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A Telehealth and Texting Intervention to Improve HIV Care Engagement, Mental Health, and Substance Use Outcomes in Youth Living with HIV: A Study Protocol

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Abstract

Introduction: Youth and young adults living with HIV (YLWH) experience worse clinical outcomes than adults and high rates of mental health and substance use challenges that impact their engagement in care and adherence to antiretroviral therapy. This study of YLWH in the San Francisco Bay area aims to evaluate the feasibility, acceptability, and preliminary clinical outcomes of a 12-session telehealth counseling series providing education, motivational enhancement, and problem-solving around HIV care, mental health, and substance use challenges. Findings from this study will provide valuable information about benefits and challenges of conducting integrated HIV, mental health, and substance use counseling for YLWH via telehealth, and will guide the development of new technology-based strategies for care.

Methods and Analysis: The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) study is a pilot randomized, crossover trial examining the feasibility and acceptability of a telehealth modality to provide counseling to improve engagement in HIV care, mental health, and substance use outcomes for YLWH. The intervention consists of twelve 20-30-minute weekly sessions with a trained counselor focused on identifying and problem-solving around barriers to HIV care access and adherence, and on addressing mental health and/or substance use issues impacting care access and adherence. Participants consent for the study in person and are randomized to receive the intervention immediately or beginning 4 months after consent. All participants receive text messages for check-ins, appointment reminders, or other messages to improve study engagement. Participants complete quantitative online surveys at baseline, 4 months, and 8 months, as well as qualitative exit interviews conducted over the telephone. Clinical outcomes, including plasma HIV RNA and CD4+ cell count, are collected from medical records. Following data collection, study staff will explore outcomes of the intervention using quantitative and qualitative methods.

Strengths and Limitations of this Study:

- Strength: The use of iterative refinement of the intervention manual throughout this pilot study increase the study's potential impact and acceptability among participants.
- Strength: The study's counseling intervention is significant in its integrated HIV and behavioral health focus which is tailored to the participant's baseline HIV knowledge, mental health status, and substance use history.
- Strength: The use of video-chat and text messaging modalities for delivery of HIV engagement, mental health, and substance use counseling is innovative, reduces the time burden to both clinicians and patients, and challenges the current delivery of health care.
- Strength: By examining the acceptability of a fully online versus hybrid in-person-online session delivery, we will be able to determine if this intervention can be offered completely remotely which will in turn increase the geographic reach for the delivery of this intervention.
- Limitations: This pilot study is limited due to its small sample size and that the data generated from this study may not be generalizable to older individuals not living in the San Francisco Bay Area.

Ethics and Dissemination: All participants will provide their written and verbal consent for participation in the study. This study and its protocols have been approved by the UCSF Institutional Review Board. Data sharing or dissemination is not applicable to this article, as no datasets have been generated or analyzed as of this time.

Trial Registration: This trial was registered with ClinicalTrials.gov, ID # NCT03681145, on 9/19/2018.

Keywords: HIV, antiretroviral therapy, mental health, substance use, counseling, telehealth, text messaging, young adults

Background

Youth and young adults ages 18-29 living with HIV (YLWH) have unique challenges with HIV diagnosis, access, and maintenance of care. In 2016, in the USA, youth ages 13-24 accounted for about 21% of all new HIV infections [1]. Among those 13-29 years of age and living with HIV, only 41% were estimated to be aware of their HIV status. In 2014, of those diagnosed with HIV, only 62% accessed HIV medical care within the first year; of those, 43% were retained in HIV care, and of those, 54% had a suppressed HIV viral load [2]. Access to care and antiretroviral therapy (ART) are crucial for the health of YLWH; high levels of ART adherence is critical for attaining HIV treatment goals including sustaining suppressed HIV viral load, decreasing risk of developing drug-resistant strains of HIV, reducing the risk of HIV transmission to others, and improving overall health [3-5].

Mental health and substance use challenges are prevalent in YLWH, though few studies have been conducted on behavioral health issues in YLWH. One study found that 18% of YLWH who were in care had clinically significant psychological symptoms such as depression or anxiety [6]. Another study of 1,706 YLWH found that 42.6% reported mental health concerns at a clinically significant level. Of those reporting these symptoms, only 39.7% reported receiving mental health care services in the past year and 21.9% reported taking medications for mental health conditions [7]. Additionally, in one sample of 12 to 26 year-olds living with HIV, 32% used tobacco, 27% used marijuana, 21% used alcohol, and 22% used other illicit substances [8].

Mental health and substance use challenges have been shown to negatively impact HIV medication adherence and clinical outcomes across the continuum of HIV care for YLWH [9-10]. For example, in one systematic review and meta-analysis, those with depression symptoms had 42% lower likelihood of achieving 80% or higher ART adherence compared to those without depression [11]. Another found that of those not taking ART, the odds of reporting clinically significant symptoms were three times as high as those on ART, showing the strong relationship between mental health and ART uptake and adherence [12]. Another review found that depression and anxiety symptoms in YLWH were

strongly associated with ART non-adherence [13]. Additionally, the review found that higher alcohol use in the past week and substance use in the past three months were also predictive of poor adherence.

There are few evidence-based counseling interventions for YLWH that address behavioral health factors impacting adherence to HIV care [14]. Interventions developed for adults have shown to be effective in improving depressive symptoms as a method of improving ART adherence [15]. However, young adults differ in multiple ways, including their technology use habits, creating an opportunity for the application of technologies to behavioral health interventions.

As 98% of people ages 18-29 have a mobile telephone and over 85% have a smartphone, telephone-based interventions are potentially accessible for the majority of YLWH [16]. Most traditional counseling interventions are provided in person and in a clinical setting; engaging in these counseling sessions may be a barrier for YLWH who experience transportation or financial issues, stigma or shame around accessing treatment, or other challenges [17]. In our formative work, YLWH reported that health-focused mobile interventions could overcome concerns about their ability to effectively and openly communicate with their providers [18]. One survey similarly found that 60% of millennials would be interested in video-chat interactions with their medical provider instead of attending in-office appointments [19].

Several HIV care adherence interventions have been developed for individuals living with HIV, though most are for adults of all ages rather than YLWH. Few of the interventions specifically developed for YLWH use telehealth, texting, or other mobile technologies as the platform for intervention delivery [20]. Although these methods have been shown to be promising in improving ART adherence and linkage to care in adults living with HIV, they have been minimally studied in YLWH [21].

The existing literature on telehealth and texting platforms for HIV-related interventions for YLWH show promising results and highlights the need for additional research in this area [22]. One text message medication reminder system for adolescents and young adults living with HIV was shown to be feasible, efficacious, and satisfactory to participants [23].

In this paper, we describe the protocol for a study to examine the feasibility and acceptability of a novel 12-session telehealth counseling series and accompanying text messages to improve engagement in HIV care, mental health, and substance use outcomes. The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) intervention is novel in its combination of telehealth and text messaging, and strategic integration of three foci (i.e., engagement in HIV care, mental health, and substance use). We will identify whether these methods are feasible and acceptable to YLWH and will examine preliminary clinical and behavioral outcomes of the intervention. We anticipate that Y2TEC will be feasible and acceptable for counseling YLWH and that participants will show preliminary evidence of improvement in clinical and behavioral outcomes.

Methods/Design

Study Overview and Design: The Y2TEC study is a single-site randomized pilot study with the primary aim of examining the feasibility and acceptability of a 12-session telehealth and text message-based counseling series for YLWH. The secondary aim is to evaluate the preliminary impact of the intervention on improved engagement in HIV care, enhanced mental health, and reduced substance use for YLWH. The University of California, San Francisco (UCSF) Institutional Review Board has reviewed and approved this study. The intervention is delivered to participants in two condition groups (i.e., intervention and waitlist control) via remote telehealth sessions delivered over 4 months, with a crossover design (see Table 1). The overall duration of participation is 8 months.

Table 1. Study Overview

		Months								
	I= Intervention Arm Participants *W= Waitlist Arm Participants* *X= All Participants*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Screening/Enrollment										
	Telephone Screening	X								

	Informed Consent		X							
Assessment Surveys										
	Baseline Survey		X							
	Follow-up Surveys					X				X
	Satisfaction and Acceptability Questionnaire					I				W
Counseling Sessions										
	Weekly Counseling Sessions (12)		I	I	I	I	W	W	W	W
Text messages										
	Monthly Check-Ins		X	X	X	X	X	X	X	X
	Session Ratings		I	I	I	I	W	W	W	W
	Goal Reminders		I	I	I	I	W	W	W	W
	Session Reminders (24 hours and 15 minutes before telehealth session)		I	I	I	I	W	W	W	W
	Community Events and Resources		X	X	X	X	X	X	X	X
Exit Interviews										
	Satisfaction Survey					I				W
	Qualitative exit interviews					I				W

Study Setting: Participants are recruited from the San Francisco Bay Area. Participants consent to the study and complete their initial baseline survey in person in a private office at a community-based location or at UCSF's Center for AIDS Prevention Studies. All other study communications are remote via the video-chat platform, text messages, and telephone calls.

Study Participants: The study sample will consist of 80 individuals ages 18-29 living with HIV, who live in and receive medical care in the greater San Francisco Bay Area. Other inclusion criteria include: English-speaking, willing and able to provide informed consent, and have access to a mobile telephone

with text messaging capability. Those planning on moving out of California in the next 8 months or with evidence of severe cognitive impairment or active psychosis that may impede their ability to provide informed consent are excluded.

Sample Size Justification: NCSS PASS will be used to compute the minimum detectable effect sizes (MDE) assuming alpha= 0.05, power= 0.80, and N= 64 reflecting anticipated attrition of 20% [24]. For estimates of means and proportions for feasibility and acceptability measures, the minimum detectable distance to the limit for confidence intervals for proportions is 12.7%, assuming a target of 70% feasibility and acceptability. For means, the standardized distance to the limit is 0.25. For primary preliminary outcome analyses proposed to compare means of continuous outcomes across the intervention and control groups at 4 months, the minimum detectable standardized mean difference *d* is 0.30. These MDEs are between cutoffs for small (*d*= 0.20) and medium (*d*= 0.50) standardized mean differences suggesting our study is powered to detect small to medium effects [25].

Patient and Public Involvement: Prior to the design of this study, we conducted formative research with healthcare providers and patients (Saberi et al, under review), which helped us refine our research questions, study design, and outcome measures. We asked YLWH about optimal methods for intervention delivery and considered the requests of several participants to have an initial session face-to-face with the counselor. Additionally, we involve participants in study recruitment by encouraging active participants to refer others and providing a $15 incentive to both the referee and referred. We will assess the effects and burden of the intervention by the participants themselves through our quantitative survey and qualitative exist interviews after the intervention. We will work with our Youth Advisory Panel and Community Action Board to disseminate the study's results to participants and the community.

General Study Procedures

Recruitment methods: Participants are recruited through in-person outreach at clinical and community sites serving YLWH, emails to clinics and providers, flyers posted at health clinics and community-based organizations, targeted online advertisements on Instagram, Craigslist, Facebook, and Grindr, and re-

contacting participants from prior studies who had expressed interest in being contacted about future studies. Finally, a participant referral method is used and a $15 incentive is provided to both the referring participant and new participant.

Eligibility Screening: Study staff provide a brief overview of the study to prospective participants, answer any questions, and complete an eligibility screening on the telephone. Those who meet the inclusion criteria and are willing to participate in the study are asked for a photo ID to verify their date of birth and proof of HIV status (a letter of diagnosis, laboratory results, or HIV medication prescription) via a photo text-messaged to the study telephone.

Consent and Enrolment Procedure: Participants review the electronic consent form (see Appendix A) with a study staff member in a private setting. Individuals who are eligible and agree to participate electronically sign the consent and a medical release form using Qualtrics (Provo, UT, USA; version March 2017) an online survey platform, and are provided a copy of the Experimental Subject's Bill of Rights.

Baseline Survey: Participants then complete the online baseline survey, which takes approximately 30-45 minutes. Study staff then help participants download a secure video-chat mobile application (i.e., Zoom, a HIPAA-compliant video-chat platform) on their telephones and demonstrate how to set up privacy settings.

Randomization: Following the baseline survey, research staff randomly assign participants to one of two condition groups (i.e., intervention or waitlist control) with a pre-numbered sealed envelope. Randomization is done using SAS (version 9.4) based on randomly permuted block sizes to ensure equal sized groups and all study staff are blinded to the randomization order. Approximately 40 participants will be randomized to the immediate intervention condition and receive their first session in person; about 40 participants will be randomized to the waitlist control condition for four months after study enrollment, and then cross-over to the treatment arm and receive the study intervention entirely remotely with no in-person session with the counselor. The counselor and clinical research coordinator will not be blinded to the randomization condition, as treatment will be prescribed as a result of the condition.

Participant Retention: A number of steps are taken to retain participants throughout the study period. Participants are asked for multiple forms of contact information (including emergency contacts, clinical contacts, and social media contacts) at the initial visit to prevent loss of contact. They receive monthly follow-up text messages to confirm their contact information, appointment reminder text messages 24 hours and 15 minutes before scheduled counseling sessions, birthday text messages, and a weekly text message with free fun local activities to facilitate rapport-building.

Participant Incentives: Participants receive up to $310 for completing all study activities, including payments for each counseling session that gradually increase throughout the study. Participants are given a ClinCard, a reloadable debit card, and instructions for use at the initial visit. Participants are also entered into two raffles for chances to win $25 Amazon gift cards when they confirm their contact information or answer two session rating questions after each telehealth session. Additionally, participants who refer others to the study are paid $15 per successful recruitment.

Risks to Participants: All risks to participants are monitored by study staff and documented at each session and study assessment. Study staff are trained to thoroughly explain these risks to participants as well as the steps taken to ensure privacy and confidentiality of all information. Safety-related risks to participants could include discomfort due to the sensitive nature of questions in study surveys including substance use, HIV health-related issues, and mental health. Non- clinical study staff conducting interviews and participant communication refer to clinical study staff if participant distress is identified. Clinical staff delivering the intervention are trained to assess distress level of participants and refer to established protocols for any participant crisis. If a participant requires treatment due to distress, this will be determined by clinical staff; they will be referred to appropriate services following the crisis protocol and the PI will be informed.

Adverse Events and Auditing: The study staff monitor post-session participant ratings (via text message) as one method for identifying those who may have experienced an adverse event. If a participant reports low satisfaction with the intervention, study staff contact them in a timely manner to determine what occurred in the session. Study staff also provide participants with the study mobile

telephone number to spontaneously report any adverse events or unintended effects of the intervention. Any adverse events will be documented on an adverse event form and follow-up will be tracked. The form along with any session notes with details will be reported to the IRB by the PI within 10 working days. The team of investigators will also meet weekly to audit and discuss general trial conduct related issues.

Protocol Amendments: Protocol amendments will be shared with all stakeholders as they occur. Study staff communicate protocol modifications to investigators during monthly meetings, submit changes to www.clinicaltrials.gov as needed, submit IRB modifications, and communicate changes to regulators during meetings every 6 months or via email as needed.

Intervention Procedure

The 12-session telehealth series is delivered by a trained behavioral health professional (such a social worker, psychologist, or psychotherapist), referred to as the "counselor" within the context of this study. Sessions use problem-solving, IMB (information-motivation-behavioral skills), and motivational interviewing and focus on engagement in HIV care, mental health, and substance use [26-28]. Telehealth sessions are completed via a secure video-chat platform, Zoom, and text messages are sent via a secure encrypted, HIPAA-compliant platform called Mosio.

Series Overview: Participants in the intervention arm meet with the counselor in person immediately after enrollment and the waitlist control arm participants meet with the counselor via video-chat after four months. Before the first meeting, the counselor reviews the participant's most recent assessment survey responses to determine the participant's level of acuity and to tailor appropriate session dosage. Mental health acuity is determined through the PHQ-9 and PCL; substance use acuity is determined through the AUDIT and ASSIST; HIV care acuity is calculated by a measure of HIV knowledge as well as current participant utilization of HIV care services and antiretroviral medications. During the first session, the counselor assesses the participant's needs and identifies current gaps in

knowledge and motivation regarding mental health, substance use, and HIV care. The first three to six of the remaining eleven sessions cover core psychoeducational and health literacy-promoting content around engagement in HIV care, mental health, and substance use challenges and treatments. Those with higher acuity receive two foundational psychoeducational modules rather than one in each of the 3 areas, amounting to a maximum of six core educational sessions.

The remaining sessions use an integrated behavioral health and HIV care-focused approach to further the conversations initiated in the core sessions. At the beginning of these sessions, the participant and counselor choose from a list of topics identified in the first session, including: (A) HIV care; (B) Mental health; (C) Substance use; (D) Lifestyle health; (E) Social support; (F) Family of origin; (G) Romantic and sexual relationships; (H) Self-identity and disclosure; (I) Subsistence Needs (housing, money, and resources) and (J) Education and vocation. These sessions can be done in any order and repeated as needed. If a participant is in crisis and unable to be re-directed to these options, a "wildcard" session (K) focused on crisis response and safety planning may be held. The final session includes reviewing the content covered and goals achieved in the previous sessions, identifying unmet needs, accessing community-based resources, and learning strategies for maintaining changes.

Scheduling Sessions: Four months are allocated to complete the 12 weekly counseling sessions to allow for missed and re-scheduled sessions. Participants are encouraged to contact the counselor or study staff to re-schedule their appointments as needed. Participants receive session reminders via text message 24 hours and 15 minutes before each session.

Session Documentation and Fidelity: The counselor completes session summary notes through a Qualtrics survey form, which includes closed-ended and multiple-choice questions such as session length, participant location, technical issues encountered, session topics selected, educational topics covered, goals set, a session content fidelity checklist, and a narrative progress note.

Evaluation and Curriculum Modifications: The initial version of the Y2TEC intervention will be delivered to participants randomized to the intervention arm. The research team plans to adjust the intervention based on lessons learned and feedback from participants to develop and disseminate a

modified version of the intervention (i.e., intervention manual version 2.0) to the waitlist control participants. As a result, the intervention will have gone through an iterative refinement process and will be ready for implementation in a larger randomized controlled trial by the end of the pilot study.

Data Collection and Management Procedure

Clinical Data Collection: At consent, participants sign a medical release form and research staff obtain medical records from participants' respective medical clinics at baseline, 4 months, and 8 months. Information collected includes appointment attendance, medications, and laboratory data including plasma HIV RNA and CD4+ cell count. The data point closest to baseline, 4 months and 8 months +/- one month are used for data analysis.

Assessment Data Collection: Participants complete assessment surveys at baseline, 4 months, and 8 months after enrollment. The surveys collect demographic, technology use, substance use, mental health, and HIV care information (see Table 2). The baseline surveys are completed online in-person at the initial visit and the other two are completed remotely on the participants' mobile devices.

Table 2. Measures in Participant Surveys

Domain (in order of the survey)	Measure	Baseline Survey	Follow-up Surveys
Demographics	Original measure	X	
Use of Technology	Original measure	X	
HIV Treatment Outcomes, Antiretroviral History, and Adherence	Original measure	X	X
HIV Knowledge	HTKS (HIV Treatment Knowledge Scale)	X	X

	[29]		
Alcohol Use	AUDIT (Alcohol Use Disorders Identification Test) [30]	X	X
Substance Use	ASSIST [31], Q2 (Alcohol, Smoking, and Substance Involvement Screening Test), DAST-10 [32] (Drug Abuse Screening Test)	X	X
Depression	PHQ-9 (Patient Health Questionnaire) [33]	X	X
Adverse Childhood Experiences	ACE (Adverse Childhood Experience Questionnaire) [34]	X	
Trauma/PTSD	PCL-5 (PTSD Check List) [35]	X	X
Anxiety	GAD-7 (Generalized Anxiety Disorder) [36]	X	X
Sleep	PSQI (Pittsburgh Sleep Quality Index) [37]	X	X
Resilience	CD-RISC (Connor-Davidson Resilience Scale) [38]	X	X
Internalized HIV Stigma	HSM (HIV Stigma Mechanisms) [39]	X	X
Mental Health and Substance Use Stigma	SAMHSA Mental Health and Alcohol Abuse Stigma Assessment [40]	X	X
Social Support	MOS-SSC (Medical Outcomes Study Social Support Scale) [41]	X	X
Social Isolation	PROMIS (Patient-Reported Outcomes Measurement Information System) [42]		X
Health Care Empowerment	HCE (Health Care Empowerment) [43]	X	X
Relationship with Health Care Provider	HCP-13 (Health Care Provider) [44]	X	X
Unmet Subsistence Needs and	MOS-SF (Medical Outcomes Study Short	X	X

Instrumental Support	Form) [45]		
Satisfaction and Acceptability	Original measure		X

Qualitative Data Collection: A subset of approximately 20 participants who have finished the intervention will be invited to complete an audio-recorded telephone semi-structured individual qualitative exit interview with study staff. Participants will be chosen to reflect a range of levels of engagement and attendance using a question adapted from the Session Rating Scale (SRS) [46] to determine level of satisfaction with each telehealth session. Using mean scores of participant satisfaction over 12 telehealth sessions and attendance, participants will be divided into four groups: 1) high attendance, high satisfaction, 2) high attendance, low satisfaction, 3) low attendance, high satisfaction, and 4) low attendance, low satisfaction. Five participants will be randomly selected from each category and interviewed. The interviews will focus on the acceptability of the intervention and participant feedback on the intervention, and the interviews will be audio-recorded and transcribed verbatim.

Confidentiality and Data Protection: All screening and consenting will take place in a private room. Study staff will use a secure, encrypted texting platform for all study text communication. Participants will receive support from study staff who will demonstrate how to set up additional privacy measures using the settings on their personal cell phones. Electronic data will be gathered through HIPAA-complaint platforms, stored on a secure network, and password protected. Subjects will be coded by numbers and with no names; linking information will be kept in locked files. The data will not be shared unless via a data-use agreement including de-identified data. The study has obtained a Certificate of Confidentiality from the National Institutes of Health to protect the privacy of potential and enrolled study participants.

Data Monitoring: A Data Monitoring Committee (DMC), interim analyses, and stopping guidelines are not needed because the study is a pilot feasibility study that has been classified as minimal risk by the University of California, San Francisco IRB.

Study Outcomes

Feasibility, Acceptability, and Clinical Outcomes: Preliminary data on feasibility, acceptability, and HIV clinical outcomes will be gathered throughout the study (see Tables 3 and 4). Acceptability of the telehealth intervention will be determined throughout the study using several methods. Study staff will administer two session rating questions via text after each weekly telehealth session, asking if the participant "felt heard, understood, and respected by the counselor" and if the "session was right" for them. Additionally, a 30-item exit survey is administered through Qualtrics after the intervention is completed, including questions pertaining to (a) the overall rating of the study; (b) satisfaction with each study procedure; (c) ease or difficulty with each study procedures; (d) helpfulness of communication with study staff; (e) self-perception of improved ART adherence, mental health, and substance use with study participation; (f) recommending a study similar to this to a friend; and (g) participating again in a similar study. Study staff will also conduct qualitative exit interviews with 20 participants to gather in-depth descriptions of participant experiences, perceptions, and acceptability of the intervention. Clinical outcomes within the two study arms include HIV RNA, CD4+ cell count, self-reported adherence, appointment attendance, substance use (DAST and ASSIST), and mental health (PHQ-9 and PCL-5) (see table 4).

Table 3. Primary Outcome Measures: Feasibility and Acceptability

Primary Outcome Measures	Metrics	Acceptance Criteria
Acceptability	Measure participant satisfaction with the telehealth intervention at completion of intervention by a 30-item questionnaire (1 Excellent-6 Unsatisfied) administered through	Mean satisfaction score ≥80%

	an online survey	
	Measure participant satisfaction with each telehealth session via 2-item scale (1-Strongly Agree-4 Strongly Disagree) administered via text messaging	Mean satisfaction score ≥80% over 12 telehealth sessions
Feasibility	Recruitment	At least 70% of the planned 80 participants (i.e., N= 56)
	Participant retention at 4 months	At least 80% of participants retained in the study at 4 months
	Participant retention at 8 months	At least 60% of participants retained in the study at 8 months
	Number of telehealth disconnections	Mean of one disconnection per videoconferencing session
	Participant response time to texts	Mean of 3 days between bi-directional text message and participants' response
	Sound quality based on a 1 item questions using Likert scale (0-10) (0= poor quality; 10= excellent quality)	Mean of 7 out of 10 sound quality
	Video quality based on a 1 item question using Likert scale (0-10) (0= poor quality; 10= excellent quality)	Mean of 7 out of 10 video quality

Table 4. Secondary Outcome Measures: Clinical Impact

Secondary Outcome Measures	Metrics
Alcohol Use	Measure participants' alcohol use from baseline to 4 and 8 months using the Alcohol Use Disorder Test (AUDIT), a 10-item questionnaire to measure severity of participants' alcohol use. Responses are summed. Scoring range is 0-20+; 0-7: Low alcohol use, 20+: High dependence.
Depression	Measure participants' depression from baseline to 4 and 8 months using the Patient Health Questionnaire (PHQ-9), a 9-item Likert scale score (0 - 3) 0 "not at all", 3 "nearly every day". Responses are summed. Scores will have a range of 0-27. PHQ-9 scores of > 10 are associated with moderate to severe depression.
Frequency of Substance Use	Measure participants' change in substance use from baseline to 4 and 8 months using a 10-item questionnaire (ASSIST) to measure frequency of participants' substance use.
Post-Traumatic Stress Disorder (PTSD)	Measure participants' self-reported PTSD from baseline to 4 and 8 months using the PTSD Checklist—revised (PCL), a 20-item Likert questionnaire administered through an online survey. Scoring: 0 points for "not at all", 1 point for "a little bit", 2 points for "moderately", 3 points for "quite a bit", 4 points for "extremely". Scores will have a range of 0-80. Responses are summed.
Self-reported medication adherence	Measure changes in participants' self-reported medication adherence based on 1-item adherence rating (1-Excellent- 6 Poor, lower rating indicates higher adherence) from baseline to 4 and 8 months.
Severity of Substance Use	Measure participants' changes in substance use from baseline to 4 and 8

	months using the Drug Abuse Screening Test (DAST), a 10-item questionnaire to measure severity of participants' substance use. Responses are summed. Scoring (0-10); 0-2 Low substance use, 9-10 Severe substance use.
Measure of participant HIV Knowledge using HIV Treatment Knowledge Scale	Assess participants' knowledge of HIV from baseline to 4 and 8 months through the HIV Treatment Knowledge measure, a 15-item self-report questionnaire. Scoring out of 15 (0-11 Inadequate, 12-15 Adequate). Scores will have a range of 0-15.

Data Analysis Plan

Quantitative analysis plan: One-way frequency tables will be generated for all baseline and follow-up survey questions and measures of central tendency and variability will be computed for continuous measures. Results from these analyses will quantify important sample characteristics and participant use of various telehealth modalities as well as proportions and means of the feasibility and acceptability measures. As needed, multiple imputation (MI) will be employed to address missing data for inferential analyses. Primary preliminary outcome analyses will use generalized estimating equations (GEE) or linear mixed models (LMM) to compare mean log10 HIV RNA across the intervention and control groups at 4 months relative to baseline. Secondary exploratory preliminary outcome analyses will use the same analytic methods to compare the 8-month time point within the intervention arm to baseline to examine whether the intervention had longer-term effects. A parallel exploratory analysis will compare waitlist controls at 4 months versus 8 months.

Additional secondary exploratory analyses will repeat this set of analyses on other secondary outcomes such as CD4+ cell count, HIV knowledge, self-reported adherence and appointment attendance, PHQ-9 and PCL-5 mental health measures, AUDIT alcohol use measure, and the DAST substance use measure. Finally, all analyses described above will be repeatedly stratified by participant sex to explore whether there is any evidence of sex differences in effects. Due to the modest sample size and pilot focus

of the study, significance testing will be de-emphasized in favor of performing inferential analyses as a feasibility check to ensure all measures and analysis protocols are in place for a larger formal efficacy trial [47-48].

Qualitative analysis plan: Study staff will complete, audio-record, and transcribe individual in-depth interviews with 20 YLWH following completion of the clinical intervention. The analytic team will identify broad themes from the interview transcripts, discuss and refine them, and then enter them into a Microsoft Excel-based matrix with a column for each theme and a row for each case.

One coder will initially identify patterns in the themes and code each interview to identify sub-themes and a second coder will double code a random subsample (N= 5) of the interview codes within the matrix. Discrepancies in coding will be discussed by the team until a consensus is reached and interrater reliability will be calculated. A sequential mixed method design will be used to integrate our quantitative and qualitative data analysis.

Dissemination plan: Study staff will work with the UCSF Center for AIDS Prevention Studies' Community Engagement Core and the Youth Advisory Board to disseminate results to the community and participants via presentations, community forums, email updates, and/or social media. Study staff will conduct town hall presentations and publish findings in peer reviewed journals to communicate results with healthcare professionals.

Discussion

This study protocol describes the Y2TEC pilot randomized, crossover study designed to impact the mental health, substance use, and HIV care challenges of YLWH. Few interventions for YLWH currently exist that address these three concerns in an integrated way, and as a result, we had few examples of similar curricula while developing the Y2TEC intervention. Therefore, we relied on formative research including qualitative interviews with healthcare providers and staff serving YLWH, as well as a mixed-methods study examining HIV care engagement, mental health, substance use, and technology-based interventions to address these issues with the target population (Saberi et al, under review) [49].

Additionally, in our review of existing telehealth interventions focusing on these areas, we discovered that there were general telehealth guidelines but few specifics for research. For example, telehealth-specific regulations on best practices for responding to mental health crises described general practices for clinicians with little mention of best clinical practices for crisis response within a research setting [50-51]. We also found that there were few sources of information about best practices for using text messaging and telehealth counseling within research settings, as many healthcare providers who are currently holding telehealth appointments are practicing within medical groups that have officially adopted these technologies [52].

This study has several unique aspects that are worth highlighting. This intervention explores non-traditional methods for care provision that deviate from the adult-care models and may be considered more "youth-friendly" [53]. The intervention was specifically designed to be tailored and adaptable to the participant by using the results of the participant's assessment responses to inform the counselor's decision-making around the number of educational and problem-solving sessions on particular topics. As a result, the counselor is given the ability to spend more or less time on HIV care, mental health, or substance use based on the acuity of the participant's need. Though this adaptive modular structure adds complexity, it has the potential to better meet the needs of participants than a more rigidly structured intervention.

Furthermore, this study simultaneously explores several unique aspects of feasibility and acceptability. In addition to exploring whether this form of intervention will impact HIV, mental health, and substance use outcomes, we are also considering the effect of a fully online versus hybrid in-person-online session delivery. Half of the participants receive the first intervention session with the counselor in person and the rest of their sessions remotely, and the other half receive the full series remotely. If shown to be similarly acceptable, this intervention can be offered completely remotely.

The Y2TEC counseling series has been designed with replication and scalability in mind. The intervention is unique in the relatively low clinician time burden (6 hours of individual counseling per participant over 4 months) compared to traditional face-to-face counseling, which often involves weekly

hour-long sessions (which may total 16 hours over 4 months). Additionally, if we find that participants perceive the remote-only counseling option as acceptable, implementing the intervention would require minimal office space and physical materials, limiting factors within healthcare settings. A remote-only counseling intervention would also potentially increase access for those living in rural areas with limited access to transportation or local services.

We anticipate that the findings of our study will show that a telehealth and text message-based counseling series for YLWH will be acceptable and feasible. We expect that the findings from this study will provide information about additional ways of using new mobile technologies to support the HIV care goals and behavioral health needs of YLWH and will help influence the development of additional mobile-based counseling strategies. The results of this pilot study will allow us to conduct a larger multi-center randomized controlled trial to examine the efficacy of this intervention.

List of Abbreviations

AIDS: Acquired Immune Deficiency Syndrome

ART: Antiretroviral Therapy

ASSIST: Alcohol, Smoking, and Substance Involvement Screening Test

AUDIT: Alcohol Use Disorders Identification Test

DAST: Drug Abuse Screening Test

GEE: Generalized Estimating Equations

HIV: Human Immunodeficiency Virus

IRB: Institutional Review Board

LMM: Linear Mixed Methods

MI: Multiple Imputation

PCL-5: PTSD Checklist for DSM-5

PHQ-9: Patient Health Questionnaire-9

PI: Principal Investigator

UCSF: University of California, San Francisco

Y2TEC: Youth to Telehealth and Text to Improve Engagement in Care

YLWH: Youth Living with HIV

Declarations

Competing interests: The authors have no conflicts of interest to declare.

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Author's contributions: PS, CDR, and MJ conceived the study and developed the experimental design and measures. AW and VG developed the telehealth counseling intervention and manual. DL and PS developed the main study protocols. AW and DL carried out the daily study activities. TN contributed to the data collection and analysis plan. All authors were involved in the revision of the draft manuscript and have agreed to the final content.

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
EXPERIMENTAL SUBJECT'S
BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,
2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,
4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
5) To be told of the other choices I have and how they may be better or worse than being in the study,
6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
7) To be told what sort of medical treatment is available if any complications arise,
8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,
9) To receive a copy of the signed and dated consent form,
10) To be free of pressure when considering whether I wish to agree to be in the study.

_____

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Institutional Review Board, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the UCSF Human Research Protection Program, Box 0962, 3333 California St., Ste. 315, San Francisco, CA 94143. Call 415- 476-1814 for information on translations.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

IRB NUMBER: 16-18538
IRB APPROVAL DATE: 09/27/2018
IRB EXPIRATION DATE: 02/20/2019

Study Title: Youth to Text or Telehealth for Engagement in HIV Care (Y2TEC)

Research Project Director:	Parya Saberi, PharmD MAS, Assistant Professor UCSF Center for AIDS Prevention Studies 3rd Floor, 550 16th St, San Francisco, CA 94158 Phone: 415-502-1000 ext. 17171 ; e-mail: parya.saberi@ucsf.edu
Study Coordinator:	Dominique Legnitto, Phone: 415.917.7686 Email: Dominique.Legnitto@ucsf.edu

This is a research study about how youth (ages 18-29) living with HIV (YLWH) engage in healthcare and the use of technology to improve their engagement in care. This study is being conducted by Dr. Parya Saberi, PharmD and Dr. Carol Dawson-Rose RN, PHD from the UCSF Department of Medicine.

Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you are:

- A young person (18-29 years old) living with HIV
- Living or receiving healthcare in the Bay area outside of San Francisco
- Can speak and understand English

Why is this study being done?

The purpose of this study is to understand ways to help youth living with HIV stay involved in their healthcare. We are interested in how clinicians can improve the resources available, particularly around mental health and substance use. Additionally, we want to see if an intervention delivered by video-chat and text message might help improve engagement in care and adherence to antiretroviral therapy, as well as impact mental health and substance use.

The California HIV/AIDS Research Program pays for the conduct of this study. The investigators of this study have no conflicts of interest to disclose.

How many people will take part in this study?

About 80 people will take part in this study. The study will enroll youth living with HIV to test an intervention delivered remotely using video chat for 12 weekly sessions. 40 participants will be randomly selected to begin receiving the intervention immediately after enrollment. The remaining 40 participants will be randomly selected to a control group for four months and will receive the study intervention at that time.

What will happen if I take part in this research study?

If you are eligible to participate, the study staff will explain the study and procedures to you and answer any questions you have. If you agree to participate, you will sign this consent form and the following procedures will occur:

Initial Visit and Survey and Randomization

- A study staff member will ask you to complete the baseline survey. The survey will include standard questions about your background, current health, HIV medical care, and substance use. This survey will last about 30 minutes.

- Upon completion of the baseline survey, the study staff will use an online tool to randomly assign you to one of the following two conditions:

  Group A –You will meet with a counselor in person for your first session and remotely for all other visits for a total of 12 sessions. You will receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Immediately after completing the baseline survey, you will follow the steps listed below.

  Or

  Group B - You will receive the revised study intervention after a waiting period of four months. At this time, you will be asked to complete an online survey that will last about 30 minutes. You will meet with a counselor remotely for 12 sessions to receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Then you will follow the steps listed below outlining the telehealth intervention.

- The first session will last 30 minutes. A member of the study staff will schedule your remaining sessions to occur weekly. The counselor will meet with you individually for 30 minutes to complete a brief assessment and to identify topic areas to address during the counseling sessions. If for any reason you are unable to make a scheduled session, you may reschedule the appointment by contacting the study staff by phone or text at (415) 917-7686.

- Remaining sessions will be delivered remotely in a private location of your choice, using a secure video chat platform on your mobile phone, tablet or computer and will last about 30 minutes. The study counselor will ask for your present location at the beginning of each video session. You can provide as little or as much detail as you want about your location. Choosing to be more specific about your location will help the study staff ensure your safety and accurate collection of data about where participants access video sessions. During the sessions, you will choose from a menu of topics to discuss including engagement in HIV care, mental health, substance use and/or other concerns affecting your life.

- You will receive between 3 and 5 text messages a week from Study staff and will be asked to respond.
  - Monthly Check in texts to collect updated contact information will occur during the 4-month waiting period when you are not receiving the study intervention.
  - Weekly reminders and appointment confirmations 24 hours before your scheduled appointment and a link to the video chat service 15 minutes before each session.
  - Routine follow-up texts between visits. These will include requested resources, a reminder of goals that were set and notifications about free stuff or events in the community.
  - Session Rating texts will be sent to you after each completed telehealth session and will ask for your response to rate your session with the counselor.

Additional Study Procedures

Surveys: At months 4 and 8, study participants will be asked to complete a brief online survey assessment. The surveys will ask demographic information, substance use and mental health information. These surveys will be completed online using Qualtrics, a UCSF approved secure survey tool on the participants' own mobile device.

Waiting period: During the 4 month waiting period when participants in either group are not receiving the intervention, participants will receive monthly text messages requesting confirmation of contact information. Study staff will request a response from participants to either confirm or update contact information. No other study activities will occur during the waiting period.

Exit Interviews: You may be asked to participate in a brief interview after you have received the intervention. A member of the research staff will interview you for about 30 minutes over the phone. You will be asked to describe your experiences receiving the telehealth intervention. The research staff will make an audio recording of your conversation. After the interview, someone will type into a computer a transcription of the interview and will remove any mention of names. The sound recording will then be destroyed.

Contact Information: A research staff member will ask you for information about how best to contact you if you miss an appointment. You will be asked to provide the names of people who know how to reach you and your social media usernames. Any information about your location that you provide will be kept in secure password protected files. You can ask to have these tracking procedures stopped at any time.

Video Chat: A member of the study staff will help you download a free and secure video chat application, Zoom, on your phone and will demonstrate how to set-up privacy settings. In the event that the application does not work, you will be offered the choice of using WhatsApp or FaceTime to complete telehealth video sessions.

Technical Issues: If you lose your phone or device used for telehealth sessions, or it is stolen, please contact the study staff at 415-917-7686. Once you find your device or obtain a new one, we will restart your text messages.

Crisis: In the event that you are a serious danger to yourself (e.g. suicidal and with plans to commit suicide), the counselor may attempt to identify your location and send emergency services for a safety check. For this reason (as well as for collection of data about where participants have access to internet), we will ask for your present location at the beginning of each video session. The counselor may also contact your emergency contact or mental health provider on file to request support for you if you are experiencing a severe mental health crisis. If you have any questions about how Y2TEC study responds to situations like these, you may talk to your counselor about them at any time during the study.

Medical Record: You will be asked to sign a form authorizing the study staff to view your medical records to get information such as laboratory tests (e.g., viral load test results) or other information related to past medical history that may be applicable to this study.

Participant Referral: If you would like to help us spread the word about Y2TEC, you may be asked to share information about the study with people you know who may be interested and eligible to participate.

Resource Guide: You will be offered verbal, printed, or electronic resources that may be helpful to you. Listed below are some of the resources you may be offered:

- Community Resource guide related to HIV care, mental and substance use.
- Information about mobile health applications and online support groups
- Information on HIV care, mental health, or substance use

Study location

The first study visit will take place in a private room or office to ensure your privacy. All other study activities will be conducted remotely using a video chat application on your mobile phone, tablet or computer in a private setting of your choice. You will be required to share the state where you are located at the beginning of each session to continue but can provide as little or as much detail as you want about your location. Choosing to be more specific about your location helps us ensure your safety and accurate collection of data about where participants access video sessions.

How long will I be in the study?

Participation in the study will last about 8 months. Total time for study activities will be about 10 hours. The telehealth visits, surveys and the exit interview will last about 30 minutes each. The total amount of time you will spend reading and responding to text messages is estimated to be between 10 and 20 minutes per month.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study. The study researcher may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Inconvenience: Participation in the study may sometimes be inconvenient. The study staff will make every effort to schedule interviews and sessions at convenient times.

Surveys: Some of the questions in the interviews or discussions with study staff might make you uncomfortable, upset or embarrassed. You are free to decline to answer any questions or to take part in any discussions at any time.

Technology: This study is using text and video-chat technology, which may have some problems. It is possible that text messages will be sent to you at a time you did not choose, text messages may come when you were not expecting them, there may be missed text messages, or too many text messages. There is a possibility that you may exceed the data or minutes in your cell phone plan and have to pay for that. Staff can provide you with tools and tips to avoid exceeding cell phone plan limits.

Loss of Privacy: Every reasonable effort has been taken to ensure your privacy and confidentiality; however, confidentiality during Internet communication cannot be guaranteed. While using the Zoom App, data is encrypted in transit not stored.
For more information about risks and side effects, please ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, the information that you provide may help the researchers better understand more about how young people (ages 18-29) living with HIV engage in health care and how their engagement in care can be improved.

What other choices do I have if I do not take part in this study?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

Will information about me be kept private?

We will do our best to make sure that the personal information gathered for this study is securely stored. You will be assigned a unique participant ID and data collected will be de-identified and stored on an encrypted server at UCSF in password-protected files. Interviews will be audio recorded and identifying information will be removed from transcripts. The audio-recordings will be destroyed after the interviews are transcribed. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The Y2TEC study staff are mandated to report information about incidents involving child abuse, elder abuse, and participants who intend to hurt themselves or others. These incidents are reported to law enforcement and/or Child Protective Services or Adult Protective Services as required by law.

To protect your privacy, the study has obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use information, documents, that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence. Information, documents, protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the California HIV/AIDS Research Program (CHRP)
- Representatives of the University of California

Are there any costs to me for taking part in this study?
You will not be charged for any of the study procedures.

Will I be paid for taking part in this study?
Yes, in return for your time, effort and travel expenses, you will be paid for completing all study activities. Payment will be given to you in the form of cash or reloadable debit card. Please refer to the complete breakdown of payments below:

- Consent and Survey # 1: $10
- Session 1: $20
- Survey #2: $10
- Session 2-3: $10 each
- Session 4-6: $15 each
- Session 7-9: $20 each
- Session 10-12: $25 each
- Survey #3: $30
- Monthly Check-in Texts and Session Rating Texts: Each time you respond to the monthly text confirming your contact information or the test rating after each completed telehealth session, you will be entered into a drawing and could receive a $25 Amazon Gift card.
- Exit Interview: Participants selected to be interviewed will receive $30
- Referral: $10 per referral if you refer eligible participants to the study.

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you in any way. You will not lose any of your regular benefits.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

IRB NUMBER: 16-18538
IRB APPROVAL DATE: 09/27/2018
IRB EXPIRATION DATE: 02/20/2019

Who can answer my questions about the study?

You can talk to the researchers about any questions, concerns, or complaints you have about this study. Contact the researchers Parya Saberi at 415-502-1000 ext. 17171 or Carol Dawson Rose at 415-514-0428 or Y2TEC@ucsf.edu.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the UCSF Institutional Review Board at 415-476-1814.

Would you like to be contacted if we have other studies for which you might be eligible?

Your initials _____ ☐ Yes ☐ No

Do you consent to allow study staff to locate you through contacting your friends, family, agencies and institution? Indicate your preference below:

Your initials _____ ☐ Yes ☐ No

CONSENT

You have been given a copy of this consent form to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Obtaining Consent

BMJ Open

A Telehealth and Texting Intervention to Improve HIV Care Engagement, Mental Health, and Substance Use Outcomes in Youth Living with HIV: A Pilot Feasibility and Acceptability Study Protocol

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A Telehealth and Texting Intervention to Improve HIV Care Engagement, Mental Health, and Substance Use Outcomes in Youth Living with HIV: A Pilot Feasibility and Acceptability Study Protocol

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Abstract

Introduction: Youth and young adults living with HIV (YLWH) experience worse clinical outcomes than adults and high rates of behavioral health challenges that impact their engagement in care and adherence to antiretroviral therapy. This study in the San Francisco Bay area aims to evaluate the feasibility, acceptability, and preliminary clinical outcomes of a 12-session telehealth counseling series provided to 80 YLWH, including education, motivational enhancement, and problem-solving around HIV care, mental health, substance use, and other challenges. Findings will provide information about benefits and challenges of telehealth counseling for YLWH and will guide the development of new technology-based strategies for care.

Methods and Analysis: The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) study is a pilot randomized, crossover trial examining the feasibility and acceptability of a telehealth counseling intervention consisting of twelve 20-30-minute weekly sessions focused on identifying and problem-solving around barriers to HIV care access and adherence, and on addressing mental health, substance use, and/or other issues. Participants also receive text messages for check-ins, appointment reminders, and to improve engagement. Participants complete quantitative online surveys at baseline, 4, and 8 months, as well as qualitative exit interviews. Clinical outcomes, including plasma HIV RNA and CD4+ cell count, are collected from medical records. Study staff will explore outcomes of the intervention using quantitative and qualitative methods.

Ethics and Dissemination: This study and its protocols have been approved by the UCSF Institutional Review Board. Study staff will work with the UCSF Center for AIDS Prevention Studies' Community Engagement Core and the Youth Advisory Panel to disseminate results to the community, participants, and the academic community.

Trial Registration: This trial was registered with ClinicalTrials.gov, ID # NCT03681145, on 9/19/2018.

Keywords: HIV, antiretroviral therapy, mental health, substance use, counseling, telehealth, text messaging, young adults

Strengths and Limitations of this Study:

- Strength: The use of iterative refinement of the intervention manual throughout this pilot study increases the study's potential impact and acceptability among participants.
- Strength: The study's counseling intervention is significant in its integrated HIV and behavioral health focus which is tailored to the participant's baseline HIV knowledge, mental health status, and substance use.
- Strength: The use of video-chat and text messaging modalities for delivery of HIV engagement, mental health, and substance use counseling with youth living with HIV is important, reduces the time burden to theclinician and patient, and challenges the current delivery of health care.
- Strength: By examining the acceptability of a fully online versus hybrid in-person-online session delivery, we will be able to determine if this intervention can be offered completely remotely which will in turn increase the geographic reach for the delivery of this intervention.
- Limitation: This pilot study is limited due to its small sample size, and the data generated from this study may not be generalizable to older individuals and those not living in the San Francisco Bay Area.

Background

Youth and young adults ages 18-29 living with HIV (YLWH) have unique challenges with HIV diagnosis, access, and maintenance of care. In 2016, in the USA, youth ages 13-24 accounted for about 21% of all new HIV infections [1]. Among those 13-29 years of age and living with HIV, only 41% were estimated to be aware of their HIV status. In 2014, of those diagnosed with HIV, only 62% accessed HIV medical care within the first year; of those, 43% were retained in HIV care, and of those, 54% had a suppressed HIV viral load [2]. Access to care and antiretroviral therapy (ART) are crucial for the health of YLWH; high levels of ART adherence is critical for attaining HIV treatment goals including sustaining suppressed HIV viral load, decreasing risk of developing drug-resistant strains of HIV, reducing the risk of HIV transmission to others, and improving overall health [3-5].

Mental health and substance use challenges are prevalent in YLWH, though few studies have been conducted on behavioral health issues in YLWH. One study found that 18% of YLWH who were in care had clinically significant psychological symptoms such as depression or anxiety [6]. Another study of 1,706 YLWH found that 42.6% reported mental health concerns at a clinically significant level. Of those reporting these symptoms, only 39.7% reported receiving mental health care services in the past year and 21.9% reported taking medications for mental health conditions [7]. Additionally, in one sample of 12 to 26 year-olds living with HIV, 32% used tobacco, 27% used marijuana, 21% used alcohol, and 22% used other illicit substances [8].

Mental health and substance use challenges have been shown to negatively impact HIV medication adherence and clinical outcomes across the continuum of HIV care for YLWH [9-10]. For example, in one systematic review and meta-analysis, those with depression symptoms had 42% lower likelihood of achieving 80% or higher ART adherence compared to those without depression [11]. Another found that of those not taking ART, the odds of reporting clinically significant symptoms were three times as high as those on ART, showing the strong relationship between mental illness symptoms and ART uptake and adherence [12]. Another review found that depression and anxiety symptoms in YLWH were strongly associated with ART non-adherence [13]. Additionally, the review found that

higher alcohol use in the past week and substance use in the past three months were also predictive of poor adherence.

There are few evidence-based counseling interventions for YLWH that address behavioral health factors impacting adherence to HIV care [14]. Interventions developed for adults have shown to be effective in improving depressive symptoms as a method of improving ART adherence [15]. However, young adults differ in multiple ways, including their technology use habits, creating an opportunity for the application of technologies to behavioral health interventions.

As 98% of people ages 18-29 have a mobile telephone and over 85% have a smartphone, telephone-based interventions are potentially accessible for the majority of YLWH [16]. Most traditional counseling interventions are provided in person and in a clinical setting; engaging in these counseling sessions may be a barrier for YLWH who experience transportation or financial issues, stigma or shame around accessing treatment, or other challenges [17]. In our formative work, YLWH reported that health-focused mobile interventions could overcome concerns about their ability to effectively and openly communicate with their providers [18]. One survey similarly found that 60% of millennials would be interested in video-chat interactions with their medical provider instead of attending in-office appointments [19].

Several HIV care adherence interventions have been developed for individuals living with HIV, though most are for adults of all ages rather than YLWH. Few of the interventions specifically developed for YLWH use telehealth, texting, or other mobile technologies as the platform for intervention delivery [20]. Although these methods have been shown to be promising in improving ART adherence and linkage to care in adults living with HIV, they have been minimally studied in YLWH [21].

The existing literature on telehealth and texting platforms for HIV-related interventions for YLWH show promising results and highlights the need for additional research in this area [22]. One text message medication reminder system for adolescents and young adults living with HIV was shown to be feasible, efficacious, and satisfactory to participants [23]. However, a study of 15-22-year-old YLWH found that neither a one-way or two-way text messaging intervention significantly improved HIV

medication adherence [24]. This highlights the need for additional research on the effectiveness of interventions that combine text messaging with other elements, which may improve efficacy.

In this paper, we describe the protocol for a study to examine the feasibility and acceptability of a novel 12-session telehealth counseling series and accompanying text messages to improve engagement in HIV care, mental health, and substance use outcomes. The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) intervention is novel in its combination of telehealth and text messaging, and strategic integration of three foci (i.e., engagement in HIV care, mental health, and substance use). We will identify whether these methods are feasible and acceptable to YLWH and will examine preliminary clinical and behavioral outcomes of the intervention. We anticipate that Y2TEC will be feasible and acceptable for counseling YLWH and that participants will show preliminary evidence of improvement in clinical and behavioral outcomes.

Methods/Design

Study Overview and Design: The Y2TEC study is a single-site randomized pilot study with the primary aim of examining the feasibility and acceptability of a 12-session telehealth and text message-based counseling series for YLWH. The secondary aim is to evaluate the preliminary impact of the intervention on improved engagement in HIV care, enhanced mental health, and reduced substance use for YLWH. The University of California, San Francisco (UCSF) Institutional Review Board has reviewed and approved this study. The intervention was designed based on the results of our formative mixed-methods and qualitative research on youth-friendly HIV counseling methods. The intervention is delivered to participants in two condition groups (i.e., intervention and waitlist control) via remote telehealth sessions delivered over 4 months, with a crossover design (see Table 1). The overall duration of participation is 8 months.

Table 1. Study Overview

		Months								
	I= Intervention Arm Participants *W= Waitlist Arm Participants* *X= All Participants*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Screening/Enrollment										
	Telephone Screening	X								
	Informed Consent		X							
Assessment Surveys										
	Baseline Survey		X							
	Follow-up Surveys					X				X
	Satisfaction and Acceptability Questionnaire					I				W
Counseling Sessions										
	Weekly Counseling Sessions (12)		I	I	I	I	W	W	W	W
Bi-Directional Text messages										
	Monthly Check-Ins			W	W	W		I	I	I
	Session Ratings		I	I	I	I	W	W	W	W
	Goal Reminders		I	I	I	I	W	W	W	W
	Session Reminders (24 hours and 15 minutes before telehealth session)		I	I	I	I	W	W	W	W
	Community Events and Resources		X	X	X	X	X	X	X	X
Exit Interviews										
	Satisfaction Survey					I				W

	Qualitative exit interviews					I				W

Study Setting: Participants are recruited from the San Francisco Bay Area. Participants consent to the study and complete their initial baseline survey in person in a private office at a community-based location or at UCSF's Center for AIDS Prevention Studies. All other study communications are remote via the video-chat platform, text messages, and telephone calls.

Study Participants: The study sample will consist of 80 individuals ages 18-29 living with HIV, who live in and receive medical care in the greater San Francisco Bay Area. We have chosen to include young adults in this age range as they are in a distinct developmental phase with unique needs and challenges compared to minors or those over 29 years of age. Other inclusion criteria include: English-speaking, willing and able to provide informed consent, and have access to a mobile telephone with text messaging capability. Those planning on moving out of California in the next 8 months or with evidence of severe cognitive impairment or active psychosis that may impede their ability to provide informed consent are excluded.

Sample Size Justification: NCSS PASS will be used to compute the minimum detectable effect sizes (MDE) assuming alpha= 0.05, power= 0.80, and N= 64 reflecting anticipated attrition of 20% [25]. For estimates of means and proportions for feasibility and acceptability measures, the minimum detectable distance from the estimate of the proportion to the upper or lower confidence limit for confidence intervals for proportions is 12.7%, assuming a target of 70% feasibility and acceptability.

For means, the standardized distance to the limit is 0.25. For primary preliminary outcome analyses proposed to compare means of continuous outcomes across the intervention and control groups at 4 months, the minimum detectable standardized mean difference *d* is 0.30. These MDEs are between cutoffs for small (*d*= 0.20) and medium (*d*= 0.50) standardized mean differences suggesting our study is powered to detect small to medium effects [26].

Patient and Public Involvement: Prior to the design of this study, we conducted formative research with healthcare providers and patients (Saberi et al, under review), which helped us refine our research

questions, study design, and outcome measures. We asked YLWH about optimal methods for intervention delivery and considered the requests of several participants to have an initial session face-to-face with the counselor. Additionally, we involve participants in study recruitment by encouraging active participants to refer others and providing a $25 incentive to both the referee and referred. We will assess the effects and burden of the intervention by the participants themselves through our quantitative survey and qualitative exist interviews after the intervention. We will work with our Youth Advisory Panel and Community Action Board to disseminate the study's results to participants and the community.

General Study Procedures

Recruitment methods: Participants are recruited through in-person outreach at clinical and community sites serving YLWH, emails to clinics and providers, flyers posted at health clinics and community-based organizations, targeted online advertisements on Instagram, Craigslist, Facebook, and Grindr, and re-contacting participants from prior studies who had expressed interest in being contacted about future studies. Finally, a participant referral method is used and a $25 incentive is provided to both the referring participant and new participant.

Eligibility Screening: Study staff provide a brief overview of the study to prospective participants, answer any questions, and complete an eligibility screening on the telephone. Those who meet the inclusion criteria and are willing to participate in the study are asked for a photo ID to verify their date of birth and proof of HIV status (a letter of diagnosis, laboratory results, or HIV medication prescription) via a photo text-messaged to the study telephone or by bringing these documents to the initial in-person visit.

Consent and Enrollment Procedure: The enrollment visit will be completed in person with a study staff member. Participants review the electronic consent form (see Appendix A) with a study staff member in a private setting. Individuals who are eligible and agree to participate electronically sign the consent and a medical release form using Qualtrics (Provo, UT, USA; version March 2017) an online survey platform, and are provided a copy of the Experimental Subject's Bill of Rights.

Baseline Survey: Participants then complete the online baseline survey, which takes approximately 30-45 minutes. Study staff then help participants download a secure video-chat mobile application (i.e., Zoom, a HIPAA-compliant video-chat platform) on their telephones. Study staff demonstrate how to set up privacy settings on mobile telephones, such as keeping text message previews from showing up on locked screens and adding a security code to lock the telephone.

Randomization: Following the baseline survey, research staff randomly assign participants to one of two condition groups (i.e., intervention or waitlist control) with a pre-numbered sealed envelope. Randomization is done using SAS (version 9.4) based on randomly permuted block sizes to ensure equal sized groups and all study staff are blinded to the randomization order. Approximately 40 participants will be randomized to the immediate intervention condition and receive their first session in person; about 40 participants will be randomized to the waitlist control condition for four months after study enrollment, and then cross-over to the treatment arm and receive the study intervention entirely remotely with no in-person session with the counselor. The counselor and clinical research coordinator will not be blinded to the randomization condition, as treatment will be prescribed as a result of the condition.

Participant Retention: A number of steps are taken to retain participants throughout the study period. Participants are asked for multiple forms of contact information (including emergency contacts, clinical contacts, and social media contacts) at the initial visit to prevent loss of contact. They receive 3 monthly follow-up text messages during the waiting period to confirm their contact information, appointment reminder text messages 24 hours and 15 minutes before scheduled counseling sessions, birthday text messages, and a weekly text message with free fun local activities to facilitate rapport-building (see table 2).

Table 2. Text Messages

Message	Schedule	Text & Response

24 Hour Reminder* (A)	24 hours before appointment	If Y: "Thank you for confirming, Please text us with any questions." If N: "Thank you for replying, we will contact you to reschedule."
15 Minute Reminder (A)	15 min before appointment	"UCSF Team: Appointment Reminder: See you in 15 minutes, here is the link (zoom link)."
Resource (M)	As needed	"UCSF Team: Resources: Here are the resources you requested (link to resources)."
Goals* (M)	3 business days after session	"UCSF Team: Goals: Were you able to attempt your goal? Yes Or Not Yet" Response: "Got it!"
Free Stuff (A)	Weekly	"UCSF Team: Fun Free Stuff: Enjoy Free Yoga in the Park this Saturday from 10-11 am, Downtown Oakland. Here's the link (website)."
Monthly Check-in* (A)	Monthly during waiting period	"UCSF Study Team: Update or confirm your contact info for a chance to win one of 5 $25 Amazon e- Gift cards at the end of the study. Has your phone number or email address changed? Please reply 1 Yes 0 No " If yes: "Please send us your updated phone number and email address._____ Thank you! You have been entered in the raffle, good luck!" If No: Thank you! You have been entered in the raffle, good luck!"

Survey Link (M)	Baseline, 4 and 8 months	"UCSF Team: It's time for your survey. Click on the link below to complete the feedback survey and receive $10. Thank you! (Survey Link)"
Session Rating* (A)	After each session	"UCSF Team: Please tell us about the session today for a chance to win one of five $25 Amazon e-Gift cards at the end of the study: I felt heard, understood, and respected by the counselor: Strongly agree Agree Neither agree nor disagree Disagree Strongly disagree Overall, today's session was right for me: Strongly agree Agree Neither agree nor disagree Disagree Strongly disagree" Response: "Thanks for your responses! Please let us know if you have any additional comments by texting us."
Session Completion (M)	After completion of all sessions	"Congratulations on completing the 1st half of the Y2TEC study! Next, you will receive a survey on xx/xx/xx & a final survey on yy/yy/yy. Please let us know if you have any questions. Thanks!"
Waiting Period Completion (M)	After completing waiting period	"Congratulations, you have finished the 1st half of the Y2TEC study! Next, you will receive a survey on xx/xx/xx & we will contact you to schedule your 1st video chat session after you complete your survey. Please let us know if you have any questions. Thanks!"
Birthday Message (M)	On participant's birthday	"UCSF Team: Happy Birthday, we are sending you all our best wishes for a very happy birthday today, cheers!"

Away Message (A)	After hours and holidays	"Thank you for your message! The Y2TEC Study staff are out of the office until XX/XX/XX and will respond after this date. If this is an emergency, please call 911."
Study Referral (M)	As needed	"UCSF Team: Participants can receive up to $310 for completing all study activities plus $25 per person they refer who enrolls in the study!"

Key:
* = Bi-Directional
(A) = Automated message
(M) = Manually-sent message

Participant Incentives: Participants receive up to $310 for completing all study activities, including payments for each counseling session that gradually increase throughout the study (in $10-$25 increments). Participants are given a ClinCard, a reloadable debit card, and instructions for use at the initial visit. Participants are also entered into two raffles for chances to win $25 Amazon gift cards when they confirm their contact information or answer two session rating questions after each telehealth session. Additionally, participants who refer others to the study are paid $25 per successful recruitment.

Risks to Participants: All risks to participants are monitored by study staff and documented at each session and study assessment. Study staff are trained to thoroughly explain these risks to participants as well as the steps taken to ensure privacy and confidentiality of all information. Safety-related risks to participants could include discomfort due to the sensitive nature of questions in study surveys including substance use, HIV health-related issues, and mental health. Non- clinical study staff conducting interviews and participant communication refer to clinical study staff if participant distress is identified. Clinical staff delivering the intervention are trained to assess distress level of participants and refer to established protocols for any participant crisis. If a participant requires treatment due to distress, this will be determined by clinical staff; they will be referred to appropriate services following the crisis protocol and the PI will be informed.

Adverse Events and Auditing: The study staff monitor post-session participant ratings (via text message) as one method for identifying those who may have experienced an adverse event. If a participant reports low satisfaction with the intervention, study staff contact them in a timely manner to determine what occurred in the session. Study staff also provide participants with the study mobile telephone number to spontaneously report any adverse events or unintended effects of the intervention. Any adverse events will be documented on an adverse event form and follow-up will be tracked. The form along with any session notes with details will be reported to the IRB by the PI within 10 working days. The team of investigators will also meet weekly to audit and discuss general trial conduct related issues.

Protocol Amendments: Protocol amendments will be shared with all stakeholders as they occur. Study staff communicate protocol modifications to investigators during monthly meetings, submit changes to www.clinicaltrials.gov as needed, submit IRB modifications, and communicate changes to regulators during meetings every 6 months or via email as needed.

Intervention Procedure

The 12-session telehealth series is delivered by a trained behavioral health professional (such a social worker, psychologist, or psychotherapist), referred to as the "counselor" within the context of this study. Sessions use problem-solving, IMB (information-motivation-behavioral skills), and motivational interviewing and focus on engagement in HIV care, mental health, and substance use [27-29]. Telehealth sessions are completed via a secure video-chat platform, Zoom, and text messages are sent via a secure encrypted, HIPAA-compliant platform called Mosio.

Series Overview: Participants in the intervention arm meet with the counselor in person immediately after enrollment and the waitlist control arm participants meet with the counselor via video-chat after four months. Before the first meeting, the counselor reviews the participant's most recent assessment survey responses to determine the participant's level of acuity and to tailor appropriate session dosage. Mental

health acuity is determined through the PHQ-9 and PCL; substance use acuity is determined through the AUDIT and ASSIST; HIV care acuity is calculated by a measure of HIV knowledge as well as current participant utilization of HIV care services and antiretroviral medications. During the first session, the counselor assesses the participant's needs and identifies current gaps in knowledge and motivation regarding mental health, substance use, and HIV care. The first three to six of the remaining eleven sessions cover core psychoeducational and health literacy-promoting content around engagement in HIV care, mental health, and substance use challenges and treatments. Those with higher acuity receive two foundational psychoeducational modules rather than one in each of the 3 areas, amounting to a maximum of six core educational sessions.

The remaining sessions use an integrated behavioral health and HIV care-focused approach to further the conversations initiated in the core sessions. At the beginning of these sessions, the participant and counselor choose from a list of topics identified in the first session, including: (A) HIV care; (B) Mental health; (C) Substance use; (D) Lifestyle health; (E) Social support; (F) Family of origin; (G) Romantic and sexual relationships; (H) Self-identity and disclosure; (I) Subsistence Needs (housing, money, and resources) and (J) Education and vocation. These sessions can be done in any order and repeated as needed. If a participant is in crisis and unable to be re-directed to these options, a "wildcard" session (K) focused on crisis response and safety planning may be held. The final session includes reviewing the content covered and goals achieved in the previous sessions, identifying unmet needs, accessing community-based resources, and learning strategies for maintaining changes.

Scheduling Sessions: Four months are allocated to complete the 12 weekly counseling sessions to allow for missed and re-scheduled sessions. Participants are encouraged to contact the counselor or study staff to re-schedule their appointments as needed. Participants receive session reminders via text message 24 hours and 15 minutes before each session.

Session Documentation and Fidelity: The counselor completes session summary notes through a Qualtrics survey form, which includes closed-ended and multiple-choice questions such as session length,

participant location, technical issues encountered, session topics selected, educational topics covered, goals set, a session content fidelity checklist, and a narrative progress note.

Evaluation and Curriculum Modifications: The initial version of the Y2TEC intervention will be delivered to participants randomized to the intervention arm. The research team plans to adjust the intervention based on lessons learned and feedback from participants to develop a modified version of the intervention (i.e., intervention manual version 2.0). This version will be provided to all waitlist control participants and outcome differences between the two arms will be explored during analysis. As a result, the intervention will have gone through an iterative refinement process and will be ready for implementation in a larger randomized controlled trial by the end of the pilot study.

Data Collection and Management Procedure

Clinical Data Collection: At consent, participants sign a medical release form and research staff obtain medical records from participants' respective medical clinics at baseline, 4 months, and 8 months. Information collected includes appointment attendance, medications, and laboratory data including plasma HIV RNA and CD4+ cell count. The data point closest to baseline, 4 months and 8 months +/- one month are used for data analysis.

Assessment Data Collection: Participants complete assessment surveys at baseline, 4 months, and 8 months after enrollment. The surveys collect demographic, technology use, substance use, mental health, and HIV care information (see Table 3). The baseline surveys are completed online in-person at the initial visit and the other two are completed remotely on the participants' mobile devices.

Table 3. Measures in Participant Surveys

Domain (in order of the survey)	Measure	Baseline Survey	Follow-up Surveys

Demographics	Original measure	X	
Use of Technology	Original measure	X	
HIV Treatment Outcomes, Antiretroviral History, and Adherence	Original measure	X	X
HIV Knowledge	HTKS (HIV Treatment Knowledge Scale) [30]	X	X
Alcohol Use	AUDIT (Alcohol Use Disorders Identification Test) [31]	X	X
Substance Use	ASSIST [32], Q2 (Alcohol, Smoking, and Substance Involvement Screening Test), DAST-10 [33] (Drug Abuse Screening Test)	X	X
Depression	PHQ-9 (Patient Health Questionnaire) [34]	X	X
Adverse Childhood Experiences	ACE (Adverse Childhood Experience Questionnaire) [35]	X	
Trauma/PTSD	PCL-5 (PTSD Check List) [36]	X	X
Anxiety	GAD-7 (Generalized Anxiety Disorder) [37]	X	X
Sleep	PSQI (Pittsburgh Sleep Quality Index) [38]	X	X
Resilience	CD-RISC (Connor-Davidson Resilience Scale) [39]	X	X
Internalized HIV Stigma	HSM (HIV Stigma Mechanisms) [40]	X	X
Mental Health and Substance Use Stigma	SAMHSA Mental Health and Alcohol Abuse Stigma Assessment [41]	X	X

Social Support	MOS-SSC (Medical Outcomes Study Social Support Scale) [42]	X	X
Social Isolation	PROMIS (Patient-Reported Outcomes Measurement Information System) [43]		X
Health Care Empowerment	HCE (Health Care Empowerment) [44]	X	X
Relationship with Health Care Provider	HCP-13 (Health Care Provider) [45]	X	X
Unmet Subsistence Needs and Instrumental Support	MOS-SF (Medical Outcomes Study Short Form) [46]	X	X
Satisfaction and Acceptability	Original measure		X

Qualitative Data Collection: A subset of approximately 20 participants who have finished the intervention will be invited to complete an audio-recorded telephone semi-structured individual qualitative exit interview with study staff for a $30 payment. Participants will be chosen to reflect a range of levels of engagement and attendance using a question adapted from the Session Rating Scale (SRS) [47] to determine level of satisfaction with each telehealth session. Using mean scores of participant satisfaction over 12 telehealth sessions and attendance, participants will be divided into four groups: 1) high attendance, high satisfaction, 2) high attendance, low satisfaction, 3) low attendance, high satisfaction, and 4) low attendance, low satisfaction. Five participants will be randomly selected from each category and interviewed. Participants will receive information and consent for the qualitative interviews during the initial visit, along with the consent for the rest of the study. The interviews will focus on the acceptability of the intervention and participant feedback on the intervention, and the interviews will be audio-recorded and transcribed verbatim.

Confidentiality and Data Protection: All screening and consenting will take place in a private room. Study staff will use a secure, encrypted texting platform for all study text communication. Participants

will receive support from study staff who will demonstrate how to set up additional privacy measures using the settings on their personal mobile telephones. Electronic data will be gathered through HIPAA-compliant platforms, stored on a secure network, and password protected. Subjects will be coded by numbers and with no names; linking information will be kept in locked files. The data will not be shared unless via a data-use agreement including de-identified data. The study has obtained a Certificate of Confidentiality from the National Institutes of Health to protect the privacy of potential and enrolled study participants.

Data Monitoring: A Data Monitoring Committee (DMC), interim analyses, and stopping guidelines are not needed because the study is a pilot feasibility study that has been classified as minimal risk by the University of California, San Francisco IRB.

Study Outcomes

Feasibility, Acceptability, and Clinical Outcomes: Preliminary data on feasibility, acceptability, and HIV clinical outcomes will be gathered throughout the study (see Tables 4 and 5). Acceptability of the telehealth intervention will be determined throughout the study using several methods. Study staff will administer two session rating questions via text after each weekly telehealth session, asking if the participant "felt heard, understood, and respected by the counselor" and if the "session was right" for them. Additionally, a 30-item exit survey is administered through Qualtrics after the intervention is completed, including questions pertaining to (a) the overall rating of the study; (b) satisfaction with each study procedure; (c) ease or difficulty with each study procedures; (d) helpfulness of communication with study staff; (e) self-perception of improved ART adherence, mental health, and substance use with study participation; (f) recommending a study similar to this to a friend; and (g) participating again in a similar study. Study staff will also conduct qualitative exit interviews with 20 participants to gather in-depth descriptions of participant experiences, perceptions, and acceptability of the intervention. Clinical outcomes within the two study arms include HIV RNA, CD4+ cell count, self-reported adherence,

appointment attendance, substance use (DAST and ASSIST), and mental health (PHQ-9 and PCL-5) (see table 5).

Table 4. Primary Outcome Measures: Feasibility and Acceptability

Primary Outcome Measures	Metrics	Acceptance Criteria
Acceptability	Measure participant satisfaction with the telehealth intervention at completion of intervention by a 30-item questionnaire (1 Excellent-6 Unsatisfied) administered through an online survey	Mean satisfaction score ≥80%
	Measure participant satisfaction with each telehealth session via 2-item scale (1-Strongly Agree-4 Strongly Disagree) administered via text messaging	Mean satisfaction score ≥80% over 12 telehealth sessions
Feasibility	Recruitment	At least 70% of the planned 80 participants (i.e., N= 56)
	Participant retention at 4 months	At least 80% of participants retained in the study at 4 months
	Participant retention at 8 months	At least 60% of participants retained in the study at 8 months
	Number of telehealth disconnections	Mean of one disconnection per videoconferencing session

	Participant response time to texts	Mean of 3 days between bi-directional text message and participants' response
	Sound quality based on a 1 item questions using Likert scale (0-10) (0= poor quality; 10= excellent quality) as rated by counselor	Mean of 7 out of 10 sound quality
	Video quality based on a 1 item question using Likert scale (0-10) (0= poor quality; 10= excellent quality) as rated by counselor	Mean of 7 out of 10 video quality

Table 5. Secondary Outcome Measures: Clinical Impact

Secondary Outcome Measures	Metrics
Alcohol Use	Measure participants' alcohol use from baseline to 4 and 8 months using the Alcohol Use Disorder Test (AUDIT), a 10-item questionnaire to measure severity of participants' alcohol use. Responses are summed. Scoring range is 0-20+; 0-7: Low alcohol use, 8-19: Moderate alcohol use, 20+: High alcohol use / dependence.
Depression	Measure participants' depression from baseline to 4 and 8 months using the Patient Health Questionnaire (PHQ-9), a 9-item Likert scale score (0 - 3) 0 "not at all", 3 "nearly every day". Responses are summed. Scores will have a range of 0-27. PHQ-9 scores of > 10 are associated with moderate to severe depression.

Frequency of Substance Use	Measure participants' change in substance use from baseline to 4 and 8 months using a 10-item questionnaire (ASSIST) to measure frequency of participants' substance use.
Post-Traumatic Stress Disorder (PTSD)	Measure participants' self-reported PTSD from baseline to 4 and 8 months using the PTSD Checklist—revised (PCL), a 20-item Likert questionnaire administered through an online survey. Scoring: 0 points for "not at all", 1 point for "a little bit", 2 points for "moderately", 3 points for "quite a bit", 4 points for "extremely". Scores will have a range of 0-80. Responses are summed.
Self-reported medication adherence	Measure changes in participants' self-reported medication adherence based on 1-item adherence rating (1-Excellent- 6 Poor, lower rating indicates higher adherence) from baseline to 4 and 8 months.
Severity of Substance Use	Measure participants' changes in substance use from baseline to 4 and 8 months using the Drug Abuse Screening Test (DAST), a 10-item questionnaire to measure severity of participants' substance use. Responses are summed. Scoring (0-10); 0-2 Low substance use, 9-10 Severe substance use.
Measure of participant HIV Knowledge using HIV Treatment Knowledge Scale	Assess participants' knowledge of HIV from baseline to 4 and 8 months through the HIV Treatment Knowledge measure, a 15-item self-report questionnaire. Scoring out of 15 (0-12 Inadequate, 13-15 Adequate). Scores will have a range of 0-15.

Data Analysis Plan

Quantitative analysis plan: One-way frequency tables will be generated for all baseline and follow-up survey questions and measures of central tendency and variability will be computed for continuous

measures. Results from these analyses will quantify important sample characteristics and participant use of various telehealth modalities as well as proportions and means of the feasibility and acceptability measures. Primary preliminary outcome analyses will use linear mixed models (LMM) to compare mean log10 HIV RNA across the intervention and control groups at 4 months relative to baseline. Secondary exploratory preliminary outcome analyses will use the same analytic methods to compare the 8-month time point within the intervention arm to baseline to examine whether the intervention had longer-term effects. A parallel exploratory analysis will compare waitlist controls at 4 months versus 8 months.

Additional secondary exploratory analyses will repeat this set of analyses on other secondary outcomes such as CD4+ cell count, HIV knowledge, self-reported adherence and appointment attendance, PHQ-9 and PCL-5 mental health measures, AUDIT alcohol use measure, and the DAST substance use measure. Finally, all analyses described above will be repeatedly stratified by participant gender to explore whether there is any evidence of sex differences in effects. Due to the modest sample size and pilot focus of the study, significance testing will be de-emphasized in favor of performing inferential analyses as a feasibility check to ensure all measures and analysis protocols are in place for a larger formal efficacy trial [48-49].

Qualitative analysis plan: Study staff will complete, audio-record, and transcribe individual in-depth interviews with 20 YLWH following completion of the clinical intervention. The analytic team will identify broad themes from the interview transcripts, discuss and refine them, and then enter them into a Microsoft Excel-based matrix with a column for each theme and a row for each case. One coder will initially identify patterns in the themes and code each interview to identify sub-themes and a second coder will double code a random subsample (N= 5) of the interview codes within the matrix. Discrepancies in coding will be discussed by the team until a consensus is reached and interrater reliability will be calculated. A sequential mixed-method design will be used to integrate our quantitative and qualitative data analysis.

Dissemination plan: Study staff will work with the UCSF Center for AIDS Prevention Studies' Community Engagement Core and the Youth Advisory Board to disseminate results to the community

and participants via presentations, community forums, email updates, and/or social media. Study staff will conduct town hall presentations and publish findings in peer reviewed journals to communicate results with healthcare professionals.

Discussion

This study protocol describes the Y2TEC pilot randomized, crossover study designed to impact the mental health, substance use, and HIV care challenges of YLWH. Few interventions for YLWH currently exist that address these three concerns in an integrated way, and as a result, we had few examples of similar curricula while developing the Y2TEC intervention. Therefore, we relied on formative research including qualitative interviews with healthcare providers and staff serving YLWH, as well as a mixed-methods study examining HIV care engagement, mental health, substance use, and technology-based interventions to address these issues with the target population [Saberi et al, under review, 50].

Additionally, in our review of existing telehealth interventions focusing on these areas, we discovered that there were general telehealth guidelines but few specifics for research. For example, telehealth-specific regulations on best practices for responding to mental health crises described general practices for clinicians with little mention of best clinical practices for crisis response within a research setting [51-52]. We also found that there were few sources of information about best practices for using text messaging and telehealth counseling within research settings, as many healthcare providers who are currently holding telehealth appointments are practicing within medical groups that have officially adopted these technologies [53].

This study has several unique aspects that are worth highlighting. This intervention explores non-traditional methods for care provision that deviate from the adult-care models and may be considered more “youth-friendly” [54]. The intervention was specifically designed to be tailored and adaptable to the participant by using the results of the participant’s assessment responses to inform the counselor’s decision-making around the number of educational and problem-solving sessions on particular topics. As a result, the counselor is given the ability to spend more or less time on HIV care, mental health, or

substance use based on the acuity of the participant's need. Though this adaptive modular structure adds complexity, it has the potential to better meet the needs of participants than a more rigidly structured intervention.

Furthermore, this study simultaneously explores several unique aspects of feasibility and acceptability. In addition to exploring whether this form of intervention will impact HIV, mental health, and substance use outcomes, we are also considering the acceptability of a fully online versus hybrid in-person-online session delivery. Half of the participants receive the first intervention session with the counselor in person and the rest of their sessions remotely, and the other half receive the full series remotely. If shown to be similarly acceptable, this intervention can be offered completely remotely.

The Y2TEC counseling series has been designed with replication and scalability in mind. The intervention is unique in the relatively low clinician time burden (6 hours of individual counseling per participant over 4 months) compared to traditional face-to-face counseling, which often involves weekly hour-long sessions (which may total 12-16 hours over 4 months). Additionally, if we find that participants perceive the remote-only counseling option as acceptable, implementing the intervention would require minimal office space and physical materials, limiting factors within healthcare settings. A remote-only counseling intervention would also potentially increase access for those living in rural areas with limited access to transportation or local services.

We anticipate that the findings of our study will show that a telehealth and text message-based counseling series for YLWH will be acceptable and feasible. We expect that the findings from this study will provide information about additional ways of using new mobile technologies to support the HIV care goals and behavioral health needs of YLWH and will help influence the development of additional mobile-based counseling strategies. The results of this pilot study will allow us to conduct a larger multi-center randomized controlled trial to examine the efficacy of this intervention.

List of Abbreviations

AIDS: Acquired Immune Deficiency Syndrome

ART: Antiretroviral Therapy

ASSIST: Alcohol, Smoking, and Substance Involvement Screening Test

AUDIT: Alcohol Use Disorders Identification Test

DAST: Drug Abuse Screening Test

GEE: Generalized Estimating Equations

HIV: Human Immunodeficiency Virus

IRB: Institutional Review Board

LMM: Linear Mixed Methods

MI: Multiple Imputation

PCL-5: PTSD Checklist for DSM-5

PHQ-9: Patient Health Questionnaire-9

PI: Principal Investigator

UCSF: University of California, San Francisco

Y2TEC: Youth to Telehealth and Text to Improve Engagement in Care

YLWH: Youth Living with HIV

Declarations

Competing interests: The authors have no conflicts of interest to declare.

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Author's contributions: PS, CDR, and MJ conceived the study and developed the experimental design and measures. AW and VG developed the telehealth counseling intervention and manual. DL and PS developed the main study protocols. AW and DL carried out the daily study activities. TN contributed to

the data collection and analysis plan. All authors were involved in the revision of the draft manuscript and have agreed to the final content.

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
EXPERIMENTAL SUBJECT'S
BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,
2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,
4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
5) To be told of the other choices I have and how they may be better or worse than being in the study,
6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
7) To be told what sort of medical treatment is available if any complications arise,
8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,
9) To receive a copy of the signed and dated consent form,
10) To be free of pressure when considering whether I wish to agree to be in the study.

_____

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Institutional Review Board, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the UCSF Human Research Protection Program, Box 0962, 3333 California St., Ste. 315, San Francisco, CA 94143. Call 415- 476-1814 for information on translations.

Study Title: Youth to Text or Telehealth for Engagement in HIV Care (Y2TEC)

Research Project Director:	Parya Saberi, PharmD MAS, Assistant Professor UCSF Center for AIDS Prevention Studies 3rd Floor, 550 16th St, San Francisco, CA 94158 Phone: 415-502-1000 ext. 17171 ; e-mail: parya.saberi@ucsf.edu
Study Coordinator:	Dominique Legnitto, Phone: 415.917.7686 Email: Dominique.Legnitto@ucsf.edu

This is a research study about how youth (ages 18-29) living with HIV (YLWH) engage in healthcare and the use of technology to improve their engagement in care. This study is being conducted by Dr. Parya Saberi, PharmD and Dr. Carol Dawson-Rose RN, PHD from the UCSF Department of Medicine.

Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you are:

- A young person (18-29 years old) living with HIV
- Living or receiving healthcare in Northern California
- Can speak and understand English

Why is this study being done?

The purpose of this study is to understand ways to help youth living with HIV stay involved in their healthcare. We are interested in how clinicians can improve the resources available, particularly around mental health and substance use. Additionally, we want to see if an intervention delivered by video-chat and text message might help improve engagement in care and adherence to antiretroviral therapy, as well as impact mental health and substance use.

The California HIV/AIDS Research Program pays for the conduct of this study. The investigators of this study have no conflicts of interest to disclose.

How many people will take part in this study?

About 80 people will take part in this study. The study will enroll youth living with HIV to test an intervention delivered remotely using video chat for 12 weekly sessions. 40 participants will be randomly selected to begin receiving the intervention immediately after enrollment. The remaining 40 participants will be randomly selected to a control group for four months and will receive the study intervention at that time.

What will happen if I take part in this research study?

If you are eligible to participate, the study staff will explain the study and procedures to you and answer any questions you have. If you agree to participate, you will sign this consent form and the following procedures will occur:

Initial Visit and Survey and Randomization

- A study staff member will ask you to complete the baseline survey. The survey will include standard questions about your background, current health, HIV medical care, and substance use. This survey will last about 30 minutes.

- Upon completion of the baseline survey, the study staff will use an online tool to randomly assign you to one of the following two conditions:

  Group A –You will meet with a counselor in person for your first session and remotely for all other visits for a total of 12 sessions. You will receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Immediately after completing the baseline survey, you will follow the steps listed below.

  Or

  Group B - You will receive the revised study intervention after a waiting period of four months. At this time, you will be asked to complete an online survey that will last about 30 minutes. You will meet with a counselor remotely for 12 sessions to receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Then you will follow the steps listed below outlining the telehealth intervention.

- The first session will last 30 minutes. A member of the study staff will schedule your remaining sessions to occur weekly. The counselor will meet with you individually for 30 minutes to complete a brief assessment and to identify topic areas to address during the counseling sessions. If for any reason you are unable to make a scheduled session, you may reschedule the appointment by contacting the study staff by phone or text at (415) 917-7686.

- Remaining sessions will be delivered remotely in a private location of your choice, using a secure video chat platform on your mobile phone, tablet or computer and will last about 30 minutes. The study counselor will ask for your present location at the beginning of each video session. You can provide as little or as much detail as you want about your location. Choosing to be more specific about your location will help the study staff ensure your safety and accurate collection of data about where participants access video sessions. During the sessions, you will choose from a menu of topics to discuss including engagement in HIV care, mental health, substance use and/or other concerns affecting your life.

- You will receive between 3 and 5 text messages a week from Study staff and will be asked to respond.
  - Monthly Check in texts to collect updated contact information will occur during the 4-month waiting period when you are not receiving the study intervention.
  - Weekly reminders and appointment confirmations 24 hours before your scheduled appointment and a link to the video chat service 15 minutes before each session.
  - Routine follow-up texts between visits. These will include requested resources, a reminder of goals that were set and notifications about free stuff or events in the community.
  - Session Rating texts will be sent to you after each completed telehealth session and will ask for your response to rate your session with the counselor.

Additional Study Procedures

Surveys: At months 4 and 8, study participants will be asked to complete a brief online survey assessment. The surveys will ask demographic information, substance use and mental health information. These surveys will be completed online using Qualtrics, a UCSF approved secure survey tool on the participants' own mobile device.

Waiting period: During the 4 month waiting period when participants in either group are not receiving the intervention, participants will receive monthly text messages requesting confirmation of contact information. Study staff will request a response from participants to either confirm or update contact information. No other study activities will occur during the waiting period.

Exit Interviews: You may be asked to participate in a brief interview after you have received the intervention. A member of the research staff will interview you for about 30 minutes over the phone. You will be asked to describe your experiences receiving the telehealth intervention. The research staff will make an audio recording of your conversation. After the interview, someone will type into a computer a transcription of the interview and will remove any mention of names. The sound recording will then be destroyed.

Contact Information: A research staff member will ask you for information about how best to contact you if you miss an appointment. You will be asked to provide the names of people who know how to reach you and your social media usernames. Any information about your location that you provide will be kept in secure password protected files. You can ask to have these tracking procedures stopped at any time.

Video Chat: A member of the study staff will help you download a free and secure video chat application, Zoom, on your phone and will demonstrate how to set-up privacy settings. In the event that the application does not work, you will be offered the choice of using WhatsApp or FaceTime to complete telehealth video sessions.

Technical Issues: If you lose your phone or device used for telehealth sessions, or it is stolen, please contact the study staff at 415-917-7686. Once you find your device or obtain a new one, we will restart your text messages.

Crisis: In the event that you are a serious danger to yourself (e.g. suicidal and with plans to commit suicide), the counselor may attempt to identify your location and send emergency services for a safety check. For this reason (as well as for collection of data about where participants have access to internet), we will ask for your present location at the beginning of each video session. The counselor may also contact your emergency contact or mental health provider on file to request support for you if you are experiencing a severe mental health crisis. If you have any questions about how Y2TEC study responds to situations like these, you may talk to your counselor about them at any time during the study.

Medical Record: You will be asked to sign a form authorizing the study staff to view your medical records to get information such as laboratory tests (e.g., viral load test results) or other information related to past medical history that may be applicable to this study.

Participant Referral: If you would like to help us spread the word about Y2TEC, you may be asked to share information about the study with people you know who may be interested and eligible to participate.

Resource Guide: You will be offered verbal, printed, or electronic resources that may be helpful to you. Listed below are some of the resources you may be offered:

- Community Resource guide related to HIV care, mental and substance use.
- Information about mobile health applications and online support groups
- Information on HIV care, mental health, or substance use

Study location

The first study visit will take place in a private room or office to ensure your privacy. All other study activities will be conducted remotely using a video chat application on your mobile phone, tablet or computer in a private setting of your choice. You will be required to share the state where you are located at the beginning of each session to continue but can provide as little or as much detail as you want about your location. Choosing to be more specific about your location helps us ensure your safety and accurate collection of data about where participants access video sessions.

How long will I be in the study?

Participation in the study will last about 8 months. Total time for study activities will be about 10 hours. The telehealth visits, surveys and the exit interview will last about 30 minutes each. The total amount of time you will spend reading and responding to text messages is estimated to be between 10 and 20 minutes per month.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study. The study researcher may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Inconvenience: Participation in the study may sometimes be inconvenient. The study staff will make every effort to schedule interviews and sessions at convenient times.

Surveys: Some of the questions in the interviews or discussions with study staff might make you uncomfortable, upset or embarrassed. You are free to decline to answer any questions or to take part in any discussions at any time.

Technology: This study is using text and video-chat technology, which may have some problems. It is possible that text messages will be sent to you at a time you did not choose, text messages may come when you were not expecting them, there may be missed text messages, or too many text messages. There is a possibility that you may exceed the data or minutes in your cell phone plan and have to pay for that. Staff can provide you with tools and tips to avoid exceeding cell phone plan limits.

Loss of Privacy: Every reasonable effort has been taken to ensure your privacy and confidentiality; however, confidentiality during Internet communication cannot be guaranteed. While using the Zoom App, data is encrypted in transit not stored.
For more information about risks and side effects, please ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, the information that you provide may help the researchers better understand more about how young people (ages 18-29) living with HIV engage in health care and how their engagement in care can be improved.

What other choices do I have if I do not take part in this study?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

Will information about me be kept private?

We will do our best to make sure that the personal information gathered for this study is securely stored. You will be assigned a unique participant ID and data collected will be de-identified and stored on an encrypted server at UCSF in password-protected files. Interviews will be audio recorded and identifying information will be removed from transcripts. The audio-recordings will be destroyed after the interviews are transcribed. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The Y2TEC study staff are mandated to report information about incidents involving child abuse, elder abuse, and participants who intend to hurt themselves or others. These incidents are reported to law enforcement and/or Child Protective Services or Adult Protective Services as required by law.

To protect your privacy, the study has obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use information, documents, that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence. Information, documents, protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the California HIV/AIDS Research Program (CHRP)
- Representatives of the University of California

Are there any costs to me for taking part in this study?
You will not be charged for any of the study procedures.

Will I be paid for taking part in this study?
Yes, in return for your time, effort and travel expenses, you will be paid for completing all study activities. Payment will be given to you in the form of cash or reloadable debit card. Please refer to the complete breakdown of payments below:

- Consent and Survey # 1: $10
- Session 1: $20
- Survey #2: $10
- Session 2-3: $10 each
- Session 4-6: $15 each
- Session 7-9: $20 each
- Session 10-12: $25 each
- Survey #3: $30
- Monthly Check-in Texts and Session Rating Texts: Each time you respond to the monthly text confirming your contact information or the test rating after each completed telehealth session, you will be entered into a drawing and could receive a $25 Amazon Gift card.
- Exit Interview: Participants selected to be interviewed will receive $30
- Referral: $25 per referral if you refer eligible participants to the study.

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you in any way. You will not lose any of your regular benefits.

IRB NUMBER: 16-18538
IRB APPROVAL DATE: 02/19/2019
IRB EXPIRATION DATE: 02/07/2020

Who can answer my questions about the study?

You can talk to the researchers about any questions, concerns, or complaints you have about this study. Contact the researchers Parya Saberi at 415-502-1000 ext. 17171 or Carol Dawson Rose at 415-514-0428 or Y2TEC@ucsf.edu.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the UCSF Institutional Review Board at 415-476-1814.

Would you like to be contacted if we have other studies for which you might be eligible?

Your initials _____ ☐ Yes ☐ No

Do you consent to allow study staff to locate you through contacting your friends, family, agencies and institution? Indicate your preference below:

Your initials _____ ☐ Yes ☐ No

CONSENT

You have been given a copy of this consent form to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____ _____

Date Participant's Signature for Consent

_____ _____

Date Person Obtaining Consent

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym Title page (pg 1), Abstract (pg 2-3)
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Abstract (pg 3)
	2b	All items from the World Health Organization Trial Registration Data Set Abstract (pg 3), Declarations (pg 27)
Protocol version	3	Date and version identifier Declarations (pg 27)
Funding	4	Sources and types of financial, material, and other support Declarations (pg 27)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Declarations (pg 27)
	5b	Name and contact information for the trial sponsor Declarations (pg 27)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities Declarations (pg 27)
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) Data Monitoring (pg 19), Declarations (pg 27)

Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention Background (pg 5-7)
	6b	Explanation for choice of comparators Background (pg 5-7)
Objectives	7	Specific objectives or hypotheses Study Overview and Design (pg 7)
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) Abstract (pg 2-3), Study Overview and Design (pg 7)

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained Study Overview and Design (pg 7), Study Setting (pg 9)
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) Study Participants (pg 9)
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered General Study Procedures (pg 10-14), Intervention Procedure (pg 15-16)
		Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) Risks to Participants (pg 14)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) Session Documentation and Fidelity (pg 16), Data Monitoring (pg 19)

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial N/A – behavioural study with no restrictions in this area
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended Study Outcomes (pg 19-23)
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Study Overview (table 1, pg 8)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations Study Participants (pg 9), Sample Size Justification (pg 9)
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size Recruitment Methods (pg 10)
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions Randomization (pg 11)
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned Randomization (pg 11)
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions General Study Procedures (pg 10- 11), Randomization (pg 11)

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how Randomization (pg 11)
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial Randomization (pg 11)
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Data Collection and Management Procedure (pg 17), Measures in Participant Surveys and Outcome Measures, (Tables 3-5, pg 17-23)
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Participant retention (pg 11)
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol Session Documentation and Fidelity (pg 16), Data collection and management (pg 17-19)
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Quantitative Analysis Plan (pg 23-24)
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) Qualitative Analysis Plan (pg 24)
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) Quantitative Analysis Plan (pg 23-24)

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed Data monitoring (pg 19), Declarations (pg 27)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial Risks to Participants (pg 14), Data monitoring (pg 19)
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct Adverse Events and Auditing (pg 14), Data monitoring (pg 19)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor Adverse Events and Auditing (pg 14)

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval Ethics and Dissemination (pg 3)
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) Protocol amendments (pg 15)
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Consent and Enrolment Procedure (pg 10), Consent form (Appendix A)
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable N/A – no ancillary studies

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial Data Collection and Management Procedure (pg 17-19), Confidentiality and Data Protection (pg 19)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site Completing interests (pg 27), Funding (pg 27)
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators Ethics and Dissemination (pg 3), Dissemination Plan (pg 24)
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation Adverse Events and Auditing (pg 14)
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions Ethics and Dissemination (pg 3), Patient and Public Involvement (pg 9), Dissemination Plan (pg 24)
	31b	Authorship eligibility guidelines and any intended use of professional writers Author's Contributions (pg 27)
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code N/A – no plans
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates Appendix A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable N/A- not applicable to this study

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

A Telehealth and Texting Intervention to Improve HIV Care Engagement, Mental Health, and Substance Use Outcomes in Youth Living with HIV: A Pilot Feasibility and Acceptability Study Protocol

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A Telehealth and Texting Intervention to Improve HIV Care Engagement, Mental Health, and Substance Use Outcomes in Youth Living with HIV: A Pilot Feasibility and Acceptability Study Protocol

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Abstract

Introduction: Youth and young adults living with HIV (YLWH) experience worse clinical outcomes than adults and high rates of behavioral health challenges that impact their engagement in care and adherence to antiretroviral therapy. This study in the San Francisco Bay area aims to evaluate the feasibility, acceptability, and preliminary clinical outcomes of a 12-session telehealth counseling series provided to 80 YLWH, including education, motivational enhancement, and problem-solving around HIV care, mental health, substance use, and other challenges. Findings will provide information about benefits and challenges of telehealth counseling for YLWH and will guide the development of new technology-based strategies for care.

Methods and Analysis: The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) study is a pilot randomized, crossover trial examining the feasibility and acceptability of a telehealth counseling intervention consisting of twelve 20-30-minute weekly sessions focused on identifying and problem-solving around barriers to HIV care access and adherence, and on addressing mental health, substance use, and/or other issues. Participants also receive text messages for check-ins, appointment reminders, and to improve engagement. Participants complete quantitative online surveys at baseline, 4, and 8 months, as well as qualitative exit interviews. Clinical outcomes, including plasma HIV RNA and CD4+ cell count, are collected from medical records. Study staff will explore outcomes of the intervention using quantitative and qualitative methods.

Ethics and Dissemination: This study and its protocols have been approved by the UCSF Institutional Review Board. Study staff will work with the UCSF Center for AIDS Prevention Studies' Community Engagement Core and the Youth Advisory Panel to disseminate results to the community, participants, and the academic community.

Trial Registration: This trial was registered with ClinicalTrials.gov, ID # NCT03681145, on 9/19/2018.

Keywords: HIV, antiretroviral therapy, mental health, substance use, counseling, telehealth, text messaging, young adults

Strengths and Limitations of this Study:

- Strength: The use of iterative refinement of the intervention manual throughout this pilot study increases the study's potential impact and acceptability among participants.
- Strength: The study's counseling intervention is significant in its integrated HIV and behavioral health focus which is tailored to the participant's baseline HIV knowledge, mental health status, and substance use.
- Strength: The use of video-chat and text messaging modalities for delivery of HIV engagement, mental health, and substance use counseling with youth living with HIV is important, reduces the time burden to theclinician and patient, and challenges the current delivery of health care.
- Strength: By examining the acceptability of a fully online versus hybrid in-person-online session delivery, we will be able to determine if this intervention can be offered completely remotely which will in turn increase the geographic reach for the delivery of this intervention.
- Limitation: This pilot study is limited due to its small sample size, and the data generated from this study may not be generalizable to older individuals and those not living in the San Francisco Bay Area.

Background

Youth and young adults ages 18-29 living with HIV (YLWH) have unique challenges with HIV diagnosis, access, and maintenance of care. In 2016, in the USA, youth ages 13-24 accounted for about 21% of all new HIV infections [1]. Among those 13-29 years of age and living with HIV, only 41% were estimated to be aware of their HIV status. In 2014, of those diagnosed with HIV, only 62% accessed HIV medical care within the first year; of those, 43% were retained in HIV care, and of those, 54% had a suppressed HIV viral load [2]. Access to care and antiretroviral therapy (ART) are crucial for the health of YLWH; high levels of ART adherence is critical for attaining HIV treatment goals including sustaining suppressed HIV viral load, decreasing risk of developing drug-resistant strains of HIV, reducing the risk of HIV transmission to others, and improving overall health [3-5].

Mental health and substance use challenges are prevalent in YLWH, though few studies have been conducted on behavioral health issues in YLWH. One study found that 18% of YLWH who were in care had clinically significant psychological symptoms such as depression or anxiety [6]. Another study of 1,706 YLWH found that 42.6% reported mental health concerns at a clinically significant level. Of those reporting these symptoms, only 39.7% reported receiving mental health care services in the past year and 21.9% reported taking medications for mental health conditions [7]. Additionally, in one sample of 12 to 26 year-olds living with HIV, 32% used tobacco, 27% used marijuana, 21% used alcohol, and 22% used other illicit substances [8].

Mental health and substance use challenges have been shown to negatively impact HIV medication adherence and clinical outcomes across the continuum of HIV care for YLWH [9-10]. For example, in one systematic review and meta-analysis, those with depression symptoms had 42% lower likelihood of achieving 80% or higher ART adherence compared to those without depression [11]. Another found that of those not taking ART, the odds of reporting clinically significant symptoms were three times as high as those on ART, showing the strong relationship between mental illness symptoms and ART uptake and adherence [12]. Another review found that depression and anxiety symptoms in YLWH were strongly associated with ART non-adherence [13]. Additionally, the review found that

higher alcohol use in the past week and substance use in the past three months were also predictive of poor adherence.

There are few evidence-based counseling interventions for YLWH that address behavioral health factors impacting adherence to HIV care [14]. Interventions developed for adults have shown to be effective in improving depressive symptoms as a method of improving ART adherence [15]. However, young adults differ in multiple ways, including their technology use habits, creating an opportunity for the application of technologies to behavioral health interventions.

As 98% of people ages 18-29 have a mobile telephone and over 85% have a smartphone, telephone-based interventions are potentially accessible for the majority of YLWH [16]. Most traditional counseling interventions are provided in person and in a clinical setting; engaging in these counseling sessions may be a barrier for YLWH who experience transportation or financial issues, stigma or shame around accessing treatment, or other challenges [17]. In our formative work, YLWH reported that health-focused mobile interventions could overcome concerns about their ability to effectively and openly communicate with their providers [18]. One survey similarly found that 60% of millennials would be interested in video-chat interactions with their medical provider instead of attending in-office appointments [19].

Several HIV care adherence interventions have been developed for individuals living with HIV, though most are for adults of all ages rather than YLWH. Few of the interventions specifically developed for YLWH use telehealth, texting, or other mobile technologies as the platform for intervention delivery [20]. Although these methods have been shown to be promising in improving ART adherence and linkage to care in adults living with HIV, they have been minimally studied in YLWH [21].

The existing literature on telehealth and texting platforms for HIV-related interventions for YLWH show promising results and highlights the need for additional research in this area [22]. One text message medication reminder system for adolescents and young adults living with HIV was shown to be feasible, efficacious, and satisfactory to participants [23]. However, a study of 15-22-year-old YLWH found that neither a one-way or two-way text messaging intervention significantly improved HIV

medication adherence [24]. This highlights the need for additional research on the effectiveness of interventions that combine text messaging with other elements, which may improve efficacy.

In this paper, we describe the protocol for a study to examine the feasibility and acceptability of a novel 12-session telehealth counseling series and accompanying text messages to improve engagement in HIV care, mental health, and substance use outcomes. The Youth to Telehealth and Text to Improve Engagement in Care (Y2TEC) intervention is novel in its combination of telehealth and text messaging, and strategic integration of three foci (i.e., engagement in HIV care, mental health, and substance use). We will identify whether these methods are feasible and acceptable to YLWH and will examine preliminary clinical and behavioral outcomes of the intervention. We anticipate that Y2TEC will be feasible and acceptable for counseling YLWH and that participants will show preliminary evidence of improvement in clinical and behavioral outcomes.

Methods/Design

Study Overview and Design: The Y2TEC study is a single-site randomized pilot study with the primary aim of examining the feasibility and acceptability of a 12-session telehealth and text message-based counseling series for YLWH. The secondary aim is to evaluate the preliminary impact of the intervention on improved engagement in HIV care, enhanced mental health, and reduced substance use for YLWH. The University of California, San Francisco (UCSF) Institutional Review Board has reviewed and approved this study. The intervention was designed based on the results of our formative mixed-methods and qualitative research on youth-friendly HIV counseling methods. The intervention is delivered to participants in two condition groups (i.e., intervention and waitlist control) via remote telehealth sessions delivered over 4 months, with a crossover design (see Table 1). The overall duration of participation is 8 months.

Table 1. Study Overview

		Months								
	I= Intervention Arm Participants *W= Waitlist Arm Participants* *X= All Participants*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Screening/Enrollment										
	Telephone Screening	X								
	Informed Consent		X							
Assessment Surveys										
	Baseline Survey		X							
	Follow-up Surveys					X				X
	Satisfaction and Acceptability Questionnaire					I				W
Counseling Sessions										
	Weekly Counseling Sessions (12)		I	I	I	I	W	W	W	W
Bi-Directional Text messages										
	Monthly Check-Ins			W	W	W		I	I	I
	Session Ratings		I	I	I	I	W	W	W	W
	Goal Reminders		I	I	I	I	W	W	W	W
	Session Reminders (24 hours and 15 minutes before telehealth session)		I	I	I	I	W	W	W	W
	Community Events and Resources		X	X	X	X	X	X	X	X
Exit Interviews										
	Satisfaction Survey					I				W

	Qualitative exit interviews					I				W

Study Setting: Participants are recruited from the San Francisco Bay Area. Participants consent to the study and complete their initial baseline survey in person in a private office at a community-based location or at UCSF's Center for AIDS Prevention Studies. All other study communications are remote via the video-chat platform, text messages, and telephone calls.

Study Participants: The study sample will consist of 80 individuals ages 18-29 living with HIV, who live in and receive medical care in the greater San Francisco Bay Area. We have chosen to include young adults in this age range as they are in a distinct developmental phase with unique needs and challenges compared to minors or those over 29 years of age. Other inclusion criteria include: English-speaking, willing and able to provide informed consent, and have access to a mobile telephone with text messaging capability. Those planning on moving out of California in the next 8 months or with evidence of severe cognitive impairment or active psychosis that may impede their ability to provide informed consent are excluded.

Sample Size Justification: NCSS PASS will be used to compute the minimum detectable effect sizes (MDE) assuming alpha= 0.05, power= 0.80, and N= 64 reflecting anticipated attrition of 20% [25]. For estimates of means and proportions for feasibility and acceptability measures, the minimum detectable distance from the estimate of the proportion to the upper or lower confidence limit is 12.7%, assuming a target of 70% feasibility and acceptability. For means, the standardized distance to the limit is 0.25. For primary preliminary outcome analyses proposed to compare means of continuous outcomes across the intervention and control groups at 4 months, the minimum detectable standardized mean difference *d* is 0.30. These MDEs are between cutoffs for small (*d*= 0.20) and medium (*d*= 0.50) standardized mean differences suggesting our study is powered to detect small to medium effects [26].

Patient and Public Involvement: Prior to the design of this study, we conducted formative research with healthcare providers and patients (Saberi et al, under review), which helped us refine our research questions, study design, and outcome measures. We asked YLWH about optimal methods for intervention delivery and considered the requests of several participants to have an initial session face-to-face with the counselor. Additionally, we involve participants in study recruitment by encouraging active participants to refer others and providing a $25 incentive to both the referee and referred. We will assess the effects and burden of the intervention by the participants themselves through our quantitative survey and qualitative exist interviews after the intervention. We will work with our Youth Advisory Panel and Community Action Board to disseminate the study's results to participants and the community.

General Study Procedures

Recruitment methods: Participants are recruited through in-person outreach at clinical and community sites serving YLWH, emails to clinics and providers, flyers posted at health clinics and community-based organizations, targeted online advertisements on Instagram, Craigslist, Facebook, and Grindr, and re-contacting participants from prior studies who had expressed interest in being contacted about future studies. Finally, a participant referral method is used and a $25 incentive is provided to both the referring participant and new participant.

Eligibility Screening: Study staff provide a brief overview of the study to prospective participants, answer any questions, and complete an eligibility screening on the telephone. Those who meet the inclusion criteria and are willing to participate in the study are asked for a photo ID to verify their date of birth and proof of HIV status (a letter of diagnosis, laboratory results, or HIV medication prescription) via a photo text-messaged to the study telephone or by bringing these documents to the initial in-person visit.

Consent and Enrollment Procedure: The enrollment visit will be completed in person with a study staff member. Participants review the electronic consent form (see Appendix A) with a study staff member in a private setting. Individuals who are eligible and agree to participate electronically sign the consent and a

medical release form using Qualtrics (Provo, UT, USA; version March 2017) an online survey platform, and are provided a copy of the Experimental Subject's Bill of Rights.

Baseline Survey: Participants then complete the online baseline survey, which takes approximately 30-45 minutes. Study staff then help participants download a secure video-chat mobile application (i.e., Zoom, a HIPAA-compliant video-chat platform) on their telephones. Study staff demonstrate how to set up privacy settings on mobile telephones, such as keeping text message previews from showing up on locked screens and adding a security code to lock the telephone.

Randomization: Following the baseline survey, research staff randomly assign participants to one of two condition groups (i.e., intervention or waitlist control) with a pre-numbered sealed envelope. Randomization is done using SAS (version 9.4) based on randomly permuted block sizes to ensure equal sized groups and all study staff are blinded to the randomization order. Approximately 40 participants will be randomized to the immediate intervention condition and receive their first session in person; about 40 participants will be randomized to the waitlist control condition for four months after study enrollment, and then cross-over to the treatment arm and receive the study intervention entirely remotely with no in-person session with the counselor. The counselor and clinical research coordinator will not be blinded to the randomization condition, as treatment will be prescribed as a result of the condition.

Participant Retention: A number of steps are taken to retain participants throughout the study period. Participants are asked for multiple forms of contact information (including emergency contacts, clinical contacts, and social media contacts) at the initial visit to prevent loss of contact. They receive 3 monthly follow-up text messages during the waiting period to confirm their contact information, appointment reminder text messages 24 hours and 15 minutes before scheduled counseling sessions, birthday text messages, and a weekly text message with free fun local activities to facilitate rapport-building (see table 2).

Table 2. Text Messages

Message	Schedule	Text & Response

24 Hour Reminder* (A)	24 hours before appointment	If Y: "Thank you for confirming, Please text us with any questions." If N: "Thank you for replying, we will contact you to reschedule."
15 Minute Reminder (A)	15 min before appointment	"UCSF Team: Appointment Reminder: See you in 15 minutes, here is the link (zoom link)."
Resource (M)	As needed	"UCSF Team: Resources: Here are the resources you requested (link to resources)."
Goals* (M)	3 business days after session	"UCSF Team: Goals: Were you able to attempt your goal? Yes Or Not Yet" Response: "Got it!"
Free Stuff (A)	Weekly	"UCSF Team: Fun Free Stuff: Enjoy Free Yoga in the Park this Saturday from 10-11 am, Downtown Oakland. Here's the link (website)."
Monthly Check-in* (A)	Monthly during waiting period	"UCSF Study Team: Update or confirm your contact info for a chance to win one of 5 $25 Amazon e- Gift cards at the end of the study. Has your phone number or email address changed? Please reply 1 Yes 0 No " If yes: "Please send us your updated phone number and email address._____ Thank you! You have been entered in the raffle, good luck!" If No: Thank you! You have been entered in the raffle, good luck!"

Survey Link (M)	Baseline, 4 and 8 months	"UCSF Team: It's time for your survey. Click on the link below to complete the feedback survey and receive $10. Thank you! (Survey Link)"
Session Rating* (A)	After each session	"UCSF Team: Please tell us about the session today for a chance to win one of five $25 Amazon e-Gift cards at the end of the study: I felt heard, understood, and respected by the counselor: Strongly agree Agree Neither agree nor disagree Disagree Strongly disagree Overall, today's session was right for me: Strongly agree Agree Neither agree nor disagree Disagree Strongly disagree" Response: "Thanks for your responses! Please let us know if you have any additional comments by texting us."
Session Completion (M)	After completion of all sessions	"Congratulations on completing the 1st half of the Y2TEC study! Next, you will receive a survey on xx/xx/xx & a final survey on yy/yy/yy. Please let us know if you have any questions. Thanks!"
Waiting Period Completion (M)	After completing waiting period	"Congratulations, you have finished the 1st half of the Y2TEC study! Next, you will receive a survey on xx/xx/xx & we will contact you to schedule your 1st video chat session after you complete your survey. Please let us know if you have any questions. Thanks!"
Birthday Message (M)	On participant's birthday	"UCSF Team: Happy Birthday, we are sending you all our best wishes for a very happy birthday today, cheers!"

Away Message (A)	After hours and holidays	"Thank you for your message! The Y2TEC Study staff are out of the office until XX/XX/XX and will respond after this date. If this is an emergency, please call 911."
Study Referral (M)	As needed	"UCSF Team: Participants can receive up to $310 for completing all study activities plus $25 per person they refer who enrolls in the study!"

Key:
* = Bi-Directional
(A) = Automated message
(M) = Manually-sent message

Participant Incentives: Participants receive up to $310 for completing all study activities, including payments for each counseling session that gradually increase throughout the study (in $10-$25 increments). Participants are given a ClinCard, a reloadable debit card, and instructions for use at the initial visit. Participants are also entered into two raffles for chances to win $25 Amazon gift cards when they confirm their contact information or answer two session rating questions after each telehealth session. Additionally, participants who refer others to the study are paid $25 per successful recruitment.

Risks to Participants: All risks to participants are monitored by study staff and documented at each session and study assessment. Study staff are trained to thoroughly explain these risks to participants as well as the steps taken to ensure privacy and confidentiality of all information. Safety-related risks to participants could include discomfort due to the sensitive nature of questions in study surveys including substance use, HIV health-related issues, and mental health. Non- clinical study staff conducting interviews and participant communication refer to clinical study staff if participant distress is identified. Clinical staff delivering the intervention are trained to assess distress level of participants and refer to established protocols for any participant crisis. If a participant requires treatment due to distress, this will be determined by clinical staff; they will be referred to appropriate services following the crisis protocol and the PI will be informed.

Adverse Events and Auditing: The study staff monitor post-session participant ratings (via text message) as one method for identifying those who may have experienced an adverse event. If a participant reports low satisfaction with the intervention, study staff contact them in a timely manner to determine what occurred in the session. Study staff also provide participants with the study mobile telephone number to spontaneously report any adverse events or unintended effects of the intervention. Any adverse events will be documented on an adverse event form and follow-up will be tracked. The form along with any session notes with details will be reported to the IRB by the PI within 10 working days. The team of investigators will also meet weekly to audit and discuss general trial conduct related issues.

Protocol Amendments: Protocol amendments will be shared with all stakeholders as they occur. Study staff communicate protocol modifications to investigators during monthly meetings, submit changes to www.clinicaltrials.gov as needed, submit IRB modifications, and communicate changes to regulators during meetings every 6 months or via email as needed.

Intervention Procedure

The 12-session telehealth series is delivered by a trained behavioral health professional (such a social worker, psychologist, or psychotherapist), referred to as the "counselor" within the context of this study. Sessions use problem-solving, IMB (information-motivation-behavioral skills), and motivational interviewing and focus on engagement in HIV care, mental health, and substance use [27-29]. Telehealth sessions are completed via a secure video-chat platform, Zoom, and text messages are sent via a secure encrypted, HIPAA-compliant platform called Mosio.

Series Overview: Participants in the intervention arm meet with the counselor in person immediately after enrollment and the waitlist control arm participants meet with the counselor via video-chat after four months. Before the first meeting, the counselor reviews the participant's most recent assessment survey responses to determine the participant's level of acuity and to tailor appropriate session dosage. Mental

health acuity is determined through the PHQ-9 and PCL; substance use acuity is determined through the AUDIT and ASSIST; HIV care acuity is calculated by a measure of HIV knowledge as well as current participant utilization of HIV care services and antiretroviral medications. During the first session, the counselor assesses the participant's needs and identifies current gaps in knowledge and motivation regarding mental health, substance use, and HIV care. The first three to six of the remaining eleven sessions cover core psychoeducational and health literacy-promoting content around engagement in HIV care, mental health, and substance use challenges and treatments. Those with higher acuity receive two foundational psychoeducational modules rather than one in each of the 3 areas, amounting to a maximum of six core educational sessions.

The remaining sessions use an integrated behavioral health and HIV care-focused approach to further the conversations initiated in the core sessions. At the beginning of these sessions, the participant and counselor choose from a list of topics identified in the first session, including: (A) HIV care; (B) Mental health; (C) Substance use; (D) Lifestyle health; (E) Social support; (F) Family of origin; (G) Romantic and sexual relationships; (H) Self-identity and disclosure; (I) Subsistence Needs (housing, money, and resources) and (J) Education and vocation. These sessions can be done in any order and repeated as needed. If a participant is in crisis and unable to be re-directed to these options, a "wildcard" session (K) focused on crisis response and safety planning may be held. The final session includes reviewing the content covered and goals achieved in the previous sessions, identifying unmet needs, accessing community-based resources, and learning strategies for maintaining changes.

Scheduling Sessions: Four months are allocated to complete the 12 weekly counseling sessions to allow for missed and re-scheduled sessions. Participants are encouraged to contact the counselor or study staff to re-schedule their appointments as needed. Participants receive session reminders via text message 24 hours and 15 minutes before each session.

Session Documentation and Fidelity: The counselor completes session summary notes through a Qualtrics survey form, which includes closed-ended and multiple-choice questions such as session length,

participant location, technical issues encountered, session topics selected, educational topics covered, goals set, a session content fidelity checklist, and a narrative progress note.

Evaluation and Curriculum Modifications: The initial version of the Y2TEC intervention will be delivered to participants randomized to the intervention arm. The research team plans to adjust the intervention based on lessons learned and feedback from participants to develop a modified version of the intervention (i.e., intervention manual version 2.0). This version will be provided to all waitlist control participants and outcome differences between the two arms will be explored during analysis. As a result, the intervention will have gone through an iterative refinement process and will be ready for implementation in a larger randomized controlled trial by the end of the pilot study.

Data Collection and Management Procedure

Clinical Data Collection: At consent, participants sign a medical release form and research staff obtain medical records from participants' respective medical clinics at baseline, 4 months, and 8 months. Information collected includes appointment attendance, medications, and laboratory data including plasma HIV RNA and CD4+ cell count. The data point closest to baseline, 4 months and 8 months +/- one month are used for data analysis.

Assessment Data Collection: Participants complete assessment surveys at baseline, 4 months, and 8 months after enrollment. The surveys collect demographic, technology use, substance use, mental health, and HIV care information (see Table 3). The baseline surveys are completed online in-person at the initial visit and the other two are completed remotely on the participants' mobile devices.

Table 3. Measures in Participant Surveys

Domain (in order of the survey)	Measure	Baseline Survey	Follow-up Surveys

Demographics	Original measure	X	
Use of Technology	Original measure	X	
HIV Treatment Outcomes, Antiretroviral History, and Adherence	Original measure	X	X
HIV Knowledge	HTKS (HIV Treatment Knowledge Scale) [30]	X	X
Alcohol Use	AUDIT (Alcohol Use Disorders Identification Test) [31]	X	X
Substance Use	ASSIST [32], Q2 (Alcohol, Smoking, and Substance Involvement Screening Test), DAST-10 [33] (Drug Abuse Screening Test)	X	X
Depression	PHQ-9 (Patient Health Questionnaire) [34]	X	X
Adverse Childhood Experiences	ACE (Adverse Childhood Experience Questionnaire) [35]	X	
Trauma/PTSD	PCL-5 (PTSD Check List) [36]	X	X
Anxiety	GAD-7 (Generalized Anxiety Disorder) [37]	X	X
Sleep	PSQI (Pittsburgh Sleep Quality Index) [38]	X	X
Resilience	CD-RISC (Connor-Davidson Resilience Scale) [39]	X	X
Internalized HIV Stigma	HSM (HIV Stigma Mechanisms) [40]	X	X
Mental Health and Substance Use Stigma	SAMHSA Mental Health and Alcohol Abuse Stigma Assessment [41]	X	X

Social Support	MOS-SSC (Medical Outcomes Study Social Support Scale) [42]	X	X
Social Isolation	PROMIS (Patient-Reported Outcomes Measurement Information System) [43]		X
Health Care Empowerment	HCE (Health Care Empowerment) [44]	X	X
Relationship with Health Care Provider	HCP-13 (Health Care Provider) [45]	X	X
Unmet Subsistence Needs and Instrumental Support	MOS-SF (Medical Outcomes Study Short Form) [46]	X	X
Satisfaction and Acceptability	Original measure		X

Qualitative Data Collection: A subset of approximately 20 participants who have finished the intervention will be invited to complete an audio-recorded telephone semi-structured individual qualitative exit interview with study staff for a $30 payment. Participants will be chosen to reflect a range of levels of engagement and attendance using a question adapted from the Session Rating Scale (SRS) [47] to determine level of satisfaction with each telehealth session. Using mean scores of participant satisfaction over 12 telehealth sessions and attendance, participants will be divided into four groups: 1) high attendance, high satisfaction, 2) high attendance, low satisfaction, 3) low attendance, high satisfaction, and 4) low attendance, low satisfaction. Five participants will be randomly selected from each category and interviewed. Participants will receive information and consent for the qualitative interviews during the initial visit, along with the consent for the rest of the study. The interviews will focus on the acceptability of the intervention and participant feedback on the intervention, and the interviews will be audio-recorded and transcribed verbatim.

Confidentiality and Data Protection: All screening and consenting will take place in a private room. Study staff will use a secure, encrypted texting platform for all study text communication. Participants

will receive support from study staff who will demonstrate how to set up additional privacy measures using the settings on their personal mobile telephones. Electronic data will be gathered through HIPAA-compliant platforms, stored on a secure network, and password protected. Subjects will be coded by numbers and with no names; linking information will be kept in locked files. The data will not be shared unless via a data-use agreement including de-identified data. The study has obtained a Certificate of Confidentiality from the National Institutes of Health to protect the privacy of potential and enrolled study participants.

Data Monitoring: A Data Monitoring Committee (DMC), interim analyses, and stopping guidelines are not needed because the study is a pilot feasibility study that has been classified as minimal risk by the University of California, San Francisco IRB.

Study Outcomes

Feasibility, Acceptability, and Clinical Outcomes: Preliminary data on feasibility, acceptability, and HIV clinical outcomes will be gathered throughout the study (see Tables 4 and 5). Acceptability of the telehealth intervention will be determined throughout the study using several methods. Study staff will administer two session rating questions via text after each weekly telehealth session, asking if the participant "felt heard, understood, and respected by the counselor" and if the "session was right" for them. Additionally, a 30-item exit survey is administered through Qualtrics after the intervention is completed, including questions pertaining to (a) the overall rating of the study; (b) satisfaction with each study procedure; (c) ease or difficulty with each study procedures; (d) helpfulness of communication with study staff; (e) self-perception of improved ART adherence, mental health, and substance use with study participation; (f) recommending a study similar to this to a friend; and (g) participating again in a similar study. Study staff will also conduct qualitative exit interviews with 20 participants to gather in-depth descriptions of participant experiences, perceptions, and acceptability of the intervention. Clinical outcomes within the two study arms include HIV RNA, CD4+ cell count, self-reported adherence,

appointment attendance, substance use (DAST and ASSIST), and mental health (PHQ-9 and PCL-5) (see table 5).

Table 4. Primary Outcome Measures: Feasibility and Acceptability

Primary Outcome Measures	Metrics	Acceptance Criteria
Acceptability	Measure participant satisfaction with the telehealth intervention at completion of intervention by a 30-item questionnaire (1 Excellent-6 Unsatisfied) administered through an online survey	Mean satisfaction score ≥80%
	Measure participant satisfaction with each telehealth session via 2-item scale (1-Strongly Agree-4 Strongly Disagree) administered via text messaging	Mean satisfaction score ≥80% over 12 telehealth sessions
Feasibility	Recruitment	At least 70% of the planned 80 participants (i.e., N= 56)
	Participant retention at 4 months	At least 80% of participants retained in the study at 4 months
	Participant retention at 8 months	At least 60% of participants retained in the study at 8 months
	Number of telehealth disconnections	Mean of one disconnection per videoconferencing session

	Participant response time to texts	Mean of 3 days between bi-directional text message and participants' response
	Sound quality based on a 1 item questions using Likert scale (0-10) (0= poor quality; 10= excellent quality) as rated by counselor	Mean of 7 out of 10 sound quality
	Video quality based on a 1 item question using Likert scale (0-10) (0= poor quality; 10= excellent quality) as rated by counselor	Mean of 7 out of 10 video quality

Table 5. Secondary Outcome Measures: Clinical Impact

Secondary Outcome Measures	Metrics
Alcohol Use	Measure participants' alcohol use from baseline to 4 and 8 months using the Alcohol Use Disorder Test (AUDIT), a 10-item questionnaire to measure severity of participants' alcohol use. Responses are summed. Scoring range is 0-20+; 0-7: Low alcohol use, 8-19: Moderate alcohol use, 20+: High alcohol use / dependence.
Depression	Measure participants' depression from baseline to 4 and 8 months using the Patient Health Questionnaire (PHQ-9), a 9-item Likert scale score (0 - 3) 0 "not at all", 3 "nearly every day". Responses are summed. Scores will have a range of 0-27. PHQ-9 scores of > 10 are associated with moderate to severe depression.

Frequency of Substance Use	Measure participants' change in substance use from baseline to 4 and 8 months using a 10-item questionnaire (ASSIST) to measure frequency of participants' substance use.
Post-Traumatic Stress Disorder (PTSD)	Measure participants' self-reported PTSD from baseline to 4 and 8 months using the PTSD Checklist—revised (PCL), a 20-item Likert questionnaire administered through an online survey. Scoring: 0 points for "not at all", 1 point for "a little bit", 2 points for "moderately", 3 points for "quite a bit", 4 points for "extremely". Scores will have a range of 0-80. Responses are summed.
Self-reported medication adherence	Measure changes in participants' self-reported medication adherence based on 1-item adherence rating (1-Excellent- 6 Poor, lower rating indicates higher adherence) from baseline to 4 and 8 months.
Severity of Substance Use	Measure participants' changes in substance use from baseline to 4 and 8 months using the Drug Abuse Screening Test (DAST), a 10-item questionnaire to measure severity of participants' substance use. Responses are summed. Scoring (0-10); 0-2 Low substance use, 9-10 Severe substance use.
Measure of participant HIV Knowledge using HIV Treatment Knowledge Scale	Assess participants' knowledge of HIV from baseline to 4 and 8 months through the HIV Treatment Knowledge measure, a 15-item self-report questionnaire. Scoring out of 15 (0-12 Inadequate, 13-15 Adequate). Scores will have a range of 0-15.

Data Analysis Plan

Quantitative analysis plan: One-way frequency tables will be generated for all baseline and follow-up survey questions and measures of central tendency and variability will be computed for continuous

measures. Results from these analyses will quantify important sample characteristics and participant use of various telehealth modalities as well as proportions and means of the feasibility and acceptability measures. Primary preliminary outcome analyses will use linear mixed models (LMM) to compare mean log10 HIV RNA across the intervention and control groups at 4 months relative to baseline. Secondary exploratory preliminary outcome analyses will use the same analytic methods to compare the 8-month time point within the intervention arm to baseline to examine whether the intervention had longer-term effects. A parallel exploratory analysis will compare waitlist controls at 4 months versus 8 months.

Additional secondary exploratory analyses will repeat this set of analyses on other secondary outcomes such as CD4+ cell count, HIV knowledge, self-reported adherence and appointment attendance, PHQ-9 and PCL-5 mental health measures, AUDIT alcohol use measure, and the DAST substance use measure. Finally, all analyses described above will be repeatedly stratified by participant gender to explore whether there is any evidence of gender differences in effects. Due to the modest sample size and pilot focus of the study, significance testing will be de-emphasized in favor of performing inferential analyses as a feasibility check to ensure all measures and analysis protocols are in place for a larger formal efficacy trial [48-49].

Qualitative analysis plan: Study staff will complete, audio-record, and transcribe individual in-depth interviews with 20 YLWH following completion of the clinical intervention. The analytic team will identify broad themes from the interview transcripts, discuss and refine them, and then enter them into a Microsoft Excel-based matrix with a column for each theme and a row for each case. One coder will initially identify patterns in the themes and code each interview to identify sub-themes and a second coder will double code a random subsample (N= 5) of the interview codes within the matrix. Discrepancies in coding will be discussed by the team until a consensus is reached and interrater reliability will be calculated. A sequential mixed-method design will be used to integrate our quantitative and qualitative data analysis.

Dissemination plan: Study staff will work with the UCSF Center for AIDS Prevention Studies' Community Engagement Core and the Youth Advisory Board to disseminate results to the community

and participants via presentations, community forums, email updates, and/or social media. Study staff will conduct town hall presentations and publish findings in peer reviewed journals to communicate results with healthcare professionals.

Discussion

This study protocol describes the Y2TEC pilot randomized, crossover study designed to impact the mental health, substance use, and HIV care challenges of YLWH. Few interventions for YLWH currently exist that address these three concerns in an integrated way, and as a result, we had few examples of similar curricula while developing the Y2TEC intervention. Therefore, we relied on formative research including qualitative interviews with healthcare providers and staff serving YLWH, as well as a mixed-methods study examining HIV care engagement, mental health, substance use, and technology-based interventions to address these issues with the target population [Saberi et al, under review, 50].

Additionally, in our review of existing telehealth interventions focusing on these areas, we discovered that there were general telehealth guidelines but few specifics for research. For example, telehealth-specific regulations on best practices for responding to mental health crises described general practices for clinicians with little mention of best clinical practices for crisis response within a research setting [51-52]. We also found that there were few sources of information about best practices for using text messaging and telehealth counseling within research settings, as many healthcare providers who are currently holding telehealth appointments are practicing within medical groups that have officially adopted these technologies [53].

This study has several unique aspects that are worth highlighting. This intervention explores non-traditional methods for care provision that deviate from the adult-care models and may be considered more “youth-friendly” [54]. The intervention was specifically designed to be tailored and adaptable to the participant by using the results of the participant’s assessment responses to inform the counselor’s decision-making around the number of educational and problem-solving sessions on particular topics. As a result, the counselor is given the ability to spend more or less time on HIV care, mental health, or

substance use based on the acuity of the participant's need. Though this adaptive modular structure adds complexity, it has the potential to better meet the needs of participants than a more rigidly structured intervention.

Furthermore, this study simultaneously explores several unique aspects of feasibility and acceptability. In addition to exploring whether this form of intervention will impact HIV, mental health, and substance use outcomes, we are also considering the acceptability of a fully online versus hybrid in-person-online session delivery. Half of the participants receive the first intervention session with the counselor in person and the rest of their sessions remotely, and the other half receive the full series remotely. If shown to be similarly acceptable, this intervention can be offered completely remotely.

The Y2TEC counseling series has been designed with replication and scalability in mind. The intervention is unique in the relatively low clinician time burden (6 hours of individual counseling per participant over 4 months) compared to traditional face-to-face counseling, which often involves weekly hour-long sessions (which may total 12-16 hours over 4 months). Additionally, if we find that participants perceive the remote-only counseling option as acceptable, implementing the intervention would require minimal office space and physical materials, limiting factors within healthcare settings. A remote-only counseling intervention would also potentially increase access for those living in rural areas with limited access to transportation or local services.

We anticipate that the findings of our study will show that a telehealth and text message-based counseling series for YLWH will be acceptable and feasible. We expect that the findings from this study will provide information about additional ways of using new mobile technologies to support the HIV care goals and behavioral health needs of YLWH and will help influence the development of additional mobile-based counseling strategies. The results of this pilot study will allow us to conduct a larger multi-center randomized controlled trial to examine the efficacy of this intervention.

List of Abbreviations

AIDS: Acquired Immune Deficiency Syndrome

ART: Antiretroviral Therapy

ASSIST: Alcohol, Smoking, and Substance Involvement Screening Test

AUDIT: Alcohol Use Disorders Identification Test

DAST: Drug Abuse Screening Test

GEE: Generalized Estimating Equations

HIV: Human Immunodeficiency Virus

IRB: Institutional Review Board

LMM: Linear Mixed Methods

MI: Multiple Imputation

PCL-5: PTSD Checklist for DSM-5

PHQ-9: Patient Health Questionnaire-9

PI: Principal Investigator

UCSF: University of California, San Francisco

Y2TEC: Youth to Telehealth and Text to Improve Engagement in Care

YLWH: Youth Living with HIV

Declarations

Competing interests: None declared.

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Author's contributions: PS, CDR, and MJ conceived the study and developed the experimental design and measures. AW and VG developed the telehealth counseling intervention and manual. DL and PS developed the main study protocols. AW and DL carried out the daily study activities. TN contributed to

the data collection and analysis plan. All authors were involved in the revision of the draft manuscript and have agreed to the final content.

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
EXPERIMENTAL SUBJECT'S
BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,
2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,
4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
5) To be told of the other choices I have and how they may be better or worse than being in the study,
6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
7) To be told what sort of medical treatment is available if any complications arise,
8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,
9) To receive a copy of the signed and dated consent form,
10) To be free of pressure when considering whether I wish to agree to be in the study.

_____

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Institutional Review Board, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the UCSF Human Research Protection Program, Box 0962, 3333 California St., Ste. 315, San Francisco, CA 94143. Call 415- 476-1814 for information on translations.

Study Title: Youth to Text or Telehealth for Engagement in HIV Care (Y2TEC)

Research Project Director:	Parya Saberi, PharmD MAS, Assistant Professor UCSF Center for AIDS Prevention Studies 3rd Floor, 550 16th St, San Francisco, CA 94158 Phone: 415-502-1000 ext. 17171 ; e-mail: parya.saberi@ucsf.edu
Study Coordinator:	Dominique Legnitto, Phone: 415.917.7686 Email: Dominique.Legnitto@ucsf.edu

This is a research study about how youth (ages 18-29) living with HIV (YLWH) engage in healthcare and the use of technology to improve their engagement in care. This study is being conducted by Dr. Parya Saberi, PharmD and Dr. Carol Dawson-Rose RN, PHD from the UCSF Department of Medicine.

Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you are:

- A young person (18-29 years old) living with HIV
- Living or receiving healthcare in Northern California
- Can speak and understand English

Why is this study being done?

The purpose of this study is to understand ways to help youth living with HIV stay involved in their healthcare. We are interested in how clinicians can improve the resources available, particularly around mental health and substance use. Additionally, we want to see if an intervention delivered by video-chat and text message might help improve engagement in care and adherence to antiretroviral therapy, as well as impact mental health and substance use.

The California HIV/AIDS Research Program pays for the conduct of this study. The investigators of this study have no conflicts of interest to disclose.

How many people will take part in this study?

About 80 people will take part in this study. The study will enroll youth living with HIV to test an intervention delivered remotely using video chat for 12 weekly sessions. 40 participants will be randomly selected to begin receiving the intervention immediately after enrollment. The remaining 40 participants will be randomly selected to a control group for four months and will receive the study intervention at that time.

What will happen if I take part in this research study?

If you are eligible to participate, the study staff will explain the study and procedures to you and answer any questions you have. If you agree to participate, you will sign this consent form and the following procedures will occur:

Initial Visit and Survey and Randomization

- A study staff member will ask you to complete the baseline survey. The survey will include standard questions about your background, current health, HIV medical care, and substance use. This survey will last about 30 minutes.

- Upon completion of the baseline survey, the study staff will use an online tool to randomly assign you to one of the following two conditions:

  Group A –You will meet with a counselor in person for your first session and remotely for all other visits for a total of 12 sessions. You will receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Immediately after completing the baseline survey, you will follow the steps listed below.

  Or

  Group B - You will receive the revised study intervention after a waiting period of four months. At this time, you will be asked to complete an online survey that will last about 30 minutes. You will meet with a counselor remotely for 12 sessions to receive an intervention focused on reducing barriers to engagement in HIV care and improving your overall wellness. Then you will follow the steps listed below outlining the telehealth intervention.

- The first session will last 30 minutes. A member of the study staff will schedule your remaining sessions to occur weekly. The counselor will meet with you individually for 30 minutes to complete a brief assessment and to identify topic areas to address during the counseling sessions. If for any reason you are unable to make a scheduled session, you may reschedule the appointment by contacting the study staff by phone or text at (415) 917-7686.

- Remaining sessions will be delivered remotely in a private location of your choice, using a secure video chat platform on your mobile phone, tablet or computer and will last about 30 minutes. The study counselor will ask for your present location at the beginning of each video session. You can provide as little or as much detail as you want about your location. Choosing to be more specific about your location will help the study staff ensure your safety and accurate collection of data about where participants access video sessions. During the sessions, you will choose from a menu of topics to discuss including engagement in HIV care, mental health, substance use and/or other concerns affecting your life.

- You will receive between 3 and 5 text messages a week from Study staff and will be asked to respond.
  - Monthly Check in texts to collect updated contact information will occur during the 4-month waiting period when you are not receiving the study intervention.
  - Weekly reminders and appointment confirmations 24 hours before your scheduled appointment and a link to the video chat service 15 minutes before each session.
  - Routine follow-up texts between visits. These will include requested resources, a reminder of goals that were set and notifications about free stuff or events in the community.
  - Session Rating texts will be sent to you after each completed telehealth session and will ask for your response to rate your session with the counselor.

Additional Study Procedures

Surveys: At months 4 and 8, study participants will be asked to complete a brief online survey assessment. The surveys will ask demographic information, substance use and mental health information. These surveys will be completed online using Qualtrics, a UCSF approved secure survey tool on the participants' own mobile device.

Waiting period: During the 4 month waiting period when participants in either group are not receiving the intervention, participants will receive monthly text messages requesting confirmation of contact information. Study staff will request a response from participants to either confirm or update contact information. No other study activities will occur during the waiting period.

Exit Interviews: You may be asked to participate in a brief interview after you have received the intervention. A member of the research staff will interview you for about 30 minutes over the phone. You will be asked to describe your experiences receiving the telehealth intervention. The research staff will make an audio recording of your conversation. After the interview, someone will type into a computer a transcription of the interview and will remove any mention of names. The sound recording will then be destroyed.

Contact Information: A research staff member will ask you for information about how best to contact you if you miss an appointment. You will be asked to provide the names of people who know how to reach you and your social media usernames. Any information about your location that you provide will be kept in secure password protected files. You can ask to have these tracking procedures stopped at any time.

Video Chat: A member of the study staff will help you download a free and secure video chat application, Zoom, on your phone and will demonstrate how to set-up privacy settings. In the event that the application does not work, you will be offered the choice of using WhatsApp or FaceTime to complete telehealth video sessions.

Technical Issues: If you lose your phone or device used for telehealth sessions, or it is stolen, please contact the study staff at 415-917-7686. Once you find your device or obtain a new one, we will restart your text messages.

Crisis: In the event that you are a serious danger to yourself (e.g. suicidal and with plans to commit suicide), the counselor may attempt to identify your location and send emergency services for a safety check. For this reason (as well as for collection of data about where participants have access to internet), we will ask for your present location at the beginning of each video session. The counselor may also contact your emergency contact or mental health provider on file to request support for you if you are experiencing a severe mental health crisis. If you have any questions about how Y2TEC study responds to situations like these, you may talk to your counselor about them at any time during the study.

Medical Record: You will be asked to sign a form authorizing the study staff to view your medical records to get information such as laboratory tests (e.g., viral load test results) or other information related to past medical history that may be applicable to this study.

Participant Referral: If you would like to help us spread the word about Y2TEC, you may be asked to share information about the study with people you know who may be interested and eligible to participate.

Resource Guide: You will be offered verbal, printed, or electronic resources that may be helpful to you. Listed below are some of the resources you may be offered:

- Community Resource guide related to HIV care, mental and substance use.
- Information about mobile health applications and online support groups
- Information on HIV care, mental health, or substance use

Study location

The first study visit will take place in a private room or office to ensure your privacy. All other study activities will be conducted remotely using a video chat application on your mobile phone, tablet or computer in a private setting of your choice. You will be required to share the state where you are located at the beginning of each session to continue but can provide as little or as much detail as you want about your location. Choosing to be more specific about your location helps us ensure your safety and accurate collection of data about where participants access video sessions.

How long will I be in the study?

Participation in the study will last about 8 months. Total time for study activities will be about 10 hours. The telehealth visits, surveys and the exit interview will last about 30 minutes each. The total amount of time you will spend reading and responding to text messages is estimated to be between 10 and 20 minutes per month.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study. The study researcher may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Inconvenience: Participation in the study may sometimes be inconvenient. The study staff will make every effort to schedule interviews and sessions at convenient times.

Surveys: Some of the questions in the interviews or discussions with study staff might make you uncomfortable, upset or embarrassed. You are free to decline to answer any questions or to take part in any discussions at any time.

Technology: This study is using text and video-chat technology, which may have some problems. It is possible that text messages will be sent to you at a time you did not choose, text messages may come when you were not expecting them, there may be missed text messages, or too many text messages. There is a possibility that you may exceed the data or minutes in your cell phone plan and have to pay for that. Staff can provide you with tools and tips to avoid exceeding cell phone plan limits.

Loss of Privacy: Every reasonable effort has been taken to ensure your privacy and confidentiality; however, confidentiality during Internet communication cannot be guaranteed. While using the Zoom App, data is encrypted in transit not stored.
For more information about risks and side effects, please ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, the information that you provide may help the researchers better understand more about how young people (ages 18-29) living with HIV engage in health care and how their engagement in care can be improved.

What other choices do I have if I do not take part in this study?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

Will information about me be kept private?

We will do our best to make sure that the personal information gathered for this study is securely stored. You will be assigned a unique participant ID and data collected will be de-identified and stored on an encrypted server at UCSF in password-protected files. Interviews will be audio recorded and identifying information will be removed from transcripts. The audio-recordings will be destroyed after the interviews are transcribed. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The Y2TEC study staff are mandated to report information about incidents involving child abuse, elder abuse, and participants who intend to hurt themselves or others. These incidents are reported to law enforcement and/or Child Protective Services or Adult Protective Services as required by law.

To protect your privacy, the study has obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use information, documents, that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence. Information, documents, protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the California HIV/AIDS Research Program (CHRP)
- Representatives of the University of California

Are there any costs to me for taking part in this study?
You will not be charged for any of the study procedures.

Will I be paid for taking part in this study?
Yes, in return for your time, effort and travel expenses, you will be paid for completing all study activities. Payment will be given to you in the form of cash or reloadable debit card. Please refer to the complete breakdown of payments below:

- Consent and Survey # 1: $10
- Session 1: $20
- Survey #2: $10
- Session 2-3: $10 each
- Session 4-6: $15 each
- Session 7-9: $20 each
- Session 10-12: $25 each
- Survey #3: $30
- Monthly Check-in Texts and Session Rating Texts: Each time you respond to the monthly text confirming your contact information or the test rating after each completed telehealth session, you will be entered into a drawing and could receive a $25 Amazon Gift card.
- Exit Interview: Participants selected to be interviewed will receive $30
- Referral: $25 per referral if you refer eligible participants to the study.

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you in any way. You will not lose any of your regular benefits.

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IRB EXPIRATION DATE: 02/07/2020

Who can answer my questions about the study?

You can talk to the researchers about any questions, concerns, or complaints you have about this study. Contact the researchers Parya Saberi at 415-502-1000 ext. 17171 or Carol Dawson Rose at 415-514-0428 or Y2TEC@ucsf.edu.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the UCSF Institutional Review Board at 415-476-1814.

Would you like to be contacted if we have other studies for which you might be eligible?

Your initials _____ ☐ Yes ☐ No

Do you consent to allow study staff to locate you through contacting your friends, family, agencies and institution? Indicate your preference below:

Your initials _____ ☐ Yes ☐ No

CONSENT

You have been given a copy of this consent form to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____ _____

Date Participant's Signature for Consent

_____ _____

Date Person Obtaining Consent

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym Title page (pg 1), Abstract (pg 2-3)
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Abstract (pg 3)
	2b	All items from the World Health Organization Trial Registration Data Set Abstract (pg 3), Declarations (pg 27)
Protocol version	3	Date and version identifier Declarations (pg 27)
Funding	4	Sources and types of financial, material, and other support Declarations (pg 27)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Declarations (pg 27)
	5b	Name and contact information for the trial sponsor Declarations (pg 27)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities Declarations (pg 27)
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) Data Monitoring (pg 19), Declarations (pg 27)

Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention Background (pg 5-7)
	6b	Explanation for choice of comparators Background (pg 5-7)
Objectives	7	Specific objectives or hypotheses Study Overview and Design (pg 7)
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) Abstract (pg 2-3), Study Overview and Design (pg 7)

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained Study Overview and Design (pg 7), Study Setting (pg 9)
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) Study Participants (pg 9)
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered General Study Procedures (pg 10-14), Intervention Procedure (pg 15-16)
		Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) Risks to Participants (pg 14)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) Session Documentation and Fidelity (pg 16), Data Monitoring (pg 19)

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial N/A – behavioural study with no restrictions in this area
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended Study Outcomes (pg 19-23)
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Study Overview (table 1, pg 8)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations Study Participants (pg 9), Sample Size Justification (pg 9)
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size Recruitment Methods (pg 10)
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions Randomization (pg 11)
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned Randomization (pg 11)
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions General Study Procedures (pg 10- 11), Randomization (pg 11)

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how Randomization (pg 11)
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial Randomization (pg 11)
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Data Collection and Management Procedure (pg 17), Measures in Participant Surveys and Outcome Measures, (Tables 3-5, pg 17-23)
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Participant retention (pg 11)
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol Session Documentation and Fidelity (pg 16), Data collection and management (pg 17-19)
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Quantitative Analysis Plan (pg 23-24)
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) Qualitative Analysis Plan (pg 24)
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) Quantitative Analysis Plan (pg 23-24)

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed Data monitoring (pg 19), Declarations (pg 27)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial Risks to Participants (pg 14), Data monitoring (pg 19)
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct Adverse Events and Auditing (pg 14), Data monitoring (pg 19)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor Adverse Events and Auditing (pg 14)

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval Ethics and Dissemination (pg 3)
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) Protocol amendments (pg 15)
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Consent and Enrolment Procedure (pg 10), Consent form (Appendix A)
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable N/A – no ancillary studies

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial Data Collection and Management Procedure (pg 17-19), Confidentiality and Data Protection (pg 19)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site Completing interests (pg 27), Funding (pg 27)
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators Ethics and Dissemination (pg 3), Dissemination Plan (pg 24)
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation Adverse Events and Auditing (pg 14)
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions Ethics and Dissemination (pg 3), Patient and Public Involvement (pg 9), Dissemination Plan (pg 24)
	31b	Authorship eligibility guidelines and any intended use of professional writers Author's Contributions (pg 27)
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code N/A – no plans
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates Appendix A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable N/A- not applicable to this study

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.