Acceptability, Effect and Cost of Mobile-Health on Art Adherence and Assessment of Covid-19 Knowledge Among Youths: A Mixed Methods Sequential Study in Kiryandongo. A Study Protocol Youth Trial

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COLLEGE OF HEALTH SCIENCES

**ACCEPTABILITY, EFFECT AND COST OF MOBILE-HEALTH ON ART ADHERENCE
AND ASSESSMENT OF COVID-19 KNOWLEDGE AMONG YOUTHS: A MIXED
METHODS SEQUENTIAL STUDY IN KIRYANDONGO**

STUDENT: 2018/HD07/19451U

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2 Contents

3	OPERATIONAL DEFINITIONS	5
4	ABSTRACT	6
5	CHAPTER ONE: INTRODUCTION.....	8
6	1.1 Background.....	8
7	1.2 Problem Statement.....	14
8	1.3 Objectives	15
9	1.3.1 General Objectives.....	15
10	1.3.2 Specific Objectives	16
11	1.4 Study Justification.....	16
12	1.5 Conceptual Framework:.....	17
13	1.6 Theoretical Framework:	18
14	CHAPTER TWO: LITERATURE REVIEW	20
15	2.1. Youth and mobile phone use.....	20
16	2.2 Acceptability of mHealth in HIV positive population	21
17	2.3 mHealth and ART adherence virological outcomes	23
18	2.4 mHealth and retention in care	25
19	2.5 mHealth technologies costs.....	27
20	2.6 Hypotheses and Research Questions.....	28
21	CHAPTER THREE: METHODS	29

22	3.1	Study Design: Mixed Methods Sequential study.....	29
23	3.2	Study setting.....	29
24	3.3	Study population	30
25	3.4	Materials and Methods.....	30
26		Study Objectives:.....	30
27		Study Objective 2:	35
28		Study Objective 3:	50
29	3.5	Quality control	52
30	4.	REFERENCES	59

31

32

33

34

35

36

OPERATIONAL DEFINITIONS

Adherence to ART: Self- reported adherence to ART as depicted on the mHealth dash board or HIV card

Loss to follow-up: Missing 2 visits consecutively, not able to ascertain vitals

mHealth: use of mobile technology e.g. mobile phones and other wireless technology for health-related activities

Retention in care: Continuous engagement in clinical care for 1 year

Virological suppression: Viral load less than 1000 copies/ml

Youth Living with HIV/AIDS: Persons living with human immunodeficiency virus/ acquired immunodeficiency syndrome aged 15 to 24yrs (United Nations General Assembly Resolution A/RES/50/81 (“World Programme of Action for Youth to the Year 200 and Beyond”))

ABSTRACT

Background: AIDS is the leading cause of death among young people in sub-Saharan Africa. Adherence to antiretroviral therapy is the principal determinant for achieving and sustaining viral suppression, which decreases progression to AIDS and reduces risk of mortality.

Few studies have evaluated mHealth adherence tools among youths in resource-limited settings.

We aim to evaluate whether mHealth tool improves ART adherence outcomes among youth receiving ART at a rural district in Western Uganda.

The Corona virus disease outbreak was announced a Public Health Emergency of International concern on Jan 2020; and declared a global pandemic by World Health Organization on Mar, 2020. In rural areas, there is little data on knowledge and myths on COVID among youths.

General objective: To assess acceptability, effect and cost of the mHealth tool on ART adherence, knowledge and myths on COVID-19 among youth initiating and on ART at Kiryandongo District.

Methods: This is a mixed method sequential exploratory study, with the qualitative study conducted first followed by a randomized control trial and healthcare cost evaluation. The qualitative study will assess barriers, enablers of adherence and acceptability of mHealth among youths receiving care at three health facilities in Kiryandongo District. The randomized control trial of 206 youth initiating ART to either Standard of Care or mHealth tool plus Standard of care to assess effect of mHealth tool on ART adherence and retention in care. Through a basic cell phone, participants in the intervention arm will receive pill reminders, clinic appointment reminders, health voice messages and self-reported symptoms in addition to standard of care. Collection of data on knowledge and myths on COVID-19, HIV and sexual behavior. The health care evaluation nested within randomized trial, will assess the cost of intervention in comparison to Standard of care.

Discussion: This project will determine acceptability, effectiveness of mHealth, knowledge & myths on COVID-19 and cost of delivering pill and clinic appointment reminders, and voice messages to a population with suboptimal ART adherence in a resource-limited setting.

Trial registration: Fully registered under clinicaltrials.gov by 20th Jan 2021. The study is ongoing. Recruitment started Aug 2020.

Clinical Trial registration: **NCT 04718974**

<https://ichgcp.net/nl/clinical-trials-registry/NCT04718974>

Key words: mHealth, Youth, HIV, ART adherence, Barriers, Enablers, cost evaluation

This manuscript is written following the SPIRIT checklist and the structure guide by the Directorate of Research and Graduate Training, Makerere University, Kampala Uganda..

CHAPTER ONE: INTRODUCTION

1.1 Background

Human Immunodeficiency Virus (HIV) continues to be a global public health threat. Globally, about 37.9 million [32.7-44.0 million] people were living with HIV (PLWH) in 2018 of whom 25.7 million were in sub-Saharan Africa (1). An estimated 3.9 million[2.1-5.7 million] youth were living with HIV (YLWH) globally in 2017, most of whom live in sub-Saharan Africa (2, 3). Every week in 2018, 6,200 young women aged 15-24 years became infected with HIV around the world (4). In sub-Saharan Africa, 80% of new HIV infections, among young people aged 15-24, occur in girls. Young women (15-24 years) are twice as likely to be living with HIV as young men (5). Young people are the only population group in which AIDS-related deaths are increasing (6). AIDS is the leading cause of death among young people in sub-Saharan Africa (2).

In Uganda, there were 160,000 YLWH in 2018 (4). An estimated 53,000 new HIV infections occurred among youth in 2018, accounting for 26% of HIV incidence in the country (2). Uganda is implementing the Joint United Nations Programme on HIV and AIDS (UNAIDS) 90-90-90 targets, which aim to achieve 90% of PLWH knowing their status, 90% of those who know their status accessing antiretroviral therapy (ART) and 90% of people on ART achieving virologic suppression by 2020 (7). With regard to attaining global 90-90-90 targets, this means that 81% of people with HIV globally receive ART and 73% of them are virally suppressed. In 2018 in Uganda, 84% of people with HIV knew their status, 72% of PLWH were on ART and 64% of PLWH were virally suppressed [(2, 4). Viral suppression rates were much lower among youth in Uganda in

2017: 44.9% for females and 32.5% in males (8). Young people (15-19 years) in Uganda are more likely to drop out of HIV care than children or adults because of fear of disclosure, stigma and discrimination (9)

The Infectious Diseases Institute (IDI) is an implementing partner for the President's Emergency Plan for AIDS Relief (PEPFAR) in three of Uganda's seven regions, and provides care for approximately one-in-three of the 1,167,107 Ugandans receiving ART. In 2017, 18 districts supported by the IDI had viral suppression rates between 38% and 87%. Kiryandongo Hospital, one of the HIV care facilities supported by the IDI, was chosen as the study site because it had a total of 1,322 youth (15-24 years) registered in care by June 2019. The number of YLWH accessing care at this hospital has increased over the years, from 1,107 in 2017 to 1,308 in 2018. In 2018, a total of 637 new youth were registered for care at the unit, and by Jun 2019, an additional 218 youths had been registered into care. Overall retention in care at the hospital was 76% in 2017 and improved to 79% in 2018. The viral suppression rate was 72% and 79% in 2017 and 2018, respectively, but this is still below the national and UNAIDS target of 90%.

The World Health Organization (WHO) defines mobile health (mHealth) as "medical or public health practice supported by mobile devices" including mobile phones (10). The WHO recommends mHealth interventions to support HIV adherence. Prior mHealth research studies have shown improved virological outcomes, decreased risk of non-adherence, good retention in care, strengthened health systems through ART adherence and clinic reminder support and improved self-reported adherence and viral load suppression among non-adherent youth (11) (12) (13, 14) (Rebecca Schnall, M.R.,2010). The Call for Life Study (CFL) was an mHealth intervention trial which aimed to improve outcomes in HIV patients using mobile phone based interactive software support (ClinicalTrials.gov NCT 02953080). Between August 2016 and

November 2018, 1,031 PLHIV were screened and 600 participants enrolled (300 per site). They were randomised in a 1:1 ratio, and followed at an urban site (Infectious Diseases Institute Clinic) and a peri-urban HIV clinic (Kasangati Health Centre) to either Standard of Care (SoC) face-to-face counsellor adherence support or SoC plus the Call for Life Uganda (CFLU) mHealth tool. CFLU used Interactive Voice Response (IVR) or text messages delivered to participants via MOTECH-based Connect for Life™ (Janssen, Global Public Health-J&J). The CFLU tool offered daily pill reminders, appointment visit reminders, symptom reporting and management and weekly health information tips. The primary objective of the study was to assess quality of life utilizing medical outcome study scores (MOS) and physical health scores (PHS) in people living with HIV (PLWHIV) accessing mobile phone-based support using the CFLU tool. Despite having no statistically significant observed difference in mean percentage scores of MOS-HIV, Mental Health Scores and PHS at baseline and 6 months between CFL and SoC arms, a 5-point improvement in PHS favoring the intervention group was noted among participants starting first line ART or switching to second line (ANCOVA 4.01; $p=0.048$) (15).

Adherence to ART is the principal determinant for achieving and sustaining viral suppression, which decreases progression to AIDS and reduces risk of mortality (16). Suboptimal adherence includes missed or late doses, sub-therapeutic dosing and treatment interruptions or discontinuations (17) (18). Sustaining adherence to ART among youth is challenging perhaps because of treatment fatigue (for those congenitally infected), side effects, drug interactions, drug toxicities, sub-optimal regimens, viral fitness, malabsorption, incomplete emotional and psychological development, lifestyle choices and lack of dedicated health services (19). Sub-optimal adherence leads to sub-therapeutic plasma concentrations of antiretroviral drugs which may speed up the development of drug resistance, limit future drug options and permit

transmission of resistant strains (20). These factors highlight the difficulty of maintaining high adherence among youth.

HIV services oriented toward adult care are perceived by youth as poor quality and intimidating which discourages retention in care (21). Thus, youth are more likely to drop out of HIV care than adults (22) (23). There is urgent need to develop interventions to improve ART adherence among youth. Few studies have evaluated mHealth adherence tools among youths in resource-limited settings. This study aims to evaluate whether the CFLU mHealth tool improves ART adherence outcomes among youth receiving ART at a rural district in Western Uganda.

When initiated on ART, a high level of sustained adherence is necessary to suppress viral replication and improve immunological and clinical outcomes, decrease risk of developing ARV drug resistance and reduce the risk of HIV transmission (24). The proportion of youth with viral load suppression in Uganda is suboptimal; only 44.9% of females and 32.5% of males achieved viral suppression in 2017. Effective implementation of evidence-based interventions is needed if the last two 90s of the UNAIDS 90-90-90 targets are to be achieved.

Previous work has shown that mHealth interventions improve virological outcomes (25) (26), decrease risk of non-adherence (27), improve retention in care (28), strengthen health systems through ART adherence and clinic reminder support (29) and improve self-reported adherence and viral load suppression among non-adherent youth (30). The Call for Life Uganda mHealth tool was developed by Janssen Global Public Health Research and Development, in close collaboration with the Infectious Diseases Institute (IDI), and tailored it to the needs of PLHIV in Uganda. Call for Life Uganda (CFLU) is based on the CONNECT FOR LIFE™ technology and the MOTECH platform. CONNECT FOR LIFE™ is an m-health technology initially developed as a community information technology platform for health initiatives to improve care in patients in developing

countries. The platform interacts with patients using basic mobile phone technology and with healthcare providers through a web-based interface. This Interactive Voice Response (IVR) software was first piloted by Janssen and the Grameen Foundation in India, and was called “Treatment advice by Mobile Alerts”(TAMA) to support HIV patients in India.

The Call for Life Uganda (CFLU) study randomized 600 PLHIV to receive enhanced adherence support with daily SMS or Interactive Voice Response (IVR) call reminders, standardized health education messages and facility based standard of care (intervention arm) or facility standard of care only (SOC) in a 1:1 ratio (ClinicalTrials.gov NCT 02953080). A total of 331 health education messages were designed and developed by IDI and Straight Talk Foundation-Uganda staff, using National HIV prevention guidelines. These messages were piloted with expert patients at the Infectious Diseases Clinic (IDC) at Mulago Hospital in Kampala, Uganda, translated into three local languages (Luganda, Kiswahili and Runyakitara) and relayed to patients using the platform once a week or on request during the daily pill reminder call. Patients could also call in using a toll-free number to request health education messages, or report any symptoms related to the disease, drug or any concomitant illness. The CFLU study participants were prospectively followed 6 monthly for 24 months. The study’s main outcome was to assess quality of life utilizing Medical Outcome Study Scores-HIV (MOS-HIV), Mental Health Scores (MHS) and Physical Health Scores (PHS) in PLWHIV accessing mobile phone-based adherence using the CFLU tool. There was no statistically significant observed difference in mean percentage score of MOS-HIV, MHS and PHS at baseline and 6 months between CFLU and SoC arms. In those starting first line ART or switching to second line, there was a significant improvement in PHS (ANACOVA 4.01, $p=0.048$) of 5-points difference or greater. Qualitative data suggested high acceptance and positive

experiences with the CFLU tool in PLHIV. Nearly all participants (98%) selected interactive voice response over text messages (15, 31).

IVR is a useful and flexible mHealth tool which can be used for computer-assisted screening of a population (32) or in-depth daily assessments of risk behaviours (33, 34). It can also be used as an external aid to promote participant medication adherence (35, 36) or used as a medium to relay health messages or advice intended to improve health behaviours(32). IVR may be programmed to receive incoming calls from participants, place automated outgoing calls, or a combination of both (37). Using this strategy in CFLU, this mHealth tool is able to track study participants, allows investigators to receive data nearly in real-time and to intervene should a problem occur with the study participant, before it is too late. The Call for Life System has functionality to support individualised pill reminders, visit reminders, health message calls and self-reported symptoms and management. mHealth apps have been developed for asthma, chronic obstructive pulmonary disease, diabetes, malaria, tuberculosis, and HIV as well as for specific populations, e.g., mother and baby (38). Call for Life System can be adopted for use in Ugandan YLWH to aid in ART and clinic adherence, knowledge sharing and symptom management.

Coronavirus disease (COVID-19), a viral infection with high infectivity and human-human transmissibility, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 is probably of zoonotic potential, due to the allegations that the virus was transferred to people at a food market that trades in wildlife in Wuhan, China (39).

The state of lock-down due to COVID-19 in many parts of the world has led to the halting of services (40)and Uganda health service provision has not been spared either. Uganda got first country wide lockdown on 22nd Mar 2020, this lockdown disrupted treatment continuity and globally the supply chains were halted and most patients in chronic care faced challenges (40).

There is moderate awareness and knowledge of COVID-19 among educated population in India(40), but little is document among youths in rural areas, literature search revealed one documentation on knowledge, attitude and practices of HCW in Makerere University teaching hospital(41). A poor understanding of the disease among youths can result in delayed identification and treatment leading to rapid spread of infections.

1.2 Problem Statement

About 5 million[2.1–5.7 million] youth were living with HIV (YLWH) globally in 2018, most of whom live in sub-Saharan Africa (2, 3) (<https://www.who.int>adolescents>). AIDS is the leading cause of death in Africa (<https:// www.avert.org>). Globally, 30% of all new HIV infections occur among youth 15-24 years (UNAIDS).

Youths living with HIV (YLWH) have low viral load suppression rates due to poor ART adherence compared with older adults. According to the UPHIA 2017 report, a household-based national survey conducted in Uganda from August 2016 to March 2017, approximately 55% of young females and 68% of young males had unsuppressed HIV viral load (42). Persistent viremia is associated with development of drug resistance, low immunity which increases the risk of opportunistic infections and death (20). AIDS-related illnesses remain the second leading cause of death for young women aged 15-24 years in Africa (43).

Improved linkage and retention in care coupled with improved adherence for viral suppression are paramount in contributing to the UNAIDS second and third 90s and improving the HIV treatment continuum (44). Poor viral load suppression is mainly due to non-compliance to clinic visits, lack of knowledge on ART, inconsistent swallowing of pills and poor pill adherence (45). We hypothesize that early follow-up of missed appointments coupled with adherence support

for the first 6 to 12 months of initiating ART could overcome the current problem faced by youth. Existing evidence indicates that Intensive Adherence Counselling (IAC) for those who are not suppressed may not be effective. A retrospective chart review demonstrated that suppression rates were low among ART-treated children with virological failure that completed the three recommended IAC sessions (46).

Mobile health interventions have been effective in improving ART adherence and viral suppression is a proxy measure for the adherence. A study of SMS text messaging in Italy found that the proportion with undetectable HIV RNA viral load increased from 42.3% at baseline to 76.8%, 71.5%, 76.2% at months 3, 6, and 9, respectively ($P=0.001$) (47). In rural Uganda, text messaging was effective in increasing ART adherence and the authors recommended that it be explored in youth (13, 48).

Poor ART adherence due to missed clinic visits and lack of drug refills, forgetfulness, stigma comorbid conditions and psychosocial issues are the leading causes of poor viral suppression in youth. Current use of Intensive Adherence Counselling for non-adherent, non-suppressed patients has not been shown to be effective, and there is still a gap in providing daily pill reminders, visit reminders, HIV and ART knowledge and adherence support. All this can be achieved through use of interactive voice response tool (IVR), which this study will provide through the Call for Life tool.

1.3 Objectives

1.3.1 General Objectives

To assess acceptability, cost and effect of mHealth tool on ART adherence and knowledge of COVID-19 among youths initiating ART in Kiryandongo.

1.3.2 Specific Objectives

- I. To assess barriers, enablers of adherence for ART among Youth in Kiryandongo at baseline and study end.
- II. To assess acceptability of mHealth for ART adherence among Youth in Kiryandongo at baseline and study end
- III. To evaluate effect of the mHealth CFLU tool on ART adherence at months 6 and 12
- IV. To evaluate the cost of the mHealth CFLU tool in comparison to standard of care at 12 months
- V. To assess knowledge of COVID-19 among youths in rural setting

1.4 Study Justification

Over 55% of YLWH in Uganda are not virologically suppressed. Patient-centered approaches exploiting mHealth have been shown to improve adherence to ART and viral suppression. Due to poor clinic attendance by youth, Intensive Adherence Counselling (IAC) alone cannot help suppress detectable viral load in this group. Evidence-based interventions are needed to complement standard of care adherence counseling. The 2013 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, suggested use of automated Short Message System (SMS) reminders of scheduled clinic visit to improve clinic attendance (49). Experience with the recently concluded mHealth study (Call for Life Study) at IDI shows that 98% of the study participants preferred voice calls instead of text messages. Participants cited confidentiality, voice tone and privacy related to voice calls as reasons for this preference. CFLU is an open source mobile-phone based software designed to send short messaging services (SMS) and Interactive Voice response (IVR) calls. Additional services include

pill reminder support, adherence support, visit appointment reminders, symptom report management and health information tips (FIGURE1). However, this mHealth intervention has not been implemented among the YLWH in Uganda.

It is estimated that 53.2 % of Ugandans have access to mobile phones; 23.2 million Ugandans were mobile phone subscribers in 2016 (50). According to the Pew Research Centre, Ugandan youth are more likely to use mobile phones than adults (51). This study found that 66% and 51% youth had ever used text messages or sent/viewed videos or pictures, respectively, highlighting their ease and comfort with cell phone use. In a systematic review of 25 mHealth programs targeting youth sexual reproductive health (SRH) found that most (67%) were conducted in Africa. Nearly all (87%) used mHealth as a health promotion tool to facilitate knowledge and behavior change. A minority (18%) used mHealth to link users to essential SRH services including family planning counselling services, medical abortion, post-abortion care and HIV treatment. Evidence is emerging that mobile phones are an effective way to reach youth and to achieve knowledge and behavior change (52).

Few studies have evaluated mHealth adherence tools among youths in resource-limited settings. This study aims to evaluate whether the CFLU mHealth tool improves ART adherence outcomes among youth receiving ART at a rural hospital in Western Uganda.

This study will join Uganda in implementing the Joint United Nations Programme on HIV and AIDS (UNAIDS) 90-90-90 targets, which aim to achieve 90% of PLWH knowing their status, 90% of those who know their status accessing antiretroviral therapy (ART) and 90% of people on ART achieving virologic suppression by 2020 (7).

1.5 Conceptual Framework:

FIGURE 2: CONCEPTUAL FRAME WORK

Conceptual framework showing different factors which affect antiretroviral therapy (ART) adherence and resultant viral suppression

1.6 Theoretical Framework:

Theoretical framework, is based on the Information-Motivation-Behavioral Skills Model (53)). IMB model commonly utilized in HIV to understand behaviors, in this study, we plan to provide information to the youth, motivate through use of mHealth tools in order to impact behavior change and improve pill adherence (Figure 3).

The IMB Model, (54) was developed to explain HIV risk and preventive behavior. The model recognizes three key constructs needed to engage in a given health behavior: information, motivation and behavioral skills. Information involves the provision of correct information and dismissing of incorrect information. Motivation refers to both personal and social motivation (perceived social support for engaging in certain behavior) and behavioral skills refer to perceived self-efficacy for carrying out a certain behavior (55).

Based on the IMB model (56), existing information affecting adherence will be elicited first, and this information may be around social-psychological factors, anthropological factors, stigma and HIV/ART knowledge among youth. Most of the information regarding adherence of ART in this group will be assessed at baseline and study end during the qualitative data collection, stigma will be prospectively collected under the second objective.

Secondly, the mHealth tool has been used previously for health promotion where it improved knowledge in sexual reproductive health and facilitated behavior change (52). The IMB model posits that provision of information and motivation influences behaviours. We hypothesize that the CFLU tool will address existing knowledge gaps among YLWH through provision of

health messages about HIV, ART and medication adherence. Daily pill reminders and visit reminders will motivate youth and will help to address forgetfulness and busy schedules, factors which were the main causes of medication non-adherence and missed visits in the Call for Life study. Addressing these factors will influence adherence behaviours.

Prior work suggests that patients with higher HIV knowledge are twice as likely to keep their appointments as those who are less knowledgeable. Knowledge of HIV coupled with a good client-provider was associated with increased CD4 count and a five-fold likelihood of achieving undetectable VL (57). Lack of knowledge of correct dosing and time to take drugs was associated with non-adherence in those starting ART (58). HIV knowledge has also been shown to be associated with improved quality of life (59).

Lastly, evaluation of the effect mHealth tool will include assessment of stigma scores at baseline and follow-up, HIV knowledge at baseline and follow-up, and adherence as measured by clinic attendance (visit adherence), phone interaction and viral suppression.

The IMB model was chosen because the intervention will provide information through health tip messages and motivation through daily calls. According to prior recipients of the CFLU mHealth intervention, voice calls and voice tones encouraged and motivated them to continue taking medication, which impacted their behaviours including honoring clinic visit appointments, taking medication on time and willingness to report any symptoms they may have had. These factors may have improved clinic attendance, ART adherence and viral suppression. This model is a better fit for the CFLU mHealth tool than similar behavior models e.g. the Capability-Opportunity-Motivation-Behavioral (COM-B) model.

CHAPTER TWO: LITERATURE REVIEW

2.1. Youth and mobile phone use

The use of mobile phones and other mobile technologies for improving health through research and practice is growing quickly, particularly in areas with difficult-to-reach populations or where the healthcare infrastructure is less developed (38). In the Kampala Youth Survey 2014, it was noted that nearly half of the youth owned and used phones daily (60). The study assessed psychosocial characteristics based on phone ownership and use and found that those who initially owned and used mobile phones were educated, young, wealthy, male and living in urban areas (60). More recently, cell phone use has expanded to include those living in rural areas, the elderly, and those with less resources to an estimated 23 million subscribers in Uganda (61). In the prior Kampala Youth Survey (2011), 47% of youth reported owning a mobile phone. Ownership did not vary by sex but was more common among youth above 18 years of age. Mobile phone ownership was more common among those who reported taking care of themselves at night, who reported current drug use and who reported trading sex for money, food or other goods.

As the burden of HIV continues to grow among adolescents and youth, mHealth technology could address many of the healthcare needs of YLWH including adherence to HIV medications, retention in care and self-management (62), which are critical needs for this priority population. mHealth technology could bridge the divide in healthcare delivery in underserved minority groups. Since ownership of a mobile device is common among the youth, use of mHealth can help increase engagement in HIV care (52). Due to the high incidence of HIV among minorities, adolescents and underserved youth, and their reliance on mobile technology, it is

imperative to develop health information technology (HIT) tools tailored to the needs of this population (63, 64) (12).

Overall HIV incidence in Uganda has been declining since 2010. However, the new HIV infections are disproportionately concentrated among young people. Given high penetration of mobile phone technology, there is growing support for using mobile health (mHealth) programs to reach vulnerable populations (65, 66). Given that nearly half of youth in Uganda own or use mobile phones daily, new research is needed to determine next steps for mobile health (mHealth), including the feasibility of using mobile phones for data collection and interventions with this hard-to-reach population (Swahn et al, Aug 2014).

2.2 Acceptability of mHealth in HIV positive population

Several studies on the acceptability and feasibility of mHealth in PLWH have been done, but few of these were conducted among YLWH. One study in South Africa examined short message service (SMS) and/or community-based directly observed antiretroviral therapy (cDOT) as interventions to improve ART adherence for preventing mother- to-child HIV transmission. This study showed that SMS and or cDOT are feasible in this setting. However, safe HIV status disclosure to treatment supporters and confidentiality of text messaging content about HIV and ART were deemed to be crucial implementation factors (67).

Few mHealth studies have been conducted among youths despite several studies of mHealth apps (68, 69), usability of the devices (70), and negative effects of sexualized video apps (71). Brown et al, conducted 6 focus group discussions to explore adolescent use of mobile technology for meeting their health information needs in Columbia, when given smart phones with mHealth apps. The study assessed health seeking information behavior among adolescents and found that

the main motivation for using mHealth app was their performance speed and information needs. Barriers for use of the app included use of non-phone app technology (i.e. phone, books), non-mobile resources (i.e. parents, teachers, siblings), and other health related entities not directly related to the usability of mHealth (72) (73).

Breach of confidentiality may occur following receipt of text messages. In an mHealth study among diabetics in Ethiopia, willingness to receive text messages for appointment reminders was 70.5%, (74). In North West Ethiopia, willingness to receive text message medication reminders among PLWH was only 50.9%, perhaps because use of SMS can't guarantee privacy and participants may have felt it was not safe to receive the mHealth support (75). In the rural United States, a survey carried out among 24 respondents, showed a demand for mHealth services, out of the 24 respondents, 63% were in good health, a total of 65% were willing to receive prerecorded messages for appointment reminders from the doctor (76). In rural India, willingness to receive mobile phone reminders for drug adherence was high (98%) among the 479 respondents. Of these, 424 (89%) preferred voice calls alone to other forms of communication (77).

In a rural Ugandan setting, a cross-sectional study found that over 60% of patients could potentially benefit from a mobile phone-based ART adherence support (78). Most of the mHealth studies conducted are SMS studies and only one used IVR. A qualitative study among youth assessed SMS based intervention to improve ART adherence in 2 clinics in Kampala, Uganda. Results suggested improved adherence could be achieved through reminders and social support. However, youth also suggested “intervention logistics related to content, frequency, timing and two-way messages” would be helpful to practitioners in the field (79). Another qualitative study in South–Western Uganda nested within sixty-two pilot intervention study participants found that SMS reminders and real-time adherence monitoring led to the habit of adherence, and real-time

monitoring was interpreted as “being seen”, “being cared about” which transformed their moods (80). In rural Uganda cohort of 276 participants on ART, more than half (64%) possessed a mobile phone and were willing to be contacted after a missed clinic appointment. In 79% of episodes of missed visits, patients presented for refills within a mean duration of 2.2 days (SD = 1.2 days) after mobile phone call reminder (81). Another cross-sectional survey among PLWH in rural Uganda assessed the “acceptability of and preferences for text messaging, preferences for laboratory results notification, privacy and confidentiality and cell phone use and literacy”. All the participants expressed interest in the service although they had challenges regarding “interpreting messages, discouragement upon learning bad news, and technical issues” (82). In a feasibility, validity and acceptability study of real-time adherence monitoring using a Wise pill wireless electronic adherence monitor (EAM) and self-reported missed doses via interactive voice response (IVR) and short message service (SMS), among 49 adults and 46 children in Mbarara, Uganda, adherence was higher in children than adults (92.8% vs 89.5%) by EAM, and 99–100% for both adults and children by IVR/SMS self-report (83).

2.3 mHealth and ART adherence virological outcomes

Poor adherence to antiretroviral treatment is a public health challenge associated with development of drug resistant strains necessitating initiation of costly second line therapy, and possibility of transmission of drug-resistant HIV by the non-adherent spouse (84-86).

A quasi-experimental cohort study involving 150 HIV-infected individuals from Bangalore, India, showed that among participants on antiretroviral therapy (ART) between April and July 2010, optimal adherence increased from 85% to 91% patients during the intervention period, an effect that was maintained 6 months after the intervention was discontinued ($p=0.016$). Both, IVR

calls and SMS reminders were considered nonintrusive and not a threat to privacy. A significantly higher proportion agreed that the IVR was helpful compared to the SMS ($p < 0.001$) (87).

A systematic review done by Ridgeway K et al, of the peer-reviewed and grey literature published between 2010 and 2015 to identify interventions designed to improve antiretroviral adherence among adults and adolescents in low and middle-income countries, found 43 interventions for adults, 6 involved both adults and adolescents and only 2 were among adolescents (88). Two systematic reviews (89, 90) found modest evidence for the benefits of mHealth technology. Both reviews recommended mHealth implementation, but argued that high quality (and adequately powered) clinical trials that measure clinical outcomes are essential (91).

Garofalo *et al*, May 2016, conducted a randomized trial of a two-way, personalized daily text messaging intervention to improve adherence to antiretroviral therapy (ART) among 105 poorly adherent HIV-positive adolescents and youth, ages 16–29. The average effect estimate over the 6-month intervention period was significant for $\geq 90\%$ adherence (OR=2.12, 95% CI=1.01–4.45, $p < .05$) and maintained at 12-months (6-months post-intervention) (30).

Patient-centered approaches exploiting mobile phone communications (mHealth) have been shown to improve adherence to cART and promote achievement of suppressed HIV plasma viral loads(92, 93). A systematic review by H. Anglada-Martine et al, revealed that the use of text messages or mobile applications to enhance adherence to medication do seem to have been beneficial, as 65% of the studies evaluated had positive outcomes. However, they recommended that more high-quality studies be conducted in order to demonstrate whether this type of technology reduces the considerable costs to the health system generated by non-adherence (94).

During the WelTel Kenya 1 SMS trial, participants who received SMS support had significantly improved ART adherence and rates of viral suppression compared with control

participants (27). In rural Uganda, text messaging was effective with regard to increasing ART adherence among adults, and this study aims to explore this effect among adolescents with poor virological suppression (48).

Medication adherence is the “Plus” in the 90-90-90-Plus global challenge, emphasizing the importance of ART adherence in achieving viral suppression. Many gaps remain in meeting these goals, adherence self-efficacy, depression, stressful life events, and perceived stigma were significant predictors of medication adherence (95). Mobile phone applications that support treatment adherence address forgetfulness, knowledge gap; an important barrier to treatment adherence, and this needs to be explored among the youths in Uganda.

2.4 mHealth and retention in care

Predictors of poor retention in HIV care include younger age, male sex, racial or ethnic minority status, low socioeconomic status, no usual source of health care, less advanced HIV disease, fewer non-HIV-related comorbidities, and greater unmet psychosocial needs (96). Thus, interventions to improve retention in care should incorporate informational, motivational, and behavioral skill components (97).

Retaining individuals who have initiated ART in care is challenging. A review by Fox and Rosen 2010, estimated that 20% of patients in resource-limited settings are lost to follow-up within 12 months of initiating therapy (98). Prior the era of “test and treat”, the ART naïve “ART-ineligible” patients’ clinic retention rate was estimate at 63% at month 12 (99). There are many challenges for continuity of care, financial constraints, travel difficulties and stigma are factors that can prevent PLWH who start treatment from continuing in care (100).

Many people newly diagnosed with HIV are lost to follow-up shortly before or after timely initiation of antiretroviral therapy. One study in Kenya documented that people living with HIV

felt that increased communication via the text messaging intervention had the potential to enable early identification of problems, leading to timely problem solving that could improve retention and engagement in care during the first year after diagnosis. Engaging PLWH at all points along the cascade of care is essential for transforming the management of the disease from a fatal condition to a chronic one (101, 102).

In a recently published community-based individual randomized trial in Uganda, no statistically significant differences in retention were observed in the first 6 months between those randomized to either mobile-phone or physical contact tracing reminders. Retention was higher among those who received physical contact reminders at month 12 (91.5% versus 82.1%; $p=X$) (103). Although physical contact tracing reminders had higher retention at 12 and 18 months, mobile technology has several advantages which may be cost saving. The challenges of physical contact included structural barriers, time consuming, health care worker exhaustion and physical infrastructure challenges.

Various studies in Uganda have shown that patient-related factors resulting in loss to follow-up include transportation costs, distance to health centers, inconsistent income and lack of social support. Financing of transport improved retention, but this option is not cost effective nor sustainable in resource poor countries (104-106).

Mobile health interventions may improve engagement in care. Mobile apps provide a convenient vehicle for reaching a large audience and offer the potential to create personalized and interactive interventions that can be used anonymously and discretely. In a study evaluating how youth use technology and mobile apps and how their use of technology could support their health and influence their engagement in care, participants suggested that a mobile health application should have the ability to connect to a community of other youth living with HIV, readily access

healthcare providers, track personal data and information (such as laboratory data), and obtain health news and education (107).

2.5 mHealth technologies costs

Information systems, such as electronic health records (EHRs) and mobile phones and handheld computers (also called mHealth), can be of enormous value in providing health care in multiple settings. A review done in 2011 showed that with the exception of personal digital assistant (PDA)-based data collection, there are still few scientifically rigorous data on the effectiveness and cost-effectiveness of e-health systems in developing countries (108). The World Health Organization (WHO) published a manual on implementing EHRs for developing countries. The manual states that a thorough cost-benefit analysis should be conducted to compare the options against each other and the costs of any proposed system against the perceived benefits, so as to determine the value of the system to institution/ government (109).

A systematic review of peer-reviewed mHealth literature in Africa published between 2003 and 2013 identified 44 studies on mHealth and found that mHealth interventions were associated with positive health-related outcomes. Their success was based on the accessibility, acceptance and low-cost of the technology, effective adaptation to local contexts, strong stakeholder collaboration, and government involvement. In this review, it was clearly noted that threats such as dependency on funding, unclear healthcare system responsibilities, unreliable infrastructure and lack of evidence on cost-effectiveness challenge mHealth implementation (108).

2.6 Hypotheses and Research Questions

1. What is the acceptability of mHealth among YLWH at three (03) of Kiryandongo District HIV Centres, and what are the barriers, facilitators/enablers of ART and clinic visit adherence?

Hypothesis: YLWH will have a high acceptability for mHealth with 70% accepting to use mHealth.

2. What is the effect of the mHealth-CFLU tool on ART adherence among YLWH?

Hypothesis: More than 79% of YLWH using the mHealth-CFLU tool will be adherent to ART (using viral load suppression as a proxy measure for ART adherence we anticipate an increment of 15%).

3. What is the cost of the mHealth CFLU intervention compared to standard of care over a 12 month period?

Hypothesis: mHealth will be cost effective by increasing proportion in care and proportion with viral suppression compared to standard of care

CHAPTER THREE:

3.1 Study Design: Mixed Methods Sequential study

The study design is a mixed method sequential, where the qualitative study will be done first, followed by the randomized controlled trial and thereafter the cost evaluation study.

3.2 Study setting

The study will be based at three HIV care and treatment centres in Kiryandongo District (figure 4).

Kiryandongo District has 19 government health units (one hospital, 5 Health Centre IIIs and 13 Health Centre II) which serve a population over 317,500 people. The study sites will include Kiryandongo Hospital ART clinic, Panyandoli Health Centre III and Nyakadote Health Centre (HC)II. Kiryandongo is located 225 km on the Kampala –Gulu highway, with a viral load suppression prevalence of 55.3%(UPHIA, 2017). Kiryandongo hospital has been chosen as the study site, because it is an IDI implementing site with >1000 YLWH in care and a viral suppression rate of 79% below the UNAIDS target of 90% (Table 1). In 2018, a total of 637 youths were enrolled in care and retention in care was 79%. The current total of YLWH at the site is 1,322. The two government centres Panyadoli and Nyakadoti are 44 mins /19 mins drive from Kiryandongo hospital which 30 KM and 16 KM from the Hospital. The HCIII serves a population of over 80,000 people and are included as they serve a big population of youth living with HIV in the district.

Study population

The study population will comprise of YLWH aged 15 -24 years who are ART naïve or on ART since Jun 2019.

Target population:

Youth living with HIV registered to receive ART at any of the 3 ART clinic in Kiryandongo district; Kiryandongo Hospital, Panyandoli HCIII and Nyakadoti HCII

Accessible population:

Youths consented/assented for CFLU, registered for care at Kiryandongo hospital, Panyadoli Health Centre III and Nyakadoti Health Centre II.

3.3 Materials and Methods

Study Objectives:

1a: To assess barriers, enablers of adherence among youth living with HIV in Kiryandongo at baseline and study end.

1b: To assess acceptability of mHealth among youth living with HIV in Kiryandongo at baseline and study end.

Study design: Qualitative study with narrative approach

Study purpose: To identify the key behavioral constructs that enable or hinder ART adherence among the youths, and to assess acceptability of mHealth interventions for adherence support.

Study population: YLWH 15-24 years attending Kiryandongo Hospital, Panyadoli Health Centre III or Nyakadote Health Centre II HIV/ART clinic, ART naïve or on ART since Jun 2019.

598 **Sampling:** Participants will be purposively selected, each group will include 6-10 YWLH, and
599 there will be a total of 3-5 groups ((110). The participant groups will comprise of those who are
600 naïve or initiating and on ART since Jun 2019. YWLH will be stratified by age group (≤ 18 ys and
601 > 18 ys) and gender.

602 **Study Procedure:**

603 **Selection criteria:**

604 **Inclusion:** Youth living with HIV, with a documented HIV test result, aged 15-24 yrs, ART naïve
605 or on ART since Jun 2019.

606 **Exclusion Criteria:** Youth unable to express themselves verbally, those unable to attend 2
607 sessions of the discussion

608 **Selection of participants:** We shall liaise with the clinic counsellor to refer YLWH aged 15-24
609 years with a documented HIV test result, patients who are ART naïve or initiating ART and have
610 gone through routine counselling and testing. Stratification by age group and gender will be
611 considered in selection of study participants. Eligible youth will be identified by the clinic
612 counsellor and will be referred to study team which will be located at the HIV clinic. We shall sit
613 one on one with the potential participant, give information about the purpose of the study, and
614 request them to join the focus group discussion on the scheduled date if they agree to take part.
615 This procedure will be repeated until the sample size of a particular group is reached.

616 **Sample Size:** Focus group discussions will be held until data saturation is achieved.

617 **Data Collection:**

Focus group discussions: On the day of the discussion, study information will be given to the participant including the purpose of the study, risks and benefits. We will address any questions they may have and obtain consent. An experienced person (Social Sciences group at the Academy) in conducting FGDs will facilitate the discussion assisted by two note takers (the PI and a research assistant). Ground rules will be set and choice of languages to use will be Runyoro, Kiswahili and English which are the dominant languages at the site. FGDs have been preferred and not in-depth interviews, because this study is generating information on collective views which will be used for later , and we want to generate a rich understanding of the youths experiences and beliefs (111).

At baseline, we will administer an interview guide consisting of structured questions on the CFLU mHealth tool and ART adherence, as well as open-ended qualitative questions with probes, to allow exploration of YLWH views and opinions regarding these themes. The key issues to be explored are whether the youth would accept or refuse use of an mHealth tool, what they would/wouldn't like the system to offer in terms of health education, frequency and timing of pill reminders and why. Regarding ART adherence, ART naïve participants will be asked what factors will likely facilitate / hinder their adherence to clinic attendance and ART. ART exposed participants will be asked what has facilitated or hindered their clinic attendance and ART adherence. The FGD will last for about 40 to 45 minutes. It will be audio recorded and refreshments (light snack and a soft drink) will be served. Themes to be assessed at baseline include acceptability of mHealth, assessing knowledge, usage, specifics needed, frequency timing.

At the end of the study, the groups will be subdivided according to the themes of acceptability and adherence. For acceptability, further segmentation will be based on those who have utilized the mHealth tool above or below 75% of times. For ART adherence, we shall subgroup according to

641 viral suppression (VL <1000 or >1000 copies/mL), gender and age-group below or above 18 years.
 642 The FGD guide (appendix IV) will explore the different barriers and enablers for adherence, and
 643 the responses to mHealth intervention. The discussion will be captured on an audio recorder and
 644 handwritten notes.

645 **Data collection for the FGD at study entry, before randomization:** Participants' grouping
 646 based on ART duration, age and gender at baseline (Table1).

647 **Table 1. Themes and focus groups at base line**

Themes	ART experienced (ART 3-months Plus)		Less experienced (<= 3months)	
	Male		Female	
	≤18 yrs	>18yrs	≤18yrs	> 18yrs
Acceptability: Why accept or refuse mHealth How can the system be used for adherence support (probe on time, frequency)? What they would like the system to do for them(Probe on pill reminders, Health tips/advice , symptom reporting and management and use of secret pin)				
Adherence checks: Enablers/barriers: (what has facilitated/hindered for those who are ART experienced) (what will likely facilitate- for those who are naïve or less experienced)				

648

649 **Data collection for the FGD at study end;** groups will be divided according to how well they
 650 interacted with mHealth tool ($> 50\% \leq 50\%$), age group ($>18\text{yrs} \leq 18\text{yrs}$) and sex (male or
 651 female) (Table 2).

652 **Table 2: Themes and groups for FGD at study endline**

Themes	Groups			
	$\leq 50\%$ interaction/engagement with tool		$> 50\%$ interaction/engagement with tool)	
	Male		Female	
	$\leq 18\text{yrs}$	$> 18\text{yrs}$	$\leq 18\text{yrs}$	$> 18\text{yrs}$
Acceptability: Comfort/ease using the tool Following advice from Health tips Likes/dislikes for tool Improvements & recommendations				
Adherence: Enablers (what has facilitated) Barriers(What has hindered)				

653

Data Management and analysis:

The FGD audio-recordings will be translated and transcribed into English by a group of two qualitative research assistants from the Academy at Infectious Diseases Institute. Transcripts will be read, to identify themes and subthemes. Themes will be discussed, coded and the coded book with the transcripts will be imported to Nvivo for coding and content analysis. The analysis will be done by the qualitative social sciences Lead from the Academy at IDI. Audio files will be electronically stored in password protected files which will only be accessible to the study team. The analysis will be guided by the themes already contained in the interview guide, which will further be refined following multiple readings of interview scripts to better understand the data, identify sub-themes and to group the data according to themes for analysis and interpretation. Quotations reflecting the youths' views, opinions and experiences will be identified and will be used in the presentation of study findings.

Study Objective 2:

To assess effect of mHealth tool (CFLU) on ART adherence and knowledge of COVID-19 among YLWH naïve, initiating ART or on ART since Jun 2019.

Study design: Randomized control trial with two parallel arms (Standard of Care or CFLU with Standard of Care)

Study purpose: To assess effect of CFLU on ART adherence among youth measured by interactive voice response to daily adherence calls mapped in the database and proportion with viral suppression of copies below 1000 copies/mL.

The intervention (CFLU) uses IVR calls or text messages delivered via MOTECH™ based Connect for Life technology™. The calls are delivered in 4 languages (Luganda, Luo English and

Runyakitara) and the participant has to make a choice of the preferred language during registration to the system. The system offers adherence pill reminders, health message tips, visit appointment reminders and receipt of self-reported symptoms.

A poor understanding of the disease among youths can result in delayed identification and treatment leading to rapid spread of infections among the community.

Study setting: Kiryandongo District, three sites offering HIV-ART. Kiryandongo hospital, Panyandoli Health Centre III and Nyakadote Health Centre II have been chosen as the study sites, the hospital has 1,322 YLWH and a viral suppression rate of 79% (Table 1). In 2018, a total of 637 YLWH were enrolled in care. By Jun 2019 and additional 218 YLWH had been enrolled in care. The current total at the site for age between 15-24 is 1,322. Overall retention was 79%. We have included the lower level health facilities since ART delivery is done majorly in these grassroot levels.

Study Population: Inclusion: YLWH (15-24 years), ART naïve or initiating ART since Jun 2019.

Exclusion: Hearing loss, severe illness likely to shorten life span, boarding school YLWH, Inability to use a basic mobile phone.

Sample size calculation:

Size: X-Sectional, Cohort, & Randomized Clinical Trials (Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15; Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 & 3.19)

The sample size formula for the method described in Kelsey et. al. is:

$$n_1 = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \bar{p}\bar{q}(r+1)}{r(p_1 - p_2)^2}$$

697

698 *and*699 $n_2 = rn_1$ 700 *where*701 n_1 =number of cases in the intervention702 n_2 =number of controls

703 $Z_{\alpha/2}$ = standard normal deviate for two-tailed test based on alpha level (relates to the
704 confidence interval level)

705 Z_{β} = standard normal deviate for one-tailed test based on beta level (relates to the power
706 level)

707 r = ratio of controls to cases708 p_1 = proportion of cases with exposure and $q_1 = 1-p_1$ 709 p_2 = proportion of controls with exposure and $q_2 = 1-p_2$

$$\bar{p} = \frac{p_1 + rp_2}{r+1} \quad \text{and} \quad \bar{q} = 1 - \bar{p}$$

710

711 The sample size formula *without* the correction factor by Fleiss is:

$$n_{1cc} = \frac{n_1}{4} \left[1 + \sqrt{1 + \frac{2(r+1)}{n_1 r |p_2 - p_1|}} \right]$$

$$n_{2cc} = r n_{1cc}$$

712

713 When the input is provided as an odds ratio (OR) rather than the proportion of cases exposed, the

714 proportion of cases exposed is calculated as:

$$p_1 = \frac{p_2 OR}{1 + p_2 (OR - 1)}$$

715

Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials (112)

(<https://www.openepi.com/SampleSize/SSCohort.htm>)

Two-sided significance level (1- α):	95
Power (1- β , % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	79
Percent of Exposed with Outcome:	94(83)
Odds Ratio:	4.2
Prevalence Ratio:	1.2
Prevalence difference:	15

Kelsey Fleiss Fleiss with CC

Sample size- Exposed(intervention):	81	80	93
Sample Size-Nonexposed (Control):	81	80	93
Total Sample Size:	162	160	186

CC= continuity correction. Results are rounded up to the nearest integer.

*Factoring 10% loss to follow-up, the total sample size will be **206(103 for each arm)***

Data collection procedures: Figure 5, illustrates the study schema, from screening to enrollment and data collection.

The intervention is mobile phone based IVR. However, the CLFU trial found that, it was observed that a good number of participants (50 of 256) at the urban site were not enrolled due to absence of a basic mobile phone, or had malfunctioning phone keyboards (for Poster Exhibition at the 20th International Conference on AIDS and STIs in Africa (ICASA 2019). Therefore, we shall provide a basic mobile phone to everyone in the study (SoC and intervention arm). To avoid stigma associated with a particular phone, we shall get 4 or more types of basic phones. Issues regarding simcard registration will be dealt with by the individuals.

Four study questionnaires will be administered at baseline and 6-monthly until the 12-month exit visit.

The questionnaires will capture:

- Sociodemographic and medical history
- Stigma scores
- Knowledge assessment
- Sexual behavior assessment

- Knowledge of COVID-19 (only at baseline) (Figure 5).

The data will be entered using REDCap. Blood for viral load will be collected at baseline and at the 6 and 12-month visit.

Intervention: mHealth Call For Life Uganda tool

The tool capitalises on a basic mobile phone's core utilities of voice and short messaging services. The system design, development, testing and evaluation was done by Janssen and the Grameen Foundation (<http://motechsuite.org/index.php/implementations>). In 2015, Janssen Global Public Health Research and Development, in close collaboration with the Infectious Diseases Institute Kampala (IDI), developed Call for Life Uganda (CFLU) tailored to the needs of PLHIV in Uganda. The CFLU system follows the Health Insurance Portability and Accountability Act (HIPAA) Privacy and Security rules. While the Privacy rules deals with electronic Protected Health Information, the security rule covers administrative, physical and technical safeguards to ensure confidentiality, integrity and security of electronic protected health information. Data transaction between patient and system is encrypted when it comes to human subjects. The system is password protected, and interaction of system and patient is personalised with a secret code. The system interacts with the patient through a basic mobile phone via a keypad and with the health worker through a web-based interface. The system has options to either use interactive voice response or short message service and the user has to make a choice, get a secret pin code which ensures privacy to enduser.

Screening-Enrolment procedures:

All potential participants will be written on the screening log, and a screening form completed, reasons for screen failure will be documented on the screening log. Following

successful screening, the participant will be referred to the Research Assistant (RA) to receive a thorough explanation of the study and informed consent is obtained. The RA then administers the stigma questionnaire along with the sociodemographic and medical information, , HIV knowledge and sexual behaviour questionnaires. A client locator form will be completed which will help in physical contact tracing, and the participant will be registered on the enrolment log.

Randomization will follow (see details of randomization procedure-standard operating procedure) thereafter and the result in the sealed envelope will dictate whether the patient will be registered onto the Call for Life System for the intervention or continue with standard of care as per MoH HIV Management guidelines.

Registration onto the CFLU system: Refer to Standard operating procedures on registration.

However, all patients will be registered onto the electronic and hard copy of the enrolment log and a next appointment date is given to them. Finally, the lab request forms are filled and the patient sent for a blood draw. The patient returns from the lab, receives their transport refund of UGX 20,000, with a basic mobile phone (only at baseline visit, to all participants) and is allowed to go home.

No intervention: Standard of care arm (SOC)

The Ministry of Health developed a minimum healthcare services package for PLHIV to standardize the programming, implementation and delivery of integrated HIV services in Uganda

The standard of care arm is based on the Apr 2018, consolidated guidelines for prevention and treatment of HIV in Uganda (113), and will also follow the healthcare services package for PLHIV (114).

The SOC arm will follow the services below:

- Care and support for people living with HIV, and the first line ART regimen is

TDF/3TC/DTG

- First-Line Regimen for Adults and Adolescents aged above 10 Initiating ART:

Preferred First-Line Regimen: TDF+3TC+DTG All HIV-infected adults and adolescents aged 10 years and above should be initiated on tenofovir, lamivudine and dolutegravir (TDF+3TC+DTG) as a once-daily fixed dose combination. When to use TDF+3TC+EFV: Adults and adolescents aged 10 years and above should only be initiated on TDF+3TC+EFV if their weight does not allow for use of the currently available DTG formulations (containing 50mg). Note: DTG 50mg should only be given to adults and adolescents weighing 40kg and above. When the 10mg and 25mg formulations become available, DTG will be administered to children and adolescents weighing less than 40kg.

- When to use ABC+3TC+DTG:

Adults and adolescents aged 10 years and above should only be initiated on ABC+3TC+DTG if TDF is contraindicated, including the following conditions:

1. Kidney disease and estimated glomerular filtration rate (GFR) below 60 ml/min
2. Adolescents below 35 kg of weight.

- Adherence Preparation, Monitoring, And Support:

The study team will use the 5 As principles for chronic care as a guide to offer pre-ART adherence counselling and psychosocial support. These are Assess, Advise, Agree, Assist and Arrange. The youths will be followed-up every 6 months as per MoH guidelines.

The standard Adult Care and Treatment Package includes the following services:(114)

1. HIV counselling and testing

800 2. HIV prevention services

801 3. Nutritional Counseling and support

802 4. Opportunistic infection screening and management

803 5. Screening and management of non-communicable diseases

804 6. Diagnostics and laboratory monitoring

805 7. Sexual and reproductive health

806 8. Counseling and Psychosocial support

807 9. ARV preparation, initiation and monitoring

808 10. Adherence and retention into care

809 11. Palliative care

810 12. Mental health

811 **The outcome variables include:**

- 812 • ART adherence scores at 6 and 12 months, as assessed by HIV Care Card for those on SoC
- 813 arm and Self- reported adherence to ART as depicted on the mHealth dash board.
- 814 • Viral load suppression at 6 and 12 months, as test results from blood collected at months 6
- 815 and 12 with time to viral suppression.
- 816 • Retention rates at 6 and 12 months with time to loss to follow-up
- 817 • Stigma scores at study start and end
- 818 • HIV Knowledge and sexual behaviour assessment at study start and end

Data Management Analysis Plan

Data collected on paper CRF will be entered using Research Electronic Data Capture software (REDCap) which is a safe, secure, HIPAA-compliant, web-based application and facilitates offline and online data entry. Data will be exported to STATA 14.0, for analysis. Data will then be backed up and archived in both soft and hard copy to avoid losses. The data collected will be stored securely under lock and key to maintain patient confidentiality.

Data regarding call details in the system will be extracted from Call For Life tool database, exported into Stata for analysis.

Visit dates will be extracted from database and proportions lost to follow-up drawn and time to loss to follow-up estimated. Viral load results will be extracted and time to viral suppression with survival analysis curves drawn for both arms.

Data from the Ministry of Health HIV card regarding the ART regimen and start dates will be transcribed to the data collection tool and later entered on the REDCap system.

General data analysis

Data will be analyzed at three levels, first at the univariate level, then at the bivariate level and lastly at the multivariate level. A consort diagram will be drawn to show the screening, enrolment, randomization, follow-up and analysis flow of the study.

Univariate Analysis

Descriptive analysis will be done for the factors that influence adherence, virological suppression, stigma and retention in care. In addition, the distribution of the independent variables will be done with categorical data summarized using frequencies and percentages. Numerical data will be

840 summarized using means and standard deviations for normally distributed data, and median and
 841 inter-quartile range for data that is not normally distributed.

842 **Bivariate Analysis**

843 The relationship between independent variables (age, gender, ART duration, marital status,
 844 education status, occupation and religion) and adherence and virological suppression will be
 845 analyzed using bivariate analysis made using cross tabular analysis and associations investigated
 846 using the Pearson Chi-square test.

847 The Chi-square test is based on the computational formulae below:

$$\chi^2 = \sum_{i=1}^r \sum_{j=1}^c \frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

848

849 Where

850 r is the number of categories of the i^{th} explanatory variable

851 c is the number of categories of the dependent variable

852 O_{ij} is the observed number of observations in the i^{th} explanatory

853 and j^{th} dependent variable

854 E_{ij} is the expected number of observations in the i^{th} explanatory?

855 and j^{th} dependent variable

Further, odds ratios shall be used to analyze the relationship between the dependent variable and the independent variables. Variables found to be significant at p value of $p \leq 0.05$ will be considered for the multivariable analysis.

Multivariate Analysis

Multivariable logistic regression will be used to determine the factors that influence adherence or virological suppression and retention in care. Variables found to be statistically significant at $p \leq 0.05$ in bivariate analysis and those considered to have a scientific explanation will be entered into the multivariable model.

The multivariate logistic regression adopted is based on the formulae below:

$$\ln \left[\frac{p_i}{1 - p_i} \right] = \beta_0 + \beta_1 X_1 + \dots + \beta_k X_k$$

Where;

X_i = independent variables

p_i = Probability of being adherent and viralogically suppression

$1 - p_i$ = Probability of not non-adherence or not suppressed virologically

β_0 = constant ; β_i = coefficient of the determinant

The study findings will be reported as odds ratios, confidence interval and independent variables found to have p value ≤ 0.05 at 95% confidence interval will be considered to be statistically significant in the final model.

874 After the final model, significant factors for ART adherence/ viral suppression will be computed.

875 **Data Monitoring Committee:**

876 The DMC will consist independent members with expertise in relevant clinical specialties, and
877 statistical data management the PhD supervisors will be among the committee. Their responsibility
878 is to ensure that the safety of study subjects is protected while the scientific goals of the study are
879 being met, and generate data queries to study team. The previous CFL-RCT at IDI, had no major
880 safety issues and neither were there any gender-based violence, so the DMC will suffice and will
881 be involved in:

- 882 • Review the research protocol and plan for data safety and monitoring.
- 883 • Generate data queries at a regular interval from the REDCap website
- 884 • Evaluate the progress of the trial, including periodic assessments of data quality and
885 timeliness, participant recruitment, accrual and retention, participant risk versus benefit,
886 performance of the trial site, and other factors that can affect study outcome.
- 887 • Make recommendations to the PI about continuation, termination, or other modifications
888 of the trial based on the observed beneficial or adverse effects of the intervention under
889 study.
- 890 • If appropriate, conduct interim analysis of efficacy in accordance
- 891 • Recommend solutions to address problems with study conduct, enrolment, and sample size
892 and/or data collection.

893 **Study visits (scheduled and unscheduled visit codes)**

894 The total duration of the study is 18 months; follow up period is up to 12 months. The participant
895 has a baseline visit (00.0) and is followed up at month 6 (168 days $\pm$ 14 days) visit code 01.0, last
896 visit is at month 12 (336 days $\pm$ 14 days) visit code 02.0.

897 The participant might return at the clinic due to an illness, or repeat blood draw, this interim visit
898 codes will be numbered sequentially from the previous scheduled visit. (00.01, 00.02 if its next to
899 the baseline, if next to second visit, the code will be 01.01, 01.02 etc., if its next to last visit it will
900 be coded 02.1, 02.2, etc.).

901 The study visit window is 2 weeks (14 days), beyond this period a visit code denoting an interim
902 visit is given; e.g. Visit code 01.1 first contact with patient past visit 01.0 and 01.2 denotes second
903 contact with patient past visit 01.0.

904 During enrolment, it is important to obtain the names and contact information for several
905 individuals closely related to the participant (e.g., next of kin, friends, etc.). Such individuals can
906 be contacted in the event that a participant does not return for follow-up visits. Physical contact
907 tracing will happen if the patient takes 2 weeks past the scheduled visit.

908 **Table 3: Study schedule of procedures:**

909

Study schedule of procedures	Baseline 00 + 2 weeks	Month 6± 2 weeks	Month 12± 2 weeks
Eligibility Screening	√		
Informed Consent	√		
Barriers, enablers of adherence and acceptability (Qualitative data collection at baseline)	√		
Randomization : Intervention (Call for life mHealth IVR) with Standard of care Versus Standard of care alone
COVID-19 Knowledge Assessment	√		
Stigma Scores	√		√
<ul style="list-style-type: none"> • Demographic and socio-economic assessment, • Knowledge questionnaire, • Sexual behavior questionnaire 	√	√	√
Randomization	√		
Laboratory			
Viral load ±CD4*	√*	√	√
Resistance testing(If funds allow)			√**
Qualitative assessment-study end-line			√

*Those initiating or ART naïve at study entry ** Depending on availability of funds
CD4: cluster differentiation four

912

913 Missed visit:

914 When the appointment is not honoured and the 14-day window passes, this is a missed visit. If a
915 participant misses a visit (Visit window inclusive) a missed visit form is completed documenting
916 the reason for missing (if known) and the attempts made to contact the participant, through mobile
917 phone or physical tracing. Several attempts to contact the participants must be made to ensure good
918 retention. The attempts may include: Checking the General clinic schedule to sync the appointment
919 visit, Calling the participant; Calling a relative who was disclosed to, or Visiting the participant's
920 home: To minimise missed visits, through the web-interface on CFLU system, any dropped calls
921 monitored on the dashboard, will trigger active follow-up and tracing of the participants.

922

923 Loss to follow-up:

924 If a participant misses 2 consecutive visits and unable to ascertain the vital status, this patient will
925 be declared lost to follow-up, alternatively, if 3 months consecutively elapse, without
926 acknowledging the patient's status, the patient will be labelled lost to follow-up. If a participant's
927 where about is not known for 3 months and the contact tracing is uneventful after 3 documented
928 attempts, this participant is deemed lost to follow-up and a withdraw form is completed. In case
929 the participant re-surfaces to the clinic when the study is still active/ongoing, the withdraw form
930 is cancelled out and patient re-joins the study and a study visit is conducted.

931 Study Objective 3:

932 To evaluate the cost of mHealth in comparison to Standard of Care

933 **Study design:** Cost evaluation analysis

Study Purpose: To assess cost of mHealth intervention in comparison to standard of care

Primary outcome measure: Costs spent on the intervention participants in comparison to standard of care participants

A cost analysis of the intervention from a governmental perspective will be performed. The principle of marginal costing will be used to cost the resources utilised in the alternative strategies. All costs of a historical nature, the sunk costs such as resources invested in buildings, equipment, and vehicles will be ignored. Only costs related to the future, from the onset of the study, will be recorded.

Sources of cost information: The following costs will be assessed and classified under direct or indirect cost: Sources of cost data will be; program/ project documents, financial records.

Capital costs:

I. System Costs:

- Software monthly hosting (internet, cloud hosting, call bills,)
- Support maintenance
- Hard ware
 - Computers
 - Internet modem

Recurrent costs:

I. Supplies (blood collection tubes, vacutainer holders, needle, cotton swabs)

II. Transport to fro (clinic visit):

III. Staff/ personnel salaries:

Induced costs:

I. Transport costs

II. Number of sick visits attended outside the clinic costs/fees incurred

III. Airtime fees

Health outcomes:

The number of patients with viral suppression (<1000 copies) will listed per study arm at month 6 and 12, and these will be compared across arms.

Analysis:

Primary measure will be Cost for mHealth Intervention.

3.5 Quality control

All data collection tools will be checked for completeness and validated prior to entry on REDCap. Research assistants (research nurse counsellors) will follow the research protocol, have prior protocol training, Human subject protection (HSP), and Good Clinical practice (GCP) course training. After randomization the participant on the intervention (CFL arm) will be registered on a standalone CFL-PhD clinic for this study. The viral load results entered on the CFL tool will be cross-checked and verified by the second research nurse -counsellor, as the second data entrant. All patients consented for the study will get a basic phone to eliminate issues regarding phone technologies such as some buttons not functioning well. The study will be over seen by the DMC based at infectious Diseases Institute, the PhD supervisors who review the student's progress on

the quarterly period, and these supervisors are part of doctoral committee. The internal monitor provided by the sponsor is responsible for bi annual monitoring of the study.

Data Security: All study data will be double encrypted, maintaining the confidentiality and safety of all data communications. The communication between the call for life browser and the server is encrypted using 128-bit SSL. System servers are hosted by Amazon Web Services (AWS) and are secured by Amazon VPC and AWS WAF firewalls to allow private networks and prevent unauthorized access, while data is protected from virus threats using BitDefender anti-virus technology. The YLWH database will be housed on the IDI server.

Study limitations:

The intervention involves information technology and requires reliable electricity supply, stable mobile phone network, and internet connectivity. Any disruption will lead to the CFLU system not operating as planned.

For the end user lack of experience with use of pin codes, multiple sim lines and failure to register simcard may lead to system failure Because entry of a wrong pin code will lead to blockage from use of the system. Use of multiple sim cards may lead to sim swapping and a call reminder may be received when the registered/authorised sim card number is not available because the other line is in use. Finally, unregistered simcards may be blocked by the Uganda Communications Commission.

Another limitation may be parental restrictions in phone use for YLWH enrolled in the study. The study participant's response to daily pill reminders calls assumes that self-reporting is accurate.

The Call for life health messages are in 4 main languages, due to lack of funds, the Swahili language is missing and this may affect many potential participants.

Discussion: This project will determine acceptability, effectiveness of mHealth, knowledge & myths on COVID-19 and cost of delivering pill and clinic appointment reminders, and voice messages to a population with suboptimal ART adherence in a resource-limited setting.

Trial status

The protocol current version number and date is 3.1, Jan 2021, the date recruitment began was 12th Aug 2020 and recruitment ended 30th Jun 2021. We are still following up the study participants, and the last follow-up will be 30th May 2022. I was not able to publish the protocol earlier, this is because the country underwent lockdown due to COVID-19 pandemic, just after receiving regulatory approval, when lockdown was eased, I put emphasis on recruitment to catch up with the PhD timelines and the funding period expiring in the next year.

This protocol has been amended twice, as explained below:

First amendment on version

- Revised the **study population and subject selection to include youth who initiated ART by Jun 2019**. Previously the study population was Youth who are ART naive , initiating or on ART for ≤ 3 months, this was revised to ; youth who are ART naive, initiating or **on ART since Jun 2019**.

- **Added a new questionnaire to assess knowledge of and myths about COVID-19 among youths in rural area**

Reason for first amendment/modification on version 2.2, Jan 2020:

Due to COVID-19 lockdown, disruption of normal service delivery and impact it has had on health seeking behaviour, we realised that the youth coming to Kiryandongo hospital for HIV testing and thus initiating ART markedly declined in the past 3 months. This was likely to

impact on the recruitment and timelines for this PhD study, and hence the need to amend the protocol.

1. To increase on the enrolment rate of this study, the subject selection has been amended.

2. We have also used this opportunity while amending to add a new questionnaire to assess knowledge of and myths about COVID-19 amongst this population.

Second amendment/modification on version 3.0, Jul 2020

Revised the **study sites to include two more low level facilities (Health Centre level III and II) near Kiryandongo Hospital**. Previously the study site was only at Kiryandongo Hospital

Reason for second amendment/modification:

Due to COVID-19 lockdown, there was disruption of normal service delivery and most patients requested to get ART transfer out to sites nearer their home. This led to low recruitment and delays to sample size accrual and hence the need to amend the protocol.

1. To increase on the enrolment rate for study, we requested addition of two sites which are Panyandol Health Centre and Nyakadot Health Centre which are within Kiryandongo district. Inclusion of low level health facility involved in HIVcare

List of abbreviations

AIDS: Acquired Immuno Deficiency Syndrome

cART: Combined Antiretroviral Therapy

1043	CD4 cell: Cluster Differentiated cells
1044	cDOT: Community based Directly Observed Treatment
1045	CFLU: Call for Life Uganda
1046	CITI: Collaborative Institutional Training Initiative
1047	COVID-19: CORONA VIRUS DISEASE 2019
1048	GCP: Good Clinical Practice
1049	HIT: Health Information Technology
1050	HIV RNA: Human Immunodeficiency Virus Ribonucleic Acid
1051	HSP: Human Subjects Protection
1052	IAC: Intensive Adherence Counselling
1053	IDI: Infectious Diseases Institute
1054	IVR: Interactive Voice Response
1055	MoH: Ministry of Health
1056	PEPFAR: President's Emergency Plan for AIDS Relief
1057	PHS: Physical Health Scores
1058	PLWH: People living with HIV
1059	SMS: Short Messaging Service
1060	UBOS: Uganda Bureau of Statistics
1061	UNAIDS: United Nations Programme on HIV and AIDS
1062	UNCST- Uganda National Council of Science & Technology
1063	UPHIA: Uganda Population-Based HIV Impact Assessment
1064	VL: Viral load
1065	YLWH: Youth living with HIV

1066 **Ethical approval and consent to participate**

1067 Permission to carry out the study will be sought from the Department of Medicine, School of
1068 Medicine, College of Health Sciences and ethical approval from the Higher Degrees Ethics and
1069 Research Committee of School of Medicine, Makerere University College of Health Sciences and
1070 research clearance from Uganda National Council for Science Technology. Clearance will also be
1071 sought from Kiryandongo Hospital administration, Health centre in-charges, Kiryandongo District
1072 Health Office and Infectious Diseases Institute –scientific research committee. The PI is Good
1073 Clinical Practice (GCP) compliant with a CITI certificate in GCP and Human Research Subject
1074 Protection (HSP). Informed consent and assent will be obtained and documented from all
1075 participants. Confidentiality will be maintained at all times. All data collected will be secured
1076 under lock and key. The CFLU is password protected and data is encrypted once extracted from
1077 database.

1078 The National IT Authority policy will be followed and adhered to in relation to data protection,
1079 safety and confidentiality for patients.

1080 **Consent for publication**

1081 Not applicable

1082 **Availability of data and materials**

1083 The principle investigator will have access to the final trial datasets and can be availed on request,
1084 after signing the agreement from the study sponsor who is Infectious Diseases Institute.

1085 **Competing interests**

1086 There are no competing interests for all the authors

1087 **Funding**

1088 ABN received funding for a scholarship from the Academy at Infectious Diseases Institute- The

1089 scholarship covered university tuition, student stipend and research.

1090 **Authors' contributions**

1091 ABN is the Principle Investigator, PhD student at Makerere University, conceived the study
1092 developed concept, study design, proposal development, protocol writing , ethical and regulatory
1093 approvals.

1094 RPR, DBM, PW, and RJ are PhD supervisors at Makerere University, provide scientific overview,
1095 give guidance on study designs, methodology, edited and reviewed protocol until final approval.
1096 Provide progress assessment of the student. All authors read and approved the final manuscript.

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1099 **Authors' information**

1100 The Author is a PhD student at Makerere University, College of Health Sciences, School of
1101 Medicine, she got a scholarship from the Academy for hhealth Innovations at Infectious Diseases
1102 Institute.

1103

1104 **4. REFERENCES**1105 <https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics>

1106 UNAIDS. UNAIDS Data FactSheet. 2018.

1107 Avert.Org. Young People HIV and AIDS 2019 [updated 21 Aug 2018; cited 2019 7 Oct].

1108 UNAIDS. Youth and HIV. 2018.

1109 UNAIDS. Global AIDS Update 2019. 2019.

1110 AIDSInfo. Young People (15-24yrs) living with HIV-by sex 2019 [cited 2019]. Available from:

1111 <https://aidsinfo.unaids.org/>.

1112 UNAIDS. Ending the AIDS epidemic among children, adolescents and young women 2019 [updated

1113 2019; cited 2018 27 Apr]. Available from:

1114 [https://www.unaids.org/en/resources/presscentre/featurestories/2018/april/ending-aids-epidemic-](https://www.unaids.org/en/resources/presscentre/featurestories/2018/april/ending-aids-epidemic-among-children-adolescents-young-women)
1115 [among-children-adolescents-young-women](https://www.unaids.org/en/resources/presscentre/featurestories/2018/april/ending-aids-epidemic-among-children-adolescents-young-women).

1116 UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014.

1117 UPHIA. UGANDA POPULATION-BASEDHIV IMPACT ASSESSMENT. 2017.

1118 Nabukeera-Barungi N, Elyanu P, Asire B, Katureebe C, Lukabwe I, Namusoke E, et al. Adherence
1119 to antiretroviral therapy and retention in care for adolescents living with HIV from 10 districts in Uganda.
1120 BMC Infectious Diseases. 2015;15(1):520.

1121 WHO. mHealth: New horizons for health through mobile technologies. 2011.

1122 Musiimenta A, Atukunda EC, Tumuhimbise W, Pisarski EE, Tam M, Wyatt MA, et al. Acceptability
1123 and feasibility of real-time antiretroviral therapy adherence interventions in rural Uganda: Mixed-method
1124 pilot randomized controlled trial. JMIR Mhealth Uhealth. 2018;6(5):e122.

1125 Schnall R, Bakken S, Rojas M, Travers J, Carballo-Diequez A. mHealth Technology as a Persuasive
1126 Tool for Treatment, Care and Management of Persons Living with HIV. AIDS and behavior. 2015;19 Suppl
1127 2(0 2):81-9.

1128 Haberer JE, Musiimenta A, Atukunda EC, Musinguzi N, Wyatt MA, Ware NC, et al. Short message
1129 service (SMS) reminders and real-time adherence monitoring improve antiretroviral therapy adherence
1130 in rural Uganda. Aids. 2016;30(8):1295-300.

1131 Campbell AR, Kinvig K, Côté HC, Lester RT, Qiu AQ, Maan EJ, et al. Health Care Provider Utilization
1132 and Cost of an mHealth Intervention in Vulnerable People Living With HIV in Vancouver, Canada:
1133 Prospective Study. JMIR Mhealth Uhealth. 2018;6(7):e152.

1134 Rosalind M. Parkes-Ratanshi, Maria S. Nabaggala, Agnes N. Bwanika, Mohammed Lamorde,
1135 Rachel King, Noela Owarwo, et al. CALL FOR LIFE UGANDA TM: An RCT Using Interactive Voice Response
1136 for PLHIV on ART. Abstract 1037. . Conference on Retroviruses and Opportunistic Infections,; March 4-7;
1137 Seattle2019.

1138 CDC. Report of the NIH Panel to Define Principles of Therapy of HIV Infection and Guidelines for
1139 the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents. U.S. DEPARTMENT OF HEALTH
1140 AND HUMAN SERVICES

1141 Centers for Disease Control and Prevention (CDC), SERVICES USDOHAH, (CDC) CfDCaP; 1998 Apr 24.
1142 Report No.

1143 Vreeman RC, Nyandiko WM, Liu H, Tu W, Scanlon ML, Slaven JE, et al. Measuring adherence to
1144 antiretroviral therapy in children and adolescents in western Kenya. J Int AIDS Soc. 2014;17(1):19227.

1145 Hawkins A, Evangeli M, Sturgeon K, Le Prevost M, Judd A, Committee AS. Episodic medication
1146 adherence in adolescents and young adults with perinatally acquired HIV: a within-participants approach.
1147 AIDS care. 2016;28(sup1):68-75.

1148 Gardner EM, Burman WJ, Steiner JF, Anderson PL, Bangsberg DR. Antiretroviral medication
 1149 adherence and the development of class-specific antiretroviral resistance. AIDS (London, England).
 1150 2009;23(9):1035.

1151 Oyugi JH, Byakika-Tusiime J, Ragland K, Laeyendecker O, Mugerwa R, Kityo C, et al. Treatment
 1152 interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination
 1153 antiretroviral therapy in Kampala, Uganda. Aids. 2007;21(8):965-71.

1154 WHO. Guidelines on HIV self-testing and partner notification; Supplement to consolidated
 1155 guidelines on HIV testing services. . 2016.

1156 Koirala S, Deuba K, Nampaisan O, Marrone G, Ekström AM, group C-S. Facilitators and barriers for
 1157 retention in HIV care between testing and treatment in Asia—a study in Bangladesh, Indonesia, Lao,
 1158 Nepal, Pakistan, Philippines and Vietnam. PLoS One. 2017;12(5):e0176914.

1159 Hudelson C, Cluver L. Factors associated with adherence to antiretroviral therapy among
 1160 adolescents living with HIV/AIDS in low-and middle-income countries: a systematic review. AIDS care.
 1161 2015;27(7):805-16.

1162 Agwu AL, Bethel J, Hightow-Weidman LB, Sleasman JW, Wilson CM, Rudy B, et al. Substantial
 1163 multiclass transmitted drug resistance and drug-relevant polymorphisms among treatment-naïve
 1164 behaviorally HIV-infected youth. AIDS patient care and STDs. 2012;26(4):193-6.

1165 Lawrence Mbuagbaw, Lahana Thabane, Pierre Ongolo-Zogo, Richard T Lester, Edward Mills,
 1166 Jimmy Volmink, et al. The cameroon mobile phone sms (CAMPS) trial: a protocol for a randomized
 1167 controlled trial of mobile phone text messaging versus usual care for improving adherence to highly active
 1168 anti-retroviral therapy Trials. 2011;12(5).

1169 Ammassari AM, et al. Timed Short Messaging Service Improves Adherence and Virological
 1170 Outcomes in HIV-1–Infected Patients With Suboptimal Adherence to Antiretroviral Therapy. JAIDS.
 1171 2011;58(4):e113–e5.

1172 Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short
 1173 message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. The
 1174 Lancet. 2010;376(9755):1838-45.

1175 van der Kop ML OD, Patel A, et al. The effect of weekly short message service communication on
 1176 patient retention in care in the first year after HIV diagnosis: study protocol for a randomised controlled
 1177 trial (WelTel Retain). BMJ. 2013.

1178 Natalie Leon HSaED. Applying a framework for assessing the health system challenges to scaling
 1179 up mHealth in South Africa. BMC Medical Informatics and Decision Making. 2012;12(123).

1180 Garofalo R, Kuhns LM, Hotton A, Johnson A, Muldoon A, Rice D. A Randomized Controlled Trial of
 1181 Personalized Text Message Reminders to Promote Medication Adherence Among HIV-Positive
 1182 Adolescents and Young Adults. AIDS and behavior. 2016;20(5):1049-59.

1183 Byonanebye DM NM, Naggirinya AB, Lamorde M, Oseku E, King R, Owarwo N, Laker E, Orama R,
 1184 Castelnovo B, Kiragga A, Parkes-Ratanshi R. An interactive voice response software to improve the
 1185 quality of life of people living with HIV in Uganda: A Randomized Controlled Trial. JMIR mHealth and
 1186 uHealth. 2021.

1187 Corkrey R, Parkinson L, Bates L, Green S, Htun AT. Pilot of a novel cervical screening intervention:
 1188 interactive voice response. Australian and New Zealand Journal of Public Health. 2005;29(3):261-4.

1189 Schroder KE, Johnson CJ, Wiebe JS. Interactive Voice Response Technology applied to sexual
 1190 behavior self-reports: a comparison of three methods. AIDS and behavior. 2007;11(2):313-23.

1191 Perrine MW, Mundt JC, Searles JS, Lester LS. Validation of daily self-reported alcohol consumption
 1192 using interactive voice response (IVR) technology. Journal of Studies on Alcohol. 1995;56(5):487-90.

1193 Hettema JE, Hosseinbor S, Ingersoll KS. Feasibility and Reliability of Interactive Voice Response
 1194 Assessment of HIV Medication Adherence: Research and Clinical Implications. HIV clinical trials.
 1195 2012;13(5):271-7.

1196 Reidel K, Tamblyn R, Patel V, Huang A. Pilot study of an interactive voice response system to
1197 improve medication refill compliance. BMC medical informatics and decision making. 2008;8(1):46.

1198 Kerstin E. E. Schroder, Johnson CJ. Interactive Voice Response Technology to Measure HIV-related
1199 Behavior. Behavioral Aspects of HIV Management. 2009:210- 6.

1200 Qudrat-Ullah H, Tsasis P. Innovative healthcare systems for the 21st century 2017. Available from:
1201 <http://public.ebib.com/choice/publicfullrecord.aspx?p=5576718>.

1202 Haider N, Rothman-Ostrow P, Osman AY, Arruda LB, Macfarlane-Berry L, Elton L, et al. COVID-
1203 19—Zoonosis or Emerging Infectious Disease? Frontiers in Public Health. 2020;8(763).

1204 Roy D, Tripathy S, Kar SK, Sharma N, Verma SK, Kaushal V. Study of knowledge, attitude, anxiety
1205 & perceived mental healthcare need in Indian population during COVID-19 pandemic. Asian Journal of
1206 Psychiatry. 2020;51:102083.

1207 Olum R, Chekwech G, Wekha G, Nassozi DR, Bongomin F. Coronavirus Disease-2019: Knowledge,
1208 Attitude, and Practices of Health Care Workers at Makerere University Teaching Hospitals, Uganda. (2296-
1209 2565 (Print)).

1210 UPHIA. UGANDA POPULATION-BASED HIV IMPACT ASSESSMENT UPHIA 2016–2017. 2017.

1211 UNAIDS. STATE OF THE AIDS EPIDEMIC-UNAIDS DATA 2017. 2017.

1212 Babalola Stella ea. A Framework for Health Communication Across the
1213 HIV Treatment Continuum Journal of Acquired Immune Deficiency Syndromes. 2017;74:S5-
1214 S14.

1215 Lee-Ann Crystal D. Exploration of adherence to antiretroviral treatment amongst adolescents
1216 in a low socio-economic urban setting in Cape Town, South Africa: University of the Western Cape; 2017.

1217 Nasuuna E, Kigozi J, Babirye L, Muganzi A, Sewankambo NK, Nakanjako D. Low HIV viral
1218 suppression rates following the intensive adherence counseling (IAC) program for children and
1219 adolescents with viral failure in public health facilities in Uganda. BMC public health. 2018;18(1):1048.

1220 Ammassari A, Trotta MP, Shalev N, Tettoni MC, Maschi S, Di Sora F, et al. Timed Short Messaging
1221 Service Improves Adherence and Virological Outcomes in HIV-1–Infected Patients With Suboptimal
1222 Adherence to Antiretroviral Therapy. JAIDS Journal of Acquired Immune Deficiency Syndromes.
1223 2011;58(4):e113-e5.

1224 Musiimenta A, Atukunda EC, Tumuhimbise W, Pisarski EE, Tam M, Wyatt MA, et al. Acceptability
1225 and Feasibility of Real-Time Antiretroviral Therapy Adherence Interventions in Rural Uganda: Mixed-
1226 Method Pilot Randomized Controlled Trial. JMIR Mhealth Uhealth. 2018;6(5):e122.

1227 WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV
1228 infection 2013.

1229 50. UBOS. UGANDA BUREAU OF STATISTICS : 2017 Statistical_Abstract: Communication Statistics.
1230 2017.

1231 Jacob PR, Oates. Cell-Phone in Africa: Communication LifelineAL-April-15-2015. Pew-Research-
1232 Center-Africa. 2015.

1233 Ippoliti NB, L'Engle K. Meet us on the phone: mobile phone programs for adolescent sexual and
1234 reproductive health in low-to-middle income countries. Reprod Health. 2017;14(1):11-.

1235 Fisher JD, Fisher WA. The information-motivation-behavioral skills model. Emerging theories in
1236 health promotion practice and research: Strategies for improving public health. 2002;1:40-70.

1237 Fisher WA, Fisher JD, Harman J. The information-motivation-behavioral skills model: A general
1238 social psychological approach to understanding and promoting health behavior. Social psychological
1239 foundations of health and illness. 2003;22:82-106.

1240 Fisher WA, Fisher JD, Harman J. The Information-Motivation-Behavioral Skills Model: A General
1241 Social Psychological Approach to Understanding and Promoting Health Behavior. 2003:82-106.

1242 Jeffrey D.Fisher WAF. <Changing AIDS-Risk Behavior>. Psychological Bulletin. 1992;111(3):455-74.

1243 Jones D, Cook R, Rodriguez A, Waldrop-Valverde D. Personal HIV knowledge, appointment
1244 adherence and HIV outcomes. AIDS and behavior. 2013;17(1):242-9.

1245 Miller LG, Liu H, Hays RD, Golin CE, Ye Z, Beck CK, et al. Knowledge of antiretroviral regimen dosing
1246 and adherence: a longitudinal study. Clinical infectious diseases : an official publication of the Infectious
1247 Diseases Society of America. 2003;36(4):514-8.

1248 Swindells S, Mohr J, Justis JC, Berman S, Squier C, Wagener MM, et al. Quality of life in patients
1249 with human immunodeficiency virus infection: impact of social support, coping style and hopelessness.
1250 International journal of STD & AIDS. 1999;10(6):383-91.

1251 Swahn MH, Braunstein S, Kasirye R. Demographic and Psychosocial Characteristics of Mobile
1252 Phone Ownership and Usage among Youth Living in the Slums of Kampala, Uganda. Western Journal of
1253 Emergency Medicine. 2014.

1254 UBOs. Statistical Report 2018.

1255 Steve Kanfers JJHP, Keith Chan, Maria Eugenia Socias, Nathan Ford, Jamie I Forrest, Kristian
1256 Thorlund, Jean B Nachega, Edward J Mills. Interventions to improve adherence. www.thelancet.com/HIV.
1257 2016.

1258 Schnall R, Rojas M, Bakken S, Brown W, Carballo-Diequez A, Carry M, et al. A user-centered model
1259 for designing consumer mobile health (mHealth) applications (apps). Journal of biomedical informatics.
1260 2016;60:243-51.

1261 Schnall R, Bakken S, Brown W, Carballo-Diequez A, Iribarren S. Usability Evaluation of a
1262 Prototype Mobile App for Health Management for Persons Living with HIV. Studies in health technology
1263 and informatics. 2016;225:481-5.

1264 Chang LW, Kagaayi J, Arem H, Nakigozi G, Ssempiijja V, Serwadda D, et al. Impact of a mHealth
1265 intervention for peer health workers on AIDS care in rural Uganda: a mixed methods evaluation of a
1266 cluster-randomized trial. AIDS and behavior. 2011;15(8):1776-84.

1267 Chib A, Harris R. Linking Research to Practice: Strengthening ICT for Development Research
1268 Capacity in Asia: ISEAS- Yusof Ishak Institute.

1269 Nachega JB, Adetokunboh O, Uthman OA, Knowlton AW, Altice FL, Schechter M, et al. Community-
 1270 Based Interventions to Improve and Sustain Antiretroviral Therapy Adherence, Retention in HIV Care and
 1271 Clinical Outcomes in Low- and Middle-Income Countries for Achieving the UNAIDS 90-90-90 Targets. *Curr*
 1272 *HIV/AIDS Rep.* 2016;13(5):241-55.

1273 Luxton DD, June JD, Chalker SA. Mobile Health Technologies for Suicide Prevention: Feature
 1274 Review and Recommendations for Use in Clinical Care. *Current Treatment Options in Psychiatry.*
 1275 2015;2(4):349-62.

1276 Amith M, Loubser PG, Chapman J, Zoker KC, Rabelo Ferreira FER. Optimization of an EHR mobile
 1277 application using the UFuRT conceptual framework. *AMIA Annu Symp Proc.* 2012;2012:209-17.

1278 Doris Caliz XA. Usability Evaluation Method for Mobile Applications for the Elderly: A
 1279 Methodologica Proposal.

1280 Burnay J, Bushman BJ, Laroi F. Effects of sexualized video games on online sexual harassment.
 1281 *Aggressive behavior.* 2019;45(2):214-23.

1282 Sheehan B, Lee Y, Rodriguez M, Tiase V, Schnall R. A comparison of usability factors of four mobile
 1283 devices for accessing healthcare information by adolescents. *Applied clinical informatics.* 2012;3(04):356-
 1284 66.

1285 Sparkes J, Valaitis R, McKibbin A. A usability study of patients setting up a cardiac event loop
 1286 recorder and BlackBerry gateway for remote monitoring at home. *Telemedicine and e-Health.*
 1287 2012;18(6):484-90.

1288 Jemere AT, Yeneneh YE, Tilahun B, Fritz F, Alemu S, Kebede M. Access to mobile phone and
 1289 willingness to receive mHealth services among patients with diabetes in Northwest Ethiopia: a cross-
 1290 sectional study. *BMJ open.* 2019;9(1):e021766-e.

1291 Kebede M, Zeleke A, Asemahagn M, Fritz F. Willingness to receive text message medication
 1292 reminders among patients on antiretroviral treatment in North West Ethiopia: A cross-sectional study.
 1293 *BMC medical informatics and decision making.* 2015;15:65-.

1294 Sankaranarayanan J, Sallach RE. Rural patients' access to mobile phones and willingness to receive
1295 mobile phone-based pharmacy and other health technology services: a pilot study. *Telemedicine journal*
1296 *and e-health : the official journal of the American Telemedicine Association*. 2014;20(2):182-5.

1297 DeSouza SI, Rashmi MR, Vasanthi AP, Joseph SM, Rodrigues R. Mobile phones: the next step
1298 towards healthcare delivery in rural India? *PLoS One*. 2014;9(8):e104895.

1299 Kim J, Zhang W, Nyonyitono M, Lourenco L, Nanfuka M, Okoboi S, et al. Feasibility and
1300 acceptability of mobile phone short message service as a support for patients receiving antiretroviral
1301 therapy in rural Uganda: a cross-sectional study. *J Int AIDS Soc*. 2015;18(1):20311-.

1302 Rana Y, Haberer J, Huang H, Kambugu A, Mukasa B, Thirumurthy H, et al. Short Message Service
1303 (SMS)-Based Intervention to Improve Treatment Adherence among HIV-Positive Youth in Uganda: Focus
1304 Group Findings. *PLoS One*. 2015;10(4):e0125187.

1305 Ware NC, Pisarski EE, Tam M, Wyatt MA, Atukunda E, Musiimenta A, et al. The Meanings in the
1306 messages: how SMS reminders and real-time adherence monitoring improve antiretroviral therapy
1307 adherence in rural Uganda. *AIDS (London, England)*. 2016;30(8):1287-94.

1308 Kunutsor S, Walley J, Katabira E, Muchuro S, Balidawa H, Namagala E, et al. Using Mobile Phones
1309 to Improve Clinic Attendance Amongst an Antiretroviral Treatment Cohort in Rural Uganda: A Cross-
1310 sectional and Prospective Study. *AIDS and behavior*. 2010;14(6):1347-52.

1311 Siedner MJ, Haberer JE, Bwana MB, Ware NC, Bangsberg DR. High acceptability for cell phone text
1312 messages to improve communication of laboratory results with HIV-infected patients in rural Uganda: a
1313 cross-sectional survey study. *BMC medical informatics and decision making*. 2012;12(1):56.

1314 Haberer JE, Kiwanuka J, Nansera D, Muzoora C, Hunt PW, So J, et al. Realtime adherence
1315 monitoring of antiretroviral therapy among HIV-infected adults and children in rural Uganda. *AIDS*
1316 *(London, England)*. 2013;27(13):2166-8.

1317 De Costa A, Shet A, Kumarasamy N, Ashorn P, Eriksson B, Bogg L, et al. Design of a randomized
1318 trial to evaluate the influence of mobile phone reminders on adherence to first line antiretroviral
1319 treatment in South India--the HIVIND study protocol. BMC medical research methodology. 2010;10:25.

1320 Chesney MA, Morin M, Sherr L. Adherence to HIV combination therapy. Social science & medicine
1321 (1982). 2000;50(11):1599-605.

1322 Paraskevis D, Kostaki E, Gargalianos P, Xylomenos G, Lazanas M, Chini M, et al. Transmission
1323 Dynamics of HIV-1 Drug Resistance among Treatment-Naive Individuals in Greece: The Added Value of
1324 Molecular Epidemiology to Public Health. Genes. 2017;8(11).

1325 Rodrigues R, Shet A, Antony J, Sidney K, Arumugam K, Krishnamurthy S, et al. Supporting
1326 adherence to antiretroviral therapy with mobile phone reminders: results from a cohort in South India.
1327 PLoS One. 2012;7(8):e40723.

1328 Ridgeway K, Dulli LS, Murray KR, Silverstein H, Dal Santo L, Olsen P, et al. Interventions to improve
1329 antiretroviral therapy adherence among adolescents in low- and middle-income countries: A systematic
1330 review of the literature. PLoS One. 2018;13(1):e0189770.

1331 Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, et al. The effectiveness of mobile-health
1332 technology-based health behaviour change or disease management interventions for health care
1333 consumers: a systematic review. PLoS medicine. 2013;10(1):e1001362.

1334 Caroline Free GP, Louise Watson, et al. The effectiveness of mobile health technologies to improve
1335 health care service delivery processes. A systematic review and meta analysis. PLoS medicine.
1336 2013;10(1):e1001363.

1337 Tomlinson M, Rotheram-Borus ea. Scaling up mHealth: where is the evidence? PLoS medicine.
1338 2013;10(2):e1001382.

1339 Campbell JI, Haberer JE. Cell Phone-Based and Adherence Device Technologies for HIV Care and
1340 Treatment in Resource-Limited Settings: Recent Advances. Current HIV/AIDS reports. 2015;12(4):523-31.

1341 Campbell AR, Kinvig K, Côté HC, Lester RT, Qiu AQ, Maan EJ, et al. Health Care Provider Utilization
1342 and Cost of an mHealth Intervention in Vulnerable People Living With HIV in Vancouver, Canada:
1343 Prospective Study. JMIR mHealth and uHealth. 2018;6(7).

1344 Anglada-Mart H, #237, nez, Martin-Conde M, Rovira-Illamola M, Sotoca-Momblona JM, et al. An
1345 Interactive Mobile Phone---Website Platform to Facilitate Real-Time Management of Medication in
1346 Chronically ill Patients. J Med Syst. 2017;41(8):1-8.

1347 Corless IB, Hoyt AJ, Tyler-Viola L, Sefcik E, Kemppainen J, Holzemer WL, et al. 90-90-90-Plus:
1348 Maintaining Adherence to Antiretroviral Therapies. AIDS patient care and STDs. 2017;31(5):227-36.

1349 Giordano TP, Hartman C, Gifford AL, Backus LI, Morgan RO. Predictors of retention in HIV care
1350 among a national cohort of US veterans. HIV clinical trials. 2009;10(5):299-305.

1351 Giordano TP. Retention in HIV care: what the clinician needs to know. Topics in antiviral medicine.
1352 2011;19(1):12-6.

1353 Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on
1354 treatment in sub-Saharan Africa, 2007-2009: systematic review. Tropical medicine & international health
1355 : TM & IH. 2010;15 Suppl 1:1-15.

1356 Kohler PK, Chung MH, McGrath CJ, Benki-Nugent SF, Thiga JW, John-Stewart GC. Implementation
1357 of free cotrimoxazole prophylaxis improves clinic retention among antiretroviral therapy-ineligible clients
1358 in Kenya. AIDS (London, England). 2011;25(13):1657-61.

1359 Mebal Namwabira EKN, Nigel Livesley, Alex R Ario,. Improving Retention of patients in HIV Care
1360 in Uganda. Poster, international Conference. 2011.

1361 Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV
1362 care and its relevance to test-and-treat strategies for prevention of HIV infection. Clinical infectious
1363 diseases : an official publication of the Infectious Diseases Society of America. 2011;52(6):793-800.

1364 Smillie K, Van Borek N, van der Kop ML, Lukhwato A, Li N, Karanja S, et al. Mobile health for early
1365 retention in HIV care: a qualitative study in Kenya (WeTel Retain). Afr J AIDS Res. 2014;13(4):331-8.

1366 Kiwanuka N, Mpendo J, Asimwe S, Ssempiira J, Nalutaaya A, Nambuusi B, et al. A randomized trial
 1367 to assess retention rates using mobile phone reminders versus physical contact tracing in a potential HIV
 1368 vaccine efficacy population of fishing communities around Lake Victoria, Uganda. BMC infectious diseases.
 1369 2018;18(1):591.

1370 Tuller DM, Bangsberg DR, Senkungu J, Ware NC, Emenyonu N, Weiser SD. Transportation costs impede
 1371 sustained adherence and access to HAART in a clinic population in southwestern Uganda: a qualitative
 1372 study. AIDS and behavior. 2010;14(4):778-84.

1373 Kasigeire S. Socio-Economic Conditions and retention of clients in HIV Care and Treatment at
 1374 Kagadi Hospital, Uganda. manuscript. 2014.

1375 Emenyonu N, Muyindike W, Habyarimana J, Pops-Eleches C, Thirumurthy H, Ragland K, et al.,
 1376 editors. Cash transfers to cover clinic transportation costs improve adherence and retention in care in a
 1377 HIV treatment program in rural Uganda. 17th Conference on retroviruses and opportunistic infections;
 1378 2010.

1379 Dillingham R, Ingersoll K, Flickinger TE, Waldman AL, Grabowski M, Laurence C, et al. PositiveLinks:
 1380 A Mobile Health Intervention for Retention in HIV Care and Clinical Outcomes with 12-Month Follow-Up.
 1381 AIDS patient care and STDs. 2018;32(6):241-50.

1382 Blaya JA, Fraser HS, Holt B. E-health technologies show promise in developing countries. Health
 1383 affairs. 2010;29(2):244-51.

1384 WHO. Electronic Health Records Manual For Developing Countries 2006.

1385 Morgan DL. Designing focus group research. Tools for primary care research. Research methods
 1386 for primary care, Vol. 2. Thousand Oaks, CA, US: Sage Publications, Inc; 1992. p. 177-93.

1387 Gill P, Stewart K, Treasure E, Chadwick B. Methods of data collection in qualitative research:
 1388 interviews and focus groups. British dental journal. 2008;204(6):291-5.

1389 OpenEpi. Sample Size for Cross-Sectional, Cohort, & Randomized Clinical Trial Studies 2019 [cited
 1390 2019 Oct 2]. Available from: <https://www.openepi.com/SampleSize/SSCohort.htm>.

1391 MoH. CONSOLIDATED GUIDELINES FOR PREVENTION AND TREATMENT OF HIV IN UGANDA. In:
1392 program Ac, editor. 2018.

1393 MoH U. Intergrated Health Care Services Package for HIV Prevention, Treatment and Care
1394 Servicea for Uganda. September 2014.

1395 Amith, M.; Loubser, PG.; Chapman, J.; Zoker, KC.; Rabelo Ferreira, FE. Optimization of an EHR mobile
1396 application using the UFuRT conceptual framework.. AMIA Annual Symposium proceedings /
1397 AMIA Symposium AMIA Symposium; 2012; p. 209-17.

1398 Luxton DD, Mishkind MC, Crumpton RM, Ayers TD, Mysliwiec V. Usability and feasibility of smartphone
1399 video capabilities for telehealth care in the U.S. military. Telemedicine journal and ehealth : the
1400 official journal of the American Telemedicine Association. 2012; 18(6):409–12. [PubMed:
1401 22650351]

1402 Burnay E, Cruz-Correia R, Jacinto T, Sousa AS, Fonseca J. Challenges of a mobile application for asthma
1403 and allergic rhinitis patient enablement-interface and synchronization. Telemedicine journal and
1404 e-health: the official journal of the American Telemedicine Association. 2013; 19(1): 13–8.
1405 [PubMed: 23215639]

1406 Sheehan B, Lee YJ, Rodriguez M, Tiase V, Schnall R. A Comparison of Usability Factors of Four Mobile
1407 Devices for Accessing Healthcare Information by Adolescents. Applied clinical informatics. 2012;
1408 3(4):356–66. [PubMed: 23227134]

1409 Sparkes J, Valaitis R, McKibbon A. A usability study of patients setting up a cardiac event loop recorder
1410 and BlackBerry gateway for remote monitoring at home. Telemedicine journal and ehealth : the
1411 official journal of the American Telemedicine Association. 2012; 18(6):484–90. [PubMed:
1412 22676379]

1413 Kim J et al. 2015) Journal of the International AIDS Society 2015, 18:20311
1414 [http://www.jiasociety.org/index.php/jias/article/](http://www.jiasociety.org/index.php/jias/article/view/20311) view/20311 |
1415 <http://dx.doi.org/10.7448/IAS.18.1.20311>)

Swahn et al, 2014. Mobile Phone Ownership and Usage among Youth. Western Journal of Emergency
Medicine, Volume XV, NO. 5 : August 2014

H. Anglada-Martinez, G. Riu-Viladoms, M. Martin-Conde, et al. 2015. Does mHealth increase adherence
to medication? Results of a systematic review. Int J Clin Pract, January 2015, 69, 1, 9–32. doi:
10.1111/ijcp.12

Figure1: Illustration of Call for life mHealth Tool Functions

Figure 2: Conceptual Framework **Figure3: Theoretical Framework**

Figure 4 Map of Uganda showing Kiryandongo District where study is taking place

The 3 study sites in

Figure 5: Study Schema

Outcome assessment at month 6 and 12

ART Adherence; Viral Suppression, Retention in care, Cost-evaluation analysis

Knowledge at baseline in comparison to endline

Supplementary Files

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