



A Review of Telehealth Innovations for HIV Pre-Exposure Prophylaxis (PrEP)

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Abstract

Purpose of Review This review summarizes novel interventions that employ technology to improve HIV pre-exposure prophylaxis (PrEP) availability, uptake, and adherence.

Recent Findings Several notable technology-based programs are increasing access to PrEP in unique ways. We identified multiple models for using telehealth to bolster PrEP dissemination and adherence, such as mobile applications that offer PrEP prescribing without an in-person visit, longitudinal distance telermentoring for community provider PrEP education and clinical guidance, and electronic consults for PrEP specialist support in the primary care setting. Outcomes data for all of these modalities are limited but show promise.

Summary Technology-based interventions can address gaps in the PrEP care continuum. Future research should assess and compare outcomes, scalability, cost-effectiveness, and sustainability. Costs associated with the creation of new technological tools slow innovation and the field would benefit from a platform for technology sharing.

Keywords Telehealth · HIV prevention · Pre-exposure prophylaxis · Technology

Introduction

Pre-exposure prophylaxis (PrEP) with daily oral emtricitabine/tenofovir, disoproxil, and fumarate reduced HIV transmission risk by >90% in clinical trials and was approved by the US Food and Drug Administration (FDA) for this indication in 2012 [1]. Although the Centers for Disease Control and Prevention (CDC) reports that an estimated 1.25 million individuals in the USA have an indication for PrEP, fewer than 10% of at-risk persons currently receive it [2, 3••]. Numerous barriers prevent access to PrEP. Obstacles along the PrEP continuum of care include individual awareness of HIV risk and willingness to take PrEP, geographic distance to care, provider awareness of PrEP, and willingness

to prescribe, cost or insurance access, and adherence [4, 5]. Stigma also prevents HIV preventative care for many; for example, fewer than 50% of men who have sex with men (MSM) disclose their sexual orientation to their primary care provider due to discomfort in healthcare settings and fear of judgment [6]. Uptake of PrEP has been especially low for young MSM of color and MSM living in rural areas, for whom issues like cost and stigma may be especially pronounced [7–10]. Novel technology-based strategies are now being employed to circumvent these barriers and scale-up PrEP coverage for at-risk populations.

The US Health Resources and Service Administration (HRSA) defines telehealth as “the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care, patient and professional health-related education, public health and health administration” [11]. Telehealth encompasses a number of different modalities, ranging from synchronous video teleconferencing to store-and-forward consultations (see Table 1 for further definitions of telehealth modalities, rationale for their use, and applications for PrEP). The Infectious Diseases Society of America (IDSA) supports the use of telehealth as a means of reaching rural and urban underserved populations [18]. In recent years, telehealth modalities have been leveraged in

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Table 1 Various telehealth modalities, rationale for their use, examples of their implementation for technology-based PrEP care, along with major partnerships and references

Modality	Function and rationale	Examples	Funding/partnerships	References
Provider-to-patient	Remote PrEP prescribing; designed to overcome geographic barriers, connect at-risk persons directly to PrEP-trained providers, and may reduce barriers such as fear of discrimination.	PrEPTECH, a pilot program in California that enrolled participants via a mobile-friendly website, with PrEP intake appointments by phone, opt-in text message adherence reminders, and PrEP medication by mail. Gay City, an LGBTQ community center in Seattle, where HIV counselors provide on-site care and PrEP is prescribed using videoconference visits with a remote PrEP specialist. PrEPiOWA, an intervention in which clinical pharmacists prescribe medications and counsel patients via telemedicine, with physician support available as needed. Plusheare.com , a mobile/web platform that offers videoconference visits for PrEP prescribing in many states. Nurx.com , a mobile/web platform that offers PrEP after a text message-based intake by a physician.	California DOH; University of California, Los Angeles; YTH.org ; Gilead Washington State DOH; University of Washington; Gay City community center Iowa DOH; University of Iowa For-profit For-profit	[12, 13••] [14•] [13••]
Provider-to-provider	Distance mentorship and clinical consultation for community PrEP prescribers via videoconference with Infectious Disease specialists plus a multidisciplinary support team; designed to build capacity of primary care providers to prescribe PrEP.	The Mountain West AETC ECHO program offers quarterly PrEP didactics and case-based discussion via videoconference, connecting community PrEP providers in six states with University of Washington specialists, including ID providers as well as pharmacy, psychiatry, and social work experts.	Washington State DOH; University of Washington; HRSA	[15]
Store-and-forward consults (“e-Consults”)	EHR-based specialist consultation without a face-to-face visit; designed to reduce barriers to access to PrEP specialists, support primary care provider prescribing, and build capacity of non-specialists to prescribe PrEP.	The Veteran’s Health Administration has a well-established e-Consult system to support PCPs in PrEP prescribing and the University of Washington recently introduced Infectious Disease e-Consults, including an option for PrEP-prescribing guidance.	Washington State DOH; University of Washington; HRSA	[16, 17]

PrEP, pre-exposure prophylaxis; *DOH*, Department of Health; *HRSA*, Health Resources and Service Administration; *AETC*, AIDS Education and Training Center; *ECHO*, Extension for Community Healthcare Outcomes; *EHR*, electronic healthcare record

innovative ways to reach at-risk individuals and promote PrEP uptake, including interventions that connect at-risk persons directly to providers or that connect providers to other providers or specialists for clinical training or support.

Here, we describe and compare recent advances in the use of electronic and mobile technologies that overcome barriers to PrEP dissemination. Although outside of the scope of this review, telehealth is also being used to improve PrEP adherence, as with text message medication reminders and electronic pillbox remote monitoring. Many telehealth interventions are the subject of ongoing study. Whenever possible, we summarize peer-reviewed literature; however, due to the fast pace of technological advances and limited published data, we also rely on correspondence with telehealth developers and investigators to fill in gaps. We intend this review to serve as a resource for the design and implementation of future PrEP telehealth initiatives.

Provider-to-Patient Telehealth Interventions

Nationwide, there are a growing number of not-for-profit and for-profit initiatives that use digital or mobile platforms to connect patients directly to PrEP prescribers. Each program must address a number of problem points in the chain of PrEP care. First, the prescriber and patient need to communicate. Options include telephone, videoconference, and mobile texting. Intermediaries such as clinical pharmacists or HIV counselors may aid in this communication by delivering on-site care, counseling, or helping to navigate medication-assistance programs and insurance enrollment. Second, programs must develop a strategy for laboratory testing and delivery of medication. Finally, financial support for physicians and program support staff is a significant issue, and regulations governing which methods of communication are reimbursable vary by state. In this section, we will review how a number of existing programs attempt to address these hurdles.

As an example of a PrEP delivery program that connects patients to prescribers, a team from University of California, Los Angeles (UCLA), launched a web-based HIV prevention program called PrEPTECH, which uses a mobile-friendly, HIPAA-compliant website to facilitate PrEP initiation and adherence in young MSM of color living in the San Francisco Bay Area. The program recruits participants via ads on Grindr, a popular “hookup app.” After signing up online and completing a screening survey, eligible persons participate in a telephone visit with an infectious disease (ID) physician and return a sexually transmitted infection (STI) self-collection kit to a laboratory where they also have blood drawn. Ultimately, participants receive a 90-day supply of PrEP medication in the mail with no requirement for a face-to-face clinic visit. In this model, all care except blood draws is provided via telehealth, with follow-up telephone appointments scheduled at 1 month,

3 months, and 6 months after PrEP initiation. Participants can opt into other benefits, such as daily adherence reminders via email or text, automated appointment reminders, and access to their PrEP prescriber via an “Ask the Doctor” feature. During the pilot phase, 25 young MSM of color received PrEP through this telehealth program, with the majority successfully transitioning to a clinic-based PrEP provider at the conclusion of the study [12, personal communication]. This innovative program demonstrates that advertising on hookup apps is a useful strategy for reaching young urban MSM of color and that a telehealth-based PrEP program can effectively engage this high-risk population and overcome barriers to PrEP initiation.

Videoconference visits have been studied as a method for initiating PrEP in a community setting in Seattle, Washington. Trained HIV counselors at Gay City, an LGBTQ community center, identify PrEP candidates and help them schedule an intake appointment with an ID physician, with the option of completing this visit by telemedicine. If pursuing this option, the counselor is on site with the PrEP candidate for the intake visit, offering counseling on PrEP-related topics and instruction on STI self-testing, performing venipuncture, and assisting with health insurance applications or medication assistance paperwork. The physician participates in the intake appointment via videoconference using a computer-based, HIPAA-compliant platform (Zoom). Follow-up appointments are completed independently by the counselor following PrEP initiation. This PrEP telehealth project differs from UCLA’s PrEPTECH program in that telemedicine appointments are conducted using videoconference instead of telephone, as dictated by Washington State law, which requires prescribers to establish a patient-to-provider relationship with at least one face-to-face evaluation for reimbursement [19]. It also relies on trained HIV counselors with a broad scope of practice for the bulk of PrEP care, thus task-shifting clinical responsibilities and increasing accessibility of PrEP providers. While not home-based like PrEPTECH, it offers patients the comfort and convenience of a local community center in lieu of an unfamiliar medical office preliminary data on ten individuals who completed their intake appointment via videoconference showed that this method was feasible and acceptable for patients. When compared to individuals who completed an in-person intake visit at Gay City ($n = 38$), those who participated in the telemedicine option had similar rates of PrEP initiation, adherence at 1 month, and return for an initial follow-up visit, but lower return for a 3 month visit [14, personal communication]. Given the small numbers in this pilot study, it is difficult to interpret the lower 3-month follow-up rate, which study authors did not attribute to the telemedicine format. Overall, this telehealth approach appears to be a practical and viable format for PrEP intake and initiation.

Another unique PrEP telehealth intervention utilizes pharmacist-driven protocols combined with telemedicine.

PrEPIOWA, which launched in February 2017, is a collaborative program run by University of Iowa clinical pharmacists and ID physicians in partnership with the Iowa Department of Public Health. Public health providers refer clients with PrEP indications from STI clinics around the state. Specialist clinical pharmacists serve as the primary contact for participants, providing PrEP counseling via interactive videoconference on a mobile video app (Vidyo) that enables secure audio-video connections on tablets, phones, or computers. The collaborative practice model allows the pharmacist to prescribe the medication under the physician's name, with the physician available for consultation if necessary. Clients taking PrEP complete surveillance bloodwork and STI testing at a network of public health labs and free clinics and individuals with positive STI screening tests are referred back to the public health department to arrange treatment and partner notification. Other than lab work, the program operates completely digitally and medications are sent via mail-order pharmacy; as with PrEPTECH, the need for a face-to-face visit with a physician is eliminated. PrEPIOWA is a nascent but growing endeavor, with upwards of 80 clients enrolled during the first year and 78% of clients retained in PrEP care at 6 months [13••, personal communication].

Telemedicine for PrEP has spread to the realm of private industry as well, and there are now multiple for-profit companies that offer internet and app-based services to connect patients with PrEP prescribers. PlushCare (plushcare.com) is a large telehealth entity that offers video appointments with physicians to consumers in most states. Initially designed as a vehicle for urgent care, the company introduced PrEP-prescribing services in November 2017 and now has upwards of 1000 PrEP enrollees, the majority of whom live outside of major urban centers [13••, personal communication]. By contrast, another major PrEP-prescribing telehealth company, Nurx (nurx.com), uses an entirely text message-based mobile platform to prescribe PrEP to customers in 18 states [personal communication]. After completing a health survey and submitting insurance information, Nurx customers can communicate with their prescribing physician via text message within a HIPAA-compliant mobile app. Both Plushcare and Nurx provide an avenue for at-risk MSM in rural areas to confidentially access PrEP. However, access to these services in most states is limited to patients with private insurance.

Direct provider-to-patient telehealth interventions provide archetypes for how telemedicine can support PrEP initiation and uptake and overcome barriers to access along the PrEP continuum of care. These models connect at-risk persons directly to a provider who is knowledgeable and willing to prescribe while eliminating the need for in-person visits. This reduces the chance that geographic distance to care, fear of discrimination, or time spent searching for a prescriber will prevent a person in need from seeking PrEP. Although existing programs still require patients to travel to a laboratory

for blood draws, an upcoming multi-site randomized clinical trial will investigate the efficacy of a model that offers completely home-based PrEP care, with visits performed by telemedicine and lab monitoring done using a self-collection kit at home [20, 21••, personal communication]. This PrEP delivery trial, called ePrEP, is designed to minimize the burden of care for at-risk persons and improve PrEP access.

Challenges to these provider-to-patient strategies include funding, which the examples described here tackled in various ways, including collaboration with state departments of public health, university affiliations, medication subsidies from drug companies, and private funding sources. Additionally, each program uses a distinct telemedicine platform for communication with patients and some created their own platform, which adds cost and time. One limitation of provider-to-patient models is they do not build the capacity of primary care and other clinicians to prescribe PrEP, though clearly, these programs are valuable and replication or expansion of such prototypes could bolster dissemination of PrEP in the USA and abroad.

Provider-to-Provider Telehealth Interventions

Access to PrEP relies on medical provider awareness and comfort prescribing, which can be limited among rural community providers, for whom specialist consultation and continuing medical education are not readily available [22, 23]. Unlike interventions that connect patients directly to providers, other telehealth initiatives use technology to create communities of practice and deliver clinical mentorship around HIV treatment and prevention. For example, at the University of Washington in Seattle, Washington, a distance telementoring program called Project ECHO (Extension for Community Healthcare Outcomes) is being used to educate and support community PrEP providers in a multistate region. The Project ECHO model was developed by the University of New Mexico to support rural providers treating hepatitis C infection [24]. In 2012, the University of Washington and Mountain West AIDS Education and Training Center (MW AETC) launched a Project ECHO program to mentor community HIV providers in the Pacific Northwest region (participating sites currently span six states) [15]. The program brings together physicians, advanced practitioners, clinical pharmacists, and social workers for a weekly interactive videoconference. Sessions start with a short didactic talk led by a local or national HIV expert, then focus on discussion of challenging cases encountered by the community providers. In July 2015, in collaboration with the Washington State Department of Health, the team leading this program incorporated quarterly PrEP didactics and monthly PrEP case discussions to meet provider demand.

As of June 2018, the Project ECHO team has delivered 12 PrEP-focused talks since the program's inception (nine of these have occurred since July 2015). Furthermore, there have been 35 case discussions in which PrEP was the central question raised by the community provider plus another six case discussions in which PrEP was not the focal question but was discussed as potentially indicated for the partner of a patient discussed. The case discussions have focused on a variety of PrEP topics, such as clinical indications for PrEP, use of PrEP for conception by serodiscordant couples, financial barriers to PrEP, and other PrEP-related clinical best practices. The program currently connects over 30 clinical sites and the average participation is 35 community medical providers per week. The didactic talks are archived online and are free and available at www.hivecho.org.

This peer-to-peer PrEP telementoring program provides a virtual community for knowledge sharing, with the goal of fostering local PrEP champions. Project ECHO initiatives are now spreading internationally, with programs launched or in planning stages in multiple locations in Africa, South Asia, South America, the Caribbean, and other regions. The University of Washington monthly Project ECHO sessions provide a paradigm for how PrEP content might be incorporated into existing Project ECHO programs. Strengths of this model are that it builds capacity of community primary care providers and other non-specialist practitioners to offer and prescribe PrEP. In its current iteration, only providers with some pre-existing interest in HIV care typically participate in the UW Project ECHO, although the model could be adapted to train broader audiences and a PrEP-specific Project ECHO program for primary care providers could be considered. Challenges and limitations to this type of telehealth strategy include that there is no defined mechanism for reimbursement, the scalability is limited (only a certain number of clinical sites can join each weekly session), and patient outcomes have not been fully assessed, although evaluations are ongoing.

Store and Forward e-Consults

Another model for expanding PrEP-prescribing capacity is the store-and-forward or electronic consult ("e-Consult"). The e-Consult enables primary care practitioners to request remote specialist consultation without requiring a face-to-face visit between the patient and specialist. The primary care provider enters an e-Consult within the electronic health record (EHR), including their clinical question and an auto-population of relevant lab results. This prompts a chart review by an ID specialist, who writes a response to the consult question within 72 h that includes recommendations and the clinical reasoning underlying the recommendations, with the goal of supporting clinical care and educating the primary care provider. For

example, a PrEP-specific e-Consult system is built into the national Veterans Administration (VA) EHR. Within the VA system, this resource has strengthened the HIV prevention care delivered at the VA's many community-based outpatient clinics (CBOCs), improved the timeliness of PrEP prescribing, and minimized travel and inconvenience to geographically dispersed veterans [16, 17]. Similarly, in March 2018, the University of Washington introduced store-and-forward consults for ID, including an option for PrEP consultation.

Although the use of e-Consults is becoming more widespread, we were unable to identify other institutions that offer PrEP prescribing among their ID e-Consult options (though they may exist). Ideally, this option will continue to expand, as it is designed to build PrEP prescriber capacity and reduce the need for specialist consultation for PrEP. This has the potential to improve access by increasing the number of primary care providers willing to prescribe PrEP; additionally, primary care providers can access specialist backup without the need for an in-person visit, thus improving the likelihood that patients will receive guidelines-based, best practice care while reducing the delay and inconvenience associated with specialist referral and eliminating a potential window for loss to follow-up. The primary limitation of this telehealth modality to date is that structures for reimbursement are not available in all regions or healthcare systems, though we anticipate this will change in the future.

Conclusions and Future Directions

By reviewing the published literature on novel PrEP telehealth initiatives and communicating with developers of such interventions, we identified numerous ways in which technological innovation can overcome barriers to PrEP uptake, build capacity of the medical workforce to deliver PrEP, and promote PrEP adherence. These examples provide models for using technology to support dissemination of PrEP and illustrate both successes and challenges in the field of telehealth for HIV prevention.

Our findings demonstrate that mobile applications and web-based platforms that enable remote PrEP prescribing effectively circumvent challenges to access. These modalities mitigate geographic isolation; prescribers need only be licensed in the state and patients are not required to travel or spend time seeking out a PrEP-trained provider. By bypassing in-person clinic and pharmacy visits, mobile application-based interventions allow for scheduling flexibility and reduce fear of discrimination, again expanding access. Additionally, by advertising on popular hook-up apps, such programs telegraph that their providers are LGBTQ-friendly and PrEP knowledgeable, lowering barriers to disclosure. Some telehealth initiatives are expanding PrEP access on a system-wide level by using clinical pharmacists or HIV counselors as PrEP care managers, models

that appear to be effective and could be replicated in other regions, though not all states allow collaborative practice pharmacist prescribing. Telementoring projects like Project ECHO and EHR-integrated PrEP e-Consults also build PrEP care capacity by educating primary care providers about PrEP guidelines and best practices.

These digital interventions are not without challenges and limitations. Funding, for example, is a principal hurdle. Some telehealth programs like PrEPIOWA and the program through Gay City in Seattle have relied on collaboration with state public health departments and other public funding sources; these programs have had local success but their geographic scope remains limited. Expanded funding options for such programs are needed in order to extend their reach. On the other hand, we identified several for-profit telehealth platforms that offer PrEP on a wide geographic scale, but that primarily serve individuals with private insurance. The feasibility of large-scale telehealth prescribing programs will vary by state, as each state determines its own telehealth reimbursement standards for Medicaid and private insurers, and laws and regulations vary from state to state [25]. For example, visits conducted with a provider by telephone may be adequate in some states, while in others a video face-to-face visit may be required.

While progress has been made in developing functional web and smartphone-based PrEP interventions, there is a need for ongoing research to identify which telehealth strategies are most impactful, scalable, and cost-effective. Looking forward, an open-source platform for technological resource-sharing between institutions would be invaluable given the difficulties and cost incurred through independent mobile app development. Novel funding sources are needed and advocacy to change laws and regulations to better support and reimburse such models must occur so that they can be implemented in regions with the greatest need.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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