protected health information is collected by consultants or stored in the consultation platform. Data analytics features of this platform were used to create reports capturing all PrEPline consultations during the 4-year calendar period from January 1, 2017, through December 31, 2020. We started with 2017 to align with the release of CDCs then updated PrEP guidelines.[18] PrEPline consultation call data were then exported to Microsoft Excel by one co-author (P.S.) for further analysis.

We used a qualitative content analysis approach in which clinical topics and subtopics were developed inductively through reading, interpreting, and discussing textual data.[19] Initially, one co-author (P.S.) reviewed a random sample of 40 calls to develop preliminary overarching clinical topics (e.g., laboratory ordering/monitoring and side effects) and subtopics (e.g., HIV viral load testing and testing window period) that captured the main themes and subthemes of the caller's inquiry and/or clinical case and their subsequent discussion with the PrEPline consultant. One co-author (P.S.) then

trained three co-authors (A.S., N.J.M., and C.E.C.) to review and code all calls based on topic and subtopic and to iteratively refine the coding structure by identifying any topics/subtopics that were not originally captured by the first author.

Next, all the authors assigned up to three subtopics for each consultation. Additionally, the authors were trained to designate one of three levels of complexity for each consultation: (1) Level 1 or low complexity consultations (i.e., response to the question was available within the CDCs PrEP guidelines or other established medical guidelines); (2) Level 2 or moderate complexity consultations referred to discussions involving some complexity (i.e., cases with limited data to respond to the caller's question or questions that were partially addressed in CDC PrEP guidelines but required additional information to inform clinical decision-making); and (3) Level 3 or highly complex consultations (due to the absence of published data [i.e., no clear data/evidence-based guidance existed at the time to address the question, in some cases requiring PrEPline consultants to seek additional input from other PrEP researchers or clinical experts]).

Two co-authors (P.S. and C.E.C.) reviewed a random sample of 10% of categorized calls for quality assurance and to ensure consistency in coding across reviewers. One co-author (P.S.) used descriptive statistics to summarize caller demographic characteristics, call topics and subtopics, and the level of complexity.

Results

From 2017 through 2020, the PrEPline responded to a total of 1,754 clinical teleconsultation requests from providers across the United States (*Table 1*). There was a gradual increase in the percentage of PrEPline calls from 2017 ($n=414$, 23.6%) to 2019 ($n=500$, 28.5%) and a decrease in the percentage of calls in 2020 ($n=373$, 21.3%). Most calls were from advanced practice nurses ($n=689$, 39.3%) and physicians ($n=662$, 37.7%), with a smaller percentage from other types of health care providers, including physician assistants ($n=131$, 7.5%), pharmacists ($n=83$, 4.7%), and registered nurses ($n=57$, 3.2%).

Family Medicine ($n=372$, 56.2%) and Internal Medicine ($n=96$, 14.5%) constituted the majority of physician callers, whereas other specialists, such as Infectious Diseases ($n=80$, 12.1%), called less frequently. The highest number of calls were from the Pacific region ($n=493$, 28.1%), and the fewest number of calls were from the Southeast ($n=155$, 8.8%), South Central ($n=124$, 7.1%), and New England ($n=110$, 6.3%) regions. The majority of callers indicated that they had ever prescribed PrEP ($n=987$, 56.3%) and had at least one patient on PrEP ($n=884$, 50.4%).

Table 1. Characteristics of the National PrEPline Callers and the Patients/Cases Regarding Whom Callers Were Requesting Consultation

CHARACTERISTIC	SUBCATEGORIES	*N* = 1,754
Year, *n* (%)		
	2017	414 (23.6)
	2018	467 (26.6)
	2019	500 (28.5)
	2020	373 (21.3)
Facility type, *n* (%)		
	Outpatient	1,346 (76.7)
	Hospital	221 (12.6)
	Other	167 (9.5)
	Prefer not to respond, missing	20 (1.2)
Contact profession, *n* (%)		
	Advanced practice nurse	689 (39.3)
	Physician	662 (37.7)
	Physician assistant	131 (7.5)
	Other health-related profession	86 (4.9)
	Pharmacist	83 (4.7)
	Registered nurse	57 (3.2)
	Other non-health-related profession, missing	46 (2.7)
Specialty of physician callers, *n* (% among 662 physicians)		
	Family Medicine	372 (56.2)
	Internal Medicine	96 (14.5)
	Infectious Diseases	80 (12.1)
	Pediatrics and Neonatology	38 (5.7)
	Obstetrics and Gynecology	25 (3.8)
	Emergency Medicine	15 (2.3)
	Occupational Medicine	4 (0.6)
	Psychiatrist	3 (0.5)
	Other specialty	29 (4.4)
Region,[a] *n* (%)		
	Pacific	493 (28.1)
	Northeast/Caribbean	250 (14.3)
	Mountain West	220 (12.5)
	Mid-West	213 (12.1)
	Mid-Atlantic	165 (9.4)

continued →

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Table 1. Characteristics of the National PrEPline Callers and the Patients/Cases Regarding Whom Callers Were Requesting Consultation *continued*

CHARACTERISTIC	SUBCATEGORIES	*N* = 1,754
	Southeast	155 (8.8)
	South Central	124 (7.1)
	New England	110 (6.3)
	Unknown	24 (1.4)
Ever prescribed PrEP, *n* (%)		
	Yes	987 (56.3)
	No	474 (27.0)
	N/A or missing	293 (16.7)
Number of patients on PrEP, *n* (%)		
	0	397 (22.6)
	1–5	290 (16.5)
	6–25	288 (16.4)
	26+	306 (17.4)
	N/A, prefer to not respond, missing	473 (27.0)
Provision of direct services to people living with HIV, *n* (%)		
	Yes	334 (19.0)
	No	1,007 (57.4)
	Missing	413 (23.5)
Years of HIV service, mean (SD)		7.0 (7.3)
Patient's gender, *n* (%)		
	Cisgender man	1,011 (57.6)
	Cisgender woman	243 (13.9)
	Transgender woman	12 (0.7)
	Other	5 (0.3)
	Prefer to not respond, unknown, missing	7 (0.5)
Patient's eligibility for PrEP,[b] *n* (%)		
	MSM	891 (31.1)
	Multiple sex partners	384 (13.4)
	Inconsistent or no condom use	337 (11.8)
	Sex partner living with HIV	235 (8.2)
	Heterosexual intercourse	180 (6.3)
	Sex partner at risk for HIV	85 (2.4)
	STI diagnosis within last 6–12 months	78 (2.7)
	Transgender	40 (1.4)
	Other	104 (3.6)
	Unknown, missing	550 (19.2)

continued →

Table 1. Characteristics of the National PrEPline Callers and the Patients/Cases Regarding Whom Callers Were Requesting Consultation *continued*

[a]Based on the AETCs Program categorization.

[b]Multiple categories could be selected; therefore, total is >100%.

AETCs, AIDS Education and Training Centers; MSM, men who have sex with other men; N/A, not applicable; PrEP, pre-exposure prophylaxis; SD, standard deviation; STI, sexually transmitted infection.

Questions regarding specific medication-based HIV prevention strategies composed the greatest percentage of cases ($n = 931$, 22.7%; *Table 2*). The most commonly discussed subtopics within this topic area included PrEP medication initiation ($n = 379$, 9.3%), followed by consultations around the concept of undetectable = untransmittable or "U = U" ($n = 120$, 2.9%), transitioning from post-exposure prophylaxis (PEP) to PrEP ($n = 104$, 2.5%), PrEP continuation ($n = 100$, 2.4%), and deciding between prescribing PEP or PrEP ($n = 95$, 2.3%).

Under the topic of PrEP laboratory ordering/monitoring, general questions about which laboratory tests to order/monitor before or during PrEP use ($n = 598$, 14.6%) were the most common subtopic. Questions regarding side effects and contraindications arose least frequently; within this topic, renal side effects of PrEP were discussed for 249 calls (6.1%) and infrequent side effects such as liver toxicity were discussed in 67 calls (1.6%). Overall, 57.9% of calls fell within the Level 1 complexity group, and smaller percentages were categorized as Level 2 (25.5%) or Level 3 (5.8%).

Specific questions regarding deciding between tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide fumarate (TAF; $n = 118$, 2.9%) or alternative dosing strategies such as 2-1-1 dosing ($n = 87$, 2.1%) were frequently asked in the "PrEP medication information and dosing strategies" topic. Nearly 51 (1.2%) questions were regarding discrepant HIV screening/testing results before or after PrEP initiation (i.e., inconclusive or indeterminate testing results that were inconsistent and/or did not denote a clear negative or positive HIV serostatus). Additionally, few callers ($n = 11$, 0.3%) asked about more complex concepts of presumptive antiretroviral therapy (ART) prescribing (i.e., the use of ART to cover both prophylaxis and treatment in the event of a recent exposure within the "window period" of HIV diagnostic testing) and PrEP "failures" (i.e., HIV acquisition in PrEP users; $n = 10$, 0.2%).

Table 2. Main Topics and Subtopics of PrEPline Calls

TOPICS	SUBTOPICS	*n*	%
Medication-based HIV prevention strategies		931	22.7
	PrEP initiation (or reinitiation)	379	9.3
	U = U	120	2.9
	PEP to PrEP	104	2.5
	PrEP continuation	100	2.4
	PEP or PrEP	95	2.3
	PrEP to PEP	42	1.0
	PrEP discontinuation	38	0.9
	Same-day PrEP start	21	0.5
	Presumptive ART	11	0.3
	PrEP "failures"	10	0.2
	Other	11	0.3
PrEP laboratory ordering/monitoring		712	17.4
	Laboratory testing (general questions)	598	14.6
	HIV viral load testing	79	1.9
	HIV testing window period	35	0.9
Side effects and contraindications		598	14.6
	Renal toxicity	249	6.1
	Side effects (general)	160	3.9
	Contraindications	108	2.6
	Liver toxicity	67	1.6
	Rash	9	0.2
	Other	5	0.1
Resources		414	10.1
	PrEP resources/guidelines	368	9.0
	PrEP clinical protocols	18	0.4
	Medicolegal concerns	16	0.4
	PrEPline/NCCC program info	7	0.2
	General/other	5	0.1
PrEP medication information and dosing strategies		310	7.6
	Decision-making between TDF/FTC vs TAF/FTC	118	2.9
	2-1-1 Dosing	87	2.1
	TDF/FTC	43	1.0
	LAI	31	0.8
	TAF/FTC	27	0.7
	Generic TDF/FTC	4	0.1
Specific populations		221	5.4
	Cisgender women	72	1.8
	Adolescents	68	1.7
	Other specific populations	21	0.5
	Transgender women	18	0.4
	PWID	17	0.4
	Transgender populations (general)	11	0.3
	Transgender men	8	0.2
	Older adults	6	0.1
PrEP medication drug levels		209	5.1
	Adherence	113	2.8
	Time to protective levels	96	2.3
STIs and BBPs		202	4.9
	HBV	108	2.6
	STIs	71	1.7
	HCV	23	0.6
HIV testing/diagnostics and ARV resistance		119	2.9
	Discrepant HIV screening/testing results	51	1.2
	Acute retroviral syndrome/acute HIV	29	0.7
	ARV drug resistance	25	0.6
	Seroconversion	14	0.3
HIV risk assessment		99	2.4
Pregnancy and breastfeeding		88	2.1
	Pregnancy	71	1.7
	Breastfeeding	17	0.4
Drug–drug interactions		61	1.5

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Table 2. Main Topics and Subtopics of PrEPline Calls
continued

TOPICS	SUBTOPICS	*n*	%
Bone health (prevention)		56	1.4
	BMD evaluation	49	1.2
	Vitamin D	7	0.2
Access to PrEP		51	1.2
	Insurance coverage	48	1.2
	Pharmacy-specific concerns	3	0.1
COVID-19 and PrEP services/care		26	0.6

ART, antiretroviral therapy; ARV, antiretroviral; BBP, blood-borne pathogen; BMD, bone mineral density; COVID-19, coronavirus disease 2019; FTC, emtricitabine; HBV, hepatitis B virus; HCV, hepatitis C virus; LAI, long-acting injectables; NCCC, National Clinician Consultation Center; PEP, post-exposure prophylaxis; PWID, people who inject drugs; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; U = U, undetectable = untransmittable.

In addition to questions regarding the utility or efficacy of PrEP in cisgender women ($n = 72$, 1.8%) and adolescents ($n = 68$, 1.7%), questions related to other specific patient populations included PrEP for transgender women ($n = 18$, 0.4%), people who inject drugs ($n = 17$, 0.4%), transgender men ($n = 8$, 0.2%), older adults ($n = 6$, 0.1%), and other unique populations ($n = 21$, 0.5%) such as incarcerated people, people seeking prophylaxis against HIV-2, people with dysphagia, people with a history of bariatric surgery, or those on hemodialysis.

Discussion

This report provides unique insight on the types and complexity levels of clinical cases and questions posed to national HIV PrEPline consultants by frontline U.S. health care providers and helps describe the "real-world" landscape of clinical case scenarios and medical decision-making. While it was encouraging that a high number of advanced practice nurses and physicians used this service, the numbers of physician assistants, pharmacists, registered nurses, and other health care providers contacting the PrEPline were low. This may indicate a potential need for increased training and involvement of these professions in PrEP-related care. Specifically, given evidence of successful pharmacy-led PrEP services,[20,21] training of more pharmacy and nursing providers may increase opportunities for PrEP implementation and access and team-based care.

Additionally, Family Medicine and Internal Medicine constituted a higher number of the physician callers compared with Infectious Diseases and other specialties. This may be in line with a key barrier to HIV prevention services known as the "purview paradox" whereby HIV specialists often do not see HIV-negative individuals and primary care physicians may have varying levels of experience and comfort with PrEP.[11,13]

Most PrEPline inquiries came from providers in the Pacific region, and fewer questions were from the South region. This pattern bares resemblance to data demonstrating lower PrEP to need ratio in the South compared with other regions.[4] Our observation may be due to higher adoption of PrEP in the Pacific region, the geographic proximity among regional providers to the PrEPline, and/or familiarity with UCSFs HIV-related services. It is important to note that the PrEPline is federally funded and available at no cost to all providers nationally; therefore, the use of PrEPline as a clinical resource can be integrated into PrEP training and educational material and PrEP academic detailing efforts across all U.S. regions.[22] The use of PrEPline may also be of particular value in rural areas of the United States where family medicine residency programs lack PrEP training and programs.[23]

Even though the responses to many questions presented to the PrEPline could be found within the established CDC PrEP guidelines (i.e., Level 1 complexity), there are opportunities for future iterations of the guidelines or locally disseminated PrEP clinical guidance to develop content that clearly and succinctly addresses commonly asked questions with practical guidance and clinical decision-making support (i.e., more user-friendly). For example, step-by-step instructions on transitioning from PEP to PrEP may be useful, and case-based learning may be an approach, which holds appeal for newer PrEP providers.

While some of the questions posed by 2017–2020 PrEPline callers have been addressed in the updated 2021 CDC PrEP guidelines,[24,25] this study may inform future guidelines committee planning and PrEP research efforts by identifying areas that could benefit from additional clarification and investigation. Additionally, PrEP educators and trainers may wish to tailor information from the guidelines to make them optimally useful for providers. Finally, nearly one third of PrEPline callers asked clinical questions related to PrEP prescribing that required clinical judgment and extrapolation of data/practices from other areas of HIV prevention and treatment (i.e., Level 2 or 3 complexity). These data can offer providers and researchers a view of PrEP topics that would benefit from expert consensus around "best practices" and more research.

This study reflects the needs and questions of a self-selecting group of providers; however, despite this limitation,

these data can aid the NCCC and other organizations in development of "Frequently Asked Questions," PrEP toolkits, or "pocket cards," as well as creation of more substantial PrEP clinical training materials for health care providers. Given an abundance of evidence suggesting that providers would be more willing to provide PrEP if empowered with additional training,[26,27] these data can be used to develop such training materials and case discussions using commonly encountered, real-world clinical scenarios to improve providers' knowledge and comfort with PrEP initiation and continuation.

Given the successes of academic or public health detailing, these PrEP training materials and case discussions can be used to market PrEP directly to providers to address gaps in PrEP prescribing.[22] Finally, the widespread use of the PrEPline across the United States highlights the importance of accessible capacity-building services and programs and teleconsultation resources. Along with other innovations in PrEP care, such as mobile clinics, pharmacy-led PrEP delivery, PrEP coordinator-led PrEP delivery, mobile health and web-based technologies, social media platforms, and home collection of laboratory samples,[28–32] the PrEPline is an example of how health systems may better incorporate new technologies in health care to make PrEP care less burdensome and improve care in a sustainable and cost-effective[33] manner.

Authors' Contributions

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work, including in the concept, design, analysis, writing, or revision of the article.

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