Community Preventive Services Task Force

HIV Prevention: Digital Health Interventions to Improve Adherence to HIV Pre-Exposure Prophylaxis

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Finding and Rationale Statement
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CPSTF Finding and Rationale Statement

Context

In 2019, 1.06 million adults and adolescents in the United States were living with diagnosed HIV infection, including around 37,000 people with newly diagnosed infection (CDC 2021a [https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2018-updated-vol-32.pdf]). The highest rates of diagnosis were for males; people aged 20-29 years; Black or African American persons and Hispanic or Latino persons; gay, bisexual, and other men who have sex with men (collectively referred to as MSM); and people living in southern states (CDC 2021a [https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2018-updated-vol-32.pdf]).

Ending the HIV Epidemic in the United States [https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview] is the operational plan developed by agencies across the U.S. Department of Health and Human Services (HHS) to pursue the goal of reducing new HIV infections by 75% by 2025 and 90% by 2030. HHS identified four key strategies to achieve these goals in the United States: diagnose people living with HIV as early as possible after infection, treat people with HIV rapidly and effectively to reach sustained viral suppression, prevent new HIV transmission through evidence-based interventions such as pre-exposure prophylaxis (PrEP), and respond quickly to potential HIV outbreaks. The *HIV National Strategic Plan (2022-2025)* [https://www.hiv.gov/federal-response/hiv-national-strategic-plan/hiv-plan-2021-2025] is closely aligned with, and complements, Ending the HIV Epidemic. This plan aims to integrate coordinated efforts that address the HIV epidemic among all partners and stakeholders, prevent new HIV infections, improve health outcomes of people with HIV, and reduce HIV-related disparities and health inequities.

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians offer PrEP to persons who are at higher risk of HIV acquisition (USPSTF 2019 [https://www.uspreventiveservicestaskforce.org/uspstf/draft-update-summary/prevention-human-immunodeficiency-virus-hiv-infection-prep]). PrEP is a medicine that reduces the risk of getting HIV from sex or injection drug use. When taken daily as prescribed, PrEP reduces the risk of getting HIV from sex by 99% and from injection drug use by at least 74% (CDC HIV [https://www.cdc.gov/hiv/risk/prep/]). There is a strong connection between adherence to PrEP and its effectiveness in preventing HIV acquisition; reduced adherence is associated with marked declines in effectiveness (USPSTF 2019 [https://uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis]).

Intervention Definition

Digital health interventions to improve adherence to HIV PrEP use text messages, mobile apps, phone calls, or websites to deliver reminders, guidance, and support that may be tailored to an individual's needs. Participants must be HIV-negative and have a prescription for PrEP consistent with CDC guidelines (CDC 2021b [https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf]). Interventions provide one or more of the following:

- Information about HIV, PrEP, and strategies for medication adherence
- Services such as automated or interactive feedback, online forum discussions, virtual support groups, or adherence tracking intended to motivate participants

- Regular reminders for medications, virtual check-in appointments, and clinic visits

Interventions may be combined with in-person activities such as one-on-one counseling, peer-led group sessions, or patient navigation.

CPSTF Finding (December 2021)

The Community Preventive Services Task Force (CPSTF) recommends digital health interventions to increase adherence to HIV PrEP based on sufficient evidence of effectiveness. These interventions improve both daily-use pill taking and retention in PrEP care, thereby improving health for population groups who are not infected with HIV and engage in behaviors that may increase their chances of getting HIV.

Rationale

Basis of Finding

The CPSTF recommendation is based on evidence from a systematic review of 7 studies (search period January 2000 to June 2021). Eligible studies were identified through a three-step process. First, librarians from the Division of HIV Prevention conducted searches in databases MEDLINE, EMBASE, PsycINFO, and CINAHL (search period January 2000—June 2021) and established a database with all publications relevant to PrEP (Kamitani 2021, CDC 2021c). Second, librarians performed queries within the established database for publications relevant to digital health interventions to improve PrEP adherence. Last, a PubMed search was conducted to identify more recent publications potentially relevant to PrEP (search period January 2021—September 2021).

The systematic review found digital health interventions increased "good adherence" (defined as taking four or more doses of PrEP per week, 5 studies) and "excellent adherence" (defined as taking seven doses of PrEP per week, 3 studies). One study reported the intervention group missed fewer doses of PrEP when compared with the control group (Relative Risk 0.50; 95%CI 0.29—0.84). One study found the intervention improved retention in PrEP care (measured as the proportion of participants who attended all of their clinic visits) (Table 1).

Table 1. Effectiveness of Partner Services Interventions

Outcome Measure	Number of Studies	Median
Good adherence	5	2.4 (IQI: 1.9 to 4.9) Absolute difference: 10.0 pct pts (IQI: 2.3—23.3 pct pts) Relative difference: 11.1% (IQI: 5.6%—52.7%)
Excellent adherence	3	Absolute difference: 13.6 pct pts Min to max: 11.7 to 20.0 pct pts Relative difference: 65.4% Min to max: 36.4% to 200%
Retention	1	OR 2.62, 95% CI 1.24—5.54; p=0.01

Good adherence: consistent with four or more doses of PrEP per week
Excellent adherence: consistent with seven doses of PrEP per week
Retention: proportion of participants attending all clinical visits
IQI: interquartile interval
Pct pts: percentage points-
OR: odds ratio
CI: confidence interval
Min: minimum
Max: maximum

One study found adding visualized feedback to their PrEP adherence app increased the number of participants achieving excellent adherence (OR 2.0, 95% CI 1.1-3.8; p = 0.026) but did not reduce the number of participants with "poor adherence" (defined as less than four doses per week; OR 1.5, 95% CI 0.61-3.8; p = 0.36). The authors also reported poor adherence was associated with symptoms of depression or anxiety (OR 3.2, 95% CI 1.1-9.5) and low concern of acquiring HIV (OR 4.3, 95% CI 1.6-12).

Three studies examined intervention effects over time. While all three studies found effects diminished over time (intervention duration of 3 to 12 months), two of the studies reported higher adherence in the intervention groups when compared with the control groups.

Two studies reported HIV incidence. One study reported no HIV seroconversions in either the intervention or control groups, and the other reported two HIV seroconversions in the intervention group among patients who discontinued PrEP.

Applicability and Generalizability Issues

Intervention Settings

The included studies evaluated interventions implemented in the United States (6 studies) and The Netherlands (1 study). The U.S. studies were implemented in the Western (2 studies), Midwestern (2 study), Northeastern (1 study), and Southern (2 studies) regions as defined by the U.S. Census Bureau [https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf]. All studies were implemented in urban areas. The CPSTF finding is considered applicable to urban settings in all regions within the United States.

Population Characteristics

Four studies reported mean age of participants (median of 25 years), two studies reported median ages of 39 years and 49 years, and one study reported majority of participants below 49 years of age. No study conducted stratified analyses to examine if intervention effectiveness differed by participant's age.

Most participants were male (median of 96%, 5 studies); the two remaining studies only recruited male participants. Transgender female persons accounted for a median of 3% of participants (4 studies). Four studies only recruited MSM. Two studies reported the majority of participants self-identified as homosexual (49% and 68%). One study did not report on participants' sexual orientation.

All studies conducted in the United States reported information about racial or ethnic distributions (6 studies). Participants were Asian American (median of 7%, 3 studies), Black or African American (median of 13%, 5 studies), Hispanic or Latino (median 16%, 6 studies), and White (median of 69%, 4 studies); one study recruited only Black or African American participants. Study participants were representative of the U.S. general population, though none of the studies analyzed intervention effectiveness by race or ethnicity.

All of the studies reported at least one measure of socioeconomic status. A median 65% of participants were employed full time or part-time (4 studies); the remaining three studies did not report employment status. In two studies, the majority of participants had an annual income less than $20K (59% and 66%), and three studies reported a median of 22% of participants had an annual income less than $24-25K; two studies did not report income. Participants reported they had some college or more (median of 76%, 7 studies), or high school education or less (median of 17%, 4 studies). Most participants were insured (78% and 100%, 2 studies), covered by Medicaid or Medicare (64% and 90%, 2 studies), or paid for healthcare through private insurance or self-pay (19%, 1 study); three studies did not report insurance status.

In two studies, the majority of participants reported they engaged in "any" recreational substance use (64% and 72%). Four studies assessed participants' drug use history using questionnaires such as the Drug Abuse Screening Test [https://cde.drugabuse.gov/sites/nida_cde/files/DrugAbuseScreeningTest_2014Mar24.pdf] and reported low substance use (30%, 1 study), and excessive substance use (median of 37%, 3 studies); two studies did not report on drug use. None of the studies reported on injection drug use. Studies reported low alcohol use (100%, 1 study), and excessive alcohol use (median of 29%, 3 studies); three studies did not report on alcohol use. A median of 13% of study participants had mild depression, depression, or anxiety symptoms (3 studies); four studies did not report on mental health issues.

The CPSTF finding is considered applicable to younger MSM independent of socioeconomic status, race or ethnicity, or substance use.

Intervention Characteristics

All studies used a central location to collect data, obtain lab work, and provide information or instructions. Intervention duration was a median of nine months, with three studies lasting six months or less and four studies lasting longer than six months.

Interventions were designed to improve adherence to daily-use HIV PrEP. They used a digital application (app) only (2 studies), an app plus text messaging (1 study), text messaging only (1 study), or text messaging plus email, phone, or internet (3 studies). Digital health services included medication reminders (5 studies), information and education (4 studies), adherence tracking (2 studies), support groups (2 studies), and counseling (1 study).

Interventions communicated with participants daily (2 studies), weekly (3 studies), or monthly (1 study). Participants received feedback in one or more of the following ways: unidirectional communication (pre-set messages; 3 studies), automated bidirectional communication (questions were answered by pre-set messages; 3 studies), or personalized bidirectional communication (questions were answered by support persons in real time; 2 studies). One study provided an in-person support group. One study provided smartphones to study participants; the others required participants to have a smartphone and data plan. None of the studies provided information about the languages used for communications.

The CPSTF finding is considered applicable to digital health interventions designed to improve adherence to daily-use PrEP through text, phone, email, internet, or mobile apps.

Data Quality Issues

Studies were randomized control trials (RCT; 5 studies) or used group before-after designs (2 studies). Two common limitations were attrition and unclear description of sampling.

Potential Additional Benefits

Two included studies examined intervention impact on risky sexual behaviors and reported decreases in the mean number of anal sex partners and the proportion of study subjects who reported condomless anal sex (Colson et al. 2020; Liu et al. 2019). Similar decreases were observed, however, for both intervention and control groups.

Participants adhering to the schedule could gain additional benefit from increased clinical visits and services received (CDC 2021b). Recommended PrEP care includes clinical visits at different times:

- Every three months providers repeat HIV testing, assess and offer support for medication adherence and risk-reduction behaviors, perform bacterial STI screening for MSM and transgender women who have sex with men, and provided access to clean needles or syringes and drug treatment services for people who inject drugs.
- Every 6 months providers conduct renal function assessment, monitor estimated creatinine clearance level (eCrCl) for patients aged ≥50 years or who have an eCrCl <90 ml/minute at PrEP initiation, and perform bacterial STI screening for all sexually active patients.
- Every 12 months providers conduct renal function assessment for all patients; chlamydia screening for heterosexually active women and men; and weight, triglyceride and cholesterol levels assessment for patients on F/TAF, a combination of emtricitabine and tenofovir alafenamide.

Potential Harms

The broader literature noted increased risk compensation as a potential harm of the intervention. There is concern participants using PrEP may be more willing to engage in risk behavior. None of the included studies addressed risk compensation. Kumar et al. (2020) conducted a literature review to assess risk compensation associated with MSM before and after PrEP initiation. The review of 16 studies found inconsistent changes in condom use and a decrease in the number of sexual partners following PrEP initiation.

CPSTF noted that repeated PrEP reminders could lead participants to internalize stigma associated with being at high risk for HIV infection. One included study (Liu et al. 2019) reported that study participants experienced no social harms related to the intervention. Few participants (3%) worried about others knowing they were participating in the program.

Considerations for Implementation

Digital interventions to improve adherence to daily-use HIV PrEP were highly accepted among study participants. Of the services offered, study participants were most likely to use daily pill reminders and weekly check-ins. Included studies recruited a relatively young population who was more likely to be comfortable with digital communication, and few participants reported difficulties sending and receiving messages.

Interventions may need to be compliant with the Health Insurance Portability and Accountability Act (HIPAA). There are confidentiality concerns around receiving HIV-related text messages, and studies used innocuous language such as “time to take vitamin pills” to replace HIV-specific language. One study reported that their intervention was HIPAA compliant.

Digital health interventions have technology and equipment requirements. Six of the included studies only recruited participants who had smartphones and adequate data plans. In 2021, 85% of U.S. adults used a smartphone (Statista [https://www.statista.com/statistics/219865/percentage-of-us-adults-who-own-a-smartphone/]), 77% had high-speed broadband service at home (Pew Research Center [https://www.pewresearch.org/internet/fact-sheet/internet-broadband/]), and 93% used the Internet (Pew Research Center [https://www.pewresearch.org/internet/fact-sheet/internet-broadband/]), suggesting digital interventions could be widely implemented. The digital divide for smartphone ownership has diminished by race or ethnicity, but still exists for Americans with lower incomes (Pew Research Center [https://www.pewresearch.org/fact-tank/2021/06/22/digital-divide-persists-even-as-americans-with-lower-incomes-make-gains-in-tech-adoption/]), older adults (Pew Research Center [https://www.pewresearch.org/fact-tank/2022/01/13/share-of-those-65-and-older-who-are-tech-users-has-grown-in-the-past-decade/]), and people living in rural areas (Pew Research Center [https://www.pewresearch.org/fact-tank/2021/08/19/some-digital-divides-persist-between-rural-urban-and-suburban-america/]). It is important to consider participants’ income, age, and geographic location when implementing digital interventions.

In 2019, only 23.4% of people with indications for PrEP use received a prescription (CDC 2021d [https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-vol-26-no-2.pdf]). Structural and financial barriers exist for PrEP access, including patients' ability to get prescriptions and attend required clinic visits and testing appointments. Disparities in access lead to disparities in HIV care, morbidity, and mortality (Mayer et al. 2020). Implementers may want to consider options to address some of these barriers. For example, most insurance plans and state Medicaid programs [https://www.cdc.gov/hiv/basics/prep/paying-for-prep/index.html] cover the cost of PrEP. The Ready, Set, PrEP [https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program#:~:text=You%20can%20apply%20for%20the%20Ready%2C%20Set%2C%20PrEP,the%20United%20States%20including%20tribal%20lands%20and%20territories] program provides PrEP for free or at a reduced cost to those who qualify. Other programs include co-pay assistance programs [https://www.gileadadvancingaccess.com/] that lower costs of PrEP medications and state PrEP assistance programs [https://www.nastad.org/prep-access/state-prep-assistance-programs] that cover costs for medication, clinical visits, and lab testing.

Evidence Gaps

CPSTF identified several areas that have limited information. Additional research and evaluation could help answer the following questions and fill existing gaps in the evidence base.

Setting:

- How effective are digital health interventions for rural areas?

Population characteristics:

- How effective are these interventions for the following populations?
  - Older adults
  - Females and transgender persons
  - People in racial or ethnic minority groups
  - People with mental health issues
  - People who engage in excessive alcohol use or drug use (including injection drug use)

Intervention characteristics:

- Does intervention effectiveness change by offering participants the following?
  - All or part of the necessary equipment (e.g., mobile devices, data plan, internet access)
  - Materials and communications in languages other than English
  - In-person services

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Disclaimer

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