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eHealth to Enhance Treatment Adherence among Youth Living with HIV

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Abstract

Purpose of review—Multiple reviews have examined eHealth/mHealth interventions to address treatment adherence, including those focusing on youth living with HIV (YLWH). This review synthesizes results of prior reviews and recent studies (last 5 years) to provide a path forward for future research, acknowledging both lessons learned and gaps to be addressed.

Recent findings—Recent studies provide further evidence for the feasibility and acceptability of technology-based HIV interventions. Formative research of more comprehensive smartphone applications and pilot studies of computer-delivered interventions provide additional guidance on YLWH's preferences for intervention components and show promising preliminary efficacy for impacting treatment adherence.

Summary—Expanding access to technology among YLWH, in the United States and globally, supports the continued focus on eHealth/mHealth interventions as a means to reduce disparities in clinical outcomes. Future research should lend greater focus to implementation and scale-up of interventions through the use of adaptive treatment strategies that include costing analyses, measuring and maximizing engagement, fostering information sharing between researchers, and building upon sustainable platforms.

Keywords

eHealth; mHealth; youth; adolescents; SMS; technology; HIV treatment

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Compliance with Ethics Guidelines

Conflict of Interest

The authors declare that they have no competing interests.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

INTRODUCTION

Despite substantial declines in HIV transmission and increases in lifespan achieved over the past decade for those living with HIV, the full benefits of currently available tools and interventions are still not completely realized by youth living with HIV (YLWH). In the United States (US), only 48.1% of diagnosed HIV-positive youth (aged 13–24 years) achieve viral suppression (VS; <200 copies/mL at the most recent viral load test) [1] and it has been estimated that less than 6% of HIV-infected youth in the US remain virally suppressed [2]. A recent systematic review examining viral suppression among YLWH globally highlighted the scarcity of data on the topic, noting that among the six low- to moderate-quality studies identified, suppression rates were highly variable (ranging from 27–89% at 12-months post ART initiation) [3]. Another recent systematic review and meta-analysis of the HIV care continuum among youth in South Africa estimated that only 10% of HIV-infected youth (15–24 years) were virally suppressed [4].

Reviews of antiretroviral (ART) adherence among YLWH (12–24 years) provide evidence of poor adherence rates. A 2014 meta-analysis of adherence for YLWH found overall low self-reported adherence of 62.3% [5•]. Barriers to adherence and VS among youth include forgetting or not being motivated to take medications [6], low adherence self-efficacy [7], psychological distress (depression, anxiety) [8–10], substance use [9, 10], structural barriers (e.g., transportation, insurance) [11, 12], low social support [13, 14] and HIV related stigma [15, 14, 9]. The developmental changes that occur as youth transition from adolescence to young adulthood can create or exacerbate these adherence barriers [16, 17].

The potential utility of technology-based interventions to increase ART adherence and improve viral suppression among HIV-positive individuals was recognized in the early 2000's as global access to computers, the Internet, and mobile devices began to rapidly rise [18]. Since that time, many different types of electronic health (eHealth) and mobile health (mHealth) interventions have been developed to address ART adherence among YLWH, including those delivered using SMS/texting, social media and smartphone apps [19•, 20]. While conclusive evidence supporting the efficacy and effectiveness of many of these innovative approaches is still lacking, the feasibility and acceptability of technology-based interventions for YLWH has been well established [21, 22, 20].

Both in the US and globally, youths' access to technology continues to grow. In the US, nearly all youth have access to the Internet and a cell phone [23]. In low- and middle-income countries, youths' access to the Internet and cell phones continues to rise rapidly, though there are variations by country [24, 25]. Smartphone ownership is climbing in low- and middle-income countries (LMICs), but the digital divide remains. While smartphone ownership in the US among those 18–29 years was 92% in 2016 [26], the median smartphone adoption rate in LMICs rose to 37% in 2015, up from 21% in 2013, according to a Pew Research Center survey of 21 LMICs conducted in 2015 [24]. Across nearly all countries, younger people (ages 18–34 years), are more likely than older individuals (35+ year) to own a smartphone [24]. In the US, the majority (88%) of teens (13–17 years old) own or have access to cell phones or smartphones and 90% of those teens with phones exchange texts. A typical teen in the US sends and receives 30 texts per day [23]. Given that

access to technology among youth continues to grow and the feasibility and acceptability of technology-based adherence interventions for HIV-positive youth has been established, the rationale for delivering adherence interventions through these mechanisms remains strong. Although additional data is needed to determine efficacy and effectiveness of many types of eHealth and mHealth interventions for HIV-positive youth, many lessons have been learned that have the potential to improve intervention quality and move the field forward. In this review, we synthesize selected recent reviews [19•, 21, 22••, 27–30], and notable research conducted within the past five years focusing on treatment adherence interventions for HIV-positive youth. We aimed to provide a path forward that acknowledges both lessons learned and gaps still to be addressed.

METHODS

We searched PubMed for English language publications, published between January 1, 2013- December 31, 2017, that included >1 term in Title/Abstract field from each group listed below:

Group 1: HIV, Human Immunodeficiency Virus, AIDS

Group 2: antiretroviral, ART, therapy, medication, adherence, compliance, nonadheren*, retention, linkage, engagement, viral suppression, suppression

Group 3: technology, technology-based, SMS, text messag*, texting, online, internet, web, Web 2.0, social media, social network*, app*, application*, smartphone*, cell phone*, cellular phone*, mobile phone*, eHealth, mHealth, mobile health, digital, digital health, video conference*, videoconference*, Twitter, Grindr, Jack'd, Facebook, computerize*, computer-based, virtual reality, VR

Group 4: youth, young adult*, adolescen*, teen*, young

Publications were excluded that did not include: an intervention description, an eHealth/mHealth intervention component, a treatment adherence behavioral (e.g., self-reported medication taking, attendance at clinic visits) or bio-medical (e.g., viral load, viral suppression, and drug levels) outcome, and a focus on adolescent/young adult populations (age 10–24). Formative studies were included if they described a proposed intervention and potential outcomes. Studies were excluded if they only used the calling features of mobile phones (e.g. voice calls). Three authors reviewed citations and full texts were pulled for all citations noted as relevant by at least one reviewer. Of the 143 articles extracted, 16 articles, including 7 describing formative work for intervention development, 6 reporting on pilot or randomized controlled trial (RCT) results, and 3 published study protocols for planned/ongoing interventions met inclusion criteria and were deemed most significant to current work in the field (Table 1). In addition, to ensure our discussion included a historical perspective, review articles (including systematic reviews and meta-analyses) published in the last 5 years (January 1, 2013- January 1, 2018) that included relevant results were also extracted and reviewed.

We focus on adolescents and young adults, ages 10–24 years, in accordance with the World Health Organization (WHO) and other United Nations (UN) organizations, who define

adolescents as those people between 10–19 years of age, youth as 15–24 years old, and refer to the combined group (10–24 year olds) as “young people” [31].

WHAT DO WE KNOW?

Unpacking the Results of SMS Interventions

There is evidence for overall acceptability and feasibility as well as modest efficacy of two-way SMS interventions at improving both adherence and retention in care. Multiple studies, including meta-analyses, integrative and systematic reviews [22••, 28, 29•], provide confirmation of moderate short-term effect, however sustained effects have been less robust, particularly among youth. For example, in a recent pilot RCT evaluating the initial efficacy of personalized text message reminders to promote adherence among adolescents and young adults in Chicago (16–29 years old), the difference in mean adherence between intervention and control participants was significant during the 3-month follow-up, but this effect attenuated and was not significant at 6-months [32]. The overall acceptability of the intervention was high, with 95% of participants at 6-months reporting overall satisfaction with the intervention and 81% reporting wanting to continue receiving the text messages after the conclusion of the trial. Another study examining the feasibility of interactive daily text messages to improve adherence with youth reporting adherence difficulties (ages 14–29 years) demonstrated the feasibility of this approach in terms of participant responsiveness (participants responded to successfully sent messages 61.4% of the time over the 24-week study period) [33].

It is notable that an RCT examining the efficacy of SMS reminder messages conducted with younger youth in Kampala, Uganda (mean age = 18.5 years) did not find support for the effectiveness of SMS reminder messages on ART and cotrimoxazole prophylaxis adherence compared to the usual-care control group at 12-months [34]. The trial examined the effectiveness of both 1-way and 2-way (i.e., with a response option) SMS reminder messages, and noted low levels of user engagement in the group with the option to respond; across the 48-week study period, the response rate in the 2-way SMS group was only 28.5%. Of note, messages in this study lacked personalization/tailoring of timing and content of messages. Given that youth often communicate through animated memes, Graphics Interchange Formats (GIFs) and videos, it may be that text-based interventions, particularly those that are not personalized and/or tailored to the participants, may not adequately capture the attention of the recipients. Formative data suggests that boredom with prolonged and/or repetitive messaging may be a relevant challenge with this population [35].

Given the collective evidence suggesting modest impact, high acceptability, and ubiquity of cell phones with texting capabilities [35], consideration should be given to shifting from testing text-based SMS interventions in RCTs to focusing on implementation studies that combine and integrate SMS with either ongoing clinical activities or as part of more comprehensive adherence strategies. Two trials underway will provide evidence for the effectiveness of this approach with youth. A cluster-randomized controlled trial with HIV-positive adolescents (ages 13–19 years) in Zimbabwe [36], will examine the effectiveness of a clinic-level intervention that includes support provided by a designated community adolescent treatment supporter who organizes in-person monthly support groups in addition

to writing and sending weekly, individualized SMS messages that include motivational reminders as well as information about clinic/support group attendance. Adolescents in the intervention who are in need of enhanced support will receive biweekly home visits in addition to weekly phone calls and daily SMS messages. Another study aimed at improving linkage to HIV care and retention among diverse young HIV-positive men who have sex with men (MSM) in the US [37] will evaluate an intervention in which a Health Educator uses various social media platforms (e.g., Facebook messenger, text messaging, and app-based instant messages), based on the participants' preferences, to communicate with participants using theoretically-informed messages that are specifically tailored to each participant. The Health Educator will also manage an optional secret Facebook group and have some face-to-face interactions with the participants.

Emerging Data on YLWH Preferences for Comprehensive eHealth/mHealth Interventions

Multiple formative studies conducted recently have identified comparable preferences for intervention components across multiple settings (both in the US and globally) and populations of HIV-positive youth [38–40, 35, 41]. Features mentioned consistently include: facilitating connections to providers and other YLWH, including reminders for HIV related activities, and providing comprehensive and accurate information regarding HIV as well as general health and wellness.

Preferences for connecting with providers include the ability to directly message clinics and providers [39, 40], engage in real-time to receive individualized counseling support [38], as well as allow providers to have access to adherence data that users record in an app to trigger real-time adherence support [40]. Providing contact between clinics/providers and youth in-between scheduled visits could overcome structural barriers such as transportation and scheduling difficulties, and allow youth to be more candid in articulating questions and concerns in a less-intimidating, more comfortable format.

Youth also articulated a desire to have access to other HIV-positive youth, in hopes that these relationships would provide support and allow reflection on their own adherence challenges and subsequently decrease feelings of social isolation [38, 39, 41, 40]. However, it is not clear what is the best way to create socially supportive networks in eHealth interventions, either through the development of "new" social media platforms or through integration into established social media (e.g. Facebook) [39]. One recent study, for example, reported on the successful integration of a private Facebook group established for HIV-positive young adults (ages 16–27 years) attending an urban HIV/AIDS care and treatment center in the US [42]. Content analysis of messages posted to the group showed that emotional social support was sought and provided frequently through this platform. There is a clear tension, however, between youth wanting to connect but also having concerns regarding no inadvertent disclosures of same-sex sexual behaviors or HIV serostatus. In the private Facebook group, for example, several individuals who attended face-to-face meetings at the treatment center refused to join the online group because of privacy concerns and fears of their HIV status being revealed to their entire social network [42]. Suggestions for protection that were mentioned in other recent formative studies included: ensuring anonymity, secure (password protected) logins, pseudonyms/avatars [38, 39, 41, 40].

Youth stressed the importance of their life beyond HIV and daily "pill-taking." Interventions that take a more holistic approach to issues of relevance to youth living with HIV, through the provision of credible, up-to-date information on HIV as well as general health and wellness [38, 39, 41, 40, 35] may be more relevant and foster engagement. Similarly, incorporation of reminders into these interventions should not only focus on ART taking behavior reminders but also reminders about clinic appointments [38, 41, 40, 35].

Evidence for non-SMS eHealth/mHealth Interventions among YLWH is Scant but Emerging

Recently conducted research also provides preliminary evidence for the feasibility and acceptability of computer-delivered interventions for youth, though these studies have all been conducted in the US. For example, a pilot RCT evaluating the preliminary efficacy of a two-session computer-based motivational interviewing intervention [43] showed promise among HIV-positive youth initiating ART (ages 16–24 years) recruited from eight US cities. Intervention participants reported high levels of satisfaction with the intervention and effect sizes, while not powered for significance testing, suggested that intervention participants had a greater drop in viral load from baseline to 6-month follow-up when compared to participants in attention-matched nutrition and physical activity control condition using the same platform. Another recent pilot study that assessed the feasibility and acceptability of a telehealth (i.e., remote video-conferencing) medication counseling intervention with HIV-positive African American youth in the San Francisco Bay Area (18–29 years) [44], found that nearly all participants felt that the telehealth approach was private, and in some cases even more private than care they received at a clinic. Participants in this study reported feeling more comfortable disclosing their problems to the health care provider using the telehealth technology than in-person.

WHAT DO WE NEED TO DO BETTER?

Retention in eHealth/mHealth Interventions is Critical but Understudied and Poorly Addressed

Understanding, measuring and subsequently addressing engagement within mHealth adherence interventions is an area that requires greater attention [45, 46]. We propose three areas that can serve to focus future research, which include: 1) intervention usage (e.g. paradata), 2) youth-focused engagement strategies; and 3) adaptive intervention designs. Paradata (i.e., intervention usage metrics) have been associated with differential treatment outcomes in mHealth interventions [47–50], yet they remain under-examined and underreported in technology-based HIV prevention and care interventions [51, 52••]. The systematic collection and analysis of paradata will not only strengthen the evidence base for mHealth adherence interventions (do they work?) and improve our understanding of how interventions work (what components led to behavior change?), but also to inform reach and scale-up efforts (for whom do they work, under what conditions, and what is the optimal dose?).

A recent review of mHealth interventions to support medication adherence among HIV-positive men who have sex with men concluded that an important area for future growth includes overcoming engagement challenges, by considering incorporating gamification to

improve engagement and dynamic tailoring based on frequent assessments [19•]. In the formative work, described in Table 1, YLWH provided examples of strategies they felt would increase their engagement including examples of gamification (points, rewards, contests and game-based elements [38, 39, 41]), provision of incentives [39] and enabling social connections [39, 41]. One recent study that examined the feasibility of using voice and internet daily diaries to collect data on daily ART adherence among young HIV-positive men who have sex with men in three US cities (ages 16–24 years) [53], implemented a unique, tiered incentive structure based on principles of loss aversion and variable reinforcement; participants started with $25 in a compensation account, with increasing amounts (ranging from $2–$6) added for diaries completed and $1 removed for diaries missed. Participants were also entered into a lottery for every diary completed. Participants completed 72.4% of the daily dairies over the 60-day study window and remarked on the motivating nature of the compensation/incentive structure during debriefing interviews.

Moving Beyond Traditional Trial Designs

Advances in mobile technology offer novel opportunities for moving beyond the RCT and delivering adaptive interventions that operationalize the personalization of real-time selection and delivery of intervention strategies based on real-time data [54]. In adaptive interventions, the type or dose of the intervention is adjusted based on participant characteristics or response. Just-in-time adaptive interventions (JITAI) and sequential multiple assignment randomized trials (SMART) have numerous advantages over traditional trial designs and are an efficient and rigorous way to maximize clinical utility and real-world applicability [55–57]. While no completed studies in this review utilized these proposed methodologies, one published study protocol described a forthcoming trial in which newly diagnosed adolescent girls will be enrolled in a SMART pilot trial to determine the most effective way to support initial linkage to care after a positive diagnosis [58]. They will be randomized to standard referral (counseling and a referral note) or standard referral plus a single SMS text message; those not linked to care within 2 weeks will be re-randomized to receive an additional SMS text message or a one-time financial incentive.

Ensuring Interventions are Inclusive of YLWH from All Age Strata

There is a striking lack of research focusing specifically on HIV-positive adolescents between the ages of 10–19 years. While our review identified several studies conducted with HIV-positive youth, including formative/qualitative studies and pilot studies that span adolescence and young adulthood, the mean age in most of these studies is 20 and up. This is important as we consider that there are likely differences in mHealth/eHealth intervention feasibility and acceptability between youth at the younger age spectrum.

First of all, there may be important differences in the characteristics of younger youth living with HIV. While there are developmental changes (e.g., neurodevelopmental changes [59]) that continue to occur into the early twenties, adolescents between the ages of 10–19 years are undergoing many important physical, biological, emotional, and psychological changes during this phase of their development [60]. There may also be differences in the social environment of younger vs. older youth, with the former spending more time with their families and the latter spending more time with friends, peers, and subsequently engaging in

more intimate individual relationships [60, 61]. eHealth interventions that aim to reduce social isolation by fostering connections to others may need to address these evolving social contexts when engaging younger participants.

Perinatally-infected adolescents may also face unique challenges as they assume greater levels of independence and autonomy for their healthcare-related activities, particularly when transitioning out of pediatric care, which is typically managed by parents and guardians [62]. In fact, progression through adolescence is an established risk factor for poor adherence among perinatally-infected youth [63, 64]. This is especially important to consider when developing eHealth interventions for youth in sub-Saharan Africa since millions of children currently living with HIV will be growing into adolescence in the coming years [65]. Further, while there may be differences between perinatally- and behaviorally infected adolescents in terms of stigma dynamics surrounding their diagnosis and to whom they have disclosed, these issues must be understood and carefully addressed in mHealth/eHealth intervention designed for them.

Additionally, in many cultures, the norms with regard to autonomy and parental/caregiver oversight for adolescents are very different than those relevant for young adults in their early twenties [66]. Practically speaking, this may result in important differences in terms of phone-use restrictions, sharing and ownership among younger youth when compared to young adults, as well as in recruitment as research participants. For example, a Pew Research Center survey conducted with parents of US teens, ages 13–17 years, found that 55% of parents limit the amount of time or times of day that their teen can go online and 65% of parents reported having punished their teen by taking away their phone or access to the internet [67]. In the Rana study among YLWH (14–24 years) on ART in two clinics in Kampala, Uganda, nearly half of sample participants (41%) reported sharing phones with others. Youth were most likely to share phones with family members such as mothers, grandmothers and older siblings [35]. Phone sharing can be a large issue if youth have not disclosed their status. A recently funded suite of three technology-based interventions [68–70] aimed at cognitive precursors to HIV risk as well as HIV risk behaviors, among 13–18 year-old diverse, same-sex attracted youth, may help to inform recruitment and engagement of younger adolescents.

WHERE DO WE GO FROM HERE?

Moving from Development to Dissemination

While we have come a long way in the development and evaluation of mHealth interventions for YLWH, there are still significant gaps in moving the pilot work completed to date into large-scale, intervention implementation and dissemination. Planning for future scale-up and long-term sustainability should be taken into account during initial planning and technology development. This includes ensuring that economic evaluations that assess cost/cost-effectiveness are prioritized as key intervention outcomes of technology-based interventions. In a recent review by Badawy et al. focused on the economic evaluation of text-messaging and smartphone-based interventions aimed at improving medication adherence in adolescents with chronic health conditions (CHCs) [30], only 4 articles (text messaging [n=3], electronic directly observed therapy [n=1]) described interventions with possible

future cost-savings. However, none of the interventions included any formal economic evaluations leaving little evidence to support the cost-effectiveness of text-messaging and smartphone-based interventions in improving medication adherence in adolescents with CHCs. The recently funded UNC/Emory Center for Innovative Technology (iTech) Across the Prevention and Care Continuum [70] is developing standardized cost collection tools and analytic strategies that will be utilized across iTech's current research portfolio of 10 technology-based (e.g. apps, mobile websites, videoconferencing) interventions for youth (aged 15–24 years).

Toward a More Collaborative Future

Finally, it is likely time to stop "recreating the wheel" both in terms of the content that is included within eHealth interventions (e.g. text message reminders, HIV and general health articles, FAQs) as well as the platforms that the interventions are being built upon. For example, in review of 10 computer-based interventions focused on adherence, there was significant overlap in content related to adherence knowledge and strategies, ART side effects, and patient-provider communication [21]. Consideration should be given to the creation of a content repository for researchers that could be updated and adapted for the unique needs, developmental stage, and cultural features of the population of interest (e.g. age, race/ethnicity, gender). Additionally, building interventions for YLWH on existing platforms or using open source options would allow for more rapid development and result in substantial cost savings. Within iTech, many platforms initially developed for adults or other populations are being adapted for youth, rather than starting from scratch [71, 72].

CONCLUSIONS

Evidence of feasibility and acceptability of technology-based HIV interventions and promising preliminary outcomes of tested interventions support the continued focus on these types of interventions as a means to reduce disparities in adherence and VS among YLWH. Further, expanding access to and use of technology among youth suggests the importance of these interventions both in the US and globally. While technology allows for tailoring to the unique adherence patterns of HIV-positive youth, it is critical to include users in the design to ensure interventions appropriately address context and psychosocial factors impacting adherence. Examining evidence to date, lessons learned, and gaps in knowledge will help to identify a path forward- a path toward interventions that are best suited to addressing the adherence needs of youth today.

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Table 1

Recent eHealth/mHealth HIV treatment adherence intervention studies among young people

	Study Population	Description of Study	Key Findings
Formative/Qualitative			
Anand [38]	HIV+ Young men who have sex with men (YMSM) and young transgender women (YTW) (14–24 years) on ART recruited from multiple sites in Bangkok, Thailand, n=18	• Interviewed 18 behaviorally HIV-infected YMSM/YTW regarding care challenges, identified how eHealth could address care needs, and elicited preferences for eHealth interventions. • Preferences for eHealth interventions: a) credible HIV resources; b) forums-connection to others; c) connection to medical experts; d) reminders (with preference for participants choosing the content/timing/frequency); e) inclusion of gamification (e.g., rewards for activities and incentive structure) to increase engagement. Participants also requested video testimonials of YLWH and expert advice videos. • Privacy concerns mentioned.	**Mean age**: 22.5 years **Preferences** for interventions similar to others **Supportive Networks:** 72.2% of participants wanted to connect with other YLWH in an online forum **Privacy** concerns mentioned (e.g., 100% preferred using pseudonym in forum)
Holloway [39]	Black YMSM (18–29 years) recruited from community-based agencies serving Black YMSM in Los Angeles, California; n=41 (46% HIV+)	• Six focus groups to evaluate preferences for mHealth prevention and treatment • Recommendations: a) holistic health interventions; b) discrete connection to health educators and treatment providers; c) contests and prizes for health games • Participants also requested the ability to rate and review local clinics and providers • Privacy/confidentiality was paramount to participants	**Mean age**: 26 years **Preferences** for interventions similar to others **Supportive Networks:** participants were torn about whether they should be able to communicate with other users. Many liked the idea of incorporating social media into app to build social support networks with others **Privacy** concerns were noted (e.g., expressing hesitance about downloading app that might indicate their HIV status to others)
LeGrand [41]	HIV+ YMSM (20–28 years) in North Carolina; n=27 (Phase 2, n=20; Phase 3, n=7)	• Focus groups: Three focus groups to (1) assess ART adherence information, motivation, and behavioral skills needs and determine strategies to address these needs via a mobile app, and to gather feedback on the evolving features of an adherence app prototype (Epic Allies) as well as future feature concepts. • Suggestions: a) discrete medication reminders (e.g., including option to turn-off); b) connection with others dealing with similar adherence challenges; c) make interactive with games/rewards within app; d) customizable. • Usability testing: Usability testing to assess whether users: could successfully navigate features and functions of the app, could comprehend the educational content, and found the app to be engaging and relevant.	**Mean age** (focus groups): 24 years **Mean age (usability testing):** 23 years **Preferences** for interventions similar to others **Supportive Networks:** In Phase 2, participants requested an app that could be used to connect with other dealing with adherence challenges, while also emphasizing need to maintain anonymity **Engagement**: gamification **End-user involvement**: iterative app development incorporating ongoing user feedback in both Phases (e.g., updated clickable prototypes created prior to each focus group based on previous findings)
Outlaw [73]	YLWH (18–24 year) newly recommended to start ART, recruited from 2 sites of NIH Adolescent Medicine Network for HIV/AIDS	• Initial feasibility of an individually tailored computer- based two-session interactive motivational interviewing (MI) intervention for YLH newly recommended to start ART. Each session was approximately 1 hour, with the 2nd session occurring 1 month after the first.	**Mean age:** 20 years **Acceptability:** Retention was 100% for both intervention sessions; participants were satisfied with the sessions overall (80% very/mostly satisfied with Session 1; 89% with Session 2) and were satisfied with the amount of assistance they received for managing

	Study Population	Description of Study	Key Findings
	Interventions (ATN) sites in US; n=10	• Participants completed a semi-structured face-to-face interview with site staff after each intervention session to provide feedback. • Preferences for changes to intervention were largely technical and programmatic (e.g., changing voices of narrative characters, removing character verbalizations (sighs), and adding female characters).	their adherence to HIV medications (90% satisfied with Session 1 and 89% with Session 2) **End-user involvement**: Intervention development occurred in collaboration with three youth advisory groups.
Rana [35]	YLWH (14–24 years) on ART in two clinics in Kampala, Uganda; n=39 (51.3% male)	• Six focus groups conducted as part of formative work for developing an SMS-based intervention called Reminding Adolescents to Adhere (RATA) • 2 of 6 focus groups were with minors (<18 years old) • Challenges to the intervention (reported by youth): a) not all youth have access to mobile phones; b) sharing phones would be problematic for youth who have not disclosed their status to those with whom they share phones; c) some youth reported facing restrictions on their phone use (particularly younger as well as female participants); d) concerns about accidental disclosure of HIV status • No consensus for frequency of messages Preferences: a) reminders sent around time of medication dosing; 2) two- way SMS for support	**Mean age:** 19.5 years **Availability:** 90% knew how to write, read and send texts, 72% owned a cell phone **Acceptability**: Almost all participants (97%) felt that the RATA intervention would help them improve their adherence **Preferences** for interventions similar to others **Privacy** concerns mentioned (e.g., noted that 41% of all participants reported sharing a phone with others)
Saberi (2013) [44]	Black YLWH (18–29 years old) on ART (>30 days) recruited from HIV clinics in San Francisco, California; n=14 (86% male)	• Pilot Study with no comparison condition • Assessed the feasibility and acceptability of a telehealth (remote videoconferencing) ART counseling intervention provided by a HIV clinical pharmacist. • Participants received one private telehealth counseling session (~45 minutes long) followed by a semi-structured qualitative interview to explore likes/dislikes of the format, modality, and content; potential impact on adherence; privacy issues; and interaction quality. • Participants described telehealth as convenient and ef cient, with positive impact on their knowledge and less intimidating than in-person visits.	**Mean age:** 24 years **Privacy**: Perceived telehealth as private (participants were in private room at UCSF, not at home) **Design**: personal support and counseling via telehealth provided by the HIV clinical pharmacist
Saberi (2016) [40]	HIV+ youth (18–29 years) recruited from clinics serving individuals living with HIV in the San Francisco Bay Area; n=17 (88.2% male)	• Four focus groups to better understand preferences for mobile apps in general and to inform the design of a mHealth app aimed at improving retention and engagement in HIV care and adherence to ART. • Suggestions: a) ability to connect to a community of other YLWH; b) access to healthcare providers; c) ability to track personal data and information (such as laboratory data); d) provision of health news and education. • Privacy was a key factor for all participants (e.g., participant suggested passcodes, use of pseudonyms and avatars)	**Mean age**: 25 years **Preferences** for interventions similar to others, except that participants did not express an interest in having a game component in the mobile phone app. **Supportive Networks:** Participants wanted peer support from other YLWH (e.g., recommendations for a closed group invited by healthcare provider to have a “true community of YLWH”) **Privacy** concerns mentioned
Pilot/RCT			
Dowshen [33]	YLWH (14–29 years) on ART with adherence problems	• Analysis from Pilot Study [74] with no comparison condition	**Mean age**: 23 years **Engagement**: responded to prompts 61.4% of the time

	Study Population	Description of Study	Key Findings
	recruited from large US city; n=25 (92% male)	• Study consisted of 24 weeks of personalized daily SMS reminders (ITR-Interactive text response) with follow-up message 1 hour later asking whether participant took their medication. • Participants asked to respond with 1 to indicate yes and 2 to indicate no. Personalized messages were crafted by the participant.	**Effectiveness/Sustained response**: ITR and VAS measures moderately correlated during first 6 weeks of study. Results of pilot showed almost 20% improvement in self-reported adherence from baseline to week 12 (mean VAS baseline 73.7% and week 12 = 93.3%). This was sustained at week 24 (mean VAS = 93.1%).
Garofalo [32]	Poorly adherent YLWH (66% VS at baseline) (16–29 years) recruited from community-based health centers in Chicago, n=105 (80% male)	• Pilot RCT • Personalized 2-way text message reminders daily for 6 months with f/u 15 minutes later asking whether participant had taken their medication. • Both initial message and f/u messages were designed by the youth. • Comparison condition (and intervention) received standard -of-care adherence education at baseline (i.e., 20- minute animated tutorial on importance of adherence)	**Mean age**: 24 years **Engagement**: responded to prompts 58% of the time **Effectiveness/Sustained response:** moderate increase in self-reported adherence at 3 months, not significant at 6-months; The average effect estimate over the 6-month intervention period was significant for 90 % adherence (OR = 2.12, 95 % CI 1.01– 4.45, p < .05) and maintained at 12- months (6 months post-intervention). **Acceptability**: high satisfaction scores (e.g., 100% would recommend to a friend, 81% wanted to continue getting messages after study conclusion) **Privacy** noted as concern (e.g., to protect confidentiality, staff encouraged participants to delete messages after taking medication and to use messages that would not reveal status)
Linnemayr [34]	YLWH (15–22 years) at 2 HIV clinics in Kampala, Uganda; n=332 (39% male)	• Year-long parallel individual-RCT • Assigned in a 1-to-1-to-1 ratio to a weekly SMS message group, weekly SMS message with response option group, or a usual-care control group. • Messages in both SMS groups were sent at 9AM on Sunday and content was standardized. For the 1-way group, the message was “We hope you are feeling well today.” For the 2-way group, the message was “We hope you are feeling well today. Reply 1 if well, 2 if unwell.” Respondents in 2-way group who did not respond within 48 hours received a f/u message “How are you? We have not heard back from you. Reply 1 if well, 2 if unwell.” No additional messages or follow-up calls were provided after this to the non-responders. Those who said “unwell” received call from study coordinator within 24 hours.	**Mean age:** 18 years **Engagement:** 86.4% of messages were successfully sent/marked as “delivered” to the participant’s phone. Among those in 2-way group, response rate was 28.4% **Effectiveness/Sustained response:** electronically measured mean adherence was 67% in controls, 64% in 1-way texting group and 61% in 2-way group
Menza [75]	HIV+ Black YMSM (18 - 30 years) in North Carolina, n=199	• Observational analysis of RCT [76, 77] • Participants in healthMpowerment (intervention 3 months with follow-up to 12 months), a RCT of an Internet-based HIV prevention intervention vs. information control website, to identify time-varying correlates of self-reported viral suppression using relative risk (RR) regression.	**Median age:** 24.5 years **Feasibility/Acceptability:** Retention at the 12-month visit was 84%. **Engagement:** Moderate usage of intervention with large range from very low/no users to high/super users. Participants used their assigned Web site for a median of 11 minutes (IQR, 5–38.5 minutes; range, 1–1250 minutes) and a mean (SD) of 73 (190) minutes. **Effectiveness:** Increase in VS seen over time but no difference between intervention/control groups One hundred five (65%) of 162 participants reported being undetectable at baseline. At 3, 6, and 12 months, 83 (72%) of 115, 84 (82%) of 103, and 101 (86%) of 117 reported an undetectable VL, respectively.

	Study Population	Description of Study	Key Findings
Naar-King [43]	YLWH (16–24 years) newly prescribed ART (<12 weeks ago) recruited from 8 sites of NIH ATN sites in US; n=76 (80.3% male)	• Pilot RCT • Two session computer-delivered motivational intervention to facilitate adherence (MESA: Motivational Enhancement System for Adherence). 2nd session occurred one month after first session. Sessions took 30 minutes to complete. • Comparison was an active 2 session computer-delivered nutrition and physical activity control.	**Mean age**: 20.3 years **Feasibility/Acceptability**: high satisfaction ratings; high retention at 3 and 6 months (92% both) **Effectiveness:** Effect sizes suggested that the intervention group showed a greater drop than controls in VL from baseline to 6 months, and had greater percent undetectable by 6 months.
Stankievich [78]	YLWH (6–25 years) on ART, VL >1000 copies/mL recruited from tertiary hospital in Buenos Aires, Argentina; n=22 (32% male)	• Pilot Study with no comparison condition • Intervention based on a mobile generic contact made twice a month by a health worker using the participant's preferred mode of contact (e.g., WhatsApp, text messages, and Facebook) for 32 weeks • The messages included short questions about the status of the patient and medication-related issues. The content of messages was identical across the intervention group. If the patient or parent required additional information, a feedback phone call or contact message could be generated (i.e., "extended communication")	**Mean age:** 17.2 (range 6–25); 11 participants were minors (<18). NB: 7/11 minor participants were contacted through parents. **Engagement:** Each participant received a total of 16 contacts, 84% (296) were answered by the patient. 54%(189) of the contacts generated extended communications **Effectiveness:** After the strategy implementation VLs from 20/22 participants were available. 13/20 (65%) were undetectable
Protocols currently being developed/tested			
Inwani [58]	Adolescent girls and young women (AGYW) in the age range of 15 to 24 years in Homa Bay County, western Kenya, anticipating n=108	• Newly diagnosed AGYW with HIV will be enrolled in the SMART trial pilot to determine the most effective way to support initial linkage to care after a positive diagnosis. • Participants will be randomized to standard referral (counseling and a referral note) or standard referral plus a single SMS text message; those not linked to care within 2 weeks will be re-randomized to receive an additional SMS text message or a one-time financial incentive. • Study will also examine the incremental cost per HIV- positive female linked to care.	**Design**: SMART trial nested within larger implementation science study (also examining effective recruitment/HIV testing strategies to identify HIV+ AGYW). **SMS**: Part of package. After successful linkage to care, participants will receive motivation SMS for adherence to medication and care **Incentives:** Participants in SMART trial will be given a study phone to ensure lack of access is not barrier to enrollment)
Mavhu [36]	HIV-positive adolescents (13–19 years) and eligible for ART in 2 districts in Zimbabwe, expected n=500	• Sixteen clinics were randomized to either enhanced ART-adherence support or standard of care. • Both arms receive ART and adherence support provided by adult counselors and nursing staff. • Adolescents in the intervention arm additionally attend a monthly support group, have a designated Community Adolescent Treatment Supporter (CATS), and receive follow-up through personalized SMS and calls plus home visits from the CATS. • Type and frequency of contact is determined by whether the adolescent is "stable" or in need of enhanced support. Stable adolescents receive a monthly home visit plus a weekly, individualized SMS. An additional home visit is conducted if participants miss a scheduled clinic appointment or support-group meeting. Participants in need of	**SMS**: Part of package of community- based interventions. SMS messages written and sent by CATS **Design**: In-person + technology

	Study Population	Description of Study	Key Findings
		enhanced support receive bi-weekly home visits, weekly phone calls and daily SMS.	
Tanner [37]	Racially and ethnically diverse MSM (13–34 years), living with HIV`	• Describes the foundation and development of weCare, a tailored social media intervention designed to improve health outcomes among a diverse group of young MSM living with HIV. • The weCare Health Educator (a young, Latino MSM) will use established social media platforms (e.g., Facebook, text, apps) to send theory-based messages to participants based on the participant's preference for mode of connection • The Health Educator will also manage an optional Facebook secret group for participants and will also have some face-to-face interactions with participants (e.g., at clinic when participants come for appointments)	**Supportive networks:** utilization of existing social media platforms; Health Educator provision of support and personalized guidance **End-user involvement**: intervention development guided by a steering committee comprised of members from the local catchment area, including racially and ethnically diverse YMSM (some of whom are HIV positive) and the project team **Design**: Messages sent from Health Educator, secret group, face-to-face- sessions