



Effectiveness of eHealth on Human Immunodeficiency Viruses Pre-Exposure Prophylaxis among Key Population: A Systematic Review and Meta-Analysis

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Abstract

Background: eHealth has proven effective in changing health-related behaviors and overcoming barriers to HIV care. This systematic review and meta-analysis aimed to review the effect of eHealth on HIV Pre-Exposure Prophylaxis (PrEP).

Methods: A systematic review and meta-analysis was conducted in international databases without a time limit until August 2024 to identify studies evaluating the effectiveness of eHealth interventions for PrEP among key populations. This search strategy used a combination of keywords related to "eHealth", "HIV", and "pre-exposure prophylaxis". A random effects model was used to compute the pooled measure of association (relative risk). The results were combined using a random-effects model for meta-analysis. The I^2 index was also used to measure heterogeneity between the studies.

Results: Twelve articles involving 3,578 participants were included in the meta-analysis. The findings showed that using websites had a positive effect on PrEP ($RR=1.90$, 95% CI: 1.30-2.79). Moreover, e-health interventions had the greatest effect on PrEP uptake among female sex workers (FSWs) ($RR=2.27$, 95% CI: 1.62-3.17). Furthermore, e-health demonstrated a notable effect on PrEP uptake ($RR=1.90$, 95% CI: 1.30-2.79), particularly in studies with follow-up less than six months ($RR=1.85$, 95% CI: 1.19-2.09). Additionally, studies conducted in the United States reported the most significant effect of e-health on PrEP ($RR=1.71$, 95% CI: 1.38-2.11; $I^2=0.41\%$).

Conclusion: eHealth interventions have the potential to improve the effectiveness of PrEP among key populations. Integrating e-health interventions with comprehensive healthcare services and providing continuous support can improve PrEP uptake, adherence, and retention in the future.

Keywords: Telemedicine; eHealth; Pre-exposure prophylaxis; Human immunodeficiency viruses



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Introduction

Although the incidence of HIV has decreased, HIV continues to be a major global public health issue. According to the latest reports, 39.9 million people were living with HIV (PLHIV), with 1.3 million of these cases representing new infections in 2023 (1). HIV has a significant financial burden on healthcare systems (2, 3) and severely impacts the mental health of those living with HIV (4). Additionally, the disease disproportionately affects marginalized populations, exacerbating social inequalities (5). While harm reduction programs, including condom use, the provision of sterile syringes, and pre-exposure prophylaxis, are effective strategies for controlling HIV, they encounter a range of challenges in fully achieving their objectives (6-8). It highlights the necessity for innovative approaches like Pre-Exposure Prophylaxis (PrEP) to effectively address the transmission of HIV.

PrEP, in which non-HIV individuals take antiretroviral drugs to prevent HIV infection, is both safe and effective (9). Studies have shown that PrEP oral decreases the risk of HIV transmission by more than 90% (10). Moreover, Lenacapavir, administered via injection every six months, is 100% effective (11). However, PrEP's efficacy is strongly associated with adherence and retention (9, 12). Moreover, low PrEP uptake is a major challenge (13, 14). Previous studies have shown that some groups with the highest risk for HIV are not willing to initiate PrEP (15, 16), and discontinuation rates are high (17). In addition, the biggest gap in the PrEP cascade is PrEP uptake (18). As a result, the rising effectiveness of PrEP necessitates the development of innovative strategies such as eHealth to enhance its effectiveness.

Technology-based delivery methods for prevention and treatment, such as eHealth methods, are increasing (19). Large-scale information distribution and efficient tool delivery to support and sustain behavioral change, routine HIV testing among uninfected people, and connection to PrEP can be facilitated by these technologies (20-24). This method delivers health interventions and

enhances health services through mobile devices and the Internet (25). eHealth allows for the development of prevention programs, such as online education, telehealth consultations, and mobile-based reminders, to improve PrEP uptake and adherence by addressing barriers like limited access to health services, privacy concerns, and difficulties with daily medication routines (23, 24, 26).

eHealth tools, which include mobile applications and telemedicine platforms, can improve the uptake and adherence of PrEP by providing personalized support, educational resources, and reminders to users (22, 27-29). However, due to the differences in design, implementation, and outcomes associated with these eHealth interventions, a comprehensive study is necessary to assess the current evidence and determine their overall effectiveness. In addition, a comprehensive study is required to find which eHealth methods provide the greatest benefit to specific populations.

As a result, this systematic review and meta-analysis aimed to evaluate the effectiveness of eHealth interventions on HIV PrEP among key populations.

Methods and Materials

Study Design

This systematic review and meta-analysis evaluated the effect of eHealth interventions on the initiation, adherence, and retention of HIV PrEP. The study's findings were reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (30).

Eligibility criteria

The inclusion criteria for the studies were as follows: randomized controlled trials evaluated the effect of eHealth interventions on HIV PrEP; publications in the English language; and studies published in peer-reviewed journals. Furthermore, there were no limitations regarding sample size or the research context. The exclusion criteria in-

cluded: studies that did not focus on eHealth interventions; studies that did not provide data on PrEP; and non-original studies.

Search Strategy

An electronic search strategy was developed to identify studies that focused on eHealth, HIV, and PrEP. A comprehensive literature review was conducted across multiple electronic databases, including PubMed, Scopus, Web of Science, and the Cochrane Library. This search used a combination of Medical Subject Headings (MeSH) keywords, specifically "eHealth" and "pre-exposure prophylaxis." No time limit was considered for article searching, and all searches were conducted until Aug 20, 2024. Furthermore, the reference lists of studies that met the inclusion criteria were manually examined to uncover additional relevant publications. Detailed information regarding the search methodology is available in the online supplementary appendix 1 (Not published).

Study Selection

After removing duplicate articles, the titles and abstracts were evaluated based on predetermined inclusion and exclusion criteria. Two independent reviewers (HM and MN) conducted a thorough screening of the titles and abstracts for all identified studies. Studies lacking adequate data regarding the outcomes of interest were excluded. Any disagreement between the reviewers during both the screening and full-text review phases was resolved by discussion and judgment of a third author (SHR). The agreement and inter-reliability between the two authors were evaluated through the application of Kappa statistics, resulting in a Kappa value of 80%.

Data extraction

Two independent reviewers conducted a screening of the titles and abstracts of the identified studies to determine their eligibility. After this review, the full texts of studies deemed potentially relevant were assessed. Data were gathered using a data extraction form that included the author, publication year, country, sample size, study design, eHealth

method, intervention duration, and outcomes related to PrEP uptake and adherence. This data extraction form was developed based on previous studies.

Quality assessment

The quality of reporting in RCTs was assessed using the CONSORT 2010 checklist, while cohort studies were evaluated with the STROBE guidelines. Each item was scored on a scale from 0 to 2: a score of zero indicated "not reported," one indicated "inadequately described," and two indicated "adequately described." All items were assigned equal importance, and items that were not relevant to a particular study were marked as "not applicable." Using the mean scores, we established thresholds to classify studies into three quality categories: low (0-0.99), moderate (1-1.66), and high (1.67-2).

Intervention

In this study, eHealth was defined as follows to collect relevant documents. eHealth is the use of information and communication technology to support, educate, inform, and link healthcare professionals with the patients they serve (31, 32). We considered the following methods as its data collection method: A) Smartphone or personal digital assistant, which transmits patient information to the clinician (through text message and so on). B) Application or computer software that allows patients to transfer data to the clinician. C) Websites in which data is transferred by the patient to the clinician. D) Combination of these interventions (Multiple method). Therefore, eHealth interventions included mobile apps, telehealth, websites, and text messaging in this study.

Data analysis

To evaluate the heterogeneity of study outcomes, I^2 statistics were used to categorize heterogeneity into three levels: low heterogeneity ($\leq 25\%$), moderate heterogeneity (25% to 75%), and high heterogeneity ($\geq 75\%$) (33). Subgroup analyses were performed based on variables such as population, outcome, eHealth method, and follow-up duration. Visual funnel plot and the Egger test were

used to examine publication bias (34, 35). A random effects model was used to compute the pooled measure of association (relative risk). Data analysis was conducted using Stata 17 (Stata Corp, College Station, TX, USA). Additionally, a sensitivity analysis was conducted to determine the robustness of the findings, wherein one study was excluded at each stage, and the results were compared to those of the complete analysis.

Results

Characteristics of Included Studies

The PRISMA flow diagram outlines the search strategy to identify the articles (Fig. 1). In total, 971 publications were identified, of which 538 were excluded as duplicates or irrelevant according to title and abstract. Full-text assessment was undertaken for leaving 67 potentially relevant articles. After a detailed full-text review, 12 eligible articles were included in the analysis. Moreover, 3578 participants participated in the 12 included studies. In addition, 11 studies used were RCTs. A detailed description of the characteristics of all enrolled studies is displayed in Table 1.

Table 1: Characteristics of included studies on the effectiveness of eHealth interventions on HIV PrEP

Author (Reference)	Country	Sample size	Population*	eHealth mode	Intervention Duration	outcome	Quality
Erenrich (21)	United States	229	MSM and TW	Website	Daily; 90 and 180	Uptake	low
Lillis (22)	United States	220	Clients of sexual health center	Website	Months:1	Uptake	Moderate
Songtaweasin (51)	Thailand	200	Men and TW	Software/ Application	Months:3,6	Adherence	Moderate
Wang (23)	China	1023	MSM	Smartphone	Months: 1, 3, 6, 9, and 12	Adherence	Moderate
Kawichai (52)	Thailand	200	YMSM, YTGW	Software/ Application	Months:3,6	Adherence	high
Mbotwa (49)	Tanzania	470	Female sex workers	Software/ Application	Months:1	Retention	Moderate
Liu (28)	United States	121	MSM	Multiple method	Weeks: 4, 12,24, and 36	Retention	high
Liu (28)	United States	121	MSM	Multiple method	Weeks: 4, 12,24, and 36	Adherence	high
Whiteley (24)	United States	69	YMSM	Software/ Application	Weeks: 24	Adherence	Moderate
Colson (53)	United States	204	MSM, TGW	Multiple method	Months:9,12	Adherence	Moderate
Musinguzi (54)	Kenya and Uganda	373	high-risk heterosexual HIV	Smartphone	Months:1,12	Adherence	low
Haberer (27)	Kenya	348	Young Adult women	Smartphone	Months:1,3	Adherence	high

*Men who have sex with men (MSM), Transgender women (TW), Young Men who have sex with men (YMSM), young transgender women (YTGW)

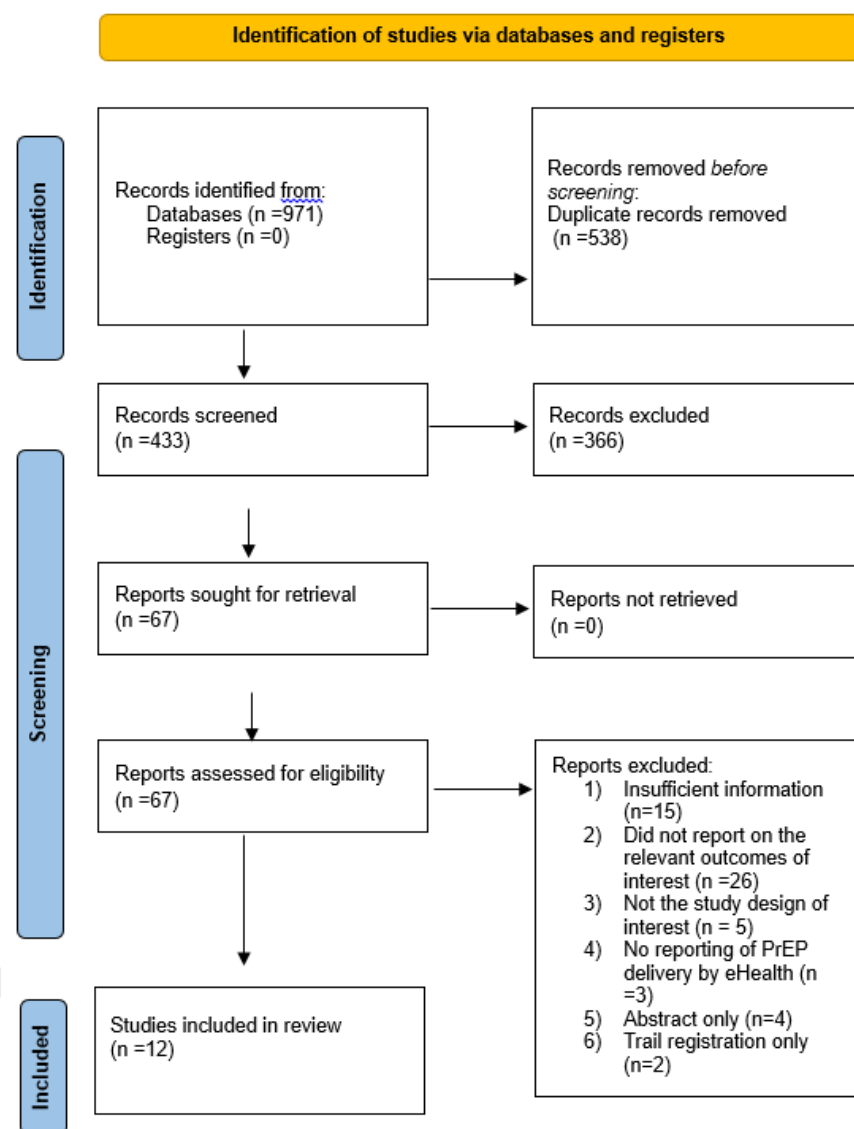


Fig. 1: PRISMA 2020 flow diagram for new systematic reviews, which included searches of databases and registers only

Heterogeneity test

The pooled relative risk for studies using multiple methods was 1.39 (95% CI: (1.11-1.75); $P < 0.001$). There was heterogeneity among the results of the included studies. The I^2 was 82% ($I^2 = 82.21\%$;

$P < 0.001$) (Fig. 2). To reduce heterogeneity and achieve greater convergence, we performed subgroup analysis based on the eHealth method, Population, Continent, Duration, Outcome, and study quality.

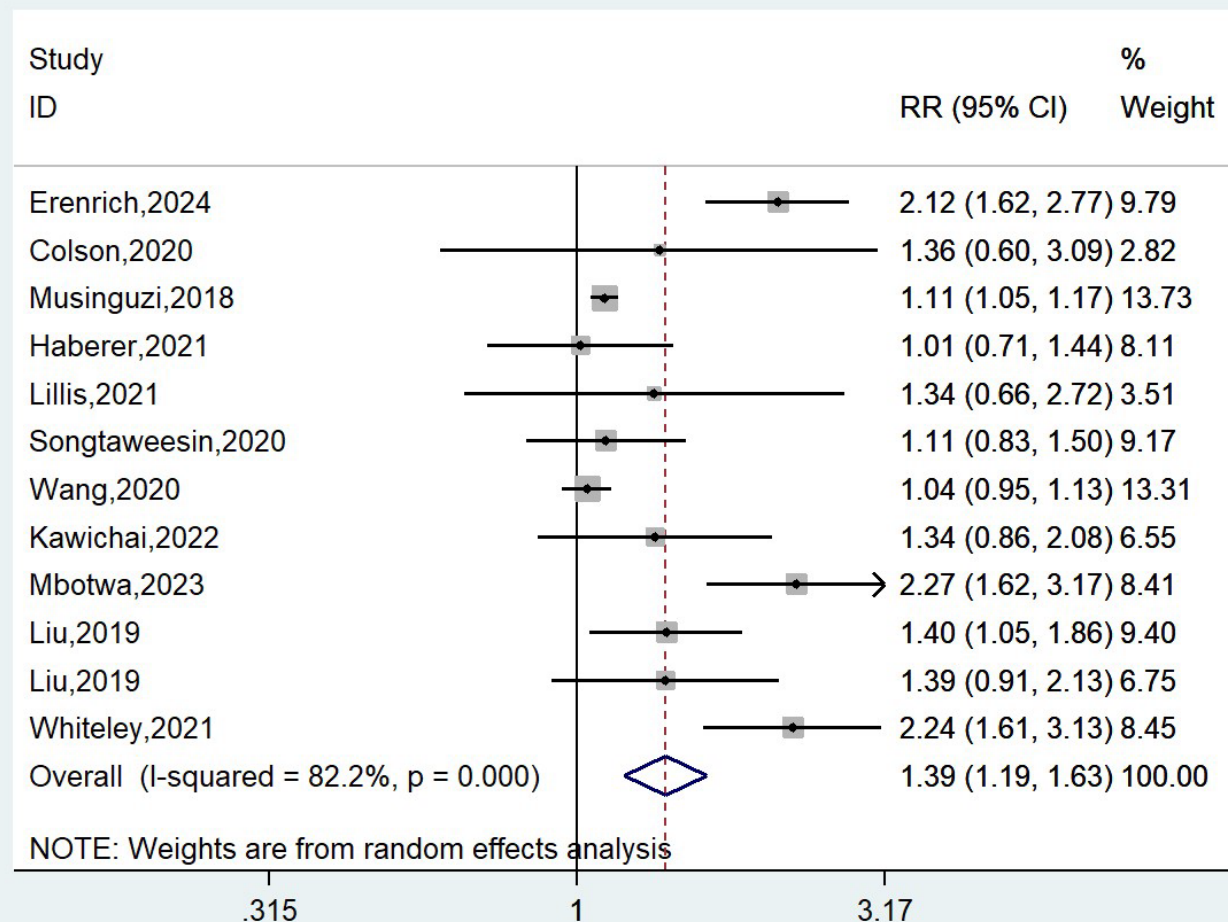


Fig. 2: Effectiveness of eHealth interventions on HIV PrEP

Sub-group analysis

To investigate the source of heterogeneity, we performed a subgroup analysis based on the eHealth method, Population, Continent, Duration, Outcome, and study quality (Table 2). The use of web-sites had a higher effect on PrEP than other e-Health methods (RR=1.90, 95% CI: 1.30-2.79; $I^2 = 29.10\%$). Moreover, the effect of e-Health on PrEP among FSWs was more than double that observed in other groups (RR=2.27, 95% CI: 1.62-

3.17; $I^2 = 22.80\%$). Furthermore, e-health interventions exhibited the most effect on PrEP uptake, with an RR of 1.90 (95% CI: 1.30-2.79; $I^2 = 29.11\%$), and demonstrated a greater effect in studies with follow-up periods of less than six months, where the RR was 1.85 (95% CI: 1.19-2.09; $I^2 = 76.31\%$). Additionally, studies conducted in the United States reported the greatest effect of e-Health on PrEP services (RR=1.71, 95% CI: 1.38-2.11; $I^2 = 0.41\%$).

Table 2: Subgroup analyses of the effectiveness of eHealth interventions on HIV PrEP by study and participant characteristics

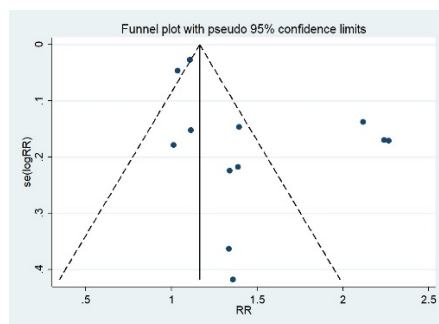
Moderator and subgroups		k (number of trials)	RR (95% CI)	I ² %	P-value for heterogeneity
Type of e-Health method					
	Website	2	1.90 (1.30-2.79)	29.1	0.23
	Multiple method	3	1.39 (1.11-1.75)	0.00	0.99
	Smartphone	3	1.09 (1.04-1.14)	0.00	0.44
	Software/application	4	1.66 (1.14-2.43)	79.0	0.00
Population*					
	MSM and TW	5	1.46 (1.12-1.90)	62.6	0.03
	High risk of heterosexual HIV	3	1.11(1.05-1.16)	0.00	0.77
	MSM	3	1.45 (0.87-2.42)	90.21	0.00
	FSWs	1	2.27 (1.62-3.17)	0.00	0.00
outcome					
	Uptake	2	1.90 (1.30-2.79)	29.1	0.23
	Adherence	8	1.20 (1.05-1.37)	67.5	0.00
	Retention	2	1.77 (1.10-2.84)	78.5	0.03
Continent					
	America	6	1.71(1.38-2.11)	0.41	0.13
	Africa	3	1.35 (0.88-2.06)	88.60	0.00
	Asia	3	1.05 (0.97-1.15)	0.01	0.49
Duration					
	<6	7	1.58 (1.19-2.09)	76.32	0.00
	6-12	5	1.11(1.03-1.20)	30.35	0.21
Quality					
	Low	2	1.51(0.80-2.85)	95.37	0.00
	Moderate	6	1.48 (1.04-2.11)	86.34	0.00
	high	4	1.27(1.06-1.52)	0.01	0.52

*Men who have sex with men (MSM), Female sex workers (FSW), Transgender women (TW), Young Men who have sex with men (YMSM), young transgender women (YTGW).

Assessment of Publication Bias

Publication bias was assessed by a funnel , and the absence of bias was represented by substantial symmetry (Fig. 3). To confirm the absence of publication bias, Egger's test was employed and did

not show the presence of bias ($P=0.249$). The metatrim test at pseudo-95% CI with a random effects model showed that there was no significant difference.

**Fig. 3:** Funnel plot to show the distribution of 12 studies

Sensitivity Analysis

Sensitivity analyses using the random effects model revealed that no single study affected the

overall effectiveness of eHealth Interventions on HIV PrEP (Fig. 4).

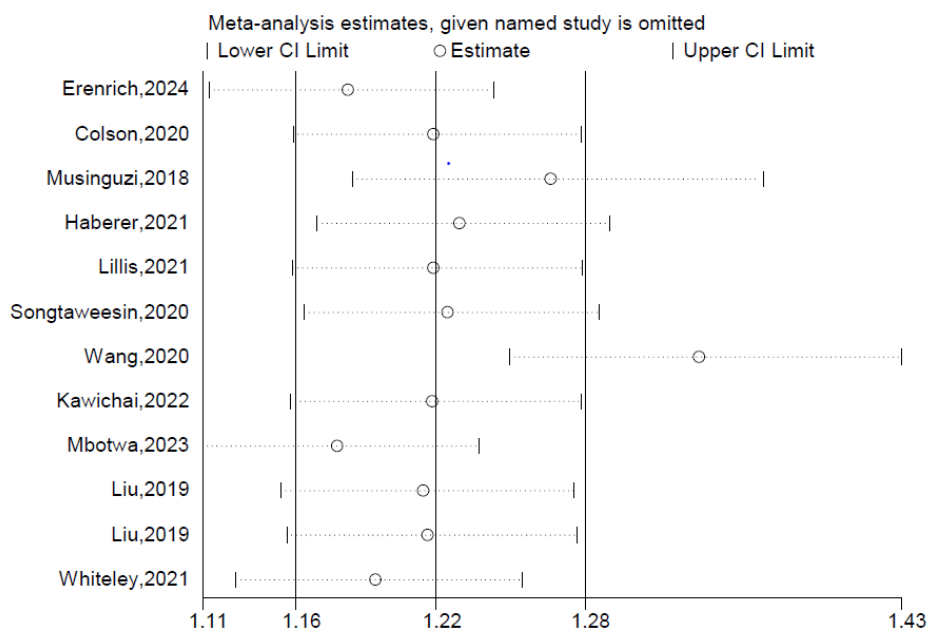


Fig. 4: Result of sensitivity analysis of the 12 studies

Discussion

Our results demonstrated that eHealth interventions were effective on PrEP. These interventions positively affected users' adherence, uptake, and retention (RR=1.39). While all eHealth methods had significant benefits, websites (RR=1.90) and mobile applications (RR=1.66) exhibited the greatest effect on PrEP outcomes. Notably, the effectiveness of these interventions was most pronounced within the first six months (RR=1.58), with a decline in effects observed over longer durations. Furthermore, eHealth interventions had a greater impact on FSWs compared to other groups (RR=2.27).

Our findings showed that in the e-health intervention group, there was a 1.39 times greater probability of adherence, uptake, and retention of PrEP compared to the control group. This finding was consistent with other studies (36-38). These studies found that the intervention group had higher

adherence and retention rates than the comparison groups. These interventions notably enhance PrEP adherence by addressing stigma-related barriers that hinder individuals' willingness to start and maintain PrEP use (39). eHealth platforms lead to anonymity, allowing users to seek information and uptake services such as PrEP without fear of judgment or discrimination. This is important as stigma can worsen mental health issues, such as anxiety and depression, which are important barriers to PrEP adherence (40). Furthermore, eHealth by text messages, mobile applications, and online platforms delivers personalized reminders for medication intake and clinic visits, increasing PrEP adherence among key populations (41). While initial engagement with digital tools may be high, maintaining long-term usage can be difficult, leading to decreased adherence over time (23). To enhance long-term usage of eHealth interventions and adherence to PrEP, it is essential to prioritize user anonymity and get user

feedback to address stigma and mental health barriers. Furthermore, integrating motivational messaging and supportive programs can encourage long-term usage of eHealth interventions and consistent engagement with PrEP.

Our findings indicated that websites (1.90 times) and mobile applications (1.66 times) had a greater effect than other eHealth intervention methods. These results were similar to the results of previous studies. They indicated that using websites and mobile applications is more effective on PrEP than control groups (42, 43). There has been a notable increase in the utilization of websites within the framework of the PrEP prevention program (44). The effectiveness of eHealth interventions in promoting PrEP differs by method and may vary based on the at-risk populations and the duration of use (45). For instance, mobile applications and SMS reminders improve accessibility and engagement but may need supplementary strategies for maintaining adherence such as counseling meetings, peer support groups, or incentives (46, 47). The growing use of these intervention methods underscores their potential to enhance accessibility and engagement among at-risk populations. However, the effectiveness of these interventions may differ based on the specific methods employed and the duration of their use, emphasizing the importance of appropriate strategies for different populations for optimal adherence and outcomes. For example, counseling sessions can address individual barriers to adherence, while peer support groups can foster a sense of community and mutual encouragement. Incentives, such as small rewards or vouchers, can further motivate participation.

The findings indicated that eHealth interventions have a significant effect on HIV PrEP among key populations, with a particularly notable effect observed among FSWs (2.27 times greater than other groups). These interventions effectively address structural and behavioral barriers through appropriate methods, such as immediate support and community-driven models. Such approaches encourage PrEP use among high-risk populations. Similar to our findings, a study found that integrating eHealth interventions, particularly mobile

health (mHealth) technology, can improve PrEP uptake, adherence, and retention among FSWs in Sub-Saharan Africa (48). In contrast to our findings, eHealth interventions were effective for PrEP prevention and management within the MSM group (21, 42). Disagreements about the effectiveness of eHealth interventions may arise from variations in sample size, intervention design, measuring methods used to assess outcomes, and research setting. In our analysis of three articles focusing on eHealth interventions for MSM, we found that two of these studies utilized relatively small sample sizes and relied on messages or phone calls as their intervention methods. In contrast, our findings demonstrate a significant effect of eHealth interventions on PrEP outcomes when the study population includes both MSM and TW. This suggests a need for further research that includes larger sample sizes and explores a broader range of eHealth intervention types within key populations.

This study found that the effectiveness of eHealth methods on PrEP declines after six months. This observation aligns with the findings of the study by Mbotwa et al. (49). Numerous eHealth interventions have proven effective in facilitating short-term behavior changes among participants. For example, a systematic review found that eHealth interventions (including web-based interventions, short message service/text messages/email reminders, online video-based, computer-assisted, multimedia-based, social network, live chat, virtual simulation intervention, and smartphone applications) successfully led to short-term behavior modifications, but only one study maintained these changes over a 12-month follow-up period (44). While eHealth interventions can effectively enhance behavior change and adherence to PrEP in the short term, their long-term effectiveness may be limited by insufficient support, such as regular people follow-up and reminder messages (50). The evidence indicates a trend of decreasing effectiveness over time, highlighting the necessity of designing interventions that incorporate follow-up strategies or booster sessions to maintain user adherence.

Limitations

This study had three limitations. First, the small number of studies focusing on key populations in the subgroup analysis indicates that we should be cautious when interpreting the findings. Second, the effectiveness of eHealth interventions may be influenced by contextual factors such as local healthcare infrastructure, cultural attitudes toward PrEP, and access to technology. These factors may affect the generalizability of findings to different settings. Finally, restricting the studies to English-language publications may introduce a language bias. Studies published in other languages, which could potentially contribute valuable insights, were excluded. This limitation may influence the generalizability of the findings.

Conclusion

eHealth interventions present a significant opportunity to enhance PrEP uptake, adherence, and retention among key populations. Furthermore, the positive effect is more evident in studies with shorter follow-up periods, demonstrating that these interventions successfully promote PrEP uptake. By implementing these interventions, we can enhance access to HIV preventive techniques and play an important role in decreasing the incidence of new HIV infections. Future studies should look into the long-term effects of these interventions, as well as customized techniques for maintaining PrEP adherence.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Availability of data and materials

Unpublished data are available upon email to the corresponding author based on a reasonable application.

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Conflict of interest

The authors declare that there is no conflict of interest.

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