Mobile Phone Adherence Support for HIV Patients in Manila, Philippines

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LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

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Abstract

Title: Mobile Phone Adherence Support for HIV Patients in Manila, Philippines

Background: In the context of a rapidly accelerating HIV epidemic in the Philippines concentrated among men who have sex with men (MSM), behavioural interventions to support delivery of HIV care and treatment are needed. Mobile health (mHealth) interventions have potential to improve adherence to HIV medicines but have not been implemented or evaluated in this setting.

Methods: This thesis examines the development, implementation, and evaluation of a mobile phone intervention to support adherence to antiretroviral therapy for people living with HIV in Metro Manila, Philippines. The behavioural science-informed, user-informed approach to intervention development is described. A mixed methods process evaluation assesses the intervention's feasibility, acceptability, and fidelity of delivery. A prospective cohort study documents the adherence to antiretroviral therapy and demographic, behavioural, and clinical characteristics of the 462 participants.

Results: The intervention consisted of a menu of services (pill reminders, health tips, appointment reminders, and adherence feedback) that could be delivered by voice call or text message on the days and at times chosen by the user. Factors negatively associated with adherence were longer time on ART, inconsistent condom use, and substance use. Being in a relationship was positively associated with adherence to ART. While the intervention was acceptable, fidelity of delivery was poor due to technological challenges related to the telecommunications provider. Improved adherence over time was observed, with the proportion of patients taking more than 95% of their ART doses increasing from 78.6% at baseline to 90.3% at 48 weeks. Viral load suppression rates did not change significantly over the course of the study. Neither adherence nor viral load was associated with exposure to the intervention.

Conclusion: Evidence regarding the efficacy of mobile phone interventions to support adherence to ART remains mixed. Interventions to support Filipino MSM living with HIV should incorporate elements that focus on social support and harm reduction for substance use.

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I left the Philippines and relocated to South Africa in 2018, and while working full-time, it has been a challenge to get this thesis over the finish line. I am immensely grateful to my co-workers who encouraged me to stick with it, even when it meant they sometimes had to pick up my slack! Naomi Hill, Rutendo Bothma, Moya Mabitsi, and Helen Struthers have been steadfast in their support.

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Acronyms and abbreviations

Acronym	Meaning
AIDS	acquired immunodeficiency syndrome
aOR	adjusted odds ratio
ART	antiretroviral therapy
ARV	antiretroviral
BCT	behaviour change technique
BCW	Behaviour Change Wheel
BPO	business process outsourcing
CEEBIT	Continuous Evaluation of Evolving Behavioural Intervention Technologies
CNS	Central Nervous System
COM-B	capability, opportunity, motivation, behaviour
CrI	credible interval
DOH	Department of Health
DTMF	dual tone multi-frequency
EC2	elastic compute cloud
EFV	efavirenz
GBP	Great British Pound
GEE	generalised estimating equations
HARP	HIV/AIDS and ART Registry of the Philippines
HIV	human immunodeficiency virus
HPV	human papilloma virus
ICF	informed consent form
IHBSS	Integrated HIV Behavioural and Serologic Survey
IMB	Information–motivation–behavioural skills
IT	information technology
IVR	interactive voice response
IVRS	interactive voice response system
KAP	knowledge, attitudes, and practices
LGBT	Lesbian, Gay, Bisexual, Transgender
LOCF	last outcome carried forward
LPV/r	lopinavir/ritonavir
LSHTM	London School of Hygiene and Tropical Medicine
LTFU	lost to follow-up
mERA	mHealth evidence reporting and assessment
mHealth	mobile health
MNAR	missing not-at-random
MOTECH	Mobile Technology for Community Health
MSM	men who have sex with men
NNRTI	nonnucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
OHAT	Outpatient HIV and AIDS Treatment
OR	odds ratio
PCP	pneumocystis pneumonia
PhilHealth	Philippine Health Insurance Corporation

PHP	Philippine Peso
PI	Protease Inhibitor
PIN	personal identification number
PLHIV	people living with HIV
PMTCT	prevention of mother-to-child transmission
PrEP	pre-exposure prophylaxis
QOL	quality of life
RCT	randomised controlled trial
RDS	relational database service
RR	risk ratio
SD	standard deviation
SHIP	Sustained Health Initiatives of the Philippines
SMS	short message service
STD	sexually transmitted disease
STI	sexually transmitted infection
TAMA	Treatment Advice by Mobile Alerts
TB	tuberculosis
TGW	transgender women
TREAT Asia	Therapeutics, Research, Education, and AIDS Training Asia
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Office on Drugs and Crime
UPMREB	University of the Philippines Manila Research Ethics Board
UP-PGH/SAGIP	The STI/AIDS Guidance Intervention & Prevention Unit at the University of the Philippines - Philippine General Hospital
VAS	visual analogue scale
VL	viral load
VOIP	voice over internet protocol
WHO	World Health Organization
WHOQOL-HIV BREF	WHO quality of life HIV brief questionnaire

Chapter 1. Background

This thesis describes a prospective cohort study of patients at an HIV clinic in Metro Manila, Philippines who participated in the Connect for Life mobile phone adherence demonstration project, a mobile health (mHealth) intervention to support adherence to treatment for HIV (human immunodeficiency virus) treatment.

In this introductory chapter I describe the context of the HIV epidemic in the Philippines, review the evidence for and potential of mobile phone interventions to improve antiretroviral therapy (ART) adherence among HIV patients, outline the aims and objectives of this thesis, and describe the study setting and timelines.

1.1 The HIV epidemic in the Philippines

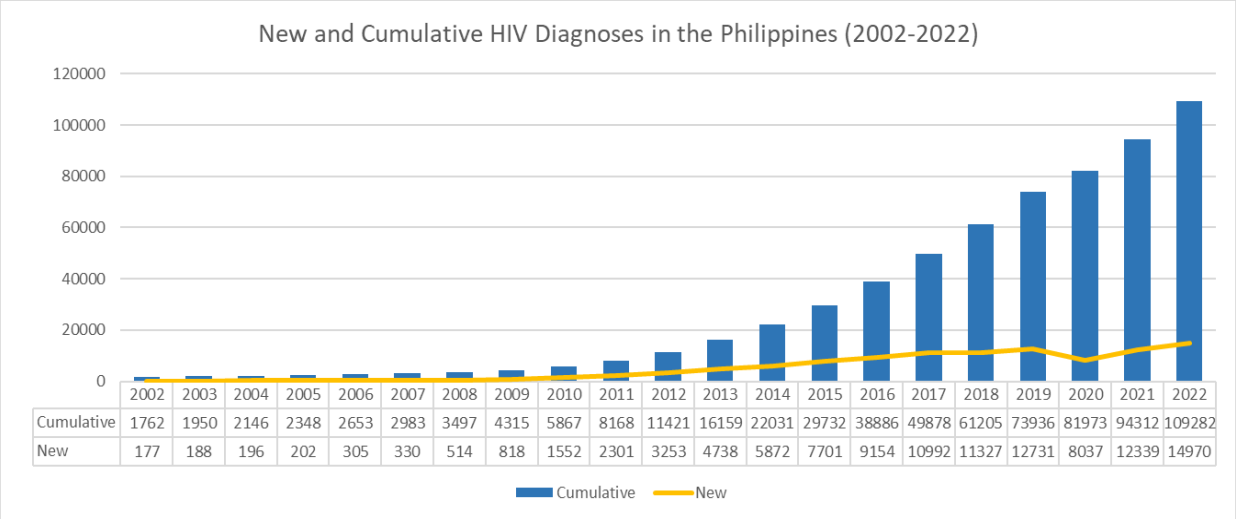
This section provides an overview of the epidemiology of HIV in the Philippines and a description of how the HIV epidemic has disproportionately affected specific key populations. I also summarise the literature that was available at the outset of this thesis when I conducted my early literature review in 2016, and the gaps in knowledge that were identified.

Overview HIV epidemic in the Philippines

HIV is a virus that attacks the body's immune system. HIV can be transmitted through exposure to the blood, semen, vaginal fluid, anal mucus or breast milk of a person living with HIV. Transmission most often occurs through anal or vaginal sex, through sharing needles, syringes, or other drug injection equipment, or from a mother to her baby during pregnancy, birth, or breastfeeding. If HIV is not treated, it can lead to AIDS (acquired immunodeficiency syndrome). There is currently no effective cure for HIV. With treatment, HIV can be controlled and people with HIV can live long, healthy lives and reduce the risk of transmission to others.(1)

The research in this thesis was conducted in the Philippines, a country of over 113 million people in Southeast Asia.(2) In May 2015, the World Health Organization (WHO) announced that the Philippines had one of the fastest-growing HIV epidemics in the world.(3–6) Between 2010 and 2021 the incidence of HIV increased by 380% from 0.05 cases per 1,000 uninfected population in 2010 to 0.19 cases in 2021, which is the second highest incidence in the Southeast Asia and Western Pacific region, following Papua New Guinea.(7) Incidence among men was more than 10 times higher than in women, at 0.36

and 0.03 new infections per 1,000 uninfected population per year, respectively.(7) The estimated number of people living with HIV in the Philippines reached 140,000 in 2021, and the cumulative number of people ever diagnosed with HIV in the Philippines reached 109,282 in December 2022 (**Figure 1**).(7,8)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Cumulative	1762	1950	2146	2348	2653	2983	3497	4315	5867	8168	11421	16159	22031	29732	38886	49878	61205	73936	81973	94312	109282
New	177	188	196	202	305	330	514	818	1552	2301	3253	4738	5872	7701	9154	10992	11327	12731	8037	12339	14970

Figure 1. HIV diagnoses in the Philippines.
Source: HIV/AIDS and ART Registry of the Philippines (HARP) Report December 2022

The Philippines has adopted the 90-90-90 United Nations targets in the Sixth AIDS Medium-Term Plan of the Philippine National AIDS Council and the Philippine HIV Health Sector Plan (2018-2020).(9,10) The Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets called for 90% of people living with HIV (PLHIV) knowing their status, 90% of people living with HIV who know their status being on ART, and 90% of people living with HIV on ART achieving viral suppression. In the Philippines, data published in 2021 indicate that 64% of PLHIV know their status, 41% of those who are HIV positive are on ART, and the proportion of people who have suppressed viral loads is unknown.(11,12) As of December 2022, the median age of new cases in the Philippines is 27 years old, and more than 79% of people newly diagnosed with HIV/AIDS in the Philippines are under 35.(8)

HIV prevention, testing, and treatment services in the Philippines have expanded in recent years, with the introduction of a pilot project for HIV pre-exposure prophylaxis (PrEP) starting in 2017. However, widespread stigma, lack of knowledge, and barriers to accessing care continue to pose challenges to engaging patients in services.(5,13–15). According to UNAIDS country data from 2020, 73.3% of all new diagnoses are late diagnoses (CD4 <350 copies/mm^3), indicating that patients are very immune compromised before seeking out or being offered testing services.(15) As in many lower- to middle-income countries, high rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence lead to poor outcomes for many HIV patients in the Philippines.(16,17)

ART can be accessed by PLHIV at more than 150 health facilities identified as Department of Health (DOH) designated treatment hubs and primary HIV care clinics across the country.(15) HIV care and treatment is freely available through the government-funded Outpatient HIV/AIDS Treatment (OHAT) package created by the Philippine Health Insurance Corporation (PhilHealth) in 2010.(18) OHAT pays up to 30,000 Philippine Pesos (478 GBP) per patient per year directly to the treatment hub where the PhilHealth member is registered.(19) This package covers ART medications, two CD4 count lab assays per year (an indicator of immune function), and one viral load assay per year (measures the amount of HIV in a blood sample). The patient must pay out of pocket for any medical expenses that are not included in the OHAT package.

Key Populations in the Philippines HIV epidemic

According to UNAIDS, the five main key population groups globally that are particularly vulnerable to HIV and frequently lack adequate access to services include: gay men and other men who have sex with men (MSM), sex workers, transgender people, people who inject drugs, and prisoners and other incarcerated people.(20) Globally, the risk of new infections faced by MSM has been increasing. UNAIDS data from 2021 show that MSM have 28 times the risk of acquiring HIV compared to people of the same age and gender identity, while people who inject drugs have 35 times the risk, sex workers have 30 times the risk, transgender women have 14 times the risk, and incarcerated people have five times the risk.(20)

In the Philippines, the predominant mode of HIV transmission has changed over time. Early in the HIV epidemic, most diagnoses were among heterosexual females, especially sex workers.(8) Beginning in 1991, more males than females were diagnosed with HIV, and in 2010 MSM transmission surpassed heterosexual transmission.(8,21)

Since 2010, incidence among gay men and other MSM increased by more than five times in the Philippines. Sex between males is the predominant mode of transmission of HIV in the Philippines, accounting for 82% of all new diagnoses.(8) There is an estimated HIV prevalence of 5% among the estimated 687,000 MSM in the Philippines.(20) The majority of MSM HIV infections (and HIV infections in general) occur in Metro Manila area, which includes Quezon City, the area with the highest documented HIV prevalence in the country (12%) among MSM and transgender women (TGW).(22)

HIV prevention, testing, and treatment do not reach the majority of MSM in the Philippines. According to UNAIDS 2020 data, less than 30% had accessed testing services in the prior 12 months, less than 15% had received combination HIV prevention interventions (i.e. received a free condom in the last 12

months and they know where they can go for an HIV test), and condom use at last sexual encounter was just 40%.(15)

Drivers of HIV incidence among MSM in the Philippines include number of sexual partners, drug and alcohol use during sex, low condom use, and infrequent HIV testing.(23–25) Results from the 2018 national Integrated HIV Behavioural and Serologic Survey (IHBSS) found that 56% of MSM and TGW respondents had at least three male sex partners in the past 12 months. In the past 12 months, 52% of MSM and TGW respondents had sex while drunk, of whom over half (52%) had sex without condoms. Meanwhile, 32.5% had attended a health facility for a sexually transmitted infection in the prior 12 months.(26) The MSM and TGW respondents were young, 87% under the age of 25, and were very active on social media, with 48% of respondents using online platforms (most commonly Facebook) to find sex partners.

HIV literacy was low; just 33% of the 2018 IHBSS respondents were aware there is treatment for HIV, and only 7.5% had heard of PrEP. Comprehensive knowledge of basic HIV prevention and transmission facts was below 50%. There were common misconceptions about HIV (i.e. that a person can get HIV from mosquito bites, using toilet bowls, and by sharing food with someone who has HIV), and respondents also had misconceptions about sex practices, such as the belief that withdrawal before ejaculation prevents HIV transmission (43%), and that taking the insertive role during anal sex has the greater risk for HIV (26%).

Sexualised Drug Use and the Philippines War on Drugs

Progress in the HIV response across the Southeast Asia region has been hampered by increases in certain higher risk behaviours, such as stimulant drug use.(20) Sexualised drug use, known as “chemsex” more broadly or as “Partee n Play” in the Philippines context, contributes to increased transmission of HIV and other STIs among MSM. This is due to the risk behaviours that accompany chemsex, including higher sex frequency, unprotected sex with multiple partners, group sex, inconsistent condom use, internal ejaculation, and less concern about HIV and sexually transmitted infection (STI) status. (27) Substance use may also negatively impact adherence to ART or PrEP.

The prevalence of sexualised drug use practices among MSM in Asia ranges from 3.1% to 30.8%, based on estimates from nine countries in the region.(27) High rates of amphetamine-type stimulant use have been reported amongst MSM in parts of Asia, including Indonesia (15.0%), Malaysia (23.9%), Thailand (32.0%), and China (13.3%).(28) The Philippines 2018 IHBSS found that 11% of MSM had used drugs in the prior year, with 70% of those men using methamphetamine (locally known as “shabu”).

Meanwhile, 3% of MSM disclosed that they had engaged in group sex and 2% had engaged in chemsex. Condom use during chemsex was just 23.8%. (26)

In the Philippines, the impact of sexualised drug use on the HIV epidemic is exacerbated by a punitive legal context, lack of clinical skills for substance use screening and harm reduction counselling, and high levels of stigma among health providers.

In line with regional trends, compulsory detention in the name of drug treatment has increased significantly in the Philippines, despite evidence documenting the financial and human costs of this punitive approach.(29) From 2012 to 2018, the number of detention centres increased from 37 to 60 and the number of people detained increased by more than 100% (from 2,744 to 5,447). In 2019, the occupancy rate in these rehabilitation facilities was 125% and the average length of detention was 10 months. (29)

Human rights groups expressed concerns about abuses and extrajudicial killings of people who use drugs during the Presidency of Rodrigo Duterte from 2016–2022. Various rights groups estimate that between 12,000 and 30,000 people were killed in President Duterte's "drug war."(30) The Philippine Drug Enforcement Agency figures record that, from 1 July 2016 to 31 May 2022, 6,252 people died during operations against illegal drugs, and 239,218 operations against illegal drugs were conducted with 345,216 people arrested.(31) The country's political climate remains tilted towards punitive approaches under President Ferdinand Marcos Jr., who is making efforts to restore the death penalty for drug offences.(32)

A systematic review of criminalisation of drug use by DeBeck et al found that in 80% of studies, criminalisation negatively affected HIV prevention and treatment.(33) In the Philippine context, it has been observed that interruption of HIV treatment is common among detainees, who were not able to access their medication for several days or weeks when placed under arrest during anti-illegal drug operations (such as raids of chemsex events).

While sexualised drug use increases transmission risk for HIV and other sexually transmitted infections, the multiple stigmas surrounding HIV, drug use, homosexuality, and sex with multiple partners often serve to prevent MSM from accessing HIV prevention, testing, and treatment services.(34,35) In 2017, a qualitative study found that experienced stigma and a lack of trust in health providers led PLHIV who use drugs to disengage from care.(36–38) A survey of 16 HIV care clinicians and 17 drug rehabilitation providers working in HIV treatment in the Philippines found that stigmatising attitudes were common, such as the belief that "people who use drugs are dangerous," or that "health care providers should report clients' illicit drug use to law enforcement authorities." (39)

HIV in the Philippines: Summarising the evidence

At the outset of this thesis in 2016 I conducted a literature search to understand the body of knowledge in the Philippines setting and to identify all relevant literature specific to HIV prevention, care, and treatment in the Philippines published in the preceding 20 years (excluding papers before 1996), which I have summarised below. I searched PubMed, Google Scholar, and Google for key words "Philippines", "HIV", "AIDS", and "antiretroviral therapy". I then used a snowball method, reviewing the bibliographies of relevant literature to identify other relevant titles. I also personally contacted colleagues in the field, including clinicians, academic colleagues, and government officials to request relevant publications, reports, and unpublished sources. Details of all relevant publications and reports identified are as follows:

Journal Articles: I identified a total of just 27 papers about HIV care and treatment in the Philippines published in academic journals between 1997 and 2016 (**Table 1**). Of the 27 papers identified, six were news, commentary, or editorial, while 21 were research articles. An additional 10 papers from the TREAT Asia consortium cohort include data from one clinical research site in the Philippines. However, in these articles, findings are reported aggregated at regional level and are not specific to the Philippines.

Until 2004, publications describe the slow pace of the spread of HIV in the Philippines. As the HIV epidemic accelerated in neighbouring countries like Thailand and Vietnam, the low incidence of HIV in the Philippines was described as a "mystery." From 2010, authors began to express concern regarding an accelerating HIV epidemic among MSM in the Philippines.

Table 1. Peer-reviewed journal articles identified in literature search.

Year	Author/Research Group	Topic of article
1997	Avelino	HIV Prevention Indicators in Quezon City, Philippines (40)
1999	Ismail	Sexually Transmitted Disease (STD) and Acquired Immunodeficiency Syndrome (AIDS) in South East Asia (41)
2000	Reid	Rapid assessment of drug use and HIV vulnerability in south-east and east Asia (42)
2001	Simbulan	High-risk behaviours and the prevalence of sexually transmitted diseases among women prisoners at the women state penitentiary in Metro Manila (43)
2003	Bosch	News: HIV mystery in the Philippines (44)
2004	Mateo	HIV/AIDS in the Philippines (45)
2006	Rojanapithayakorn	The 100% Condom Use Programme in Asia (46)
2006-2016	Morisky/Urada/ Withers/Chiao	**7 papers:** Socio-structural and behavioural risk factors associated with HIV among sex workers and trafficked people (47–53)

2009	Hernandez	Men-who-have-sex-with-other-males (MSM) in the Philippines – identities, sexualities and social mobilities: a formative assessment of HIV and AIDS vulnerabilities (23)
2010	Parry	News: Philippines faces expanding HIV epidemic, shows research (54)
2011-2013	Telan	**2 papers:** Sentinel surveillance, Possible HIV Transmission Modes Among At-Risk Groups (55,56)
2012	Yu	How are countries in the Western Pacific region tracking the HIV epidemic? Results from a 2011 survey of ministries of health (57)
2013	Ross	Commentary: HIV epidemic in men who have sex with men in Philippines (58)
2013	Lucea	The context of condom use among young adults in the Philippines: implications for HIV prevention (59)
2013	Gangcuangco	Prevalence and risk factors for HIV Infection among men having sex with men in Metro Manila, Philippines (60)
2014	Cheng	Same-Sex Behaviour and Health Indicators of Sexually Experienced Filipino Young Adults (61)
2015	Ross	Short Communication: The dire sexual health crisis among MSM in the Philippines: an exploding HIV epidemic in the absence of essential health services (25)
2015	Parry	News: Philippines records highest number of new HIV cases since 1984 (62)
2007-2015	TREAT Asia Cohort	**10 papers:** TREAT Asia regional cohort publications (17,63–71)
2015	Oyomopito	Risk group characteristics and viral transmission clusters in South-East Asian patients infected with human immunodeficiency virus-1 (HIV-1) circulating recombinant form (CRF) 01-AE and subtype B (72)
2016	The Lancet HIV Editors	Editorial: Philippine epidemic calls for urgent action on HIV (73)

Institutional Reports: The Philippines Department of Health (DOH), UNAIDS, and WHO routinely report surveillance data. Reports created by Department of Health were sometimes available online, and some were provided to me by DOH staff upon request; other reports were provided to me by colleagues in the field. These reports included four local demographic, health, or seroprevalence surveys, two reports by international agencies, monthly DOH surveillance/monitoring reports, and several other ad hoc reports and policy documents (**Table 2**).

Table 2. Institutional reports identified in literature search.

Year/Frequency	Institution	Description
Monthly	Philippines Department of Health	HIV/AIDS and ART Registry of the Philippines (HARP) Report (74)
2005	UNAIDS	Resource Needs for an Expanded Response To Aids in Low- and Middle-Income Countries (75)
2008	Philippine Statistics Authority	Philippines National Demographic and Health Survey 2008 (76)
2011	Philippines Department of Health	Philippine Estimates of the Most At-Risk Population and People Living with HIV 2011. (5)

2012	AIDS Society of the Philippines	The Global Fund Transitional Funding Mechanism proposal to Global Fund (77)
2013	Philippines Department of Health	2013 Integrated HIV Behavioural and Serologic Survey (IHBSS) Report (78)
2013	Philippine Health Insurance Corporation	An Assessment of the Outpatient HIV/AIDS Treatment Package Provided by the Philippine Health Insurance Corporation: A Discussion Paper(13)
2013	Philippine Statistics Authority	Philippines National Demographic and Health Survey 2013 (79)
2014	Philippines Department of Health	AIDS Epidemic Model Impact Modelling & Analysis Philippine Case Study Technical Report (80)
2014	UNAIDS	UNAIDS 2014 Global AIDS Response Progress Reporting Country Progress Report Philippines (6)
2015	Philippines Department of Health	2015 Integrated HIV Behavioural and Serologic Survey (IHBSS) Fact Sheets (81)
2016	WHO	WHO Western Pacific Regional Office Country Profile HIV/AIDS in the Philippines (82)
2016	National HIV/AIDS & STI Surveillance and Strategic Information Unit	Report: The Growing HIV Epidemic among Adolescents in the Philippines (83)

News/magazine Articles: The majority of journalistic coverage of the HIV epidemic in the Philippines was written by journalist Ana Santos, who wrote six feature articles under a grant from the Pulitzer Centre for Crisis Reporting.(3,84–98) These articles raised awareness of the accelerating rates of HIV in the Philippines with messages like "The Philippines largely dodged the AIDS crisis. That's changing." and "You Don't Have To Sleep Around To Get HIV." I also identified 10 news articles and podcasts published by the digital media company Rappler which also highlighted the growing epidemic as well as reporting on HIV/AIDS policy issues.(3,90–98)

Books: I identified one book, *AIDS in the Philippines*, published in 2009 and providing a broad overview of HIV/AIDS, relevant research, psychosocial aspects of HIV care, and the early response in the Philippines.(99)

Later publications: In 2018, a formal systematic review published by Restar et al identified a total of 29 HIV risk and prevention studies and 51 papers from the Philippines published from 1988–2018. Among the studies identified by Restar et al, most were focused on examining condom use-related outcomes and history of sexually transmitted infections, few had biomarkers for HIV, and none addressed biomedical HIV prevention strategies. (100)

In summary, the literature search at the outset of this thesis identified substantial gaps in knowledge in the context of a rapidly accelerating HIV epidemic in the Philippines. I identified only three published articles describing risk behaviours among MSM, the group most affected. There were no published

studies describing patterns of access to care among MSM or evaluating HIV prevention or care and treatment strategies.

1.2 Overview of health interventions delivered by mobile phone (mHealth)

Mobile phones as tools

As mobile phone technologies have become widespread in low- and middle-income countries, mobile phone interventions have become increasingly popular in the global health and development sectors as an inexpensive and efficient way to communicate with and deliver services to people.(101,102) The World Bank estimated that in 2021 there were 110 mobile phone subscriptions per 100 people globally and 107 subscriptions per 100 people in low- and middle-income countries.(103) In the Philippines, the mobile phone penetration rate is relatively high, increasing to 143 subscriptions per 100 people in 2021, from 110 in 2014.(103) When accounting for unique subscribers, 50% of the Philippines' population had mobile phones in 2014, increasing to 72% in 2021.(2,104,105) As wireless coverage is improving globally, mobile communications can be provided even in remote areas. In the Philippines, 99% of the population is reached by mobile cellular network coverage.(106)

Mobile phones are multi-functional tools that can be employed for a variety of uses that range from simple alarm functions, short message service (SMS), and telephone calls, to more complex applications (apps) and games. They allow for personalisation of message content, and can promote bidirectional communication.(107) People often carry their mobile devices with them wherever they go, so using mobile technologies allows the timing of intervention delivery to be synchronised with the most relevant time to claim the attention of the recipient.(108) This makes the mobile phone an ideal way to deliver ecological momentary interventions – treatments or services that are provided to people during their everyday lives (i.e. in real time) and in natural settings (i.e. real world).(109)

Mobile communication for health services (mHealth)

The provision of health services using mobile communications – mHealth – is a field with a growing body of evidence behind it that shows potential to improve health care services by reducing health workers workloads and decreasing the cost of health interventions.(102)

Early studies showed promise for successful application of mHealth interventions globally and across a wide variety of health issues. A 2010 systematic review of text message interventions by Cole-Lewis

et al (110) and a 2013 systematic review of mobile interventions by Free et al (108) included 12 studies and 26 randomised controlled trials (RCTs) respectively. Both reviews found that a majority of mHealth interventions for behaviour change and disease management had positive results, particularly for ART adherence among HIV patients and for smoking cessation. There was also potential for benefit in other areas including diabetes control, maternal health, and vaccination uptake.(108,110) Similar findings were shared in a 2016 systematic review that included 60 studies of text message reminders, which found that 77% of the interventions reported a positive outcome on either medication adherence, clinic attendance, or patient satisfaction.(111)

As most early mHealth studies were conducted in high-income countries, a 2014 systematic review of 44 mHealth interventions in Africa provided an important perspective on implementation in more resource-constrained settings.(112) The review found that mHealth interventions in Africa are feasible and acceptable. The success of individual interventions depends upon the accessibility, low cost of the technology, effective adaptation to local contexts, as well as strong stakeholder collaboration and government involvement. Threats such as unclear health care system responsibilities, unreliable telecommunications infrastructure, and lack of evidence on cost-effectiveness pose a challenge to mHealth projects in these settings.

While mHealth interventions have shown potential to improve health outcomes, the quality of evidence is limited by lack of scientific rigour in evaluation methodology. The studies in these early reviews tended to be pilot projects with small samples (most had less than 100 participants) and were underpowered to detect intervention effects. Many had a high risk of bias due to inability to conceal which participants received the intervention, incomplete outcome data, or lack of randomisation. Pilot projects were more likely to report positive outcomes than clinical trials.(112) Many studies have poor reproducibility of both the research methods and interventions (i.e. poor description of intervention content and implementation). (102,108,110–112)

What makes a successful mHealth intervention?

Research has documented evidence for which aspects of mHealth interventions make them more likely to achieve the desired behavioural outcomes: interventions that are informed by explicit behavioural theory,(108,110,113) targeting a specific population,(114) multi-faceted interventions (i.e. simple SMS interventions are generally not effective),(108) and interactivity and tailoring of messages.(110) Text messaging should not be considered a stand-alone model for behaviour change but rather a tool by which behaviour change methods can be delivered.(110)

1.3 mHealth for adherence to antiretroviral therapy (ART) for HIV

mHealth approaches can be used in many settings and for a variety of diseases and conditions. This thesis examines their application to HIV care and treatment, with a specific focus on adherence to ART.

Adherence to ART

WHO defines treatment adherence as "the extent to which a person's behaviour – taking medications, following a diet and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider."(115)

The efficacy of antiretroviral therapy for HIV treatment depends on patient adherence to a daily medication regimen. For ART, a high level of sustained adherence is essential to: (1) suppress viral replication and improve immunological and clinical outcomes; (2) decrease the risk of developing antiretroviral drug resistance; and (3) reduce the risk of transmitting HIV.(107,116)

Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence or lack of social support, presence of mental health disorders, and time on treatment.(17,113,117–120) In the Philippine context, issues of stigma and discrimination have also emerged as a major barrier to medication adherence.(86,93,121) In addition to these factors, people may choose to not take their medications because they have negative perceptions of treatment, feel unsatisfied with healthcare facilities, for financial reasons, or because they are trying to forget about HIV. (122,123)

It is often cited that ART adherence of ≥95% is required to prevent virologic failure. However, adherence levels as low as 80% to 90% may be adequate for viral suppression in patients taking newer antiretroviral drugs.(124) While adherence estimates vary widely between cohorts, globally, approximately 40% of patients report suboptimal adherence to ART.(118,124) In the regional TREAT Asia cohort (which includes a large site in the Philippines), 32% of 1,316 patients reported suboptimal adherence of <100% and 17% reported adherence <95% of ART doses taken in the last 30 days.(17)

Adherence to ART is measured in a variety of ways, most commonly: self-report (visual analogue scale, 3- or 4-day recall, 7-day recall), objective measures (i.e. pill count, pharmacy refill, electronic medication monitors), or biological endpoints (i.e. viral load suppression, CD4).

A systematic review and meta-analysis published by Kanters et al in 2017 assessed the full spectrum of interventions to improve adherence to ART.(125) The review included 85 trials of various ART

adherence interventions with a total of 16,721 participants, comparing each approach to standard of care. The interventions were grouped into the following categories: enhanced standard of care, telephone, SMS, behavioural skills training/medication adherence training, multimedia, cognitive behavioural therapy, treatment supporter, incentives, device reminders. The meta-analysis found that interventions that combined a treatment supporter plus a telephone component were the most efficacious at improving ART adherence (OR 6.74, 95% credible interval [CrI] 2.87-16.55), followed by cognitive behavioural therapy plus incentives (OR 2.42, CrI 0.51-12.83). The meta-analysis found that SMS interventions were superior to standard of care (OR 1.48, CrI 1.00-2.16), and that multiple interventions had additive affects.

The WHO Consolidated Guidelines on ART recommend using mHealth approaches to support HIV care and treatment and improve adherence. The 2013 guidelines stated that "Mobile phone text messages could be considered as a reminder tool for promoting adherence to ART as part of a package of adherence interventions (strong recommendation, moderate-quality evidence)."(116)

The second edition of these guidelines released in 2016 strengthened this recommendation, indicating that mobile phone text messages are low-cost interventions, have demonstrated benefit in improving adherence and viral suppression, and are backed by "moderate evidence."(126)

mHealth for ART adherence: Key studies

mHealth adherence interventions provide the user with communication (usually pill reminders, visit reminders, or health messages) via the following mechanisms:

- daily SMS messages,(127–129)
- weekly SMS messages, (128,130,131)
- automated voice messages, (132,133)
- telephone calls, (132,134,135)
- smartphone applications, (136,137) and
- combination interventions that include one of the above together with another approach (e.g. treatment supporter, non-financial incentives).(138,139)

Two important early examples of successful ART adherence interventions were implemented in Kenya. WelTel Kenya1 (published by Lester et al in 2010) was a multisite randomised clinical trial of adults living with HIV initiating ART. The study found adherence to ART (>95%) was reported by 62% (168/273) of participants receiving the SMS intervention compared with 50% (132/265) in the control group who received standard of care (relative risk [RR] for non-adherence 0.81, $P = 0.006$). Suppressed viral loads

were reported for 57% (156/273) of participants in the SMS group and 48% (128/265) in the control group, (RR for virologic failure 0.84, *P* = 0.04).(130)

It is important to note that the WelTel SMS intervention was not limited to simple one-directional SMS messages. The participants were asked to respond to each weekly SMS to indicate whether they were doing well, or if they had a problem. Participants who did not reply or who indicated they had a problem were then contacted by adherence counsellors within two days for follow-up.(130) The intensive counselling support was likely to have been a greater factor than the SMS messages themselves in the improved participant outcomes in the intervention group. However, this intervention may be difficult to replicate in settings with scarce human resources or funding limitations.

A second randomised trial in Kenya (published by Pop-Eleches et al in 2011) included 431 adult patients who had initiated ART in the three months prior to enrolment. The study compared no reminders (control), daily reminders, and weekly reminders, and also compared long and short messages. The study used simple one-way SMS reminders and MEMS caps to measure adherence. The study found that 53% of participants receiving weekly SMS reminders achieved adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group (*P* = 0.03). Participants in groups receiving weekly reminders were also significantly less likely to experience treatment interruptions exceeding 48 hours during the 48-week follow-up period than control group participants.(128) While there was no statistical evidence for a difference between control group and those receiving daily SMS reminders, less frequent weekly reminders were effective at increasing adherence.

Building on the foundations of these early mHealth ART adherence studies, recent trials have implemented more complex mHealth solutions on a larger scale in public health settings. A cluster RCT including 2,004 adults initiating ART in Mozambique provided a combination intervention strategy to improve linkage from HIV testing to ART initiation and 12-month retention. The trial compared standard of care to intervention arms consisting of a combination of SMS health tips and appointment reminders, accelerated ART initiation, and non-cash financial incentives for linkage and retention. The study found that the combination intervention increased the likelihood of linkage and retention ART at 12 months, with this outcome occurring in 35% (268/767) of participants in the standard-of-care group, 57% (425/744) of the combination-intervention group (RR = 1.58, 95% CI 1.05–2.39), and 55% (273/493) in the group with the intervention plus incentives (RR = 1.55, 95% CI 1.07–2.25). There was no difference between the arms with and without conditional financial incentives.(138) A similar combination intervention was studied in the Link4Health cluster RCT in neighbouring eSwatini with

similar results: 64% (705/1,096) of participants at the intervention sites achieved the primary outcome versus 43% (477/1,101) at the standard-of-care sites (RR 1.52, 95% CI 1.19–1.96).(140)

Of note, these key studies have focused on patients who were newly initiating ART rather than treatment-experienced patients who have been on ART for some time.

mHealth for ART Adherence: Summarising the evidence

Most relevant systematic reviews and meta-analyses (107,141–161)	**Most frequently cited articles** (127–132,134,137,139,162–171)
Sun, 2023	Lester, 2010
Mehra, 2021	Pop-Eleches, 2011
Demena, 2020	da Costa, 2012
Lee, 2020	Sabin, 2015
Nelson, 2020	Mbuagbaw, 2012
Duthely, 2020	Shet, 2014
Mills, 2019	Haberer, 2016
Shah, 2019	Hardy, 2011
Wang, 2019	Ingersoll, 2015
Amankwaa, 2018	Rodrigues, 2012
Quintana, 2018	Kalichman, 2011
Purnomo, 2018	Maduka, 2013
Daher, 2017	Orrell, 2015
Mayer, 2017	Ruan, 2017
Muessig, 2017	Huang, 2013
Anglada-Martinez, 2015	Lewis, 2013
Catalani, 2013	Perera, 2014
Chaiyachati, 2014	Simoni, 2009
Finitsis, 2013	Uzma, 2011
Mbuagbaw, 2013	
van Velthoven, 2013	
Horvath, 2012	

Figure 2. Summary of systematic reviews and meta-analyses on the topic of mHealth and HIV Adherence.

During my review of the literature, I identified more than 30 narrative reviews, systematic reviews and meta-analyses on the topic of mHealth interventions for HIV published in academic journals between 2010 and 2021. Among these, I found 22 reviews that included a specific focus on quantitative studies evaluating mHealth interventions to improve ART adherence, including pilot studies with cross-sectional analysis pre- and post-intervention, cohort studies, pilot RCTs, and full-scale RCTs. The 22 reviews referenced 97 individual publications, the most frequently cited of which are summarised in **Figure 2.**

The 2020 systematic review conducted by Demena et al is perhaps the most comprehensive review of high-quality studies evaluating mHealth interventions for ART adherence and retention in care. It included 27 studies, of which 85% were RCTs. Of these studies, 56% (15/27) reported positive and statistically significant (P≤0.05) impacts of mHealth on primary outcomes. While 48% (13/27) of studies found a positive and significant effect for adherence, only 12% (4/27) improved retention.(143) While mHealth interventions often result in improved adherence, other reviews have shown there is minimal evidence that these interventions improve other outcomes such as retention and virologic suppression.(125,150,154,172)

Several themes consistently emerged from the literature:

- Frequency and directionality of contact: Weekly contact tends to be more effective and more acceptable than daily contact. Interactive or bidirectional messages are generally more effective than one-way messages.(128,141,147)
- Combination interventions: Especially in low-resource settings, interventions that incorporate multiple strategies (e.g. SMS messages or mobile phone calls combined with social support, counselling, or incentives) are more likely to be effective.(125,149,151)
- Tailoring of messages: Incorporating bidirectional communication, personalised message content, and matching the message timing to dose schedule improved the effectiveness of interventions.(107)
- Durability of intervention effects: Very few studies followed participants for more than one year or continued to measure primary outcomes after the intervention had ended. Where information is available, it suggests that positive effects of mHealth interventions tend to wane over time. (125,173)
- Effect size: mHealth adherence interventions have small effects that require a large sample size, and studies are often underpowered to detect effect.(102,125)
- Methodological challenges: Risk of bias is high in many studies due to issues like lack of blinding, lack of random assignment, lack of control group, incomplete outcome measures, and use of self-reported outcome measures. Interventions change rapidly as technology evolves and are often not described sufficiently, leading to poor reproducibility and external validity of studies.(143,174)

In summary, a wide variety of mHealth approaches to improving adherence to ART have been applied, with high variability in trial results. There is a need to better understand the building blocks of an optimal mHealth intervention.

1.4 Study rationale

In the context of the emerging HIV crisis among MSM in the Philippines, there was an imperative to expand options for tailored HIV prevention and treatment support that respond to the specific needs of key populations.

At the inception of this thesis in 2016, there was some evidence to suggest that using an mHealth platform would be a good approach to HIV support care and treatment for MSM. Data suggested that MSM use new forms of technology at even higher rates than the general population, and significant numbers of MSM use apps and websites to meet sex partners.(114) While other studies had found high levels of feasibility and acceptability of SMS interventions targeted toward HIV-positive MSM in

the United States, in Peru, and in Asia,(175–178) there was a lack of data on interventions to improve adherence and treatment outcomes among HIV-positive MSM. Furthermore, few mHealth interventions for MSM had been evaluated in Asia and none in the Philippines. Research conducted in other settings may not be generalisable to the region since cultural context can affect the factors that influence health care-seeking and risk behaviours of MSM (such as support for others, and familial responsibility).(179)

Furthermore, I had identified that there were significant gaps in the published literature about the HIV epidemic in the Philippines, and that conducting a study describing a cohort of HIV-positive MSM in the Philippines would make an important contribution.

Through this thesis I aim to expand on the existing body of knowledge around HIV care and treatment in the Philippines, a topic about which very limited information is available in peer-reviewed, academic publications. The thesis also aims to add to the growing body of knowledge about mobile phone support interventions for HIV treatment adherence and the study we conducted was the first of its kind in the Philippines context.

1.5 Project narrative: Study setting, funding, and collaborations

Study Setting: This study was conducted at the Sustained Health Initiatives of the Philippines (SHIP) clinic, a low-cost private clinic that provides HIV treatment and comprehensive services in Mandaluyong City, Metro Manila, Philippines. Approximately 98% of SHIP's more than 900 clients are MSM, with an average age of 30 years at the initial consultation. Most are employed full-time or part-time. The patients come from all regions of Metro Manila, and some live outside of Metro Manila in other provinces.

The clinic was opened in 2012 by Dr Katerina Leyritana, and in 2014 SHIP registered as a non-profit organisation. I was the non-profit's Executive Director, and from 2014 through 2018 I was responsible for oversight of all of SHIP's programmes and operations. SHIP's Medical Director, Dr Leyritana, remained responsible for oversight of clinical care. Between 2012 and 2018, SHIP was a satellite partner clinic of the Sexually Transmitted Infection/AIDS Guidance Intervention and Prevention Unit at the Philippine General Hospital, the largest public hospital in the country. In 2018, SHIP became an independent treatment hub.

Project inception: The idea of using an mHealth platform to support patient adherence to ART came from Dr Leyritana, who contacted Jannsen after reading an online article about a pilot of the Connect for Life mHealth platform developed by the company's Global Public Health team. This initial contact led to a rich collaboration between SHIP and Janssen to adapt the Connect for Life platform to the Philippine context and to conduct a demonstration project and evaluate its implementation and impact.

Connect for Life is a technology platform created by Johnson & Johnson/Janssen Global Public Health and built on the Mobile Technology for Community Health (MOTECH) open-source software platform.(180)

From March to October 2016, Dr Leyritana and I worked closely with colleagues from the Janssen Global Public Health team (Dr Randeep Gill, Paula McKenna, Piet Knaepen) to adapt the Connect for Life platform to the Philippine setting. The intervention development process is described in Chapter 2 of this thesis.

During this period, I developed the evaluation protocol, standard operating procedures, and data collection tools, and I hired and trained a study coordinator. The protocol involved three co-investigators: 1) Dr Edsel Salvaña, an infectious disease expert from UP Manila and close collaborator of SHIP clinic, joined the project as co-Principal Investigator in May 2016, providing mentorship as well as technical input on the protocol design; 2) Dr Leyritana, Medical Director of SHIP clinic, led the clinical care for study participants; 3) Dr James Lewis from the London School of Hygiene and Tropical Medicine (LSHTM) joined the project as co-investigator and as supervisor for this PhD. I enrolled at LSHTM in September 2016 and completed upgrading in October 2016.

Researcher Positionality: Positionality refers to a researcher's world view and the position that they adopt within a given research study and its social and political context. The individual world view or 'where the researcher is coming from' is shaped by their values and beliefs, political views, religion, gender, sexuality, location, race, and social class and status, education, abilities, and so on.(181,182) Researcher positionality concerns a researcher's ontological and epistemological assumptions (assumptions about what can be known and how we can learn/know it) as well as assumptions about how we interact with and relate to our environment. Positionality influences how research is conducted, its outcomes, and results.(181,182) I came to this research as a public health professional with experience implementing health programmes and conducting clinical and operational research in Southeast Asia, Southern Africa, and the United States. Due to my academic and professional background, I had a specific interest in conducting research aimed at improving the delivery of HIV

care and treatment. Some of the more fixed aspects of my positionality included my gender, race, nationality, sexual orientation, and age: cisgender female, white, American, heterosexual, in my 30's. These factors positioned me as an "outsider" in relation to the research participants, who were predominantly young Filipino bisexual and homosexual cisgender men. This positionality, as well as the positionality of various co-investigators and research staff, created both opportunities and barriers in the research process which are described in the thesis (Chapters 2 and 7).

Study funding: Janssen provided the Connect for Life platform to SHIP as a free licence and funded the project implementation from June 2016 to April 2019 (approximately 320,000 GBP). When working with any study sponsor, a researcher must address actual and perceived conflicts of interest. In this case, Janssen was involved in various aspects of the intervention design and delivery, study design, and dissemination of results, as described below.

- **Technology platform**: Janssen developed the technology and donated the license for the Connect for Life application. As such, Janssen developers determined which technical adaptations were or were not technically feasible. Janssen staff provided technical expertise on implementation, assisting us to identify appropriate local service providers for hosting the solutions, telecommunications, and IT support, and they provided training to local IT support providers.
- **Intervention delivery**: Janssen funded the costs of implementation of Connect for Life including staff, cloud hosting of the application, and IT support. Budget limitations of the project influenced the scope of the intervention. For example, due to budget limitations there was insufficient funding for an intervention that included incoming phone calls on a zero-rated platform, and the sponsorship agreement did not provide sufficient funding for services beyond the delivery of the mHealth platform (and thereby precluded combination interventions).
- **Study design**: a stipulation of the sponsorship agreement was that the evaluation must be an observational study and not a randomised controlled trial, as a trial would have been required to undergo extensive regulatory and scientific approval processes within Janssen which were beyond the intended scope of the sponsorship agreement. Other than this stipulation that the evaluation must use an observational study design, Jannsen was not directly involved in the development of the evaluation design, and I wrote the study protocol independently.
- **Data analysis**: Jannsen did not fund the data analysis and evaluation process. I independently conducted data analysis, writing, and dissemination activities as part of my PhD, without financial support from Janssen. Janssen did not have authority over the investigators' right to

examine data independently or publish our findings. While a pharmaceutical sponsor may have an inherent bias toward dissemination of positive findings, the published evaluation included in this thesis presents both favourable and unfavourable findings about the intervention.

- **Authorship**: Janssen sponsored the subsequent open-source publication fees for three of the four published articles included in this thesis (approximately 7,000 GBP). The project lead from Jannsen, Dr. Randeep Gill, was included as a co-author in several of the articles due to his substantial contribution to the conception and implementation of the project and his editorial contributions on the manuscripts.

Project implementation and evaluation: Recruitment of study participants began in October 2016 and continued until December 2017. Follow-up continued until the final study participant completed the study in December 2018.

In January 2018 I relocated from the Philippines to South Africa. I maintained my oversight role as the co-principal investigator of the study, holding frequent virtual meetings with the study coordinator and the co-investigators in the Philippines. After the final participant completed the study in December 2018, the study coordinator continued supporting the project until August 2020, assisting with study close-out, data cleaning and data quality checks, communication with the local ethics committee, as well as supporting the continuity of patient care in the SHIP clinic and the continued implementation of the Connect for Life platform post-study.

From January 2019 until mid-2023, I conducted qualitative and quantitative analyses, prepared manuscripts for publication, and wrote up this PhD thesis. During this period, I was enrolled at LSHTM as a part-time distance learning student (self-funding) while working full-time at the Wits Reproductive Health and Research Unit (2019–2021) and later at the Anova Health Institute (2021–2023). Both employers were generous in granting study leave and flexibility for me to continue my work towards the PhD.

1.6 Aims and objectives of the thesis

The aim of this doctoral research was to adapt an interactive voice response (IVR) mobile phone platform called Connect for Life to create an intervention suited to the needs of our patient population in the study site and to the local Philippine context, and then implement and evaluate the intervention. To achieve this aim, I set out to fulfil two distinct objectives:

Objective 1: Planning and Development. Create a locally tailored intervention using a mobile phone adherence platform for HIV patients on ART at the SHIP clinic in Metro Manila, Philippines.

Objective 2: Implementation and Evaluation. Conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to assess participant adherence, retention, and treatment outcomes at baseline and over follow-up.

1.7 Ethics

Ethical clearance was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016–265–01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All patients provided written consent before inclusion in the study. Refer to ethics letters in **Appendices 1 and 2.**

1.8 Thesis structure

This research paper-style thesis contains seven chapters including this chapter. The chapters follow a logical sequence starting with literature review and description of context, followed by intervention development process, evaluation methodology, description of the cohort, process evaluation, outcome evaluation, and discussion. Four of the seven chapters are research papers which have been published or submitted for publication in scientific journals. These are presented exactly as they were published/submitted, and the only differences between the chapters and the published research papers are related to formatting (i.e. sequential numbering of tables and figures) and language conventions (i.e. US vs. UK spelling). As several of these papers were worked on simultaneously, the timing of publication of the papers is slightly different than the order in which they are presented here.

Chapter 1: Background – This introductory chapter presents a background to the context of the HIV epidemic in the Philippines, the literature on ART adherence and mHealth, the aims and objectives of the thesis, and a narrative describing the study setting, funding, and collaborations.

Chapter 2: Intervention Development – This chapter is a published research paper describing the mixed methods approach used to adapt the mHealth adherence support platform for the local setting and target population. (183)

Chapter 3: Methods – This chapter describes the observational cohort study protocol and the evaluation methods.

Chapter 4: Baseline characteristics of cohort – This chapter is a published research paper describing baseline characteristics of study participants including: sociodemographic factors, knowledge/attitudes/practices, Quality of Life as measured by the WHO quality of life HIV brief questionnaire (WHOQOL-HIV BREF), clinical characteristics, and adherence to ART. (184)

Chapter 5: Process Evaluation – This chapter is a published research paper that includes findings from the mixed methods process evaluation of the Connect for Life project. The paper includes structured observations to assess feasibility and acceptability of the intervention collected via questionnaires, routine project reports, and qualitative methods. The paper also analyses Connect for Life platform reports to quantify intervention delivery and participant usage. (185)

Chapter 6: Outcomes – This chapter is a research paper (submitted for publication, under review) which presents findings from the observational cohort study describing adherence, viral load suppression, retention in care, treatment failure and mortality, and changes in knowledge and quality of life. This paper details the associations between the key outcomes and various demographic, clinical, and behavioural factors as well as the level of exposure to the mHealth adherence support intervention.

Chapter 7: Discussion – This chapter summarises the main findings and contributions of the thesis, discusses challenges of the evaluation and the relevant methodological considerations, describes the strengths and limitations of the intervention delivered and the implications for practice.

Chapter 2: Intervention development

This chapter presents the intervention development process that was conducted in 2015-2016 to create a locally tailored intervention based on a pre-existing mobile phone adherence platform. It describes: the formative research conducted to understand adherence behaviours of patients on ART at the SHIP clinic in Metro Manila, Philippines; the mixed methods approach to adapting the technology intervention to the local context; the application of behavioural theory/models to the intervention, and; the findings of early stages of pilot testing. This relates how Objective 1 of the doctoral research (planning and development) was achieved.

This chapter is adapted from a research paper that was published in *JMIR Formative Research* as an open access article in February 2022.(183) Chronologically, this was the second of four papers published. The chapter that follows differs from the published work due to the addition of a sub-section describing the intervention theory of change in greater detail, the addition of Table 6 (Health tips topics) and Table 7 (Behavioural determinants and intervention behaviour change techniques), the addition of description of the clinician-facing aspects of the intervention in Table 5, and several minor edits to wording and use of acronyms.

Citation: O'Connor C, Leyritana K, Doyle AM, Lewis JJ, Gill R, Salvaña EM. Interactive Mobile Phone HIV Adherence Support for Men Who Have Sex With Men in the Philippines Connect for Life Study: Mixed Methods Approach to Intervention Development and Pilot Testing. JMIR Form Res [Internet]. 2022 Feb 3;6(2):e30811.

Available from: https://formative.jmir.org/2022/2/e30811

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	LSH1512747	**Title**	Ms
First Name(s)		Cara Emily	
Surname/Family Name		O'Connor	
Thesis Title		Mobile Phone Adherence Support for HIV Patients in Manila, Philippines	
Primary Supervisor		Dr Aoife Doyle	

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?		JMIR Formative Research	
When was the work published?		3 February 2022	
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion		n/a	
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	n/a
Please list the paper's authors in the intended authorship order:	n/a
Stage of publication	n/a

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the principal investigator of the study, wrote the protocol, supervised data collection, conducted data analysis, and was responsible for writing this manuscript. Co-authors contributed to study design, provided technical advice on data analysis, and provided editorial input on the manuscript.

SECTION E

Student Signature	[redacted]
Date	12/06/2023

Supervisor Signature	[redacted]
Date	07 Jun 23

2.0 Research Paper: Interactive mobile phone HIV adherence support for men who have sex with men in the Philippines: intervention development and pilot testing in the Philippines Connect for Life Study

2.1 Abstract

Background: The Philippines HIV epidemic is one of the fastest growing epidemics globally, and infections among men who have sex with men are rising at an alarming rate. The World Health Organization recommends the use of mobile health (mHealth) technologies to engage patients in care and ensure high levels of adherence to antiretroviral therapy (ART). Existing mHealth interventions can be adapted and tailored to the context and population served.

Objective: This study aims to create a locally tailored intervention using a mobile phone platform to support treatment adherence for HIV patients on ART in the Philippines.

Methods: A mixed methods approach guided by the Behaviour Change Wheel framework was used to adapt an existing mHealth adherence support platform for the local setting and target population. A literature review, retrospective clinical record review, and focus group discussions with patients were conducted to understand the drivers of ART adherence and tailor the intervention accordingly. The resulting intervention was pilot tested for eight weeks, followed by focus group discussions with patients who received the intervention to assess the acceptability of the design.

Results: Key issues contributing to nonadherence included side effects, lack of behavioural skills for pill taking, social support, mental health, and substance use. Patients identified mHealth as an acceptable mode of intervention delivery and wanted mHealth services to be highly personalisable. The study team, clinicians, and software developers integrated these findings into the intervention, which included a menu of services as follows: pill reminders, health tips, adherence feedback, appointment reminders, and symptom reporting. During the pilot phase, technical issues in the interactive voice response system (IVRS) were identified and addressed. Patients who participated in the pilot phase expressed a preference for SMS text messaging over the IVRS. Patients responded positively to the appointment reminders and health tips, whereas patient feedback on daily and weekly pill reminders and adherence feedback was mixed.

Conclusions: The mobile phone-based SMS text messaging and IVRS intervention was acceptable to men who have sex with men in Manila, Philippines, and qualitative analysis suggested that the intervention helped promote ART adherence and appointment attendance.

2.2 Introduction

HIV on the rise in the Philippines

The Philippines has the fastest growing HIV/AIDS epidemic in the Asia-Pacific region.(3,121,186) National surveillance data show that the number of new HIV cases in the Philippines has risen at an alarming rate during the past decade, with an increase from 311 cases identified in 2007 to 12,778 cases identified in 2019 – a 41-fold increase in new HIV diagnoses.(187) According to the surveillance reports by the Joint United Nations Program on HIV/AIDS, the Philippines' progress toward reaching HIV/AIDS 90-90-90 goals has been slow, with 73% of people living with HIV being aware of their status, 44% on treatment, and low coverage of viral load testing (<50%).(188,189)

The group most impacted by HIV in the Philippines is men who have sex with men (MSM), representing 84% of new diagnoses since 2015. The median age of new cases is 28 years, and >80% of people living with HIV/AIDS in the Philippines are <35.(187,190) In 2015, a national surveillance survey found that HIV prevalence among MSM who practice anal sex was 6%, an increase from 3.3% in 2013.(6,14,81,187–189)

As the prevalence and incidence of HIV increase, it is imperative that as many people living with HIV as possible are diagnosed, started on treatment, and successfully retained in care. Achieving adequate viral suppression through the use of antiretroviral therapy (ART) will be one of the key tools in ending the HIV epidemic in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and then ensuring high levels of adherence to ART and retention in care.(6,14,191) As in many low- and middle-income countries, high rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence lead to poor outcomes for many HIV patients in the Philippines.(16,17)

Evidence-based public health interventions are needed. However, a 2015 report by the World Health Organization highlights that the body of HIV research conducted in the Philippines has been limited,(192) and a systematic review of the HIV risk studies in the Philippines through April 2018 found only three publications that included data about the group most affected by HIV – MSM.(100)

Mobile health for adherence

As mobile phone technologies have become widespread in low- and middle-income countries, mobile phone interventions have become increasingly popular in the global health and development sectors as an inexpensive and efficient way to communicate with and deliver services to people.

Mobile phones are multi-functional tools that can be employed for a variety of uses that range from simple alarm functions, short message service (SMS), calls, interactive voice response systems (IVRSs), and complex apps and games. People usually have their mobile devices with them, so using mobile technologies allows the timing of the intervention delivery to be synchronised with the most relevant time to claim the attention of the recipient.(108) Moreover, mobile phones can be used almost anywhere. As wireless coverage is improving globally, mobile communications can be provided even in remote areas.

In the Philippines, 99% of the population is reached by mobile cellular network coverage, and mobile phone use is among the highest in the world, with 155 mobile connections per 100 people.(193,194) Although the coverage of mobile networks is high, smartphone coverage and mobile internet (Long-Term Evolution) speeds are lower in the Philippines than in other countries in the region,(195) which limits the potential reach of mobile internet and app-based solutions.

The 2016 WHO Consolidated Guidelines on the Use of ART for the Treatment and Prevention of HIV Infection promoted the use of SMS text messaging to improve adherence to therapy.(196) Research has shown that mobile health (mHealth) interventions have potential benefits for a wide variety of health issues, including antiretroviral adherence, smoking cessation, diabetes control, maternal health, and vaccination programs.(108,125)

Mobile phone interventions have proven successful in improving ART adherence in Africa, South Asia, and Latin America.(107,113,129,130,159,197,198) Several systematic reviews have been published about mHealth for ART adherence specifically.(161,199) A variety of mHealth approaches to improving adherence to antiretroviral medications have been studied globally, these include daily and/or weekly short text messages,(127,128,130,200) weekly long text messages,(128) weekly voice messages,(132) and fortnightly phone calls.(134,135) The outcome measures of ART adherence interventions vary; outcome measures include self-reported adherence, objective measures of adherence (i.e. pill count, pharmacy refill, and medication monitors), biological end points (i.e. viral load suppression), and quality-of-life measures.

In Kenya, two important examples of successful ART adherence interventions were implemented. At the WelTel Kenya1 multisite randomised clinical trial of adults living with HIV initiating antiretroviral

therapy (ART) adherence to ART was reported in 61.5% (168/273) of patients receiving the SMS text messaging intervention compared with 49.8% (132/265) of patients in the control group (relative risk for non-adherence 0.81; *P* = .006). Suppressed viral loads were reported in 57.1% (156/273) of patients in the SMS text messaging group and 48.3% (128/265) of patients in the control group (relative risk for virologic failure 0.84; *P* = .04).(130)

Another randomised trial of 131 adult patients who had initiated ART less than three months before enrolment found that 53% of participants receiving weekly SMS reminders achieved adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group (*P* = 0.03). Participants in groups receiving weekly reminders were also significantly less likely to experience treatment interruptions exceeding 48 hours during the 48-week follow-up period than participants.(128)

Multiple reviews of the literature on adherence programmes suggest that mobile phones are a feasible, acceptable, and effective mode of delivery for HIV interventions targeting young MSM.(175–178) There is also evidence that daily reminders can support habit forming over 2-3 months and that weekly reminders effectively support adherence.(107,161,197,201,202) It is not clear whether improvements in adherence are sustained if reminders are stopped once a habit is formed. Some evidence suggests that weekly messages with interactive elements that elicit a response from the user may be the most effective SMS text messaging adherence interventions, but many questions remain unanswered.(107,159)

Aim and objective

The investigators aim to create a locally tailored intervention using a mobile phone platform to support treatment adherence for HIV patients on ART at the study clinic in Metro Manila, Philippines.

The objective of the formative research phase of the study was to adapt an existing technology platform (Connect for Life) for the local context. We sought to answer the questions:

- What is the level of adherence in the study clinic population and similar populations in the country and region?
- What are the barriers and determinants of ART adherence among the study clinic population?
- What components should an mHealth intervention include to address these barriers and determinants?

2.3 Methods

Setting

The Sustained Health Initiatives of the Philippines (SHIP) Clinic is a public–private partnership that opened in 2012. It is a low-cost, private facility Metro Manila, a city of approximately 13 million people in the predominantly Catholic country of the Philippines and the most densely populated city in the world. As of April 2021, the SHIP clinic provided HIV primary care and wraparound services to approximately 900 patients. Between 2012 and 2018, SHIP was a satellite partner clinic of the Sexually Transmitted Infection/AIDS Guidance Intervention and Prevention Unit at the Philippine General Hospital, the largest public hospital in the country.

Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at initial consultation. Most are employed full- or part-time. The patients come from all regions of Metro Manila and some live outside of Metro Manila in other provinces. SHIP currently enrols approximately four new patients each month.

Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All patients provided written consent before inclusion in the study.

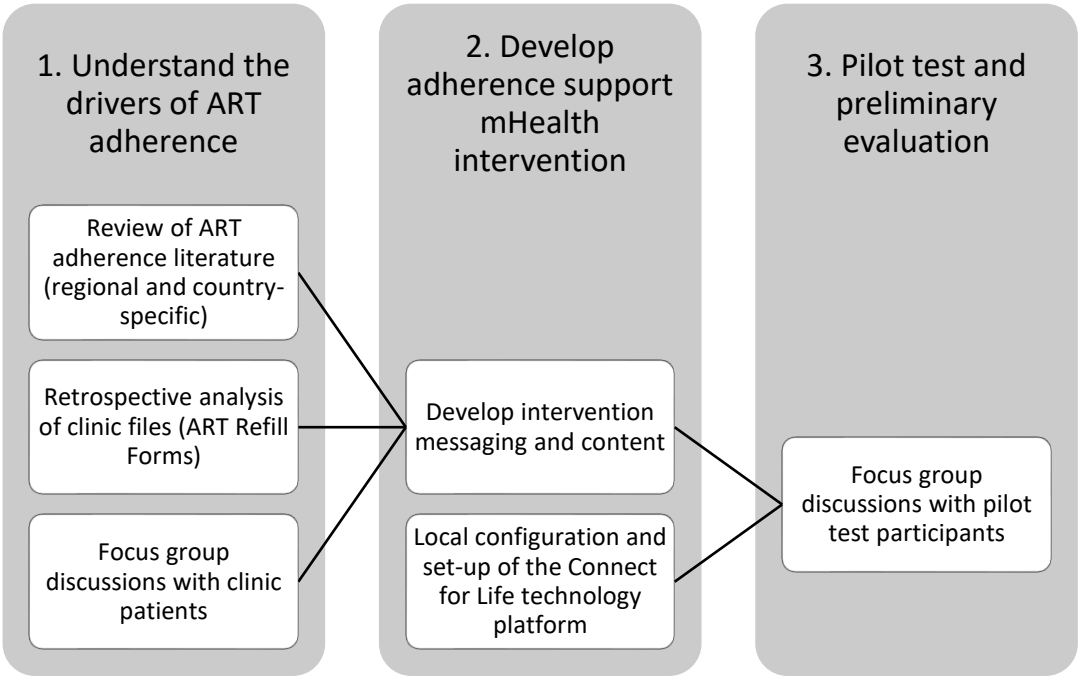
Intervention development approach

Overview

To determine the best configuration of mobile phone support services for patients in the study site, we used the following methodology (**Figure 3**):

1. Formative research to understand the drivers of ART adherence: Literature review of factors associated with ART adherence (global, regional, and country-specific data), retrospective analysis of clinic files (ART refill forms), and focus group discussions with patients in the SHIP clinic.
2. Development of mHealth intervention: We adapted an existing mHealth adherence support platform, tailored it to the setting and target population, and pilot-tested the platform, guided by the Behaviour Change Wheel (BCW) approach.
3. Pilot test and preliminary evaluation: We piloted the intervention with a subset of clinic patients for eight weeks and then conducted focus group discussions with patients who received the intervention in the pilot phase.

Figure 3. Intervention development process.



Formative Research: Understand the drivers of ART adherence

Review of ART adherence literature: A literature review of regional, country-specific, and site-level routine clinical data on ART adherence was conducted by investigators. The literature provided point estimates for adherence that could serve as comparison with our study population and outline some of the main facilitators and barriers to adherence in the Philippines context.

Retrospective analysis of clinic files: A record review of all pharmacy refill forms from the study clinic was conducted. Data were captured from 3,381 pharmacy refill forms for 682 patients collected during routine clinical care between May 2012 and August 2016. The pharmacy refill forms included basic demographic information, dispensing data, pill count, and self-report of number of doses missed in the past 30 days. Data quality for these forms was poor, with missing forms, fields left blank, and inconsistent/conflicting data in a large proportion of records. Owing to these limitations in data quality, only the most recent refill form for each patient was included in the analysis, as data were much more complete in the recent forms. The estimate of adherence was calculated as follows:

Adherence percentage = 1- (number of pills reported missed since last visit/number of pills dispensed at last visit).

Focus group discussions with clinic patients: During the formative research stage, the study team conducted focus group discussions to explore adherence challenges and possible approaches to

support adherence. The specific topics covered during the discussions were adherence challenges, use of mobile phones, attitudes towards receiving adherence reminders, priority health education topics for mHealth tips, and acceptability of receiving an adherence score as a feedback mechanism.

Focus group participants were recruited through convenience sampling of clinic patients as identified by the SHIP clinic physician. Patients were eligible to participate if they were ≥18 years, HIV-positive and on ART at the SHIP clinic, and willing to participate in a group discussion setting. Privacy around HIV-positive status was the biggest barrier to recruitment, and only patients who were publicly open about their HIV-positive status participated in focus group discussions.

Each focus group was facilitated by a qualified HIV test counsellor who was experienced in qualitative methods. A second staff member took detailed notes throughout the session, and immediately after the discussion, the notetaker and facilitator debriefed and recorded their initial observations. The focus group discussions were conducted in a mix of English and Filipino, which is common in Metro Manila. The discussions were held in a hired conference room located in the building next to the SHIP clinic, selected for the convenience of the participants. Before the discussion, the participants completed the informed consent process and provided demographic data and ART adherence data using a short questionnaire. The discussions were audio recorded on two devices, and the discussions ranged from 60 to 105 minutes. Individual debriefing and counselling by a trained counsellor was available to any participant following the groups if needed.

The focus group discussions were transcribed, and a framework-guided rapid analysis was conducted. Transcripts were manually coded using a deductive coding methodology in which initial coding grouped responses into overarching themes as per the topic areas included in the focus group discussion guide. Following initial coding, line-by-line coding assigned sub-themes. Qualitative data were consolidated in a structured template based on the a priori research questions. The template enabled consolidation of data into matrices by each category to identify salient themes.

Develop adherence support mHealth intervention

Develop intervention messaging and content: The intervention development process was broadly guided by the Behaviour Change Wheel (BCW) developed by Michie et al.(203–205) Behaviour change techniques (BCTs) related specifically to ART adherence were informed by the information–motivation–behavioural skills (IMB) model of ART adherence.(206)

The BCW is a method for characterizing and developing behaviour change interventions based on a comprehensive causal analysis of behaviour (**Figure 4**).(205) In the BCW approach, the intervention design process consists of three stages.

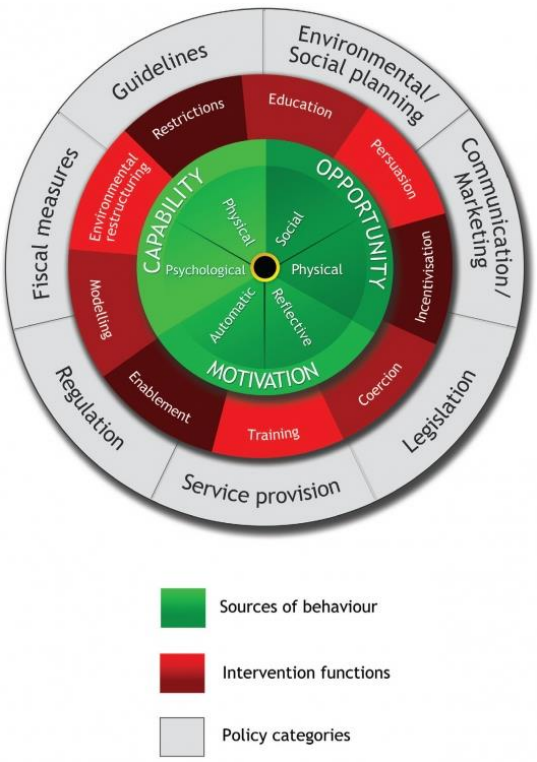


Figure 4. The Behaviour Change Wheel.

The first stage of intervention development is to understand the behaviour. In this case the specific target behaviour is optimal adherence to ART, defined as taking at least 95% of prescribed ART doses on time. To understand behaviour, the BCW approach starts with the question: *'What conditions internal to individuals and in their social and physical environment need to be in place for a specific behavioural target to be achieved?'* On the basis of the formative research findings, the components of capability, opportunity, and motivation that interact to account for behaviour were summarised.(203–205) Using the capability, opportunity, motivation, behaviour (COM-B) model, we aimed to understand the challenges faced by patients and identify opportunities to address specific behaviours through the provision of BCTs.

The second stage of intervention development in the BCW model is to identify the intervention options. In this case, we planned to use an mHealth platform that would be tailored to the setting and population.

The third stage is to identify the content and implementation options, including BCTs and mode of delivery. To better understand the most appropriate BCTs, we referenced the BCW taxonomy of BCTs

(207) and IMB skills model of ART adherence (**Figure 5**).(206) IMB is a useful behavioural theory for exploring factors that lead to adherence and is supported by robust evidence.(206,208,209) It posits that adherence-related information, motivation, and behavioural skills are the fundamental determinants of adherence to ART. The model's mediational assumption asserts that ART adherence information and motivation generally work through ART adherence behavioural skills to affect adherence behaviour. We used the IMB skills model to identify the aspects of motivation, information, and behavioural skills that our intervention might target.

The intervention services were tailored based on input from the IMB skills model, input by SHIP patients during focus group discussions, and information from clinical service providers at the study site. The study team and clinicians worked together to write 171 health tips, script the reminder messages, and map the call flows. The lead clinic physician created a symptom-reporting algorithm. A local voice talent agency was engaged to record the content. **Figure 6** provides examples of tips in each of the health tip categories.

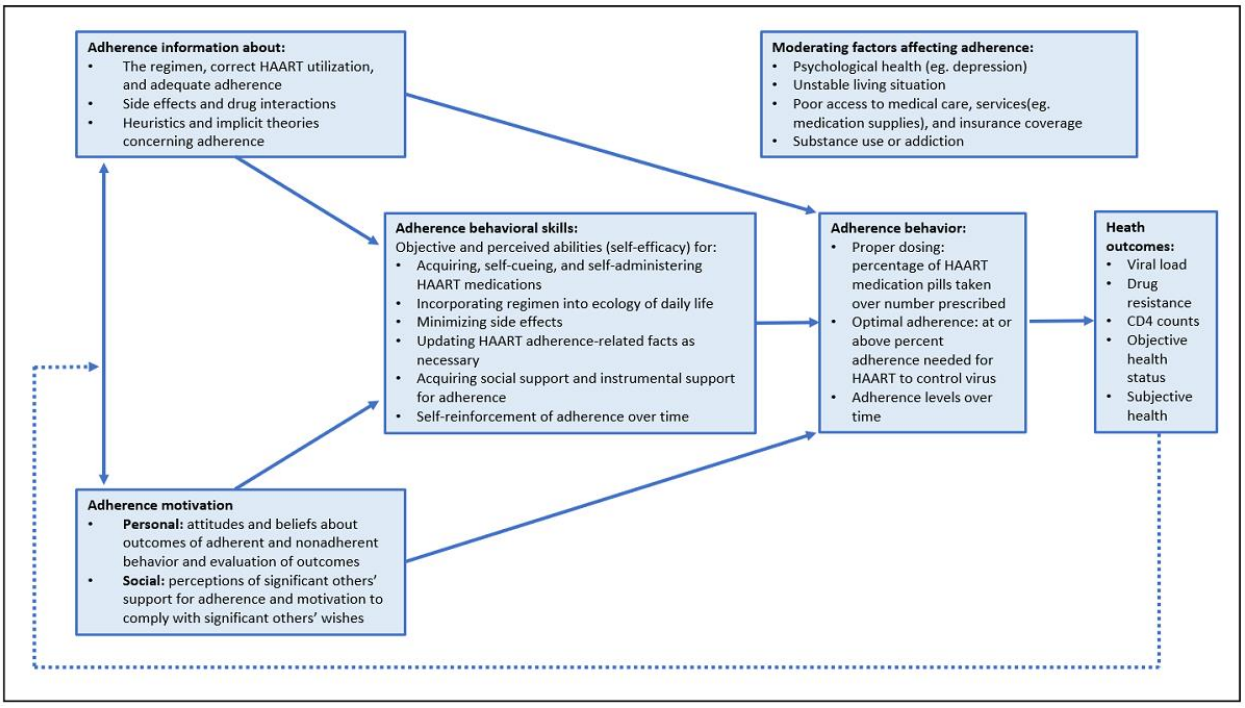


Figure 5. The information—motivation—behavioural skills model of highly active antiretroviral therapy adherence.

HAART: highly active antiretroviral therapy.

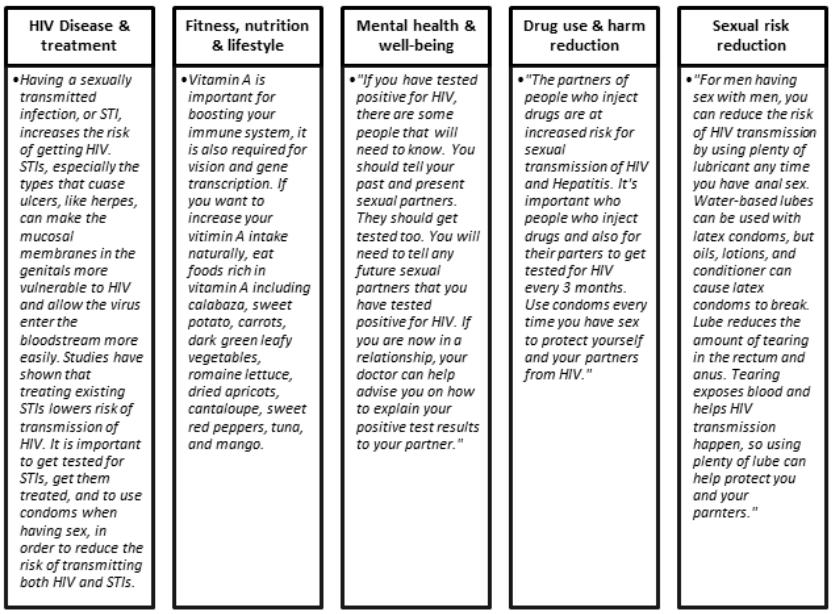


Figure 6. Health tip topic areas and sample tips.

STI: sexually transmitted infection.

Local configuration and set-up of Connect for Life technology platform: From 2015 to 2016, SHIP staff worked with internet technology specialists and public health professionals from study sponsor Janssen Global Public Health to adapt the Connect for Life platform for use at the SHIP clinic. Connect for Life is a technology built on the Mobile technology for community health (MOTECH) open-source software platform.(180) It enables health facilities to connect to patients via their cell phones/feature phones through interactive voice response system (IVRS) or through SMS. It was piloted in India and Uganda prior to roll-out in the Philippines.(210,211)

The platform has the following functionalities: pill reminders, visit reminders, symptom reporting, health tips, and adherence feedback messages. The study team worked with clinic physicians and software developers to adapt the various functions of the Connect for Life platform to align with the needs of the patients as documented in the formative research phase.

Pilot test and preliminary evaluation

Overview: During the first eight weeks of piloting the intervention, the site enrolled 62 patients in the study. These patients received adherence reminder calls, health tips, and they reported their adherence via the interactive IVRS system. During this pilot phase, the feasibility and acceptability of the intervention were analysed before moving to a larger scale implementation phase.

Feasibility: To assess feasibility of the intervention, usage data from the Connect for Life platform were analysed. This included the number of calls generated from the platform, the number of calls answered by the participants and the outcomes of those calls.

Acceptability: To assess acceptability, two focus group discussions were held to assess user experience. All eligible study participants were invited to participate in the focus groups, of which only five agreed to participate in a focus group discussion (the major barrier to participation in these focus group discussions was the difficulty of transport due to traffic congestion in Metro Manila). Participants discussed their experience with Connect for Life, their reactions to the reminders, health tips, and adherence feedback, their feedback on the call length and call frequency, and their suggestions for improving the system.

2.4 Results

Understanding drivers of ART adherence

Review of ART adherence literature (regional and country-specific): Globally, approximately 40% of patients report suboptimal adherence ART.(118,124) In the regional Therapeutics, Research, Education, and AIDS Training (TREAT) Asia cohort (which includes 12 clinical sites from Thailand, Hong Kong, Malaysia, the Philippines, and Indonesia) of 1,316 patients, 421 (31.99%) reported suboptimal adherence of <100%.(17) Similar to our Connect for Life study cohort, majority of the TREAT Asia group comprised a male (67%) population and was aged <40 years (66%); however, most participants of the TREAT Asia cohort were exposed to HIV via heterosexual contact (69%), whereas our study group was primarily homosexual. The TREAT Asia study found that the adherence rate was the lowest during the first six months on ART and the rate improved the longer the patient was on treatment.(17)

Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence of social support, and time on treatment.(17,113,117–120) In the Philippine context, issues of stigma and discrimination also emerged as a major barrier to medication adherence.(86,93,121)

Retrospective analysis of clinic files*:* On the basis of the pharmacy refill forms for SHIP clinic patients, 67.7% (317/468) of patients reported perfect adherence in the 30 days before their most recent refill, 31.8% (149/468) reported suboptimal adherence <100%, and 20% (94/468) reported adherence <95%. A retrospective review of pharmacy refill data is summarised in **Table 3**.

Table 3. Sustained Health Initiatives of the Philippines clinic adherence data from pharmacy refill forms (N=682).

	Value	Range	IQR
Total patients (N)	682		
Age (median)	32	(21-72)	(28.6-35.9)

HIV history			
Time since diagnosis (years)	3.01 years	(0-25)	(1.8-5.0)
Time from diagnosis to ART initiation (years)	0.20 years	(0-21)	(0.1-0.9)
Time on ART (years)	2.37 years	(0-10)	(1.5-3.9)
Adherence Estimates (n=468)			
100% adherence	317 (67.7%)		
Missed 1 dose—adherence (95%-100%)	55 (11.8%)		
Missed ≥2 doses—suboptimal adherence (<95%)	94 (20.1%)		

Focus group discussions with clinic patients: We also conducted focus group discussions with 1.8% (12/682) of the participants regarding their adherence challenges. All participants were male, 75% (9/12) were homosexual, 25% (3/12) were bisexual, and 67% (8/12) had full-time employment. The time patients had been on ART ranged from five months to six years, with a median time of four years. Overall, 83% (10/12) of the participants reported that they sometimes forgot to take their medications and 42% (5/12) had missed a dose within the past two weeks.

Focus group discussion findings on the causal factors for ART adherence are summarized in **Table 4**.

Table 4. Causal analysis of ART adherence behaviour.

Reason for non-adherence	Illustrative quotes from focus group discussion participants
Inconsistent daily routines/Change in habits/Behavioural skills/Difficulties with timing of dose: Common reasons that patients report missing doses include simply forgetting, being busy, being away from home, and changes in routine.(120)	*"You usually… take it at home, not in the office; there are some instances when you calculated the time… so you have to be in the office to take it properly. Then when you are there, you forget to take it, it's because you're busy already working."* *"The challenge that I faced with AR[ba]… I think it's very essential for those working in BPO [Business Process Outsourcing], is adjusting the time when your schedule shifts, because it has to be taken during your sleeping time… And, you know, you can't disclose, 'I was late because I overslept because I was really high with my ARVs."*
Low social support: Patients who have a treatment support person are more likely to be adherent.(212) Having a good relationship with the HIV primary care physician and clinic staff was an important factor.	*"My partner is really helping me a lot to adhere to the schedule in taking the medications…. When my partner gets too busy, the tendency is that we both forget that I need to take the medications."* *"The reason why most of the patients are lost to follow-up is because they feel like they are treated like patients in other [HIV treatment] hubs. The reason why we continue going to SHIP is because we feel welcome, we feel like it's like an extension of our family. Unlike in other hubs – they feel they have to wait; they don't know if they are going to die on that day or that hour. They feel that they are not that important."*
Medication side effects/type of regimen: Experiencing an adverse drug reaction is associated with poor adherence.(213) Furthermore, a large cohort study in Southeast Asia found that patients taking an NRTI[b]+NNRTI[c] regimen had poorer	*"If we open a fresh bottle of ARV sometimes it feels kind of strong… It's like the first time. You feel all the side effects of the ARV."* *"For me it really is the headache, especially this first few weeks."*

adherence than those who initiated on an NRTI+PI[d] regimen.(17) This is most likely due to difficulty tolerating the CNS[e] side effects of Efavirenz, a theme throughout our focus groups.	*"Especially when I was having a pneumonia, especially with interactions with antibacterials – It's really hard to actually take the ARV together with the other medicines because you will be getting a really, really painful stomach, even if you ate something. So sometimes in order for me to finish the whole course of the meds that's been described I have to skip if I really can't tolerate anymore."*
Shorter time on ART[f]: Some studies show that longer duration on ART is associated with better adherence.(17) Treatment-experienced focus group participants insisted that "newbies" would benefit most from the intervention.	*"For the newbies this would be a big help because for a while it's a way for them to adjust. Not all of them are still open in discussing their status with people, and this is a first step for them to accept the fact that they have this situation that they need to cope with. And to do that, it's like the IVR is helping [them]. So, it's a big help."*
Substance use/abuse: Patients who use illicit drugs or abuse alcohol may be less likely to adhere to their medication regimen.(65,118) Among our focus group participants use of methamphetamine in the context of "Partee n Play" emerged as a theme.	*"[When you are high on drugs] You tend to delay it more and more. When you are high you are more carefree, it's like 'I'll take it later, then later, then later'…"* *"I make it a point of, I have been with my friends taking drugs, and then I know that some of them have that schedule of taking the ARV. So I make it a point that I remind them to take ARV. It's like a sisterly bond, like 'Friend, it's your time…' You have to insist. It's like a responsibility within friends."*
Stress/Coping abilities/Poor mental health: People living with HIV are more likely to suffer from depression and anxiety.(117,118) Focus group participants stated that coping with a new diagnosis can be overwhelming. Interruptions in treatment for patients who have been in care for several years may be caused by episodes of depression.	*"The only reason why we really skip for days is like when you are really depressed. And drugs, with your serotonin and dopamine levels really low and you're really emotional. You tend to be like 'my life sucks and I don't want to take my meds.'"* *"You mentioned harm reduction – okay, yes. Could be. Another thing we are not really addressing is mental wellness… It's one reason why we consciously skip our medication, is our mental wellness."*
Stigma: Many PLHIV are fearful of the repercussions of disclosing their status (or having it disclosed inadvertently) to family/friends/ employers.(117,200,214,215) Focus group participants shared their fears and their experiences that disclosing can result in personal rejection, losing their housing (multi-generation family homes are the norm in Philippines), or being dismissed from their jobs. They do not want to be seen taking medicines around other people. The psychological challenges of coping with and accepting an HIV diagnosis during the early stages is a major factor for non-adherence.	*"For me I've been battling this on my own for six years. None of my relatives know that I'm positive. The only people that know that I'm positive are my friends. So, I think this reminder thing… the IVR thing, the health tips, is really good."* *"I think there is one point that I when I consciously, not really skipped, but delayed it four to six hours, just because when that alarm went really crazy everyone was looking at me…. There's this thing now that gay people are being judged when we take our meds in public… That's why it's hard to have that really loud alarm now."*

[a]ARV: antiretroviral.
[b]NRTI: nucleoside reverse transcriptase inhibitor.
[c]NNRTI: nonnucleoside reverse transcriptase inhibitor.
[d]PI: protease inhibitor
[e]CNS: central nervous system
[f]ART: antiretroviral therapy.

Development of the mHealth intervention

Overview: The intervention services were tailored based on input from SHIP patients and clinicians during formative research.

On the basis of the formative research findings, the various components of the COM-B framework were summarised, incorporating the aspects of the IMB skills model of adherence (**Figure 7**).

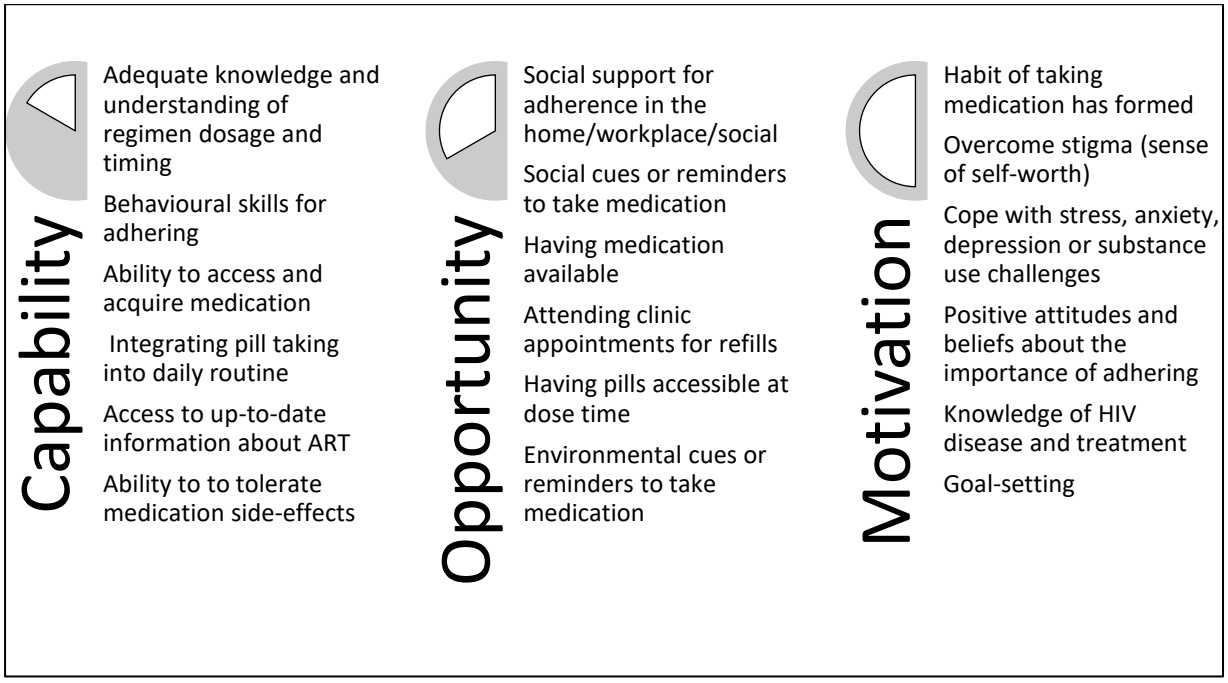


Figure 7. Summary of components contributing to optimal ART adherence based on COM-B and IMB models.

The focus group findings suggested that mobile phone would be an acceptable mode of delivery for HIV interventions targeting young MSM in the Philippines. During the focus group discussions, participants provided detailed input about the acceptability of various intervention aspects, including pill reminders, health tips, visit reminders, adherence feedback, and symptom reporting.

mHealth Intervention Preferences: Participants reported that they would like mHealth services to be personalisable. For example, participants requested to be able to select whether they receive pill and visit reminders via SMS or via calls, as well as to determine the frequency and the time of day that they receive reminders. Participants believed that newer patients who recently started ART would benefit most from daily pill reminders and experienced patients would prefer less frequent reminders. They stated that it would be important to be able to opt in or out of any call or SMS services at any time.

Participants expressed a strong interest in health tips that covered a variety of topics, not strictly HIV disease, and they wanted to personally select which categories of health tips they would hear.

In summary, participants suggested that an ideal mHealth service should be personalised based on the following factors: (1) call or SMS text messages, (2) timing of calls or messages, (3) frequency of calls or messages, and (4) content or topic areas for health education messages.

mHealth Intervention Configuration: The investigators created a standard service scheme (**Table 5**) that could be adjusted at the participant's request. The service scheme included pill reminders for all participants. For those in their first 24 weeks of ART, reminders were daily for the first 24 weeks, and weekly for the next 24 weeks. Those who were experienced on ART received weekly reminders for 24 weeks and no reminders after 48 weeks.

In addition to these patient-facing elements, the composite intervention included aspects that were provider-facing. Clinician alerts were intended to prompt clinicians to quickly identify and proactively respond to non-adherence or medication side-effects. The electronic patient medical record streamlined access to information on medical history, regimen, lab results, and appointment scheduling.

Table 5. Connect for Life services scheme.

Patient-facing intervention components				
Patient characteristics	**Pill Reminder + Adherence Feedback Messages (voice or SMS)**	**Health Tips (voice or SMS)**	**Appointment Reminders (voice or SMS)**	**Symptom Reporting (voice calls only)**
Treatment-naïve and recently initiated (less than 6 months on ART) -OR- Treatment-experienced more than 6 months with adherence below 80% at baseline	Daily reminders from 0 to 24 weeks Weekly reminders from 25 to 48 weeks	Health tips play during all Pill Reminder calls, health tips topics tailored to new patients	Yes	Yes – During all Pill Reminder calls
Treatment-experienced more than 6 months with adherence 80% or higher at baseline	Weekly reminders from 0 to 24 weeks No reminders from 25 to 48 weeks	Health tips frequency and topics selected based on the preference of clinician and patient	Yes	Yes – During all Pill Reminder calls
Provider-facing intervention components				
Clinician alerts	When clinicians log into the web-based platform, they see a list of alerts about patient nonadherence or symptom reports. The alerts are categorized into low, medium, and high priority based on the severity of the issue.			
Patient medical record	The online platform has simple electronic medical record functionality, which clinicians can use to look up laboratory results, prescriptions, diagnoses, and appointment information.			

During IVRS pill reminder calls, participants were prompted to report symptoms of illness or side effects of medications using an IVRS touch-tone menu. The participants received SMS text message recommendations for over-the-counter medications and advice depending on the algorithm outcome.

The system automatically generated an alert for the clinician of any symptom reports that required urgent attention.

All participants received SMS appointment reminders at two set times in advance of their scheduled clinic visit date.

All participants who received IVRS calls for their pill reminders could receive a weekly adherence feedback message informing them of their "score" — from 0 to 7 — based on the number of days they reported taking their doses in the prior week via the IVRS platform. The adherence feedback score was followed by a short motivational message to encourage improvement among patients with low adherence or support continued good adherence among patients with high adherence scores.

Participants would automatically receive audio health tips when they received pill reminder calls, or they could opt to receive health tips via SMS text messages. For patients new on ART, there was a tailored set of health tips that explained the basics of HIV and ART. In addition, we created tips on a variety of other health topics based on the suggestions of patients from the focus group discussions. The following five broad categories were selected for health tips: (1) HIV disease and treatment, which include tips about HIV testing and diagnosis, transmission of HIV, co-infections, and laboratory tests for people living with HIV; (2) fitness, nutrition, or lifestyle, which included tips for exercise and eating healthy; (3) mental health or well-being, which included tips on acceptance and disclosure of HIV status, and approaches for understanding and dealing with depression, anxiety, and stress; (4) drug use and harm reduction, which included medical information about common recreational drugs, safer injection, and hepatitis C; and (5) sexual risk reduction, which included tips on condoms and lubricants and tips on leading a healthy sex life with HIV. That aims of each health tips category are described in **Table 6**.

The investigators worked with two clinic providers and a local voice talent agency to write and record 171 health tips that related to the common questions and issues raised by patients and tips that incorporated the themes that emerged from the focus groups. A full inventory of health tips content is included in **Appendix 11**. The messages were crafted ensuring that they not only provided didactic information related to the health topic but also ended with a specific action or behaviour that the patient could adopt to improve or to minimise the impact of a specific behaviour.

Table 6. Health tips topics.

Topic	Aim
HIV Disease & Treatment	

	Adherence	To provide tips about how to improve adherence by integrating ART[a] into daily routine, using pill boxes, how to handle missed doses, and information about why adherence to ART is important to stay healthy and avoid drug resistance.
	Antiretroviral medications (ARVs)[b]	To provide information about what ARVs are, how ARVs work, drug interactions and side effects.
	Co-infections	To raise awareness by providing information about con-infections that may occur with HIV including other sexually transmitted infections, tuberculosis, and fungal infections.
	HIV	To provide accurate information about how HIV is transmitted, diagnosed and managed, and to dispel myths about transmission.
Mental Health & Well-being		To encourage participants to improve their general health through physical activity and eating a balanced and nutrient-rich diet, providing information about nutrition and physical activity. To encourage mental well-being by providing information about depression, anxiety, and stress, emphasizing the value of social support and disclosure of HIV status to trusted individuals.
Drug use & harm reduction		To inform and encourage protective behaviours, providing information on commonly used drugs, risks related substance use and HIV, and harm reduction practices.
Sexual risk reduction		To inform and encourage protective behaviours, providing information on a range of sexual practices.

[a]ART: antiretroviral therapy.
[b]ARV: antiretroviral.

The system was configured to protect patient privacy and prevent unintended disclosure of health information. Upon answering any call from the system, the participant would immediately hear a jingle, a song that was associated with the Connect for Life system. Upon hearing the jingle, they would enter a personal identification number to advance to the next step of the call. No health-related information would be transmitted unless the personal identification number was keyed in, to protect patient privacy and confidentiality.

Table 5 above presents the proposed service scheme. However, the services were flexible and a patient could opt out of any call or SMS text messaging service that they did not wish to receive or opt into services depending on their preference and the clinician's judgment. The clinician could reactivate or extend the pill reminders for patients who needed additional support.

Intervention theory of change

The intervention development process was informed by the Behaviour Change Wheel approach. Services in the intervention package address the three main components of the COM-B model. Capability is addressed through health tips, which aim to improve knowledge regarding ART and HIV disease and improve behavioural skills. Opportunity is addressed through the pill reminder service,

which provides an external prompt or cue for pill taking and supports habit forming through the appointment reminder service, which prompts attendance at the clinic for refill, thereby increasing accessibility and availability of medications; and through the symptom-reporting algorithm, which addresses the medical barriers to pill taking by expediting a response to side effects or medication reactions. Motivation is addressed through health tips (e.g. messages designed to help with stress, overcome stigma, and inform a positive attitude toward pill taking) and adherence feedback messages, which reward and reinforce high adherence and encourage improvement for low adherence.

Table 7 describes in greater detail the factors influencing adherence behaviour, as outlined in the IMB model and described in the formative research. The table outlines the links between these determinants, the sources of behaviour (capability, opportunity, motivation), and the mechanisms for change (intervention functions) (refer **Figure 4)**. The 15 behaviour change techniques (from Michie & Abraham's 26-item taxonomy) (207) linked to the five intervention components (pill reminders, appointment reminders, health tips, adherence feedback scores, symptom reporting) are detailed in **Appendix 10**.

Because Connect for Life was an adapted pre-existing mobile phone service, behavioural theory was applied in the intervention development process both prospectively (i.e. to inform the content of the health tips and configuration of the platform) and retrospectively (i.e. to explain the presumed mechanisms of action for automated medication reminders). Inevitably, the intervention was underpinned by priorities defined by the pharmaceutical company sponsor and by clinicians. In this sense, the intervention focused on individual behaviour of participants and providers, but did not address broader social and structural factors influencing the lives of participants.

Table 7. Behavioural determinants and intervention behaviour change techniques.

Behavioural outcome	Determinants	Features of the Behaviour Change Wheel Model		
		Source of behaviour (COM-B)	**Intervention Function**	**Connect for Life *intervention components* and related behaviour change techniques (BCTs)**
Consistent pill-taking, adherence to ART (participants)	Access to adherence information, i.e. understanding regimen, timing of doses, reason for taking medication	Improved information and understanding improves participants' *capability* to perform the desired behaviour.	Education	*Health tips* provide information about HIV and ART, provide instruction for taking ART (e.g. what to do in case of a missed dose), explain the link between adherence and good health, and provide information on consequences of non-adherence.
	Having adherence behavioural skills, i.e. incorporating medicine into daily routine, minimizing side-effects	Improved behavioural skill improves participants' *capability* to perform the desired behaviour.	Education, persuasion, incentivization, enablement	*Pill reminders* serve as external prompts/cues to take medication routinely and support habit forming. *Health tips* prompt barrier identification by sharing information about side-effects management and advice for creating a pill-taking routine. *Adherence feedback scores/messages* provide feedback on performance, prompt specific goal setting and self-monitoring of behaviour. *Symptom management* via interactive telephonic menu enables real-time information about how to deal with to side-effects and symptoms and facilitates provider-patient interaction by alerting providers to serious issues.
	Motivation to adhere to ART (personal), i.e. positive attitudes and beliefs about the importance/value of treatment adherence	Improved attitudes and beliefs about treatment adherence improve participants' *reflective motivation*.	Enablement	*Pill reminders* prompt intention formation to take ART as prescribed. *Health tips and adherence feedback scores/messages* both provide general encouragement to adhere to ART.
	Motivation to adhere to ART (social), i.e. perceived support for adherence from others, normalising ART, desire to fulfil desires/expectations of others by adhering to ART	Improved perceived social support for treatment adherence improves participants' *reflective motivation*.	Persuasion, incentivization, enablement	*Health tips* encourage participants to plan social support or social change, emphasizing the importance of treatment supporters, trusted friends, and interacting with your doctor. *Adherence feedback scores/messages* provide opportunities for social comparison and prompt identification as role model by reinforcing good adherence and encouraging improvement among those with poor adherence.

	Psychological health, substance use or addiction	Improved psychological health and reduced harms of substance use improve participants' *opportunity* to perform the desired behaviour.	Enablement	*Health tips* prompt barrier identification and provide general encouragement by sharing information about mental health, substance use, fitness, and nutrition. Messages are designed to help with stress, overcome stigma, inform positive attitudes toward pill taking. *Pill reminders* serve as prompts/cues to take medication.
	Access to health services, having medication supply available	Improved access to medications improves participants' physical *opportunity* to perform the desired behaviour.	Enablement	*Visit reminders* serve as prompts to attend clinic and support time management (i.e. prompting participant to plan for their trip to clinic ahead of the visit date), thereby enabling timely refills and availability of medication.
Timely/proactive follow-up, clinical management of patients taking ART (clinicians/providers)	Ease of access to clinical and adherence information and prioritization of cases requiring response/intervention	Expedited response by clinicians to address medical barriers (side effects) to pill taking improves participants' *opportunity* and *capability* to perform the desired behaviour.	Enablement	*Electronic medical record* provides ease of access to clinical (i.e. lab results) and visit information, enabling clinicians to more easily identify when a participant requires adherence counselling, regimen switch, or other clinical management. *Clinician alerts* prompt staff to promptly follow-up with patients who have missed visits, have abnormal lab results, and who have poor adherence, resulting in more timely clinical care and counselling.

[a]COM-B: capability, opportunity, motivation, behaviour.
[b]ART: antiretroviral therapy.

Pilot test and preliminary evaluation findings

A pilot test phase was conducted from October 2017 until January 2018, in which 62 participants were enrolled in the service. During the pilot period we received reports of several technical issues which affected the functionality of the system. Two focus group discussions were held in January and February 2018, after approximately three months of pilot project implementation. There were five participants, three in one discussion and two in the next. Focus group discussion findings on the themes emerging from the pilot test are summarized in **Table 8**.

Themes were:

Table 8. Themes emerging from the pilot test evaluation.

Themes	Illustrative quotes from focus group participants
Connect for Life (Connect for Life[a]) Technical Issues/Functionality: PIN[b] issues: DTMF[c] is the signal to the phone company that is generated when a user presses a telephone's touch keys. All focus group participants reported instances in which they attempted to enter their PIN code and the code was not recognised. The frequency of DTMF problems varied widely between the participants. Call origin: Calls are generated from an IVR platform using a US-based telecommunications provider. The service provider sets the incoming call number to be displayed as the participant's own phone number. However, participants reported that this was inconsistent, and that some incoming calls from the Connect for Life system displayed phone numbers originating in the USA, South Korea, and China.	*"Actually, I just experienced that issue last night [DTMF malfunction]. Sometimes I have been able to enter [my PIN code] and sometimes I haven't. The jingle kept going on, so I kept entering the PIN again and nothing happened, so I just hung up."* *"In my case, I think I received thrice already from various locations an unknown number that's why I didn't bother answering. One from South Korea, one from US and one from China. The problem is if the number is unknown basically I don't answer it. I'm just guessing that the number came from Connect for Life."*
SMS versus voice call preferences: There was mixed feedback about whether SMS text messages or voice calls were more effective or acceptable. Some participants said that the frequency and length of voice calls was too much. Several focus group participants requested to be changed from voice calls to SMS text messages, as texting is more convenient and less intrusive. Others preferred to stay on voice calls as they are more difficult to ignore.	*"I think SMS would be nice to have as an option. If at the time the program calls you but you didn't answer an SMS reminder would be good just to keep in touch."* *"I hated the call because I've been receiving the calls especially when I'm on my way home in an Uber. If I mistakenly answer it without the headset, the voice will be loud and basically everyone in the Uber would know."* *"If you are going to put the schedule of the consultation, I'd rather those to be in text because there's too much information that I need to remember."* *"I think it's also cultural when people don't like answering calls. Mostly Asians I know don't like answering calls. I'm not good at answering calls and most of the people I know don't also like answering calls especially if the number is unknown and overseas and then you hear this very gloomy guy voice."*

Adherence Feedback "gamification": Participants did not like receiving adherence feedback scores because it was inaccurate and it made them feel stressed.	*"[The adherence feedback score] has no effect. It has no significance to me."* *"For me I don't even care about it [the adherence score] because it just stresses me out."*
Pill Reminders: Daily pill reminder calls were not as utilised as the study team had expected based on the findings from the first two focus groups. After the pilot phase, participants reported that, even though they like the idea of regular reminder calls, in practice they are often too busy to answer the calls and report their adherence. The issue of poor uptake of pill reminder calls was further compounded by the technical issues with the entering their PIN code (DTMF issue). Some participants said that the pill reminders did not make a big difference for them as they already had other systems in place to remind them to take their medications.	*"It helped. Sometimes I would forget but it would help to remind me because I usually take my pill after work, and after work I'm just so tired, I don't check the time and sometimes I almost forget because I'm so sleepy."* *"I hate to be reminded that I have this condition every single day. I know I need to take it but I don't need to be reminded every single day that I have to."* *"If you call seven times a week that's a bit irritating for the patient. What the patient can do is have the option to get reminded through text."*
Health tips: The content of the health tips was useful and informative. All participants wanted to continue to receive health tips. Some participants would prefer SMS rather than voice recordings for the health tips. Some thought the voice recording spoke too slowly, would prefer to read it by SMS. One technical issue reported was that sometimes the same health tips were repeated for multiple days instead of receiving a new tip each day as intended.	*"The health tips are super helpful. Those are the tips about alcohol, and that say you can have sex, you are not prevented but protected. There are even those great tips on eating and what you should eat."* *"Just the voice. The girl answering the questions in the health tips is okay. The guy is very depressing."*
Other findings: Participants were enthusiastic about receiving the automated reminders for their clinic appointments. Participants stated they would have liked a more in-depth orientation or onboarding process at the outset of the intervention. They emphasised the importance of onboarding, setting expectations, thorough explanation of intervention. Not all participants understood they could change/adapt the service model.	*"But what I noticed was that it helped with the appointment. That was a big help as I was reminded that I had to go to the clinic. That's a big deal to me. But about missing the meds, it's still human."* *"I think the program's good. I could recommend that for the newbies. I think the programme should be laid on properly. For example, scheduling, the time, reminders, and the tips. Maybe after a month if the patient has already established a routine so maybe it could lessen the reminders."* *"Besides, the importance of the support group is for patients who have not disclosed to family members. There you can get support or have conversations like*

Peer support: Participants mentioned that they found participating in a focus group discussion with other PLHIV[e] very helpful and asked if there could be an opportunity for the clinic to organise in-person support groups.	*this. If there were a support group now, I'd want to be a part of it because I would like to share what I have experienced before with others."*

[a]Connect for Life: Connect for Life.
[b]PIN: personal identification number.
[c]DTMF: dial tone multifrequency.
[d]PLHIV: people living with HIV.

On the basis of the findings from the pilot phase focus group discussions, enrolment in the study was suspended because of pending solutions to technical issues. The study team worked with software developers to trace the source of the technical issues. It was determined that the platform was functioning well and that the technical failures were because of issues within the local telecommunications infrastructure (i.e. poor call quality). After the team addressed all the technical issues on the software development side, enrolment continued with SMS text messaging services only.

Since mid-2019, we have found that as telecom services improved in the Philippine setting, voice calls in the Connect for Life system can now be delivered with fewer technical issues. Following the initial pilot study, the intervention was scaled up at the SHIP clinic and currently serving 1491 patients at two HIV clinics. The platform is being further developed to move from the MOTECH base to open medical record system (OpenMRS). We plan to pilot test the new version in several HIV treatment sites across the Philippines.

2.5 Discussion

Principal findings

The intervention development approach resulted in a mHealth intervention tailored to the information needs and communication preferences of MSM in the Philippines. The intervention was designed to address various aspects of capability, opportunity, and motivation to achieve optimal adherence to ART.

The formative research found that mobile phone usage is widespread in the Philippines and is an acceptable mode of communication for health information and adherence support. The literature review and focus group discussions revealed that in our patient population key behavioural barriers to adherence included challenges around forming consistent routines and habits, low social support, stress and mental health issues, substance use, and social stigma of living with HIV. Focus group

participants strongly emphasised the need for social and family support to enable and encourage good adherence to ART. Key clinical issues affecting adherence included medication side effects (especially among efavirenz-based regimens) and shorter length of time on ART.

Following the pilot test, recipients of the intervention reported that the tone, frequency, and content of the voice messages were acceptable and appropriate. In the pre-pilot focus groups, participants preferred the male voice actor whose voice sounded more "attractive" according to several participants, whereas in the post-pilot groups, several participants mentioned that they preferred the female voice actor because her tone was warmer and she came across as a trusted friend. This finding indicates that more iterations of recording should be tested in future implementations before a full-scale roll-out and that budgets and project work plans should allow for several rounds of recording. The accounts of the focus group participants indicated that the intervention increased their knowledge and adherence behaviours. However, a large-scale cohort is needed to assess the intervention's effectiveness.

In the pre-pilot focus groups, participants were enthusiastic about receiving voice reminders via phone call, following their experience participating in the pilot most participants expressed a preference for SMS instead of voice calls. This preference may have been related to the inconvenience of answering phone calls, and it may also have been related to the technical problems experienced with the IVRS. These technical challenges posed a significant challenge to feasibility of the intervention, and delivery would need to be adapted to allow for SMS text messaging options to achieve full-scale implementation.

Strengths and limitations

The strength of the intervention development was the involvement of potential users of the intervention in the process, which included the beneficiaries or users of the potential intervention, clinical service providers, and the developers of the technology platform. The views of the target audience were collected in focus groups, which informed the tone, style, frequency, duration, and content of the intervention.

The BCW is a robust intervention development approach that provides a comprehensive understanding of the sources of a behaviour, the spectrum intervention functions, and the environment in which the behaviour occurs. A strength of this approach is the COM-B model at the hub of the BCW. By identifying the capabilities, opportunities, and motivations behind a behaviour, we can clearly identify the most relevant intervention approaches and BCTs. This approach allowed us to

develop a solid intervention plan which described technique, mode, and content to address each identified barrier to or enabler of ART adherence.

A weakness of our approach was the sampling and recruitment strategy for the participants in the focus groups. It was a challenge to identify patients who were willing to participate in a group where everyone had an HIV-positive status because many patients were not publicly out as people living with HIV, indicating that individual interviews may be an option in future studies. The patients who agreed to participate may not be representative of the wider patient population, introducing a degree of selection bias to the process. The study only included participants >18 years and the participants were almost exclusively male; thus, the findings do not address the distinct needs and challenges of adolescents and women living with HIV. In addition, there was low attendance among those who confirmed their intention to participate in the focus groups. This is reflective of the larger need to provide differentiated models of care in the Philippines, as transportation to the clinic site is not easy in Metro Manila because of traffic congestion.

Another weakness of our approach was that we had an intervention mode in mind—mobile phone—at the outset of the intervention development process. Although there are several key determinants of adherence that the Connect for Life platform can address (i.e. knowledge, habit forming, and environmental cues to take medication), there are other factors that the mHealth approach does not address (i.e. physical availability of medication and social support).

The lead author's positionality as a white, American, cisgender, heterosexual female, a public health specialist and researcher may have influenced the findings of the formative research process.(181,182) The majority of participants were young Filipino bisexual and homosexual men living with HIV, which creates some distance between the participants and researcher in terms of identity and ability to relate to one another's experience. Participants may have been reluctant to share negative perspectives of their experience in the clinic, to disclose the true reasons for not adhering to their medications, or to share negative opinions about the proposed intervention being discussed. On the other hand, participants may have been more willing to discuss topics that are perceived as stigmatised among Filipinos but less stigmatised among foreigners, such as sexual activities, drug use, and homosexual identity. In order to mitigate the impact of "outsider" positionality of the investigator, the focus group discussions were led by trained facilitators whose demographics and experience closely mirrored that of the participants.

Notably, the technical challenges experienced in delivering the intervention during the pilot phase made it difficult to assess the true acceptability and feasibility of the planned intervention. Feedback

received after the pilot phase was focused largely on the mobile phone functionality issues, which then limited the discussion regarding the content and design of the intervention as it was intended to be delivered. Conducting a small pilot phase with few participants allowed us to identify the problems with functionality and adapt the intervention before scaling up the intervention to the larger cohort; however, a more iterative process with several pilot stages would have been advantageous if budget and timeline had allowed us to do so.

Comparison with prior work

Research on ART adherence has shown that less time on ART is associated with an increased risk of poor adherence.(17,216–218) With this in mind, the intervention was designed with more frequent (daily) pill reminders for patients during their first six months on ART and less frequent (weekly) reminders for patients with longer than six months on ART. However, after the intervention design was completed and pilots, an analysis of the Philippine cohort found a different trend within the study population, observing that, even before receiving the intervention, newer patients in the Connect for Life cohort tended to be more adherent compared with patients who had taken ART for longer and showed signs of treatment fatigue.(184) This highlights the importance of the ability of clinicians to tailor the reminder frequency and other intervention functions based on individual patient needs.

Before this study, two other projects using the same technology that the Connect for Life programme was built on were implemented and evaluated in India and Uganda. First, a programme called Treatment Advice by Mobile Alerts (TAMA), provided people living with HIV in India with daily or weekly pill reminders, adherence feedback, automated algorithms for managing clinical events for patients being initiated on ART, health tips, appointment reminders, and real-time reporting to the clinics of patient interaction with TAMA. Evaluation of the TAMA pilot found that patients gave the platform a high system usability score and gave generally positive feedback about their experience with using the technology. In TAMA, patients could call a toll-free number to access health tips and a clinical event algorithm. Health tips were used by 76% (42/55) of the patients, and automated clinical advice was accessed by 64% (35/55) of the participants in the pilot study. In the Philippines, these functions were available only through outgoing system-generated calls and SMS text messaging because of the prohibitive cost of toll-free inbound telephone lines in the Philippine setting.(210,219)

The second project, the Call for Life Uganda programme, also found good uptake, acceptability, and positive response to the system. In Uganda, there was a strong preference for interactive voice response over SMS text messages, which was different from the Philippines where participants preferred SMS text messages.(220,221)

2.6 Conclusion

Our research found that a mobile phone-based SMS and IVRS intervention was acceptable to MSM in Manila, Philippines, and the focus group discussions suggested it helped promote ART adherence and appointment attendance. A comprehensive evaluation is required to establish the effects of the intervention on the clinical outcomes of HIV care and treatment.

Chapter 3. Evaluation methods

3.1 Introduction

This chapter is based on the research protocol for the study entitled "Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines", which was submitted to and approved by the LSHTM ethics committee and University of Philippines Manila institutional review board. Some sections are extracted directly from the protocol, while some sections are summarised or omitted to avoid repetition. The appendices include the informed consent form (ICF) and participant information booklet (**Appendices 3-4**), complete protocol (**Appendix 5**), and data collection tools (**Appendices 6-9**).

In Chapter 2, the methods for intervention development were described. This chapter provides a detailed description of the methods related to the observational cohort study, including study design, study population, visit schedule and procedures, data management and administrative processes, and human subjects considerations. While each of the subsequent chapters in this thesis has a section summarising the relevant methods applied in each analysis, this chapter includes a greater level of detail with regard to study procedures.

3.2 Study aim and objectives

Study aim

This study aimed to describe patient adherence, retention, and treatment outcomes, and evaluated the implementation process and the outcomes of a demonstration project of a mobile phone adherence platform for HIV patients on antiretroviral therapy (ART).

Primary objective

The primary objective of the study was to describe the adherence to medication, retention in care, and viral load suppression for the patient population participating in the Connect for Life mobile phone adherence support demonstration project.

Secondary objectives

The secondary objectives of the study were to:

- Assess the acceptability of the Connect for Life platform among the patient population of the SHIP clinic.
- Describe the HIV-related Knowledge, Attitudes, and Practices (KAP) of the participants.
- Describe the clinical outcomes of participants including treatment failure (switch to second line), AIDS-related mortality, and CD4 recovery.
- Identify factors that affect patient adherence, retention, and treatment outcomes.

3.3 Methods

Rationale for study design

This was a prospective cohort study. The prospective observational design facilitated collection of reliable adherence data through both self-report and the Connect for Life platform. In contrast, retrospective adherence data were incomplete when mining clinical records. Collection of clinical information (such as diagnoses, lab results, and drug regimens), where available in routine clinical practice, was also conducted both retrospectively at baseline, and prospectively throughout study follow-up.

Study site

Sustained Health Initiatives of the Philippines (SHIP) Clinic in Mandaluyong, Metro Manila, Philippines.

Study population

The eligible study population included all patients initiating antiretroviral therapy (ART) for HIV as well as those who were already receiving ART at the study site who consented to take part in the Connect for Life mobile phone adherence support project. During data analysis participants were stratified into subgroups for analysis based on whether they were treatment naïve or experienced, their baseline ART adherence (for treatment experienced), and their level of interaction/engagement with the Connect for Life platform.

Study duration

Participants were followed up for 48 weeks from their enrolment in the Connect for Life project. Participant questionnaires and chart extraction were conducted at four time points: baseline, 12 weeks, 24 weeks, and 48 weeks.

Study activities

The study observed and documented the clinical and adherence outcomes of participants in the Connect for Life demonstration project.

Patient Support: The Connect for Life platform generated mobile phone messages that provided participants with support in the form of pill reminders, clinic visit reminders, and health tips. Participants were able to report specific symptoms through the platform to the clinic. Participants who received pill reminder calls could report their adherence through the mobile phone and then receive weekly feedback messages regarding their adherence level for the week. These feedback messages were designed to provide positive reinforcement to participants with high adherence and to provide encouragement to improve pill-taking for participants with medium or low levels of adherence. In addition, the provider received an alert for a participant with low adherence. These alerts were followed up with a phone call from clinic staff to provide adherence counselling.

To participate in the Connect for Life platform, the patient needed to provide a mobile phone number and consent to receiving calls on this phone number from the Connect for Life platform and the medical staff in the clinic. To ensure confidentiality, whenever a call was initiated by the Connect for Life platform, the user would need to enter a personal identification number (PIN code) into their phone before hearing any message from Connect for Life.

The participant and the clinician set the frequency and time of reminders, whether they would be sent through voice or SMS, and the preferred categories for health tips. The standard Connect for Life service package was outlined in **Chapter 2, Table 5**. For participants who started on ART within the previous six months or for those who had poor adherence at baseline, the service scheme began with daily reminders and then tapered off to weekly reminders after 24 weeks and no reminders after 48 weeks. For participants who had been on ART for more than six months with adherence of >80% of pills taken in the prior 30 days, the scheme began with weekly calls for 24 weeks and then tapered down to visit reminders only. While this was the suggested service scheme, each participant could opt out of any call or SMS services that they did not wish to receive or could opt into services depending

on their preference and the clinician's judgment. The clinician could reactivate or extend pill reminders for participants that needed additional support.

Provider Adherence Monitoring: The platform served as a tool for the clinician to monitor participant adherence over time and, while not a fully functional electronic medical record, it served as a disease-specific record system securely capturing medical history, visit history, and additional clinical data (such as ART regimen, lab results, and clinic visits). The platform alerted the clinician when a participant's adherence was low or a participant reported severe symptoms. The study staff used alerts and data from the Connect for Life platform to provide responsive care to clinic patients, such as following up an alert with a phone call to provide adherence counselling. Study staff also actively followed up on alert outcomes with the participant during every regularly scheduled visit.

Ongoing Routine Care: Patients who participated in Connect for Life continued to receive the same routine clinical care. In the study site during the study period, ART initiation was recommended for patients with an AIDS-defining illness, or when CD4 count was below 500. Patients had clinic visits every three months for routine safety labs and other primary care. CD4 count was performed every six months and viral load test was performed annually. No clinical procedures or tests were performed specifically for this research study. All clinical data points were extracted from the patient records by the study staff. At regularly scheduled visits, participants completed study-related questionnaires.

Outcome measures

Primary Outcomes: To describe participant adherence, retention in care, and treatment outcomes, the following primary endpoints were used:

1. Medication adherence: Optimal adherence was defined as ≥95% of pills taken. Adherence was assessed through self-report at study visits, through participant self-reports in the Connect for Life platform during daily or weekly calls, and through pill count. A biological endpoint of viral load was also included to ensure internal validity, since the investigators did not directly observe the participant taking medications.
2. Retention in care: Proportion of participants alive and in care ("not in care" defined as not having returned for more than 30 days after last scheduled clinic visit or refill).
3. Viral load suppression: Proportion of participants whose most recent HIV RNA test result was undetectable (based on the parameters of any assay performed through routine clinical care). Viral load served as an effective proxy indicator for medication adherence, since poor adherence is associated with unsuppressed viral load.

Secondary Outcomes: The secondary outcomes of the study were:

1. Acceptability of the Connect for Life platform.
2. HIV-related knowledge, attitudes, and practices of the participants.
3. Quality of Life (QOL) score as per WHOQOL-HIV BREF questionnaire.
4. Clinical outcomes: Treatment failure (switch to second line), AIDS-related mortality, and CD4 recovery.

Acceptability was determined by:

1. Quantifying the level of interaction participants have with Connect for Life platform (i.e. proportion of adherence reminder calls responded to, number of health tips listened to, average time listened per call, number of symptoms/side effects reported through Connect for Life and proportion of positive/negative resolution of those reports).
2. Responses to participant acceptability questionnaires.
3. Participant satisfaction/concerns with Connect for Life platform and their satisfaction with the clinic services elicited in focus group discussions.
4. Documenting the potential for scale to other sites via analysis of per-participant cost to implement project in comparison to the overall cost of HIV primary care.

Process documentation consisted of monthly narrative reports on participant recruitment, ongoing use of the platform by participants, implementation challenges encountered, and participant and health care provider feedback. Process documentation also included contextual factors and events that may influence HIV care, such as changes in treatment guidelines or insurance coverage.

3.4 Study population

Inclusion criteria

1. Enrolled in HIV primary care at SHIP clinic during study recruitment period.
2. Currently on ART at the time of screening, or planned to start ART in the next 60 days.
3. Age 18 years or older.
4. Had access to a Philippines mobile phone and was willing to receive calls and messages from Connect for Life.

5. In order to provide consent and to understand the health tips, participant had to be able to understand spoken English and read written English. (Note: English was spoken fluently by all but two of the 675 patients at the study site. Since SHIP patients tend to be well-educated, employed, upper- or middle-class men, this criterion was not expected to systematically exclude any segment of the potential study population. Moreover, during formative planning stages, our patients expressed a strong desire to receive reminders and health tips in English and NOT in Filipino. The rationale was twofold. Firstly, patients believed that medical terminology and content related to sexual health would be more acceptable for them to hear in English. Secondly, patients thought it would help protect their privacy, as interactive voice response calls in English would attract less attention or "eavesdropping" compared to calls in Filipino.)

Exclusion criteria

1. Enrolled in primary HIV care at a facility other than SHIP clinic.
2. Had never taken ART and did not plan to start ART in the next 60 days.
3. Age <18 years.
4. Had no mobile phone access.
5. Unable to understand spoken or written English.

Recruitment process

All patients enrolled in care at the study site were potential study participants. Patients were approached to participate in the study by a member of the study team (study coordinator, clinic nurse, or doctor) either during a routine clinic visit or during a routine reminder phone call to schedule an upcoming clinic visit. New patients were approached about participation in the study by the clinic doctor or nurse during their initial clinic visit.

The following steps were taken during the recruitment process:

1. Initial introduction of study: A clinic staff member introduced the study to every clinic patient following the recruitment script. This introduction occurred in person at the clinic. If a patient did not attend a clinic visit during the study recruitment phase, the recruitment script could also be read to him over the phone when contacted for a routine visit reminder.
2. Recruitment log: A recruitment log was kept to document which patients had been approached and the outcome. If the patient indicated interest in the study, then the study

staff continued to the next step. If the patient declined, this was recorded in the recruitment log and the process ended there. If the patient was unsure, he could take a copy of the ICF to review on his own, or he could speak to the study investigator to get further information.

3. Screening: The potential participant was assigned a study ID number. The study staff determined patient eligibility using the inclusion and exclusion criteria on the screening checklist.
4. Informed consent: The investigator reviewed the ICF with the patient and, if the patient opted to participate, they signed the informed consent.

As an additional research activity with a subset of study participants, the investigators planned to recruit 20 to 30 participants for focus group sessions. Participants indicated on the ICF if they wished to participate in the focus group sessions. The study team selected study participants to invite to focus groups and were mindful of inviting a group that was representative of the demographic composition of the clinic population and that had diverse experiences of their HIV care.

Participant withdrawal

Participants could voluntarily withdraw from the study for any reason at any time. The Investigator could also withdraw participants from the study to protect their safety and/or if they were unwilling or unable to comply with required study procedures. In such instances, a member of the study team would be required to document the reason for withdrawal and date on the patient record, and any data entered into the patient's clinic record after the date of withdrawal from the study would not be included in the data analysis. The investigators did not anticipate any safety issues related to study participation. One foreseeable risk was the unintended disclosure of HIV status due to participation in the study, discussed in the section on Human Subjects Considerations below.

Participants who wished to stop receiving calls from the Connect for Life platform, but who were still willing to participate in the study, were maintained in follow-up as originally scheduled.

3.5 Study procedures

Screening

Screening, enrolment, and baseline visit procedures could all be conducted on the same day. The enrolment and baseline visits must have been completed within 60 days of the screening. If the subject did not enrol within 60 days from the screening visit, they could be rescreened.

Procedures:

1. Approach patient and find out if they are interested in learning about the Connect for Life (Connect for Life) demonstration project.
2. Document inclusion/exclusion criteria and confirm eligibility.

Enrolment

For each participant, independent written informed consent for screening and enrolment was obtained before any study procedures were initiated.

Procedures:

1. **Obtain informed consent:** Explain Connect for Life platform; explain study.
2. **Enrolment in Connect for Life:**
    a. Activate patient record in Connect for Life.
    b. Update patient contact details.
    c. Set up ART adherence reminders – based on ART regimen, patient's preferred call frequency, and time of day.
    d. Set up health tips preferences, based on patient and clinician selections.
    e. Provide patient with Connect for Life information sheet and copy of ICF.

Baseline

At the baseline visit, historical adherence and clinical data were extracted from the patient record. The participant completed self-administered questionnaires about adherence KAP and QOL.

Procedures:

1. **Demographic data:** Study coordinator to complete form during baseline visit via interview with participant.

2. **HIV-specific medical history:** Study coordinator to complete form during baseline visit via interview with participant plus chart extraction.
    a. Opportunistic infections/STIs/TB history.
    b. ART regimen history.
    c. Treatment failure history.
    d. Nadir CD4 count.
3. **Participant self-administered questionnaires:**
    a. KAP/QOL.
    b. Adherence.
4. **Clinical record extraction:**
    a. Most recent laboratory values: CD4 count, CD4 %, HIV RNA level.
    b. Prescription refill information (pill count).
    c. Current opportunistic infections, STIs.
    d. Current ART regimen.
    e. Concomitant medications.
    f. Treatment failure.

12 weeks and 24 weeks

Visit windows: 12-week target date = 12 weeks (84 days) from baseline visit. Window = 6 weeks–17 weeks (42–125 days) from baseline visit. 24-week target date = 24 weeks (168 days) from baseline visit. Window = 18 weeks–35 weeks (126–251 days) from baseline visit.

Procedures:

1. **Participant self-administered questionnaires.**
    a. KAP/QOL.
    b. Adherence.
    c. Connect for Life feedback.
2. **Clinical record extraction (as described above, record any new data since last visit).**
3. **Connect for Life record extraction:**
    a. Connect for Life services enrolled in.
    b. Proportion of adherence reminder calls answered.
    c. Proportion of calls responded to.
    d. Number of health tips listened to.
    e. Average time listened per call.

f. Number of symptom reports made and outcome of those calls.

4. **Adverse events and social harms monitoring.**

48 weeks

Visit window: 48-week target date = 48 weeks (336 days) from baseline visit. Window = 36 weeks–60 weeks (252–420 days) from baseline visit.

Procedures:

1. **Participant Questionnaires.**
    a. KAP/QOL.
    b. Adherence.
    c. Connect for Life feedback.
2. **Clinical record extraction (as described above).**
3. **Connect for Life record extraction (as described above).**
4. **Adverse events and social harms monitoring.**
5. **Study termination procedures.**

Schedule of events

Table 9. Schedule of events.

	Screening/ Enrolment	**Baseline (Week 0. Max 60 days from Screening)**	**12 Weeks (6–17 Weeks)**	**24 Weeks (18–35 Weeks)**	**48 Weeks (36–60 Weeks)**
Approach/recruit patient	X				
Document inclusion/exclusion criteria and confirm eligibility	X				
Informed consent	X				
Enrolment in Connect for Life platform	X				
Activation of Connect for Life services		X			
Demographic data		X			
Medical history		X			
Participant questionnaires:					
KAP/QOL		X	X	X	X
Adherence		X	X	X	X
Connect for Life feedback			X	X	X
Clinical record extraction		X	X	X	X
Connect for Life record extraction			X	X	X
Adverse events and social harms monitoring			X	X	X
Study termination procedures					X

Focus groups

The investigators planned to conduct a series of structured discussions with approximately 20–30 study participants to understand their assessment of the intervention. These discussions occurred during intervention development, pilot testing, and in the final three months of the study implementation. The discussions were intended to elicit any concerns regarding disclosure of HIV status, privacy, and perceived value of the intervention. Key informant interviews were also conducted with health care providers. As these interviews were conducted throughout the implementation period, the study team was able to respond to implementation issues and address providers' concerns throughout the study period.

Missed visits

As standard of care, all clinic patients who missed a visit received three follow-up phone calls from the clinic to reschedule their visit. If a study participant did not come to the clinic for routine care within the specified visit window, the study coordinator completed a missed visit form. For missed visits, the coordinator and clinician extracted any available data from the patient medical record and from the Connect for Life platform and completed the relevant fields on the case report forms (CRFs). If the patient had received treatment in a different facility, the study team could request release of medical records from other facilities with permission from the patient. The participant questionnaires would be marked as missed.

3.6 Data management

Data management responsibilities

My data management responsibilities were as follows: provide training and guidance to staff with respect to data management issues; oversee data quality control, including running data queries; ensure the availability of databases to capture data from participant interview and case note abstraction from medical records; ensure the safekeeping of data and access control; ensure proper data management documentation was maintained; manage data reporting processes; manage integration of data from different sources; ensure processes were in place for backup and data recovery; ensure compliance with data security and confidentiality regulations; and ensure study conduct adhered to good clinical practice standards.

The study coordinator's responsibilities were: ensure patients completed the questionnaires at each visit; extract data from Connect for Life platform and paper records; and complete paper-based and electronic CRFs.

Application and database

The Connect for Life platform was hosted in a secure cloud-based platform (Amazon Web Services) and managed by the study site.

Study data were collected on paper-based CRFs and questionnaires. Data was captured into Google Forms, which were securely stored online using SHIP's Google Workspace for non-profits. Access to the Workspace was managed by myself and my co-investigator Dr Leyritana. SHIP staff directly involved in the study were granted access to the study records, using their SHIP company credentials.

Data sources and associated outcomes

1. Routine data from patient medical records and the Connect for Life platform were used to determine clinical and retention outcomes.
2. Self-administered questionnaires collected data on KAP/QOL, self-reported adherence, and acceptability data on Connect for Life.
3. Data from Connect for Life platform database on utilisation of Connect for Life was used as an indicator of acceptability.
4. Historical programme reports from the SHIP clinic and retrospective clinical data extracted from the medical records of consenting study participants were used to establish estimated baseline retention and adherence levels.
5. Qualitative data collection methods included purposively sampled semi-structured interviews, as well as direct observation and narrative reports of intervention activities.

Quality control

Data were validated on entry, using range and consistency checks. Quality control procedures included review of paper-based and electronic CRFs for completion and correctness. Logical data checks were also performed on the data. Investigators checked for incomplete and incorrect data and sent queries to the study coordinator for error resolution. Errors were reviewed and corrected on an ongoing basis throughout the data collection period and data cleaning period post-study.

Hard copies of study records (consent forms, questionnaires) are kept in a secure location accessible only to authorised study staff, investigators, and monitors. Procedures for storage of electronic data

are described below in the section on Human Subjects Considerations. All records are to be securely archived for at least 10 years after completion of the study.

3.7 Statistical considerations

Study design

The study site implemented the Connect for Life platform as a demonstration project, with the initial goal of determining whether the platform might provide benefit to participants and whether it could be successfully implemented in real-world conditions in the setting of HIV primary care in the Philippines. For this purpose, an observational study was the most appropriate approach. However, an observational study design limits the ability to determine the causal effect of the Connect for Life intervention on participant adherence and clinical outcome. The observational study also limits the ability to control for confounding factors, although traditional regression analysis can be used to control for observed confounders. In the future, the effect of the intervention on participant adherence levels and/or clinical outcomes could potentially be evaluated in a randomised controlled trial (RCT). However, first establishing a strong proof of concept and demonstrating that the intervention is reasonably acceptable and feasible is an important step before undertaking a RCT. The outcomes of this observational study may inform future study design.

Endpoints

The primary endpoint for the study was self-reported medication adherence. Other key outcomes of interest were retention in care and viral load suppression.

The secondary endpoints were participant KAP and QOL, the use and acceptability of the Connect for Life platform, and clinical endpoints. **Table 10** summarises the key variables that we planned to include in the descriptive analysis. Data collection tools are included in **Appendices 6-9**.

Table 10. Endpoints.

Primary Outcomes
Adherence
Self-reported % of medications taken (30-day recall)
Connect for Life-generated % of medications taken (as per response to daily/weekly pill reminder calls)
Pill count % of medications taken at each refill
% of participants with suboptimal adherence (<95%) – composite measure
Retention in Care

Proportion of participants alive and in care (“alive and in care” if they are between visits and were known to have refilled their HAART within the prior 30 days, “not in care” defined as not having returned for more than 30 days after last scheduled clinic visit or refill)
Proportion of study visits missed
Viral Load Suppression
Proportion of participants whose most recent HIV RNA test result was undetectable (based on the parameters of any assay performed through routine clinical care)
Secondary Outcomes
Connect for Life Acceptability
Responses to Connect for Life acceptability questionnaires
Usage/engagement: proportion of adherence reminder calls responded to, number of health tips listened to, number of symptoms/side effects reported through Connect for Life during study period
Participant Knowledge Attitudes Practices and Quality of Life
Knowledge Attitudes Practices score
Quality of Life score
Clinical Outcomes
Treatment failure (switch to second line)
AIDs-related mortality

Sample size

Projected Study Size: Since the study was a demonstration project, the protocol allowed for all eligible patients at the study site to enrol in the study. At the time of protocol development, the study site provided treatment to 675 patients who were likely to be eligible for participation in the study. The clinic population continually grew as treatment-naïve patients initiated therapy throughout the course of the recruitment period. Taking into consideration the possibility of unforeseen recruitment challenges, at least 500 participants were expected to enrol. The main endpoints of the study are descriptive, not inferential. The primary objectives are descriptive, as this is an observational, single-arm study with no comparison group.

A calculation for the detectable effect size in a before–after comparison for a sample size of 500 is described below in **Table 11**. Retention estimates included in the calculation come from 2015 SHIP clinic data, estimates for suboptimal adherence and viral load suppression rates were based on published data from regional retrospective and prospective cohort studies and unpublished data from local programmes.(4,16,17)

The power calculation concluded that in a two-sample, two-sided equality test to compare proportions, a sample of 500 participants would allow for detection of the following differences between the baseline and outcome measures.(222)

Table 11. Power calculation.

	Estimated Baseline Observation (null hypothesis)	Per cent Increase detected with 80% power 5% type 1 error
Optimal adherence (≥95%)	83%	6.1% (to 89.1%)
Retention in care	95.4%	3.1% (to 98.5%)
Viral load suppressed	85%	5.8% (to 90.8%)

Data analysis

Statistical techniques: The data analysis plan included a combination of descriptive and inferential analysis. Exploratory data analyses were performed to analyse data quality, identify trends in the data, and identify associations between participant characteristics and outcomes.

The data analysis approach included descriptive statistics with precision estimates, chi-squared tests to compare outcomes between the different subgroups, and regression models as appropriate. Subgroup analyses compared treatment-naïve to treatment-experienced participants, participants with poor baseline adherence to participants with already high adherence at baseline, and participants with different levels of engagement with the platform. Data analysis was conducted in Stata 15 (StataCorp LLC).

The specific statistical techniques applied were as follows:

1. Baseline analysis of cohort (**Chapter 4**): Using data from the baseline visit only, categorical variables were described with proportions and continuous variables were described with means and 95% confidence intervals. I examined which demographic, behavioural, and clinical factors were related to self-reported adherence to ART of ≥95%. Crude odds ratios (ORs) were calculated with logistic regression. Factors significant at *P*-value <0.1 in the univariate analysis were included in a multivariate logistic regression analysis.

2. Process evaluation (**Chapter 5**): Descriptive analysis calculated the count, proportion, and mean number of calls sent, number answered, responses to the calls, and SMS text messages delivered. Data distributions were explored to categorise the responses to the acceptability questionnaires. Where questionnaires had blank or missing fields, all available data points were included in the analysis. Associations between acceptability of the intervention and independent variables (time point, treatment experience, and reminder frequency) were calculated using chi-squared tests.

3. Outcome evaluation (**Chapter 6**): Demographic and clinical characteristics were described as means or proportions with 95% confidence intervals. The treatment adherence and viral load suppression outcomes were assessed by comparing the baseline data (i.e. immediately pre-intervention) with data collected 12, 24 and 48 weeks after enrolment. McNemar's chi-squared tests were used to compare frequencies between baseline and 48 weeks.

   Adjusted odds ratios were estimated using a generalised estimating equations (GEE) model with an exchangeable correlation structure and robust variance. GEE was selected to allow for clustering of outcomes within an individual. The model included intervention exposure, treatment experience, baseline adherence, and other factors which had a *P*-value <0.1 in unadjusted univariate analyses (with some factors excluded a priori due to collinearity). For both main outcomes, all observations from follow-up visits were included in outcome analyses, and the models adjusted for baseline adherence and baseline viral load, respectively. Wald tests were used to calculate *P*-values of each variable.

   Several sensitivity analyses were conducted. Both univariable and multivariable analyses were reproduced using continuous variables for intervention exposure (unique number of days participant received call or SMS) and adherence (per cent adherence from 0 to 100) in place of the respective categorical and binary variables. The analyses were also reproduced using mixed-effects logistic regression models instead of GEE. Finally, the descriptive and inferential analyses were reproduced using an "intention to treat" approach, in which the dataset was updated to include data points for participants who were lost to follow-up or who died with the assumption that they were non-adherent and virally unsuppressed for the period from the time they became lost to follow-up or deceased to the date when they would have completed the study.

Other data analysis techniques: Qualitative data analysis used a structured thematic analysis to describe themes from focus group discussions. The embedded process evaluation used data on participant uptake and usage of the intervention to characterise the intervention and relate it to participant outcomes.

Stratification: Descriptive analyses of adherence and viral load outcomes were performed for the entire cohort, and then according to the following categories:

1. Intervention exposure category: Exposure level was determined by the number of days a participant received a contact from the Connect for Life system. Without any precedent

for the intervention in the Philippines setting, the cut-offs for the categories/clusters could not be determined before implementation and were defined during the analysis.

2. Adherence above or below 95% at baseline: In the region, an estimated 26% of treatment-experienced patients have suboptimal adherence.(17) Suboptimal adherence rates were expected to be slightly lower among SHIP clinic population, approximately 15-20%, due to demographic and socioeconomic differences compared to public hospitals.
3. Treatment experience of more or less than six months at enrolment: The study team planned to recruit at least 150 treatment-naïve participants.

Possible confounders: The outcomes of interest in this study could have changed over time due to aspects not related to the study intervention. These confounding influences could include: individual factors related to the outcomes (e.g. age, socioeconomic status, education, employment, time on treatment, baseline adherence level, social/family support); external factors that affect adherence (e.g. health messages from other sources, availability of prescriptions, transfer in/out of treatment site, cost of care/access to PhilHealth national health insurance benefits); and cyclical/seasonal changes in adherence behaviours (e.g. holiday travel, seasonal employment variations, social events like LGBT (Lesbian, Gay, Bisexual, Transgender) Pride month, weather and natural disasters affecting ability to commute). We also had to consider survivor bias, since those participants who had already been on treatment for some time may have been less likely to become non-adherent or lost to follow-up over time. When conducting exploratory analyses these confounding factors were taken into consideration wherever possible and the limitations of the analysis are expressly stated.

3.8 Human subjects considerations

Vulnerability of subjects

People living with HIV are considered a vulnerable population because they have an incurable disease and because they face significant stigma and discrimination. The investigators acknowledge that research should be conducted on vulnerable populations only when the objectives cannot be achieved through conducting the research on non-vulnerable populations, and that specific considerations and augmented protections should be put in place for vulnerable groups in research. The mobile phone intervention studied in this protocol was intended to specifically benefit people living with HIV. This study necessarily documented the outcomes of the intervention in this specific population, and will add to the body of knowledge that may benefit people living with this disease.

Regulatory review

Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent prior to inclusion in the study.

Risks and benefits to participants

Study participants stood to benefit by receiving medication reminders, clinic visit reminders, and health tips on their mobile phones. This could increase their knowledge and help them have successful treatment outcomes.

A risk of using mobile phones in any health intervention is the possibility of unintended disclosure of the participant's disease status via the mobile phone. The study team took a variety of measures to protect participant confidentiality and prevent unintended disclosure of HIV status; these are detailed below in the section on Confidentiality. Moreover, social harms monitoring was conducted at each study visit and interviews were conducted throughout the demonstration project. The clinic staff were tasked to routinely identify threats to participant confidentiality and take measures to address any perceived risks.

Informed consent

Each participant signed a participation agreement/ICF allowing data collection and source data verification. The participation agreement/ICF was signed before collection of any patient data.

Before enrolment in the study, the investigator or an authorised member of the participating site personnel explained to potential participants the nature of their involvement in the study and procedures for data protection. Patients were informed that their participation in the study was voluntary and they could withdraw consent for data collection at any time. They were informed that choosing not to participate in this study would not affect the standard of care they received.

The patient was given sufficient time to read the participation agreement/ICF and was given the opportunity to ask questions. After this explanation and before entry into the study, consent was appropriately recorded by means of the personally dated signature. After having obtained the consent, a copy of the participation agreement/ICF was provided to the patient.

Incentives

There were no incentives offered for study participation. Those who participated in focus groups were served snacks or a meal during the session and received a stipend of 200 pesos (equivalent to approximately GBP £3) for their transportation expenses.

Confidentiality

To participate in the Connect for Life platform, the patient needed to provide a mobile phone number and consent to receive calls on this phone number from the Connect for Life platform and the medical staff in the clinic. To ensure confidentiality, whenever a call was initiated by the Connect for Life platform, the user needed to enter a personal identification number (PIN code) into their phone before hearing any message from Connect for Life. The participant and the clinician set the frequency and time of reminders, whether they would be sent through voice or SMS, and the preferred categories for health tips.

In order to mitigate the risk of accidental disclosure of HIV status, the content of the pill reminders and clinic visit reminders used generic language that was not specific to any particular disease or condition, and did not mention HIV specifically. The health tips, however, were specifically tailored to people living with HIV and were likely to contain sensitive subject matter. Health tip recordings were initiated in the call flow only after the pill reminder was complete. Participants were able to opt into or out of each service, so concerns about being overheard on phone calls or having SMS messages with HIV-specific content inappropriately read could be mitigated by opting out of those services.

To protect participant confidentiality in the course of clinic visits, appointments were set at specific times and not in blocks, which decreased the risk that a participant's confidentiality would be compromised by meeting someone in the clinic waiting room (which can be a common occurrence in crowded hospital facilities). The clinic also has a separate entrance that does not pass through the waiting room which a patient can use if they want to avoid the waiting room.

For patients participating in the focus group discussions, there were limitations to the guarantee of confidentiality. All participants agreed to keep the identities of others and the topics of discussion completely confidential. However, the investigators had limited ability to monitor and enforce that agreement. Participants in the focus group discussions were thus made aware of this risk during the recruitment and informed consent processes, and only those participants who were comfortable with the limits to confidentiality of focus groups discussions (i.e. patients who were willing to or who had already publicly disclosed their HIV status) were asked to take part.

The collection and processing of personal data from participants enrolled in this study was limited to those data necessary to fulfil the objectives of the study. Only study staff had access to personally identifiable data. The Connect for Life platform was hosted in a secure cloud-based platform (Amazon Web Services) and managed by the study site. Therefore, the study sponsor did not have access to any personally identifiable patient data.

The data were collected and processed with adequate precautions to ensure confidentiality and compliance with data privacy protection laws and regulations. In order to protect the personal data against unauthorised disclosures or access, accidental or unlawful destruction, or accidental loss or alteration, all personally identifiable electronic data were stored in a secure, encrypted cloud-based server. All data extracted from clinic records were de-identified and coded with a patient ID number. Electronic data did not include patient name. Electronic data did include mobile phone number, which is potentially personally identifiable. Upon conclusion of all analyses, a system administrator will permanently delete all mobile phone numbers from the research database. All paper forms were keyed into the database and the hard copies are stored in a locked cabinet in a secure room in the clinic. Study staff had training in Good Clinical Practice and Human Subjects Protection.

The ICF obtained from the participant included explicit consent for the processing of personal data and for the investigator to allow direct access to their original medical records (source data/documents) for audit, ethics review, and regulatory inspection as appropriate. This consent also addressed the transfer of the data to other entities and to other countries.

The participant had the right to request, through the investigator, access to their personal data and the right to request rectification of any data that were not correct or complete. Reasonable steps were taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Finally, it was also important to protect participant confidentiality in the course of routine service delivery. The study site had a strong track record of protecting participant confidentiality, as one of the main drivers for the creation of the SHIP clinic was patient demand for more discreet HIV care and treatment services than could be delivered in public sector treatment hubs. The SHIP clinic put several measures in place: discreet location in retail building, discreet signage, the provision of two separate entrances to allow patients to bypass the waiting area if they wished, and set appointment times to avoid crowding. The SHIP clinic's unique ability to protect patient confidentiality was a key factor in making it a suitable demonstration site for the Connect for Life project.

Adverse event reporting and social harms reporting

Although study investigators made every effort to protect participant privacy and confidentiality, it was possible that participants' involvement in the study could become known to others, and that a social harm might result. A social harm is defined as a non-medical adverse consequence of study participation. Social harms are often related to difficulties in personal relationships and/or stigma or discrimination from family/community/employers. Social harms may affect study participant access to housing, employment, travel/immigration, education, health/life insurance, medical/dental care, or other areas of life. Participants were asked about social harms by the study coordinator at each visit, and if any harms were reported they were recorded on CRFs during regular visits. A social harm that was judged by the investigator to be serious or unexpected was reported to the IRB.

Preventive actions to avoid unintended disclosure included: requiring a PIN code to retrieve messages, counselling the participant on risk mitigation (e.g. when and where they should or should not answer calls from Connect for Life), and minimising the content of the SMS and voice reminders that might identify the disease status of the call recipient. In the event that a participant reported a social harm, every effort was made by study staff to provide appropriate care and counselling to the participant and/or members of the participant's family or social network who were affected. The investigators were experienced in providing counselling to the partners and family members of participants. The investigators also provided referrals to appropriate resources for the safety of the participant (e.g. support group, social services, medical providers, legal assistance). Corrective actions were taken to protect the participant, such as stopping phone calls or text messages to them. If any new risks to participation were to be identified throughout the course of the study that would affect all study subjects, the ethics review committee was to be notified, the Informed Consent Form updated, and participants notified of the additional risks and required to re-consent in order to continue participation. These procedures were put in place to protect study participants.

Study discontinuation

The study also could be discontinued at any time by the implementing site, the sponsors, government or regulatory authorities, or site IRBs.

Availability of Connect for Life after study conclusion

At the outset of the study, we decided that study participants would not automatically continue receiving services from the Connect for Life platform following their final study visit. It was not yet clear whether the project would have any benefit for patients or if it should be continued after the

conclusion of the study. The investigators planned to decide whether to continue offering the service based on the following criteria:

1. The intervention was beneficial to participants (as assessed by qualitative and quantitative outcome measures).
2. The project was feasible to implement (as assessed by embedded process evaluation).
3. The investigators were able to secure funding to continue the project.

Should those criteria be met, the investigators and sponsor would arrange to renew the product licence for the Connect for Life platform and extend the service. Participants would be required to re-consent to participation in Connect for Life if they wished to continue receiving the service.

3.9 Administrative procedures

Study coordination

The investigators and site staff were responsible for protocol implementation through study close-out, including: facilitating successful study start-up and close-out; recruiting study participants; ensuring all study procedures were completed in accordance with the protocol; maintaining research records and regulatory documents; managing various aspects of the research participant's experience, from recruiting participants to conducting visits; and completing CRFs and reports.

Study implementation was directed by the study protocol as well as by the study site’s research SOPs. Study CRFs were developed by the study team. Close coordination between protocol team members was necessary to track study progress, rates of accrual, follow-up, and other issues in a timely manner. Study staff had training in Good Clinical Practice and Human Subjects Protection.

Monitoring

External monitoring or auditing of the study was not conducted. The study team conducted continuous quality assurance checks.

3.10 Post-hoc comment on differences from planned methods

There were several aspects of the study methods described in the protocol that were excluded from this thesis or that were not executed as originally intended. I will briefly describe the reasons for discrepancy or departure from the intended methods here, and the implications of these issues are discussed further in Chapter 7.

Enrolment and data collection: The protocol planned for 500 study participants, of which 150 would be new on treatment. We enrolled just 465 participants, of whom 75 were on treatment for six months or less. This was due to incorrect estimates of the rate of new ART enrolments at the clinic; we expected about 15 new ART initiations per month but just five to six enrolments occurred per month during the study period.

Planned comparison to historical control: The study protocol included a secondary objective to compare the prospective cohort data to a historical control from patient records in order to describe the possible effect of the Connect for Life intervention. At enrolment, historical data on adherence and clinical variables were extracted from the patient charts. This was intended to form a historical retrospective cohort which could be compared to the prospective cohort to evaluate possible effects of the intervention. Unfortunately, the quality of the retrospective data on adherence, which was extracted from pharmacy refill forms, was very poor. The data included refill dates, number of pills dispensed, and number of pills remaining. From these I calculated an adherence estimate. However, due to incomplete and incorrect figures in the source data, the adherence estimates I calculated produced unrealistic results and could not be used in the analysis as a historical control.

Usage data from the Connect for Life platform: Much of the data used for the process evaluation came from reports exported from the Connect for Life platform, including the details of each call and message sent by the platform, which included: date and time of call; if call was answered; PIN entry success/failure; call time (seconds); at which part of the call flow the call was terminated; and response to pill reminder prompts. This information was used to calculate several variables (included in **Table 10** above): Connect for Life-generated percentage of medications taken; average time listened per call; proportion of calls answered; and proportion of health tips listened to. I intended to use these data to calculate a composite adherence measure and to determine level of engagement with the intervention. However, as described in other parts of this thesis, technical issues with the telecommunications provider resulted in poor fidelity of intervention delivery. Most participants received SMS only, and there was a limited amount of usage data from the Connect for Life platform.

Chapter 4: Baseline characteristics of cohort

This chapter describes the characteristics of study participants at the time of enrolment into the Connect for Life Philippines study. The analysis is based on questionnaires and medical record extraction from the baseline visits of each of the 462 study participants between October 2016 and December 2017. It describes sociodemographic factors, knowledge/attitudes/practices, Quality of Life (QOL), clinical characteristics, and adherence to ART. This analysis provides additional insights into the drivers of ART adherence in the study population, building and expanding upon the learnings from the formative research described in Chapter 2.

Objective 2 of the doctoral research was to conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to assess participant adherence, retention, and treatment outcomes at baseline and over follow-up. This chapter addresses part of this objective, by assessing the above factors at baseline.

This chapter is a research paper published in *Sexual Health* as an open access article in March 2021.(184) Chronologically, this was the first of four papers published. The Chapter that follows differs from the published version only in minor edits to wording (e.g. the replacement of the term "patient" with "participant" throughout) and minor changes to the use of acronyms.

Citation: O'Connor C, Leyritana K, Calica K, Gill R, Doyle AM, Lewis JJ, et al. Risk factors affecting adherence to antiretroviral therapy among HIV patients in Manila, Philippines: A baseline cross-sectional analysis of the Philippines Connect for Life Study. Sex Health. 2021;18(1):95–103.

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	LSH1512747	**Title**	Ms
First Name(s)		Cara Emily	
Surname/Family Name		O'Connor	
Thesis Title		Mobile Phone Adherence Support for HIV Patients in Manila, Philippines	
Primary Supervisor		Dr Aoife Doyle	

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?		Sexual Health	
When was the work published?		2 March 2021	
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion		n/a	
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	n/a
Please list the paper's authors in the intended authorship order:	n/a
Stage of publication	n/a

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the principal investigator of the study, wrote the protocol, supervised data collection, conducted data analysis, and was responsible for writing this manuscript. Co-authors contributed to study design, provided technical advice on data analysis, and provided editorial input on the manuscript.

SECTION E

Student Signature	[redacted]
Date	12/06/2023

Supervisor Signature	[redacted]
Date	07 Jun 23

4.0 Risk factors affecting adherence to antiretroviral therapy among HIV patients in Manila, Philippines: A baseline cross-sectional analysis of the Philippines Connect for Life Study

4.1 Abstract

Background: The Philippines HIV epidemic is one of the fastest growing, globally. Infections among men who have sex with men (MSM) are rising at an alarming rate, necessitating targeted evidence-based interventions to reach epidemic control. Treatment as prevention is a key strategy to end AIDS, making it a priority to explore novel approaches to retain people living with HIV (PLHIV) in care, support adherence, and reach viral suppression.

Methods: This cross-sectional analysis describes HIV-related risk behaviours and adherence to antiretroviral therapy (ART) in a population of HIV-positive patients at a clinic in Metro Manila, Philippines participating in the Philippines Connect for Life cohort study.

Results: Among 426 HIV-positive adults taking ART, 79% reported ≥95% adherence over the prior 30 days. Longer time on treatment was associated with reduced adherence to ART (adjusted odds ratio (aOR) = 0.87 per year, *P* = 0.027). Being in a mixed HIV-status relationship, in which the subject's primary partner was HIV negative, increased adherence (aOR = 3.19, *P* = 0.006). Inconsistent condom use (aOR = 0.50, *P* = 0.103) and injection drug use (aOR = 0.54, *P* = 0.090) are potentially associated with reduced adherence to ART. Participants used drugs and alcohol at significantly higher rates than the general population.

Conclusions: The study found that patients in this setting require intervention to address treatment fatigue. Interventions to improve social support of PLHIV, as well as harm-reduction approaches for drug and alcohol use, could improve adherence in this population, strengthening the test-and-treat strategy to control the epidemic.

4.2 Introduction

The Philippines has the fastest growing HIV/AIDS epidemic in the Asia–Pacific region.(3,121,186) National surveillance data show that the number of new HIV cases in the Philippines has risen at an alarming rate during the past decade, with an increase from 311 cases identified in 2007 to 11,427 cases identified in 2018 – a 36-fold increase in new HIV diagnoses.(223) According to the Joint United Nations Programme on HIV/AIDS (UNAIDS)'s surveillance reports, the Philippines' progress towards reaching HIV/AIDS 90–90–90 goals is slow, with 67% of people living with HIV (PLHIV) aware of their

status, 48% of those who know their status on treatment, and low coverage of viral load testing (<50%).(188)

Young men who have sex with men (MSM) are the key population in this emerging epidemic. Early in the HIV epidemic, most diagnoses were among heterosexual females, especially sex workers. Today, 85% of new cases are in MSM, the median age of new cases in the Philippines is 28 years, and more than 80% of people living with HIV/AIDS in the Philippines are aged under 35 years.(223) In 2015, a national surveillance survey found that HIV prevalence among MSM who practice anal sex was 6%, an increase from 3.3% in 2013.(6,14,81)

As the prevalence and incidence of HIV increase, it is imperative that as many people living with HIV as possible are diagnosed, started on treatment and successfully retained in care. Achieving adequate viral suppression through the use of antiretroviral therapy (ART) will be one of the key tools in ending the HIV epidemic in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and then ensuring high levels of adherence to ART and retention in care.(6,14,191) As in many developing countries, high rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence lead to poor outcomes for many HIV patients in the Philippines.(16,17)

Evidence-based public health interventions are needed. However, a 2015 report by the World Health Organization (WHO) highlights that the body of HIV research conducted in the Philippines has been limited,(192) and a systematic review of the HIV risk studies in the Philippines through April 2018 found only three publications that included data about the group most affected by HIV, MSM.(100)

This study aims to describe the demographic profile, clinical characteristics, HIV-related risk behaviours, quality of life (QOL), and ART adherence levels in a population of HIV-positive individuals comprised primarily of MSM receiving treatment at the Sustained Health Initiatives of the Philippines (SHIP) Clinic in Metro Manila, Philippines.

4.3 Methods

Study design, participants, and setting

A cross-sectional analysis was conducted using data from the baseline visit of a cohort study of patients at the SHIP clinic. The purpose of the larger cohort study was to evaluate the Connect for Life mobile phone adherence support intervention. Data were collected from October 2016 to December 2018.

The SHIP clinic is a public–private partnership, low-cost, fee-for-service facility in Mandaluyong, Metro Manila, which has provided HIV treatment and a comprehensive package of primary health care services to more than 900 patients since it opened in 2012. SHIP is a satellite partner clinic of the STI/AIDS Guidance Intervention & Prevention Unit at the Philippine General Hospital.

All patients starting or continuing on ART at the SHIP clinic who had a mobile phone and who spoke English (one of the two official languages in the Philippines and spoken fluently by nearly all of the patients from the study site) were eligible to participate in the study. Mobile phones were required because all patients who were enrolled would receive a mobile phone adherence intervention. The study coordinator approached patients during their routine clinic visits to provide information about the study and complete the informed consent process.

Measures

At the baseline study visit, the study coordinator collected demographic data and extracted medical history from the patient charts. Each participant completed a questionnaire on HIV-related knowledge, attitudes, and practices that was specific to the mobile phone adherence intervention and the WHO HIV Quality of Life brief questionnaire (WHOQOL-HIV BREF https://www.who.int/mental_health/publications/whoqol_hiv_bref.pdf). Patients who had taken ART before also completed an adherence questionnaire that was adapted from the AIDS Clinical Trials Group tools. All questionnaires were in English. The questionnaires were self-administered, with assistance from the study coordinator as requested.

The self-reported adherence measure used a visual analogue scale (VAS) in which participants reported the proportion of ART doses taken in the prior 30 days from 0–100%. For ART to be effective, it should be taken consistently, and early studies reported that ≥95% adherence to ART was required to achieve and maintain viral suppression.(224,225) More recent studies have shown that virological suppression may be achieved with adherence levels <95%; however, this is dependent on the duration of treatment and the ART regimen.(124,226,227) Therefore, in this analysis, those who took ≥95% of their ART doses were considered adherent, and <95% as non-adherent.

Statistical analysis

Descriptive data analysis was conducted to categorise the study population. Categorical variables were described with proportions and continuous variables were described with means and confidence intervals. We examined which characteristics of individuals were associated with adherence to ART of >95%. Crude odds ratios (ORs) were calculated with logistic regression to examine which demographic, behavioural, and clinical factors are related to self-reported adherence. Factors significant at *P*-value

<0.1 on univariate analysis were included in a multivariate logistic regression analysis. Clinical variables were excluded from the multivariate if there was plausible reverse causality between ART adherence and the clinical characteristics (i.e. viral load suppression). Where possible, continuous variables were used in the multivariate model, whereas categorical variables were used for illustrative purposes in the crude OR descriptive analyses. Data analysis was conducted in Stata 15 (StataCorp LLC).

Ethics

Ethical clearance was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016–265–01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent before inclusion in the study.

4.4 Results

The cross-sectional analysis included 426 individuals. Variables were included in the following categories: Demographics, Clinical Characteristics, HIV Knowledge, Risk Behaviours, QOL, Adherence/Reasons for Missing Medication.

At the time study enrolment began, the clinic had ~600 active patients. The study coordinator screened 485 patients as they presented during routine clinic visits, of whom 483 were eligible to participate in the study (one did not speak English, one did not have a Philippine mobile phone), and 462 patients provided consent and were enrolled (of the 21 who declined, the most common reason was that they did not want to receive calls or SMS related to the intervention). Of 462 people enrolled in the Connect for Life intervention study, 31 were either ineligible to fill out the adherence questionnaire (initiated ART at the study baseline visit and had not started taking pills) or had missing questionnaires; as a result 426 individuals reported ART adherence, and are included in this analysis. All but one of these 426 subjects were male (99.8%), and almost all were MSM (419/426 or 98.4%). The mean age was 32.4 years. University or postgraduate studies had been completed by 86% of participants (365/426), and 91% were employed (389/426), which reflects the higher socioeconomic status of patients who access private fee-for-service care.

Perfect adherence of 100% of doses taken in the last 30 days was reported by 52.1% (222/426), 95–99% was reported by 26.6% (113/426), adherence of 90–94% was reported by 12.7% (54/426), and adherence of <90% was reported by 8.7% (37/426) of participants.

Medical history was extracted from patient files and included time on ART, nadir CD4 count, history of opportunistic infections (OIs), current and past ART medications and regimen changes, viral load

suppression, and CD4 recovery. Various sociodemographic and clinical factors and their association with self-reported adherence to ART at ≥95% are reported in **Table 12.**

Participant demographic and clinical characteristics

Demographics

There is evidence to suggest that low education level is associated with non-adherence (OR = 0.20, *P* = 0.031). There was no strong evidence of associations between employment/profession or age and adherence.

Participants working in the Business Process Outsourcing (BPO) sector had lower adherence than other professions; this may be due to the varying shift times worked by call centre agents in this sector. Health workers had the highest adherence of any profession, followed by self-employed individuals. However, overall, there was no strong evidence of association between employment/profession and adherence.

Relationship status appears to be an important factor in ART adherence. Of the 27.9% of subjects (119/426) who were in a relationship, most were in a mixed-HIV status relationship in which their primary partner was HIV negative. Those in mixed HIV-status partnerships had improved odds of adherence to ART compared with individuals who were not in a relationship (OR = 2.49). The evidence suggests that being in seroconcordant relationships (both HIV positive) and disclosure of HIV status to a trusted person may also be factors that improve adherence; however, the sample size in this study was insufficient to reach these conclusions with confidence.

Adherence and viral suppression

Self-reported adherent participants were more likely to be virally suppressed (OR = 3.1, *P* = 0.016).

Time on ART and virological failure

Having been on ART for a longer time led to decreased adherence (0–6 months: OR = 1.00; 6 months–1 year: OR = 0.36; 1–2 years: OR = 0.43; 2–4 years: OR = 0.32; ≥4 years: OR = 0.25; *P* = 0.013), which indicates that participants may be experiencing treatment fatigue over time.

In total, 27.9% of participants (119/426) had changed their ART medications at least once. Of those who changed regimens, 17.7% (21/119) had to change due to virological failure, whereas the remaining 98 people changed for other reasons such as intolerance/side effects or depression worsened by efavirenz (EFV). Only 7.5% of participants (32/426) were on second-line lopinavir/ritonavir (LPV/r) or multiple-resistance ART regimens, whereas 92.5% (394/426) were on efavirenz, nevirapine, or rilpivirine-based first-line ART regimens.

CD4 and opportunistic infections history

Most participants had a nadir CD4 count in the range of 200–350 cells/mm3, indicating that they were diagnosed and started on ART before disease progression to AIDS. However, 74 participants (17.4%) had nadir CD4 count <50 cells/mm3, indicating that they did not receive HIV diagnosis and treatment until they were already severely immune-compromised. Only 51.5% (206/400) of participants who had a nadir CD4 count <500 cells/mm3 had reached CD4 recovery back to levels <500 cells/mm3.

History of opportunistic infection was common, with 61% of participants (260/426) having one or more potential opportunistic infections recorded in their complete medical history. Pneumocystis pneumonia (PCP) history was recorded in the medical history of 6% of participants (27/426), and 5% had a history of thrush (20/426). Hepatitis B at 11% (46/426) and tuberculosis (TB) history at 18% (76/426) are similar to the overall population rates of these diseases, which are endemic to the Philippines.(228,229) Hepatitis C prevalence was 0.7% in our cohort (3/426), which is also similar to the general population rate.19 Over 13% of participants (57/426) had a history of syphilis and 39% (166/426) had had another sexually transmitted infection (STI). There was no evidence of an association between ART adherence and nadir CD4, CD4 recovery, or opportunistic infection history.

Table 12. Participant characteristics.

Participant characteristics	Total		Adherent ≥95%		Non-adherent <95%		Crude OR (95% CI)	*P*-value
	(*n* = 426) *n*	(%)	(*n* = 335) *n*	(%)	(*n* = 91) *n*	(%)		
Gender								
Male	425	99.77	334	78.59	91	21.41	–	
Female	1	0.23	1	100.00	0	0.00	–	
Age (years)								
18–24	19	4.46	17	89.47	2	10.53	1.00	0.498
25–29	119	27.93	95	79.83	24	20.17	0.47 (0.10–2.16)	
30–39	245	57.51	188	76.73	57	23.27	0.39 (0.09–1.73)	
≥40	43	10.09	35	81.40	8	18.60	0.51 (0.10–2.69)	
Education								
Elementary or less	10	2.35	4	40.00	6	60.00	0.20 (0.05–0.72)*	0.010*
High School/Vocational	19	4.46	15	78.95	4	21.05	1.11 (0.36–3.44)	
College/University	316	74.18	244	77.22	72	22.78	1.00	
Postgraduate	49	11.50	44	89.80	5	10.20	2.60 (0.99–6.79)	
Unknown/Did not report	32	7.51	28	87.50	4	12.50	2.07 (0.70–6.08)	
Employment								
Business Process Outsourcing (BPO)	88	20.66	66	75.00	22	25.00	1.00	0.406
Self-Employed/Other	38	8.92	34	89.47	4	10.53	2.83 (0.90–8.89)	
Health Worker	16	3.76	15	93.75	1	6.25	5.00 (0.62–40.06)	

Professional[A]	234	54.93	182	77.78	52	22.22	1.17 (0.66–2.07)	
Student	13	3.05	10	76.92	3	23.08	1.11 (0.28–4.41)	
Unemployed	37	8.69	28	75.68	9	24.32	1.04 (0.42–2.53)	
Sexual orientation								
Bisexual	128	30.05	96	75.00	32	25.00	1.00	
Heterosexual	7	1.64	6	85.71	1	14.29	2.00 (0.23–17.25)	0.467
Homosexual	290	68.08	232	80.00	58	20.00	1.33 (0.81–2.18)	
Pansexual	1	0.23	1	100.00	0	0.00	–	
Civil status								
Married/Common-law partner	21	4.93	19	90.48	2	9.52	1.00	
Single	404	94.84	315	77.97	89	22.03	0.47 (0.11–2.10)	0.282
Unknown/Did not report	1	0.23	1	100.00	0	0.00	–	
Mixed HIV-status								
Not in a relationship	262	61.50	199	75.95	63	24.05	1.00	
Same HIV-status relationship (both HIV+)	48	11.27	41	85.42	7	14.58	1.85 (0.79–4.34)	
Mixed HIV-status relationship (partner is HIV–)	71	16.67	63	88.73	8	11.27	2.49 (1.13–5.48)*	0.030*
Unknown/Did not report	45	10.56	32	71.11	13	28.89	0.78 (0.39–1.58)	
Disclosure of HIV status to family/friend								
Disclosed	137	32.16	113	82.48	24	17.52	1.00	
Not disclosed	207	48.59	155	74.88	52	25.12	0.63 (0.37–1.09)	0.181
Unknown/Did not report	82	19.25	67	81.71	15	18.29	0.95 (0.47–1.93)	
Time on ART, years (mean)	2.77 years (95% CI 2.58–2.96)		2.61 (2.40–2.82)		3.35 (2.90–3.79)			
0–6 months	46	10.80	42	91.30	4	8.70	1.00	
6 months – 1 year	38	8.92	30	78.95	8	21.95	0.36 (0.10–1.3)	
1–2 years	83	19.48	68	81.93	15	18.07	0.43 (0.13–1.39)*	0.078
2–4 years	162	38.03	125	77.16	37	22.84	0.32 (0.11–0.96)*	
>4 years	97	22.77	70	72.16	27	27.84	0.25 (0.08–0.75)*	
Nadir CD4 (cells/mm^3) (Mean)	245 (95% CI 229–260)		246 (227–263)		244 (212–275)			
0–200	163	38.26	132	80.98	31	19.02	1.00	
200–499	237	54.76	179	75.53	58	24.47	0.72 (0.44–1.18)	0.065
500+	26	6.93	24	92.31	2	7.69	2.82 (0.63–12.56)	
Viral Suppression								
Undetectable	257	92.45	207	80.54	50	19.46	3.11 (1.24–7.77)	0.020*
Detectable (>500 copies)	21	7.55	12	57.14	9	42.86	1.00	

*OR, odds ratio; CI, confidence interval; ART, antiretroviral therapy

**Adherence is self-reported over the last 30 days.

[A]'Professional' is a broad category that includes participants who work as corporate or government employees, and workers in the education, IT, science, engineering, media, and sales and marketing sectors.

Risk behaviours

The association between risk behaviours and ART adherence is outlined in **Table 13.**

Sexual partners and condom use

The mean number of sex partners for participants in the last six months was 2.73. Among participant 21.8% reported zero partners (93/426), 32.2% reported one partner (137/426), 23.2% reported between two and nine partners (99/426), and 4.2% reported >10 partners (18/426), whereas 20.9% (89/426) of participants did not provide an answer on the questionnaire. Only 6% (25/426) of the participants reported having ever engaged in transactional sex, and of those, only two participants had had transactional sex within the last six months. In the study population, 41.3% (176/426) reported they always use condoms and 35.4% (151/426) use them some of the time or most of the time. This inconsistent condom use was associated with non-adherence to ART (OR = 0.48, *P* = 0.007); however, individuals who reported never using condoms did not have reduced odds of ART adherence.

Drug and alcohol use

In our study population, 9.4% (40/426) used 'shabu' (methamphetamine hydrochloride), 8.0% (34/426) used cannabis, 4.5% (19/423) used prescription drugs for non-medical use, and 1.4% (6/426) used inhalants (e.g. 'rugby' or 'poppers') within the last three months, and 0.7% (3/426) of respondents did not complete the substance use portion of the questionnaire. Injecting drug users (IDU) were 12.2% (52/426) of the study population; 52 who had ever injected drugs and 28 who had done so within the last three months. Among injecting drug users, the odds of ART adherence were lower (IDU ever OR = 0.46, *P* = 0.015; injecting drug use in last three months OR = 0.38, *P* = 0.019). Only two individuals reported ever having shared needles for injecting drugs. There was no association between adherence and non-injecting drug use.

Although 30.5% (130/426) of participants abstained from alcohol, 37.3% (159/426) engaged in heavy episodic drinking in the last 30 days. Problem drinking, defined as two or more episodes of heavy episodic or 'binge' drinking (>five drinks) in the last month or >14 drinks per week on average,(230,231) was prevalent in 13.4% (57/426) of the study population. Alcohol use did not have an association with ART adherence.

Quality of life

The WHOHIV-QOL BREF scores QOL in six domains, a maximum of 20 points per domain and a total score of 120. The mean for each of the six domains and the total WHOHIV-QOL BREF score are as follows: Physical 15.21; Psychological 15.04; Level of Independence 15.54; Social Relationships 15.01; Environmental 13.43; and Spirituality 14.44. The domain with the lowest overall score was

Environment, which measures aspects such as safety and security; access to health care; financial resources; opportunities for learning and for leisure; and physical environment (pollution/noise/traffic/climate).(232)

The mean QOL score in the cohort was 88.68 (95% CI 87.46–89.89). Just under half (46.5%) of the 426 participants had an overall QOL score of ≥90, which represents a high QOL, and 52.3% had a medium QOL with a score between 60 and 89. Only five participants (1.3%) had a QOL score <60. One participant did not complete the QOL questionnaire. There was no significant association between ART adherence and overall QOL (**Table 13**) or individual QOL domains (data not shown).

Knowledge of HIV

There was evidence of an association between knowledge of HIV, as scored on a 16-item questionnaire, and ART adherence. There is an association between scoring 80% and 89% on the HIV knowledge questionnaire and lower adherence (OR = 0.49, *P* = 0.044). This association does not hold for those scoring >90% and the reason for the association is unclear, warranting further investigation.

Table 13. Association between risk behaviours and antiretroviral therapy adherence.

	Total (*n* = 426)		Adherent ≥95% (*n* = 335)		Non-adherent <95% (*n* = 91)		Crude OR (95% CI)	*P*-value
	n	(%)	*n*	(%)	*n*	(%)		
Condom usage in last 6 months								
Always	176	41.31	146	82.95	30	17.05	1.00	
Sometimes/Most of the time	151	35.45	106	70.20	45	29.80	0.48 (0.29–0.82)*	0.043*
Never	78	18.31	66	84.62	12	15.38	1.13 (0.54–2.35)	
N/A (not sexually active)	21	4.93	17	80.95	4	19.05	0.87 (0.27–2.78)	
Transactional sex								
Never had transactional sex	399	93.66	314	78.70	85	21.30	1.00	
Ever had transactional sex	25	5.87	20	80.00	5	20.00	1.08 (0.39–2.97)	0.662
Unknown/Refused	2	0.47	1	50.00	1	50.00	0.27 (0.02–4.37)	
Drug use in last 3 months								
No	356	83.57	282	79.21	74	20.79	1.00	
Yes	70	16.43	53	75.71	17	24.29	0.82 (0.45–1.50)	0.519

Injection drug use ever								
No	374	87.79	301	80.48	73	19.52	1.00	
Yes	52	12.21	34	65.38	18	34.62	0.46 (0.25–0.86)*	0.018*
Heavy alcohol use								
No	363	86.43	289	79.61	74	20.39	1.00	
Yes	57	13.57	41	71.93	16	28.07	0.66 (0.35–1.23)	0.201
Quality of life (QOL)	88.68 (95% CI 87.46–89.89)		89.45 (88.13–90.76)		85.85 (82.97–88.73)			
High (90–120)	183	46.45	148	80.87	35	19.13	1.00	
Medium (60–89)	206	52.28	159	77.18	47	22.82	0.80 (0.49–1.31)	0.427
Low (0–59)	5	1.27	3	60.00	2	40.00	0.35 (0.06–2.20)	
HIV knowledge Score (mean, %)	85.01% score (95% CI 83.74–86.29)		85.01% (83.53–86.49)		85.03% (82.54–87.51)			
<80	95	22.35	80	84.21	15	15.79	1.00	
80–89	163	38.35	118	72.39	45	27.61	0.49 (0.26–0.94)*	0.044*
≤90	167	39.29	136	81.44	31	18.56	0.82 (0.42–1.62)	

*OR, odds ratio; CI, confidence interval; N/A, not applicable

Adherence/reasons for missing medication

There were 228 study participants who reported having missed medications at any point in the past; the reasons they reported for ever missing medications are detailed in **Figure 8**. The most common reasons for missing medications were that the participant was busy, forgot, fell asleep, was away from home, or had a change in their daily routine. Stigma is also a factor affecting adherence, as 44% of participants who had skipped a pill at some point did so because they did not want to be seen taking medications. Issues around side effects, toxicity, and pill burden were the least likely contributors to non-adherence.

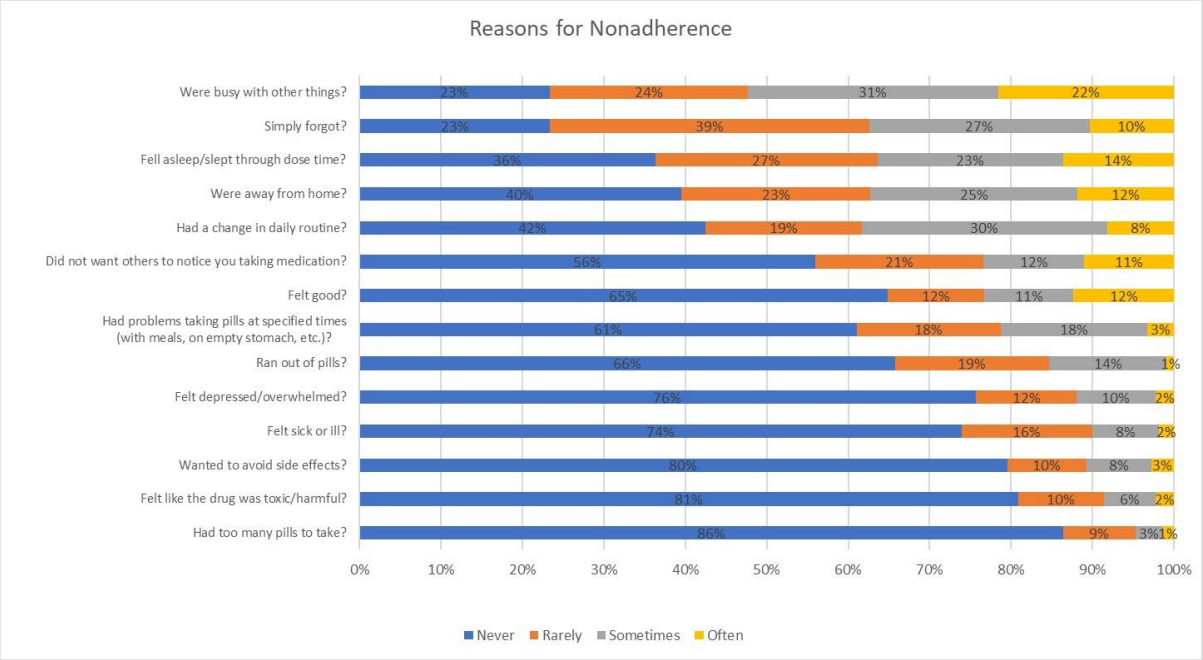

Figure 8. Reasons for missing medication (n=228).

Multivariate logistic regression model for adherence to antiretroviral therapy

In the final multivariate logistic regression model (**Table 14**), time on ART (adjusted OR (aOR) = 0.87 per year, *P* = 0.027 partner HIV status (*P* = 0.006)), and knowledge score (*P* = 0.047) were associated with ART adherence. Injection drug use and inconsistent condom use (using condoms sometimes or most of the time) may also be related to adherence, whereas the study sample may have been too small to evaluate these factors.

Table 14. Multivariate logistic regression analysis of factors associated with antiretroviral therapy (ART) adherence.

Variable	Adjusted OR	95% CI	*P*-value
Education			
Elementary or less	0.42	(0.10–1.75)	
High School/Vocational	1.16	(0.36–3.82)	
College/University	1.00		0.084
Postgraduate	2.40	(0.87–6.63)	
Unknown	2.57	(0.81–8.16)	
Partner HIV status			
N/A not in a relationship	1.00		
Same-HIV-status relationship (both HIV+)	2.37	(0.95–5.93)	0.006*
Mixed-HIV-status relationship (partner is HIV–)	3.19	(1.39–7.35)	
Unknown	0.81	(0.37–1.79)	
Time on ART, years	0.87	(0.77–0.98)	0.027*
Nadir CD4 (cells/mm^3)			
0–200	1.00		
200–499	0.78	(0.46–1.33)	0.1334
500+	2.87	(0.60–13.61)	

Condom usage (in last 6 months)			
Always	1.00		
Sometimes/Most of the time	0.50	(0.28–0.89)	0.103
Never	0.81	(0.24–2.75)	
N/A (not sexually active)	0.94	(0.43–2.06)	
Injection drug use (in last 3 months)	0.54	(0.27–1.09)	0.090
HIV Knowledge Score (mean, %)			
<80	1.00		
80–89	0.47	(0.23–0.94)	0.047*
≤90	0.81	(0.39–1.67)	

*OR, odds ratio; CI, confidence interval; N/A, not applicable

4.5 Discussion

Twenty-one per cent (91/426) of the study participants reported suboptimal adherence. By comparison, ~37% of participants globally report suboptimal adherence to ART,(118,124) and in the regional Therapeutics Research, Education, and AIDS Training in Asia (TREAT Asia) cohort (which includes a large treatment site in the Philippines), 32% of 1316 participants reported suboptimal adherence of <100%.(17) As expected, self-reported adherent participants were more likely to be virally suppressed, which indicates that participants self-report of adherence or non-adherence accurately reflects their pill-taking behaviour.

The study found that people who had been on treatment longer were less likely to be adherent to their ART. This finding is contrary to the TREAT Asia regional cohort study, which found 26% of participants self-reported suboptimal adherence levels during their first six months of treatment, and that adherence improved over time from initiation to 24 months. (17) These contradictory findings warrant further investigation. Reasons for non-adherence in this study were largely situational factors, habits, and routines, whereas clinical issues such as side effects and pill burden were less likely to impact adherence in this population.

Condom use in this study population was comparable to the general MSM population in the Philippines – 41.3% (146/405) of the sexually active SHIP population study participants always use condoms and 35.5% (151/405) use condoms most or some of the time, whereas the 2013 surveillance data showed 40.7% condom use at last anal sex among MSM. (14,60) Inconsistent condom use (using condoms sometimes or most of the time) may be associated with ART non-adherence, which suggests that motivating factors and abilities that enable a participant to adhere to ART could also be the same factors that lead to consistent condom use. The average total number of sex partners in the last six months was 2.14, which is lower than has been reported in other surveillance of MSM in the

Philippines;(14,60) this may indicate that MSM reduce their sexual activity after becoming HIV positive and starting ART, a question that warrants further investigation.

Relationship status appears to be an important factor in ART adherence. Participants in mixed HIV-status relationships were more likely to adhere to ART. The data suggest that being in a relationship, regardless of the partner's HIV status, is better than being single when it comes to ART adherence, and that disclosure of one's HIV-positive status to a trusted person can also lead to better outcomes. These findings emphasise the important role of partner, family and social support for PLHIV in order to achieve good clinical outcomes.

Another key finding in this study is that the study participants used drugs and alcohol at rates five- to 10-fold higher than the general population. In the Philippines general population, 44.7% of males abstain from alcohol and 3.5% of males engage in heavy episodic drinking,(233) whereas in our study population, only 30.5% abstained and 37.3% had engaged in heavy episodic drinking in the last 30 days. According to the United Nations Office on Drugs and Crime, 1.1% of Filipinos use 'shabu' (methamphetamine hydrochloride) and 1.6% use cannabis.(234) In our study population, 9.9% had used 'shabu' and 7.7% used cannabis within the last three months. Methamphetamine use is strongly associated with high-risk sexual behaviour and HIV acquisition,(235) and is commonly used by MSM in chemsex or 'Partee 'n' Play' activities. Compounding these risks, evidence-based HIV prevention services are not widely available in the Philippines – condom distribution is restricted,(236,237) pre- and post-exposure prophylaxis are not widely available, except through very limited pilot projects, and syringe exchange is illegal under the current administration's interpretation of the Philippines' Dangerous Drugs Act of 2002.

Limitations

This study is limited by several factors. First, adherence and risk behaviours were self-reported, and the responses are subject to social desirability bias. However, adherence was strongly associated with viral load suppression, and risk behaviours were not significantly lower than the general population (and in many cases much higher), which suggests that the self-report method was generally accurate. Furthermore, the generalisability of study data from the SHIP clinic population is limited. Due to the higher socioeconomic status and education levels of the SHIP clinic patients, and due to the fact that it is a fee-for-service clinic, the cohort may not be representative of MSM in the Philippines more broadly. Apart from employment, education, and high HIV knowledge levels, other demographic factors (age, clinical outcomes, risk profile) align with other published data on MSM and people living with HIV from the country.(5,14,60,81) Ongoing follow-up of the SHIP Connect for Life study cohort

will provide further details about incidence of opportunistic infections, retention in care, and ART adherence.

4.6 Conclusions

This study provides an in-depth analysis of demographic, clinical, and behavioural characteristics of MSM living with HIV in the Philippines, which can improve understanding of the country's epidemic and may be used to inform tailored prevention and treatment interventions.

Factors found to be associated with adherence to HIV treatment were time on ART, being in a mixed HIV-status relationship in which the person's main partner is HIV negative, and HIV knowledge level.

The issue of treatment fatigue warrants further investigation and should be addressed through implementation of tailored adherence interventions. Clinicians and other service providers should prioritise counselling and interventions to improve family and social support for PLHIV. There is also an unexplored opportunity for harm-reduction interventions among HIV-positive and HIV-negative MSM who use drugs and alcohol.

Chapter 5: Process evaluation

This chapter includes findings from the mixed methods process evaluation of the Connect for Life project. The process evaluation answers questions related to reach/recruitment, implementation fidelity, dose delivered, dose received, usability, acceptability, satisfaction, and cost. Using the mHealth Evidence Reporting and Assessment (mERA) checklist (238) and the Linnan and Steckler process evaluation framework,(239) this evaluation describes the intervention successes and challenges in a manner that is intended to be useful to others implementing or researching a similar intervention.

Objective 2 of the doctoral research was to conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to assess participant adherence, retention, and treatment outcomes at baseline and over follow-up. This chapter addresses the aspect of this objective related to evaluation of the implementation process.

This chapter is a research paper that was published in *JMIR Formative Research* as an open access article in August 2022. (185) Chronologically, this was the third of four papers published. The chapter that follows differs from the published version only in minor edits to wording (e.g. the replacement of the term “patient” with “participant” throughout) and and minor changes to the use of acronyms.

Citation: O’Connor C, Leyritana K, Doyle AM, Birdthistle I, Lewis JJ, Gill R, et al. Delivering an mHealth Adherence Support Intervention for Patients With HIV: Mixed Methods Process Evaluation of the Philippines Connect for Life Study. JMIR Form Res. 2022;6(8).

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SECTION A – Student Details

Student ID Number	LSH1512747	**Title**	Ms
First Name(s)		Cara Emily	
Surname/Family Name		O'Connor	
Thesis Title		Mobile Phone Adherence Support for HIV Patients in Manila, Philippines	
Primary Supervisor		Dr Aoife Doyle	

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?		JMIR Formative Research	
When was the work published?		12 August 2022	
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion		n/a	
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	n/a
Please list the paper's authors in the intended authorship order:	n/a
Stage of publication	n/a

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the principal investigator of the study, wrote the protocol, supervised data collection, conducted data analysis, and was responsible for writing this manuscript. Co-authors contributed to study design, provided technical advice on data analysis, and provided editorial input on the manuscript.

SECTION E

Student Signature	[redacted]
Date	12/06/2023

Supervisor Signature	[redacted]
Date	07 Jun 23

5.0 Delivering an mhealth adherence support intervention for people with HIV: Mixed methods process evaluation of the Philippines Connect for Life Study

5.1 Abstract

Background: The Philippines HIV epidemic is one of the fastest growing epidemics globally, and infections among men who have sex with men are increasing at an alarming rate. Connect for Life Philippines is a mobile health (mHealth) intervention that supports antiretroviral therapy (ART) adherence in this key population, through individualized voice calls and SMS text messages.

Objective: The objective of this process evaluation was to assess the intervention reach, dose delivered and received, fidelity, and acceptability and to describe contextual factors affecting the implementation of an mHealth adherence support intervention for patients on ART in a clinic in Metro Manila, Philippines.

Methods: A mixed methods process evaluation approach was used in an observational cohort study. Quantitative data sources for the process evaluation were call and SMS text message logs obtained from the mHealth platform and questionnaires collected at 12-, 24-, and 48-week study visits. Qualitative data were collected from process reports and through a series of focus group discussions conducted with a subset of participants during the intervention development phase, after an initial 8-week pilot phase, and at the end of the study.

Results: The 462 study participants received 31,095 interactive voice calls and 8,234 SMS text messages during the study. Owing to technical issues, intervention fidelity was low, with only 22.1% (102/462) of the participants receiving reminders via voice calls and others (360/462, 77.9%) receiving only SMS text messages during the intervention. After 48 weeks in the study, 63.5% (293/462) of the participants reported that they would be quite likely or very likely to recommend the programme to a friend, and 53.8% (249/462) of the participants reported that they benefited quite a bit or very much from the intervention. Participants who were on ART for <6 months at the beginning of the study and those who received the daily or weekly pill reminders were more likely to report that they benefited from the intervention (P = .02 and P = .01, respectively).

Conclusions: The Connect for Life intervention had high participant satisfaction and acceptability, especially among those who received high dose of the intervention. However, poor reliability of local telecommunication networks had a large impact on the intervention's usability, fidelity, and dose received.

5.2 Introduction

Background

The HIV epidemic in the Philippines is one of the fastest growing epidemics globally, with 207% increase in new HIV infections and 388% increase in AIDS deaths from 2010 to 2020. In 2020, an estimated 73% of people living with HIV in the Philippines knew their status and 44% of people living with HIV were on antiretroviral therapy (ART).(188,189,240,241) In two studies of cohorts of people with HIV in Manila, 84% to 90% of people who started ART had achieved viral suppression.(241,242) Most new and existing HIV infections occur among men who have sex with men (MSM).(240) Improving treatment coverage, retention, adherence, and viral suppression are key to slowing the spread of HIV in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging people in HIV testing and ensuring high levels of adherence to ART and retention in care.(6,14,191) High rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence lead to poor outcomes in many PLHIV in the Philippines.(16,17)

This paper describes the process evaluation of a mobile phone technology for health (mobile health [mHealth]) intervention for people living with HIV in Metro Manila, Philippines. To support ART adherence, the intervention, Connect for Life, provided participants with HIV with individualised voice calls and SMS text messages, pill reminders, appointment reminders, symptom reporting, health tips, and adherence feedback.

The Connect for Life platform was developed by Janssen Global Public Health, and before adaptation for the Philippines, its versions were piloted in India and Uganda. The mMitra (mobile friend) project in India aimed to improve maternal health outcomes through health messages to pregnant women.(243,244) The Treatment Advice using Mobile Alerts project in India (210,245) and Call for Life Uganda (220,221) supported ART adherence among people living with HIV.

Process evaluation of mHealth interventions

As mHealth technologies have become widespread in low-income and middle-income countries, mobile phone interventions have become increasingly popular in the global health and development sectors as an inexpensive and efficient way to communicate and deliver services. Several trials have shown that mHealth approaches show potential for improving self-management of chronic diseases, including adherence to HIV medications,(107,108,130,131,246) whereas systematic reviews show

mixed outcomes of mHealth interventions and highlight the need for more rigorous evaluation methods and long follow-up periods in mHealth studies.(112,143,144,148,156,197,199,247–249)

Trials assessing mHealth adherence interventions for HIV often do not include process evaluations to examine the fidelity and quality of the intervention delivery, causal mechanisms for the health outcomes, contextual factors affecting the delivery, and costs to implement.(249–251) For mHealth interventions, current guidance suggests that practitioners should also include a minimum set of information about the content, context, and technical features of the intervention, including aspects such as ease of use, content quality, privacy and security, service quality, personalisation, and perceived enjoyment.(238,252–254)

Process evaluations of SMS text messages and interactive voice response systems (IVRSs) have examined fidelity, reach, dose delivered, and user satisfaction for projects ranging from water and sanitation to prevent diarrheal disease (255); airline pilot fatigue (256); and prevention of weight gain, smoking, or HIV among young people.(257–259) A systematic review of mHealth projects in Africa found that in projects where acceptability and usability of mHealth technology among participants was measured, it was generally high. However, infrastructure issues (unreliable network and internet and electricity access) were frequently cited as key challenges in delivery.(112)

The success of mHealth projects in achieving the intended health outcomes is almost entirely dependent on the adaptation and delivery of the intervention in local contexts. Having a complete understanding of the implementation process of an mHealth intervention can enable practitioners to interpret the outcomes and replicate the intervention in other contexts. Therefore, we performed a process evaluation alongside the Connect for Life Philippines prospective cohort study. The process evaluation examined the fidelity, dose delivered and received, reach, usability, acceptability, and cost of the Connect for Life Philippines intervention.

5.3 Methods

Recruitment

The study was conducted at the Sustained Health Initiatives of the Philippines (SHIP) Clinic, a low-cost, private facility in Metro Manila, a city with approximately 13 million people in the predominantly Catholic country of the Philippines.

SHIP clinic provides HIV primary care and wraparound services to approximately 900 people living with HIV. Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at initial

consultation. Most are full-time or part-time employees. The clients come from all regions of Metro Manila, and some live in other provinces.

Recruitment into the Connect for Life study occurred in person at the study site between October 2016 and December 2017. As patients checked in for their routine clinic visits, the study coordinator approached all patients seated in the clinic waiting room, briefly introduced the study following a recruitment script, elicited their interest in participating, screened them for eligibility, completed the informed consent process, and provided a brief orientation to the intervention.

Connect for Life mobile phone ART adherence support intervention

The study team worked with IT specialists and public health professionals from Jannsen Global Public Health, University of the Philippines, and local IT companies to develop the content and functionality of the Connect for Life mHealth platform (**Figure 9**). Connect for Life is a technology built on the Mobile Technology for Community Health (MOTECH; Grameen Foundation) open-source software platform.(180) It enables health facilities to connect to participants via their mobile phones through IVRS call flows or SMS text messages. As Connect for Life works through phone calls and SMS text messages, it does not require the user to have a smartphone, install an app, or have mobile internet connection. This makes it accessible to a wide range of users in the Philippines, where, in 2015, mobile phone penetration was high, but smartphone coverage and internet access were low (with 113 mobile subscriptions per 100 people, 99% of the population reached by network coverage, and 22% of the population owning a smartphone).(104,106,260)

The study team tailored the Connect for Life platform for the Philippine context. Some existing features were retained, such as reminders sent on the recipient's preferred days and times, health tips, and symptom screening. New features were developed, such as medical record functionality and adherence feedback scores. Clinicians at the study site developed new content for the voice and SMS text messages, which were recorded by a local voice talent agency. During the formative study and intervention development stage, a series of focus groups were conducted to engage with patients at the clinic about their adherence behaviours and preferences for configuration and content, and their feedback was incorporated to ensure that the intervention was tailored to the target population.(183,184,261)

The Connect for Life system was installed in a secure cloud server environment and linked to a local telecom provider through application programming interface integration to execute calls and SMS text messages. A local IT service provider was contracted to monitor server functionality, install software updates, and troubleshoot technical issues. The Connect for Life software developers provided in-

depth technical training and software documentation to the local IT provider and training for the clinical staff on how to use the Connect for Life web-based platform.

The intervention development process was guided by the Behaviour Change Wheel and the Capability Opportunity Motivation–Behaviour model developed by Michie, Atkins, and West.(203,205,262) Behaviour change techniques related specifically to ART adherence were informed by the information–motivation–behavioural skills model of ART adherence.(206) Each service in the intervention package was designed to address ≥1 of the three main components that drive behaviour in the Capability Opportunity Motivation–Behaviour model, as outlined in **Figure 10**.(183,184)

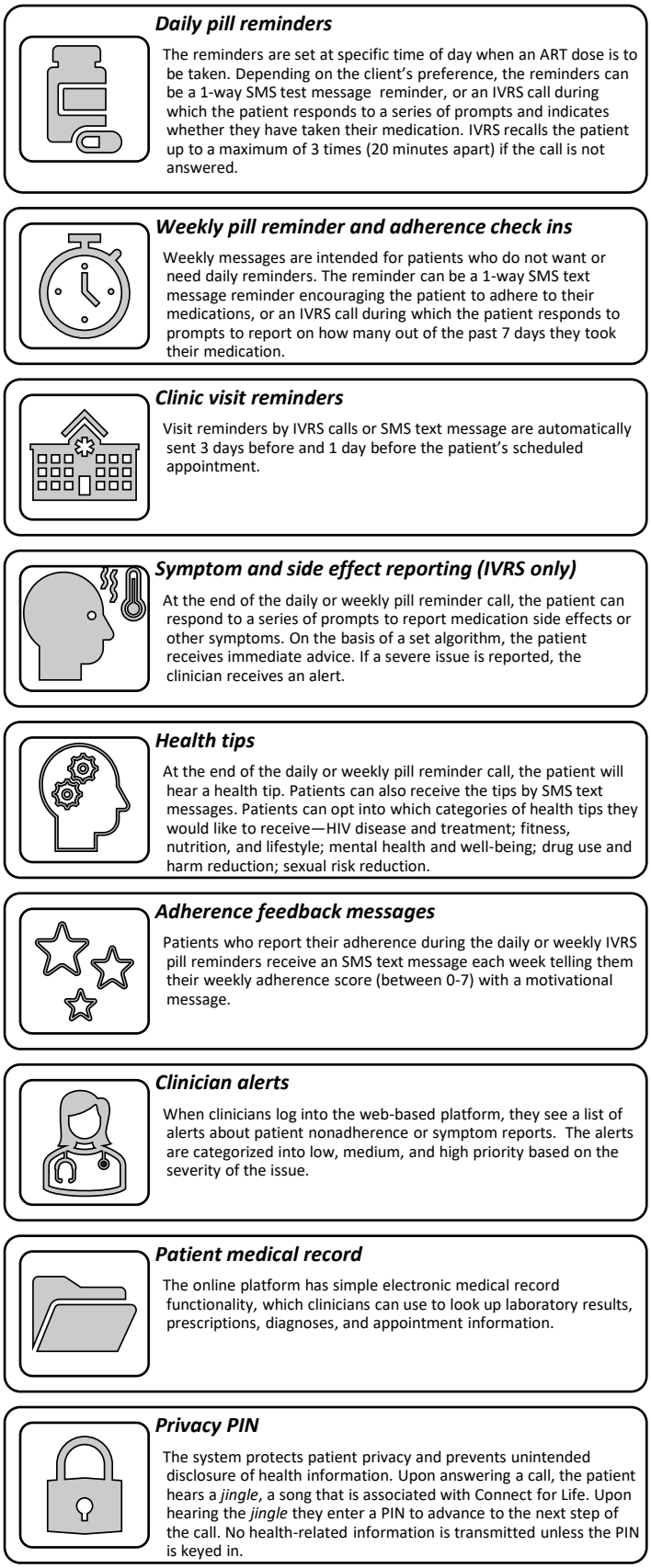

Figure 9. Connect for Life Philippines mobile health intervention functions.

*ART: antiretroviral therapy; IVRS: interactive voice response system; PIN: personal identification number.
*SMS: short message service

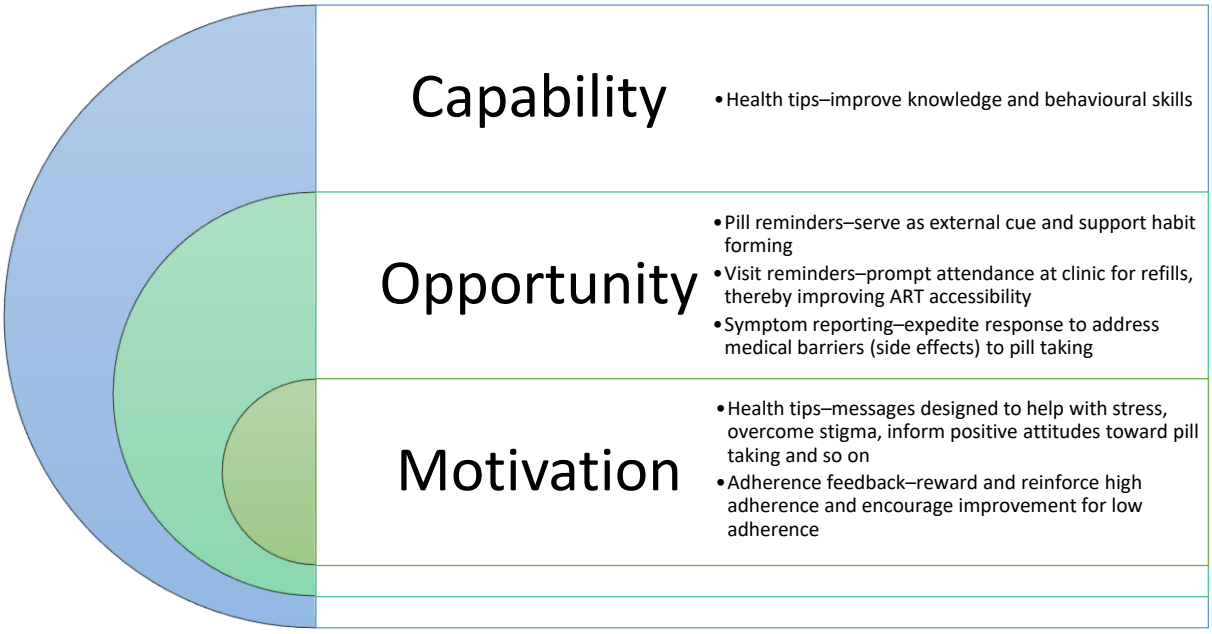

Figure 10. Intervention theory of change.

*ART: antiretroviral therapy.

Data collection and analysis

A mixed methods approach was used with qualitative data embedded in the experimental design of the 48-week prospective cohort study.(263) The design allowed us to assess participants' use of and experience with the system and use quantitative and qualitative analyses to generate complementary data about acceptability, usability, and the impact of contextual factors on the intervention.

The process evaluation measures were based on the framework proposed by Linnan and Steckler,(239) which defines the approach to adequately describe the context, reach, dose (delivered and received), acceptability, and fidelity of the intervention. Additional aspects related to reporting on mHealth technology were included based on guidance from the mHealth Evidence Reporting and Assessment (mERA) checklist.(238)

The process evaluation questions, tools, methods, and data sources are described in **Table 17** (included at end of chapter)**.**

To measure the fidelity and dose of intervention delivery, records from the mHealth platform detailing the services received by each participant were exported. To understand the usability and acceptability of the intervention, participants completed self-administered paper-based questionnaires at three time points during the study. Where questionnaires had blank or missing fields, all available data points were included in the analysis. Data distributions were explored to categorise the responses to the

questionnaires. Associations between acceptability of the intervention and independent variables (time point, treatment experience, and reminder frequency) were calculated using chi-squared tests. Data analysis was conducted using Stata 15.

Qualitative feedback was collected in several ways: routine monthly process reports from clinicians to document implementation successes and challenges, comments recorded on the acceptability questionnaires, and a series of focus group discussions. The study team conducted two focus groups with a total of 12 participants during the intervention development phase in 2016. In early 2017, a total of two additional focus groups were conducted with five participants after an 8-week pilot phase. Finally, in 2018, during the final two months of the study, three focus groups were conducted with 15 participants. The discussions were transcribed, transcripts were manually coded using a deductive coding methodology to group responses by topic areas in the focus group discussion guide, subtopics were assigned through line-by-line coding, and data were consolidated in a structured template that enabled identification of salient themes. Results from the focus group discussions in the formative and pilot phases informed the content and structure of the intervention and helped to identify implementation issues early in the project.(183)

Ethics approval

Ethics approval for the study was obtained from the University of the Philippines Manila research ethics board (protocol number 2016-265-01) and the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent before inclusion in the study.

5.4 Results

Study population and intervention delivery

Process evaluation questions 1 and 2: reach and recruitment

Of approximately 675 patients receiving ART services at the study site during the recruitment period, 485 (71.9%) were approached by the study coordinator while attending a routine visit at the clinic, 464 (68.7%) were interested in learning about the study, and 462 (68.4%) met the eligibility criteria and consented to participate.

Reasons for refusal (21/485, 4.3%) included no need or desire for adherence support, not wanting to receive messages or calls on their mobile phone, privacy concerns, and frequent travel out of the country. Of the 0.4% (2/464) of the patients who were excluded, one was ineligible because he did not speak English and the other did not have a mobile phone.

All but one of the participants in the study (461/462, 99.8%) identified as male, and 98.5% (455/462) were MSM. The mean age at enrolment was 32.4 years (SD 5.7). University or postgraduate studies had been completed by 85.9% (397/462) of the participants, and 91.3% (422/462) were employed or enrolled in university, which reflects the higher-than-average socioeconomic status of people attending the study site, a private fee-for-service clinic.

At the time of enrolment, 92.2% (426/462) of the participants were already taking ART and 7.8% (36/462) had not yet started. Of those already taking ART, perfect adherence of 100% of doses taken in the last 30 days was reported by 52.1% (222/426) of the participants, 95% to 99% adherence was reported by 26.6% (113/426), 90% to 94% adherence was reported by 12.7% (54/426), and adherence of <90% was reported by 8.7% (37/426).

Participants were followed for 48 weeks, during which time 91.1% (421/462) of the participants were retained for the study duration and active on ART at the study site, 0.6% (3/462) had withdrawn from the study but were still in care, 0.6% (3/462) had died, 3.9% (18/462) had become lost to follow-up, and 3.7% (17/462) had transferred to another clinic.

Process evaluation question 3: fidelity

The process evaluation found that the fidelity of the intervention was low. The planned intervention consisted of daily IVRS pill reminder calls for all participants in the first six months of ART and weekly IVRS calls for those on ART for more than 6 months. During the study, only 22.1% (102/462) of the participants received the IVRS intervention, whereas 72.7% (336/462) received a scaled-down SMS text message version of the intervention. The reasons for the small proportion of participants receiving the voice calls were technology-related challenges described in the Usability and Context section later in this chapter.

Process evaluation questions 4 and 5: dose delivered

Of the 462 participants, 95 (20.6%) participants received a combination of voice calls and SMS text messages, 336 (72.7%) received SMS text messages only, 7 (1.5%) received voice calls only, and 24 (5.2%) received neither.

The 22.1% (102/462) of the participants who opted for IVRS services received a total of 30,940 calls during their study enrolment period (**Table 15**). During the calls, participants listened to 3980 health tips. Only two symptom or side effect reports were made. An average of 303 calls were made per participant, which included repeat reminder calls (up to three calls per day) if the initial call was unanswered. Of all the scheduled outgoing IVRS calls by the Connect for Life system, only 0.14% (44/31,095) of the calls failed to initiate owing to a software or platform issue.

The 93.3% (431/462) of the participants who opted for SMS text messages received 8234 messages in total: 2468 (29.97%) adherence feedback, 417 (5.06%) health tips, 2272 (27.59%) pill reminders, and 3077 (37.37%) visit reminders.

Table 15. IVRS[a] and SMS text message services provided.

Services	Participants who received the service (N=462), n (%)	Total number of calls and messages delivered after enrolment (N=30,940 calls; N=8234 SMS text messages), n (%)	Number of calls and SMS text messages per participant, mean (SD)
IVRS calls (n=102)			
Any	102 (22.1)	30,940 (100)	303 (324.3)
Listened to health tip	69 (14.9)	3980 (12.86)	58 (80.1)
Reported symptoms or side effects	2 (0.4)	2 (0.01)	1 (0)
SMS text messages (n=431)			
Any	431 (93.3)	8234 (100.0)	19 (49)
Adherence feedback	70 (15.2)	2468 (30.0)	35 (17.3)
Health tip	11 (2.4)	417 (5.1)	38 (45.7)
Pill reminder	10 (2.2)	2272 (27.6)	227 (187.3)
Visit reminder	428 (92.6)	3077 (37.4)	7 (4)

[a]IVRS: interactive voice response system.

Process evaluation question 6: dose received

Including setup calls during the visits, of the 31,095 outgoing calls made by the Connect for Life system 8119 (26.11%) were answered by the participants. To listen to the message, the participant had to enter their personal identification number (PIN). A PIN attempt was recorded for 66.87% (5429/8119) of the calls that were answered, and the PIN was entered successfully in 84.56% (4591/5429) of the PIN attempts (**Figure 11**).

Of the 2,690 calls that were answered and no PIN was entered, an estimated 1846 (68.62%) went to voicemail. This estimate was based on the number of seconds the call was connected before it was automatically terminated by the software (approximately 140 seconds).

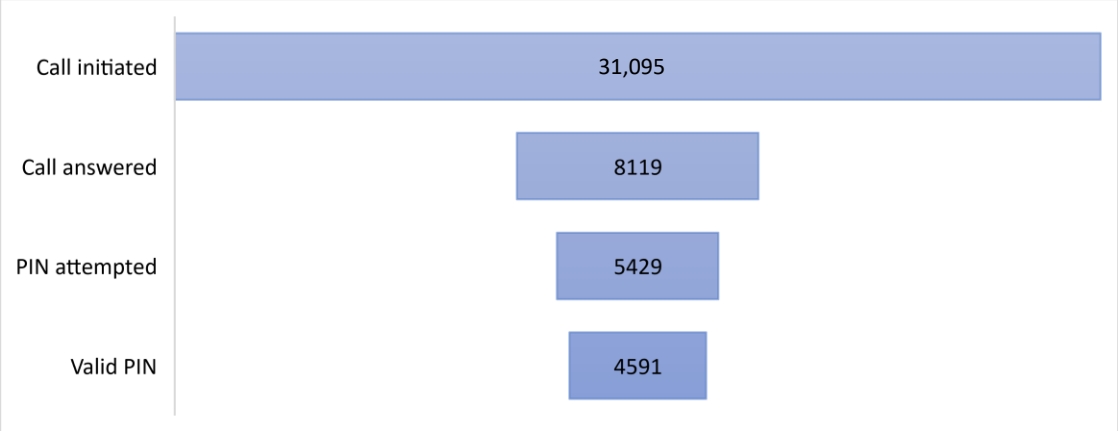

Figure 11. Interactive voice response system calls made and outcomes.

PIN: personal identification number

Experiences of participants and providers

Process evaluation questions 7 and 8: usability and context

The biggest technology challenge that the project faced was frequent dual tone multi-frequency (DTMF) malfunction during IVRS calls. This was reported by study participants and observed by the study staff during the process of activation of the IVRS service. During the DTMF malfunction, the system was unable to recognise the tones as users pressed number keys on their phones, resulting in invalid PINs or inability to navigate the IVRS menus. DTMF failure was suspected during an estimated 32.08% (2605/8119) of calls that were answered by participants (1767/2605, 67.83% of the answered calls where no PIN was entered and 838/2605, 32.17% calls where an invalid PIN was entered). Enrolment was temporarily suspended, and an investigation of the issue found that the DTMF malfunctions were related to the telecommunication infrastructure rather than the Connect for Life platform; therefore, it was not possible for the study team to correct the issues.

Only 46.1% (159/345) of the participants reported that they found the Connect for Life system quite easy or very easy to use (**Figure 12**), indicating that ease of use can be improved.

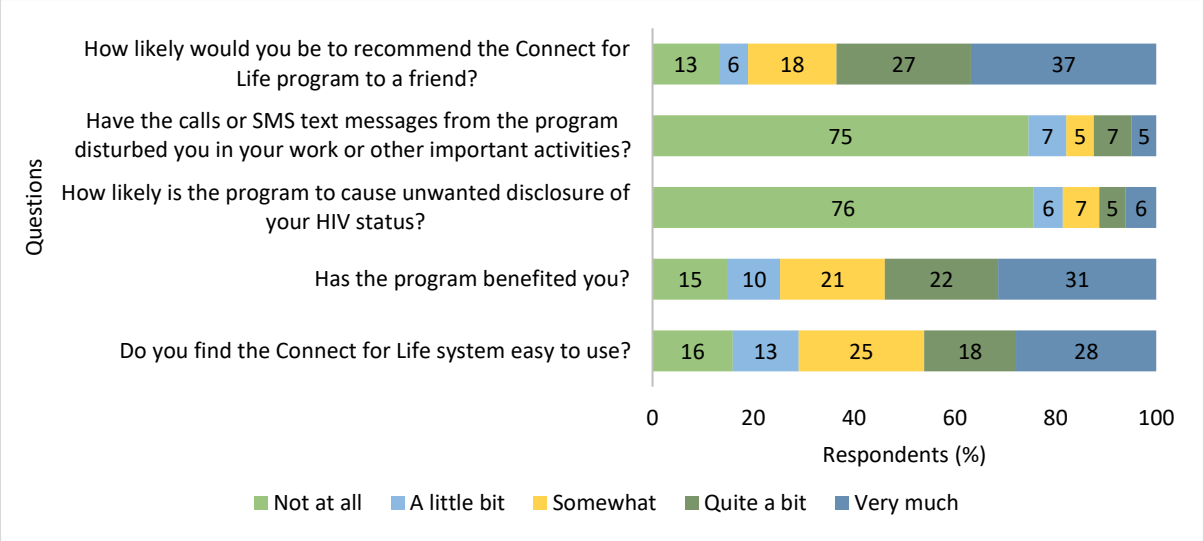

Figure 12. Intervention acceptability after 48 weeks (n=392 respondents).

The provider's experience with the system was largely positive. In monthly process reports, clinicians reported that the medical record functionality facilitated easy access to laboratory results, medication history, diagnosis, and other information, which had previously been recorded in Microsoft Word documents and paper charts. Clinicians also reported that the alert function, which flagged participants with poor adherence or side effects for the clinician to follow up, was overwhelming to use. The symptom reporting alerts were useful, but these alerts were "buried" in a long list of alerts about missed doses and missed clinic visits. This occurred when participants failed to answer calls and did not respond to the IVRS prompts, which triggered alerts for non-adherence, resulting in high numbers of inaccurate alerts for missed doses. Clinicians recommended reviewing and updating the criteria for generating alerts.

Clinic staff also observed that, across the clinic, participant appointment attendance on the scheduled date and time improved from 17% before the study to >30% after the implementation of Connect for Life. They attributed this improvement to the visit reminders sent through SMS text messages. The improved on-time visit attendance saved staff time and effort by reducing the need to call participants and reschedule appointments.

Process evaluation question 9: acceptability and satisfaction

Acceptability: Acceptability questionnaires were collected at three time points (426/462, 92.2% completed at the 12-week visit; 335/462, 72.5% at the 24-week visit; and 392/462, 84.8% at the 48-week visit). Acceptability levels are summarised in **Figure 12**.

After 48 weeks in the study, 63.5% (221/348) of the participants reported that they would be quite likely or very likely to recommend the programme to a friend, and 53.9% (187/347) of the participants reported that they benefited quite a bit or very much from the intervention.

Some participants reported concern over privacy and inconvenience, with 12.4% (43/347) of the participants reporting that the messages and calls disturbed them quite a bit or very much during their work or other important activities and 11.3% (39/345) of the participants stating it was quite likely or very likely that the intervention could cause unwanted disclosure of HIV status. Social harm monitoring was conducted at each study visit and no instances of disclosure were reported.

Associations between acceptability and several independent variables were explored.

Time on study: There was no strong evidence of difference in the acceptability indicators at different time points after enrolment. The proportion of participants who reported that the intervention benefited them quite a bit or very much was 45.2% (128/283) at the 12-week study visit, 54.3% (188/346) at the 24-week visit, and 53.9% (187/347) at the 48-week visit (*P* = .51)

Time on treatment: Among participants who had started ART <6 months before enrolment in the intervention, after 48 weeks, 65% (39/60) reported that the intervention benefited them quite a bit or very much, compared with only 51.6% (148/287) of the more experienced participants who had been on ART for >6 months at the time of enrolment (*P* = .02).

Frequency of service: People who received daily or weekly pill reminders were much more likely to report that the intervention benefited them compared with those who did not receive pill reminders. This trend was consistent across all time points. At the 48-week visit, 70% (21/30) of the participants who received weekly pill reminder and 64% (9/14) of those who received daily pill reminder reported that they benefited quite a bit or very much from the intervention compared with only 51.5% (157/305) of those who received no reminders (*P* =.01).

There was no evidence of difference between those receiving daily and those receiving weekly pill reminders in terms of acceptability of the frequency of pill reminders or participants' likelihood to recommend Connect for Life to a friend. Of those who received daily pill reminder, 14% (11/78 observations) said that there were "too many" reminders, whereas 7% (4/58 observations) of those who received weekly pill reminder said that there were "too many" reminders (*P* =.29). At week 48, a total of 80% (24/30) of the participants who received weekly pill reminders were quite likely or very likely to recommend to a friend, compared with 64% (9/14) of those who received daily pill reminders and 61.4% (188/306) of those who received no reminders (*P* =.30).

Other factors: No association was observed between viral load suppression or HIV knowledge score and intervention acceptability.

Qualitative feedback from focus group discussions and adherence questionnaires: Qualitative data were collected to facilitate better understanding of participants' experiences with the system and the contextual and motivating factors influencing the use, acceptability, and usability of the intervention.

The key findings from the acceptability questionnaires and the focus group discussions at the end of the study were that the intervention was received positively, and participants believed that the intervention should continue after the study ended. Several main themes emerged—the importance of personalised reminders, technical challenges and usability issues, desire for health tips, and importance of social support as part of HIV care (**Textbox 1**).

Textbox 1. Main themes from focus group discussions.

Personalized reminders

- Participants liked that the intervention was highly personalisable, enabling them to select the frequency and time of calls or SMS test messages and the topics of health tips. Preferences for voice calls and SMS text messages varied. Participants also reported that they found the visit reminders and pill reminders to be helpful for their adherence; however, most people were using their own alarms or pill boxes as adherence tools. Several participants who only received the visit reminder service expressed interest in trying the pill reminders and health tips after hearing the feedback from participants who received those components of the service:

  It is an advantage being reminded at work especially when you get busy so you would not miss to take your medicine on time.

  Receiving pill reminder call on a weekly basis made me more aware of the time and I think it is more beneficial to those who has tight schedule. But in my end, I never forget a dose with the aid of alarm clock.

  For me, the two times [visit] reminder is fine. Actually, it is very helpful on reminding me on my next visit. There are times that I got surprised receiving the text because I already forgot that I have a follow-up visit.

Technical challenges

- Participants who received the calls described challenges with entering their personal identification number and with navigating the interactive voice response system (these challenges were owing to failure of the dial tone multifrequency technology) and more broadly about the hassle of responding to the prompts in the calls. Even when the call went unanswered, it still served as a prompt to take medication:

  In the evening, I don't know how to use the PIN so whenever I received the call (usually an international number) and hear the music, I already know that it is the pill reminder call. I actually can't go through the IVR because I don't know exactly when I need to enter the PIN... On the other hand, the call itself serves as an alarm to take my meds though I was not able to answer or enter my PIN.

Health tips

- Participants expressed that although they use the internet to find health information, they trusted health tips from Connect for Life more, because the information was vetted by their health care provider. They liked that the health tips included information on a range of related health topics, such as nutrition and mental health, in addition to the HIV basics. However, some participants were unwilling to receive tips via SMS text message because of concerns about privacy, and some stated that they knew someone who they could ask for health information:

  In general, I think it is better that the health tips are coming from Sustained Health Initiatives of the Philippines and recommended by health care professionals. It would be more reliable as compared to information in the Google.

  It's like trivia for today, even you are on meds for a long time already.

Social support

- Almost all focus group participants mentioned the importance of human connection. Several participants mentioned that they would prefer to connect to a live person in addition to electronic information, especially regarding symptom management. Participants stressed the role of support from their health care providers or other patients in helping them to understand more about living with HIV:

  I would like to suggest having someone to reach to answer a not so relevant question like if I have stomach-ache and I want to know if it is connected to my meds or a side effect versus to searching in Google which is sometimes inaccurate.

  Exchange of experiences [is important] especially to the new patient so they would know what to do. They would feel that they are not alone, because you won't know how to avoid feeling self-pity. At least with a support group they have someone to communicate with.

Process evaluation question 10: cost

A description of the types of expenses involved in the implementation and the approximate costs from the Philippines setting are shown in **Table 16**.

Table 16. Costs involved in the intervention.

Aspect	Description	Cost
Cloud hosting of solution	The database and software require hosting on RDS[a] and EC2[b] server instance. The cost of a monthly or yearly subscription depends on the amount of storage needed and payment schedule. Our database includes data for approximately 700 participants.	US $50 per month
VOIP[c] provider	This may be the local telecommunications company (e.g. Vodacom and Globe) or a specialist service provider.	PHP 0.50 (US $0.01) per SMS text message or PHP 5 (US $0.10) per minute for voice calls

Local service provider IT[d] support	IT support monitors the server, VOIP functionality, and software updates and manages users' log-ins. Our local IT support provides up to 20 hours of support monthly and charges an hourly rate for additional support.	PHP 10,000 (US $200) per month
Staff	An administrative clerk, counsellor, or other cadre of staff will allocate time and effort to enrol participants on the system, activate their services, monitor alerts, and update details.	Cost varies (0.1-0.5 full-time equivalent of administrator)

[a]RDS: relational database service.
[b]EC2: Elastic Compute Cloud.
[c]VOIP: voice over Internet Protocol.
[d]IT: information technology.

5.6 Discussion

Principal findings

During the study, >31,000 IVRS calls and 8,000 SMS text messages were sent to 462 study participants. The Connect for Life system was acceptable to both participants and providers. Participants liked that the intervention was highly personalisable, enabling them to select the frequency and time of calls or SMS text messages and the topics of health tips. Feedback on the pill reminders, visit reminders, and health tips was very positive. Participants appreciated that health tips covered a variety of topics beyond HIV basics. The focus group discussions revealed that acceptability of the weekly adherence scores and symptom reporting functionalities of the intervention was low, as these two functions required lengthy navigation of the IVRS menu.

Owing to technical issues, the intervention was not implemented as originally intended, with only 22.1% (102/462) of the participants receiving the IVRS pill reminder intervention and others receiving a scaled-back SMS text message intervention. When the technical issues were first identified, enrolment in the study was paused for three months, while the study team assessed the cause of the issue. Ultimately, the issue of DTMF malfunction was attributed to issues in the telecommunications system that neither the telecommunications provider nor the Connect for Life developers could resolve. When enrolment was resumed, participants were provided SMS text messages rather than IVRS services. Despite the technical challenges, acceptability remained high, and only 0.6% (3/462) of the participants withdrew from the study. Following the study, the frequency of technical issues has decreased significantly, and the study site has continued to provide the service. Currently, pill reminder calls are a routine service for all new patients undergoing ART.

Notably, the technical challenges experienced in delivering the intervention were related to navigating the IVRS menu and made it difficult to distinguish whether the issues raised with ease of use or overall

satisfaction were related to the technical challenges (i.e. the dial tones were not recognised when keyed in) or to the product design (i.e. IVRS menus were very complicated). The accuracy of the adherence scores in the weekly feedback SMS text messages was dependent on successful navigation of the IVRS process. This type of feedback may have been better delivered via a smartphone app rather than an IVRS setup. The interactive component of the IVRS system was an important aspect of the study design, which was not effectively evaluated in this study owing to the low number of participants who received this part of the service, warranting ongoing monitoring and future studies.

The scaled-back intervention provided everyone with visit reminders, which addressed part of the theory of change by improving medication accessibility through timely refills, but did little to prompt pill taking, habit forming, and improvements in health knowledge. Individuals who received a high dose of the intervention (daily or weekly pill reminders) were more likely to recommend the intervention to others, suggesting that the planned intervention was more acceptable than the scaled-back version.

Our analysis of dose received shows that the call answer rate was low, with only 26.24% (8119/30,940) of outgoing calls answered, which is reflective of a preference for SMS text messages and chat services among the target population. The requirement of a PIN reduced exposure to the intervention, which was mostly owing to technological challenges. After experiencing technical difficulties several times, many participants stopped answering the calls. However, some mentioned that the phone ringing at the set time each day served as an effective adherence reminder.

Privacy considerations were paramount, with 11% (51/462) of the participants reporting that they had concerns about the potential for disclosure of their HIV status. Therefore, in situations where entering a PIN is a barrier to intervention exposure, practitioners can consider adapting the content to eliminate potentially sensitive health information and delivering the service with no PIN requirement.

Ultimately, the study showed the importance of choosing technologies that can function in local contexts. In low-resource settings, it may take time to scale up technologies that will be quick to roll out in high-resource settings. Practitioners must identify service providers with appropriate capacity and ensure that participants have the skills and motivation to use the intervention. Conducting an iterative process with several pilot stages is advantageous, as it enables practitioners to identify the problems with functionality and adapt the intervention before scaling up.

An important aspect of the intervention was that, through this regular contact from the clinic, participants felt cared for and felt that their health care provider was concerned about their well-being. This social support was a key motivator for adherence. Participants requested to be able to speak to

someone about side effects or for social support, suggesting that an intervention that links calls to counsellors more effectively may be an area for future evaluation.

Comparison with previous studies

The Connect for Life Philippines intervention was adapted from the same platform used for Call for Life Uganda and mMitra and Treatment Advice using Mobile Alerts in India. Acceptability was high in all three settings.(220,243) However, there were differences in the preferences and use patterns of the participants in the Philippines setting compared with those in Uganda and India. The Philippines had a high preference for SMS text messages over voice calls and a low call answer rate. The Connect for Life Philippines and Call for Life Uganda projects experienced similar challenges with network instability issues in the early stages.(220)

Similar to Connect for Life and Call for Life, other mHealth interventions for people living with HIV have shown improvements in ART adherence, even where participant response rates (i.e. dose received) are low.(144,249,264) For example, the PositiveLinks app used by people living with HIV in Virginia, United States, had response rates of <40% to most app prompts, but participant retention in care, CD4 results, and viral suppression improved significantly.(265) There is an important distinction between adherence to the intervention (i.e. calls, app prompts, and device use) and adherence to medication.

Strengths and limitations

A strength of the Connect for Life platform is its scalability; the project can easily be expanded to cover a large number of sites and participants with great cost efficiency, if those facilities have access to computers and internet connectivity. To deliver the project at scale, creation of content in regional languages will be an important consideration. The platform is adaptable, as the local IT provider can add and remove new data fields and update the SMS text message content, voice files, and call flows. However, changes to the functionality of the software or interoperability with other systems will require support from the software developers at Janssen Global Public Health. The Philippines Department of Health has plans to implement electronic reporting systems for HIV services at an aggregated level. If the department is ever to implement a patient-level electronic medical record, interoperability with Connect for Life will be an important consideration to ensure delivery at scale.

A strength of this process evaluation study is the mixed methods approach and the involvement of users of the intervention. The study used prospectively collected quantitative data on participants' responses to the intervention and qualitative feedback from questionnaires, monthly process reports, and focus group discussions. The evaluation included the users of the intervention, clinical service providers, and developers of the technology platform.

The methodology addressed all key components in process evaluation for public health interventions and studies (context, reach, dose delivered, dose received, fidelity, implementation, and recruitment).(239) Furthermore, the study included information on the technology platform, infrastructure, security, and cost, as guided by the mERA checklist developed by the World Health Organization mHealth Technical Evidence Review Group.(253)

A limitation of our approach was that the evaluation was conducted by the same study team responsible for planning and implementing the intervention, rather than by independent evaluators. Other limitations included the convenience sampling strategy for participants in the focus group discussions and the low participation in the focus groups. Although the study team approached many individuals to participate, it was a challenge to identify those who were willing owing to reluctance to disclose their HIV status in a group. Furthermore, owing to transportation challenges, there was low attendance among those who confirmed their intention to participate in the groups.

Incomplete data may have affected the interpretation of the results. Of the 462 participants in the study, 440 (95.2%) attended the final study visit at week 48, and 89.1% (392/440) of them completed the questionnaire during the final visit. There may be differences in the experiences of participants who transferred out, died, withdrew from the study or were lost to follow-up, attended but did not complete the questionnaire, and completed the questionnaire.

This study focused on MSM in Metro Manila, and the study population was urban and highly educated. Participants may have had alternative adherence reminders, including self-set phone alarms and email alerts. Therefore, the results are not broadly generalisable to other contexts.

Conclusions

mHealth interventions are useful to support adherence, as they have low replication costs and are highly adaptable to specific cultural contexts. On the basis of the findings of this process evaluation, we can guide practitioners implementing mHealth interventions to support medication adherence to consider the following recommendations:

1. The intervention should allow the participant to personalise the service based on their preferences for delivery by SMS text message or voice calls, timing of messages and calls, and selection of content.
2. Limit the complexity of the IVRS menus to reduce the “hassle” factor and likelihood of technical failures. As the navigation of menus is a key aspect of the intervention, consider using an app or a chatbot instead of, or in addition to, an IVRS system.

3. Consider how to use the mHealth intervention to facilitate human interaction. For example, certain responses to the intervention may prompt counsellor, clinician, or peer support.
4. Ensure that the roll-out of an existing mHealth technology in a new setting is an iterative process that includes robust process evaluation methods. Rigorous pilot-testing is needed to ensure technical function. Work plans should include ample time and budget for adaptation of the technology.

The Connect for Life mHealth intervention to support adherence to ART had high participant satisfaction and acceptability. However, the feasibility of the intervention was dependent on the reliability of local telecommunications networks, and poor reliability of the local mobile networks had a large impact on the intervention's usability, fidelity, and dose received.

The process evaluation allowed us to better understand the preferences and use patterns of mHealth services by MSM in the Philippines. This will enable the effective scale-up of mHealth services for this key population, which is essential in the context of the dual HIV and COVID-19 pandemics, where more services must be delivered virtually.

Table 17. Process evaluation methodology.

Component	Process evaluation question	Data sources	Tools/procedures	Data analysis or synthesis	Reporting
Reach/recruitment	1. What proportion of participants receiving services in the study site opted into the Connect for Life intervention? 2. What procedures were followed to recruit participants into the intervention?	Screening records	Review screening records to determine the screening and enrolment rates Recruitment script and SOP[a]	Calculate the proportion of individuals in the study site who were screened for inclusion in the study/intervention, the proportion of those who screened who were eligible, and the proportion of those eligible who enrolled in the study. Characterize main reasons for refusal.	Formative–Examined during the study enrolment period to identify intervention coverage of clinic population and direct recruitment efforts. Summative–Summarise after study enrolment period concluded.
Fidelity	3. To what extent was the Connect for Life intervention implemented as planned?	Connect for Life system reports	Review system-generated reports (call/SMS text message logs) to determine which intervention functionalities were activated for each participant and monitor changes.	Calculate the proportion of participants who received the intended intervention (according to the proposed dose in the recommended configuration of services).	Formative–Regular informal feedback to study coordinators and clinicians. Summative–Summarise overall intervention fidelity after all study visits completed.
Dose delivered	4. How many daily and weekly pill reminders, health tips, clinic visit reminders were generated by the Connect for Life System? 5. What proportion of Connect for Life calls were delivered successfully and what proportion had technical failures?	Connect for Life system reports	Review system-generated reports (call/SMS text message logs) to determine the total number of calls and SMS text messages delivered.	Calculate the total number of SMS text messages sent (per category), calls generated from the Connect for Life system, and proportion of calls with technical failures.	Formative–Regular review of system reports by IT[b] support and by study staff to monitor system functionality. Summative–Summarise after all study visits completed.
Dose received	6. What was the level of interaction between the participants and the Connect for Life system prompts?	Connect for Life system reports	Review system-generated reports (call/SMS test message logs) to determine the proportion of various call outcomes and describe participant responses to prompts in the interactive voice response system (IVRS).	Calculate the proportion of calls answered, average length of calls answered, ratio of calls to adherence reports, levels of reported adherence, and number of health tips heard, and symptom reports recorded.	Formative–Monitor technical failures. Summative–Summarise after all study visits completed.
Usability/context	7. Does the Connect for Life mHealth[c] solution function as intended? 8. What are the barriers to and facilitators of implementing the Connect for Life intervention in the local context?	Clinic staff and participants	Observations of study staff and feedback from participants. Focus groups conducted at the design stage, after 8 weeks of pilot-testing, and at the end of the study.	Narrative description of findings regarding usability of the Connect for Life intervention. Qualitative analysis of focus group discussion transcripts.	Formative–During the initial pilot phase of the intervention, to identify and resolve intervention delivery challenges. Summative–Describe the experience of study staff and participants who used the Connect for Life platform; the strengths and limitations of the solution; and contextual factors that influenced the fidelity, usability, acceptability, and cost of the intervention.

Acceptability/ satisfaction	9. What do participants like/dislike about the intervention and what is their opinion of its effectiveness?	Participants	Focus groups conducted at the design stage, after 8 weeks of pilot-testing, and at the end of the study. In-person questionnaires, self-administered at 12-, 24-, and 48-week study visits.	Qualitative analysis of focus group discussion transcripts. Descriptive analysis of Likert scale scores regarding intervention acceptability and participant satisfaction and inferential analysis of scores with participant characteristics as independent variables.	Formative–Incorporate findings from focus groups conducted during the intervention design phase into the intervention content and delivery plans. Summative–Summarise findings from quantitative analysis of questionnaires and qualitative analysis of focus group discussions after the conclusion of the study.
Cost	10. What is the cost to implement the Connect for Life intervention in the local context?	Administrative records	Review of administrative records to extract rates for infrastructure, telecommunications, and staffing of intervention.	Determine the baseline costs to set up the Connect for Life System and the average per participant cost to deliver the intervention.	Summative–Summarise after all study visits concluded, plan for the sustainability of the project beyond the study period.

[a]SOP: standard operating procedure.
[b]IT: Information technology.
[c]mHealth: mobile health.

Chapter 6: Outcome evaluation

This chapter presents findings from the observational cohort study describing adherence, viral load suppression, retention in care, treatment failure and mortality, and changes in knowledge and quality of life. The chapter details the associations between the key outcomes and various demographic, clinical, and behavioural factors as well as the level of exposure to the mHealth adherence support intervention.

Objective 2 of the doctoral research was to conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to assess participant adherence, retention, and treatment outcomes at baseline and over follow-up. This chapter addresses part of this objective, by assessing the above factors at follow-up.

This chapter is a research paper published in *AIDS and Behavior* on October 4th 2023.(266) Chronologically, this was the fourth of four papers published. The chapter that follows differs from the published version due to inclusion of brief descriptions in the Methods and Discussion section regarding the rationale for and impact of English-language inclusion criteria.

Citation: O'Connor C, Leyritana K, Calica K, Doyle AM, Lewis JJ, et al. Changes in Adherence and Viral Load Suppression Among People with HIV in Manila: Outcomes of the Philippines Connect for Life Study. *AIDS and Behavior.* 2023 Oct 4

Available from: https://link.springer.com/article/10.1007/s10461-023-04190-1

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	LSH1512747	**Title**	Ms
First Name(s)		Cara Emily	
Surname/Family Name		O'Connor	
Thesis Title		Mobile Phone Adherence Support for HIV Patients in Manila, Philippines	
Primary Supervisor		Dr Aoife Doyle	

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?		AIDS and Behavior	
When was the work published?		04 October 2023	
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion		n/a	
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the principal investigator of the study, wrote the protocol, supervised data collection, conducted data analysis, and was responsible for writing this manuscript. Co-authors contributed to study design, provided technical advice on data analysis, and provided editorial input on the manuscript.

SECTION E

Student Signature	[redacted]
Date	29 Oct 2023

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Date	29 Oct 2023

6.0 Changes in adherence and viral load suppression among people with HIV in Manila: Outcomes of the Philippines Connect for Life Study

6.1 Abstract

The Philippines HIV epidemic is among the fastest growing globally. Infections among men who have sex with men (MSM) are rising at an alarming rate, necessitating targeted evidence-based interventions to retain people living with HIV (PLHIV) in care, support adherence, and reach viral suppression. We conducted a 48-week prospective cohort study of 462 participants in which we provided a mobile health (mHealth) adherence support intervention using the Connect for Life platform. We observed an improvement in adherence, with the proportion of participants taking more than 95% of their antiretroviral therapy (ART) doses increasing from 78.6% at baseline to 90.3% at 48 weeks. Among treatment-experienced participants, adherence improved significantly (McNemar's test = 21.88, *P* <0.001). Viral load suppression did not change, with 92.6% suppression at baseline and 92.0% at 48 weeks. Illicit drug use was associated with reduced adherence (aOR = 0.56, 95%CI 0.31-1.00, *P* = 0.05) and being on second-line therapy was associated with poor viral load suppression (aOR = 0.33, 95%CI 0.14-0.78, *P* = 0.01). Quality of life (QOL) improved following ART initiation, from a mean of 84.6 points (of a possible 120) at baseline to 91.01 at 48 weeks.

Due to technical issues, fidelity to the intended intervention was low, with 22.1% (102/462) of participants receiving any voice calls and most others receiving a scaled-back SMS intervention. The mHealth intervention did not have any observed effect on adherence or on viral load suppression. While evidence of effectiveness of mHealth adherence support interventions is mixed, these platforms should continue to be explored as part of differentiated care and treatment support services.

6.2 Background

The HIV epidemic in the Philippines is one of the fastest growing HIV epidemics globally, with a doubling of the number of annual new HIV infections and the number of AIDS deaths increasing nearly by 400% from 2010 to 2020.(189,240) Most new and existing HIV infections in the Philippines occur among men who have sex with men (MSM).(240)

To slow the spread of HIV, the Philippines must continue to progress toward the Joint United Nations Program on HIV/AIDS (UNAIDS) 95-95-95 goals within all subpopulations and age groups. Currently, in the Philippines 64% of people living with HIV (PLHIV) know their status, 41% of those who are HIV

positive are on antiretroviral therapy (ART), and the proportion of PLHIV with suppressed viral loads is unknown.(11,12,241) HIV care and treatment is freely available through the government-funded Philippine Health Insurance Corporation (PhilHealth) Outpatient HIV/AIDS Treatment (OHAT) package.(18)

mHealth for medication adherence support

To achieve viral suppression, patients on ART must take their treatment consistently. However, in clinical practice achieving and maintaining optimal ART adherence is challenging.(17,118) Early clinical studies reported that ≥95% adherence to ART was required to achieve and maintain viral suppression (224,225). More recent studies have shown that virologic suppression may be achieved with adherence levels <95%; however, this is dependent on the duration of treatment and the ART regimen (124,226,227). ART non-adherence has been linked to the development of ART resistance,(267,268) progression to AIDS,(269) and death.(270)

Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence of social support, and time on treatment.(17,113,117–120) In the Philippine context, issues of stigma and discrimination have also been documented as a major barrier to medication adherence. (86,93,121,271)

As mobile phone technologies for health (mHealth) have become increasingly popular in the global health and development sectors, clinical trials have shown that mHealth approaches have promise in improving self-management of chronic disease including adherence to HIV medications (107,108,130,131,246). A 2017 systematic review and meta-analysis assessing interventions to improve adherence to ART found that SMS interventions were superior to standard of care (OR 1.48, CrI 1.00-2.16), and that multiple interventions had additive affects.(125) Systematic reviews show mixed outcomes of mHealth interventions and highlight the need for more rigorous evaluation methods and longer follow-up periods.(112,143,148,197,199,247,248)

The WHO Consolidated Guidelines on ART recommend using mHealth approaches to support HIV care and treatment and improve adherence. The 2016 guidelines endorsed mobile phone text messages as low-cost interventions that have demonstrated benefit in improving adherence and viral suppression and are backed by “moderate evidence.”(126)

During this study, we provided participants with an mHealth adherence support intervention using a platform called Connect for Life. The platform is able to send automated messages to participants via their mobile phones through interactive voice response system (IVRS) call flows or through SMS text

messages.(185) Participants received varying levels of exposure to the intervention, with the frequency of contact and types of messaging received dependent on a combination of personal preference and contextual factors.

Prior to roll-out in the Philippines, the Connect for Life platform was piloted for use in maternal health and HIV programmes in India and Uganda.(220,221,243,244) To adapt the intervention for the local setting and target population In the Philippines, we applied a mixed methods approach guided by the Behaviour Change Wheel framework and the information–motivation–behavioural skills (IMB) model.(183,205,206) The BCW is a method for characterizing and developing behaviour change interventions based on a comprehensive causal analysis of the behaviour, while the IMB model includes three primary constructs that influence behaviour changes: information and knowledge about the behaviour; the individual's motivation to perform the behaviour; and the behavioural skills necessary to perform the behaviour.

In the context of the emerging HIV crisis among MSM in the Philippines, there is an imperative to expand options for tailored HIV prevention and treatment support. While other studies have found high levels of feasibility and acceptability of SMS interventions targeted toward HIV-positive MSM in the United States, in Peru, and in Asia,(177,272–274) there is a lack of data on interventions to improve adherence and treatment outcomes among HIV-positive MSM. Furthermore, few mHealth interventions for MSM have been evaluated in Asia and none in the Philippines. In this paper we describe the outcomes of a prospective cohort study of HIV patients in the Philippines, describing adherence to medication, retention in care, and viral load suppression. We examine various factors affecting these outcomes including the mHealth adherence support intervention received.

6.3 Methods

We conducted a prospective cohort study, collecting data at four time points: baseline, 12-, 24-, and 48 weeks. The study was conducted at the Sustained Health Initiatives of the Philippines (SHIP) clinic, a low-cost, private facility providing HIV care and treatment to people in Metro Manila, Philippines. Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at initial consultation.

Recruitment into the Connect for Life study occurred in person at the SHIP clinic from October 2016 to December 2017. All patients starting or continuing on ART at the SHIP clinic who had a mobile phone and who could speak and read English were eligible to participate in the study. Mobile phones were required because all participants who were enrolled would receive a mobile phone adherence intervention. English language ability was required because formative research found that this was the

participants' preferred language for receiving health tips and medical information, particularly in regard to sexual health. Participants believed it would protect privacy and draw less attention to receive phone calls in English rather than Filipino. English is one of the two official languages in the Philippines and spoken and understood by nearly all of the residents of Metro Manila.

The study coordinator approached patients attending their routine visits while they were in the clinic waiting room. Patients were not approached or screened on days the study coordinator was not available, or if they bypassed the waiting room.

During the study, participants received a personalized combination of services, including automated pill reminders, appointment reminders, health tips, and adherence feedback messages delivered by voice call or SMS on the patient's preferred time and day. Based on findings from formative stages of the project, we planned to provide daily pill reminder calls to participants who were on ART for less than 6 months and weekly reminder calls to those on ART for 6 months or longer.(183)

Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent prior to inclusion in the study.

Objectives

The primary objective of this observational, single-arm study was to describe the adherence to medication, viral load suppression, and retention in care of the patient population participating in the Connect for Life mobile phone adherence support demonstration project. The secondary objectives were: to describe the Quality of Life and the HIV-related Knowledge, Attitudes, and Practices of participants; to describe the clinical outcomes of participants including treatment failure (switch to second line), and AIDS-related mortality; and to identify factors that affected patient adherence and treatment outcomes.

Data sources/measurements

Laboratory results, diagnoses, dispensing, and other clinical information were extracted from patient charts by the study coordinator. Each participant completed three questionnaires at each visit: HIV-related knowledge, attitudes, and practices adapted from the Brief HIV Knowledge Questionnaire (HIV-KQ-18)(275); the WHO HIV Quality of Life brief questionnaire (WHOQOL-HIV BREF)(232,276); and an adherence questionnaire that was adapted from the AIDS Clinical Trials Group adherence instrument.(120) All questionnaires were in English. The questionnaires were self-administered, with

assistance from the study coordinator as requested. Where questionnaires had blank or missing or incomplete fields, all available data points were included in the analysis.

Outcomes

The main outcomes of interest were adherence, viral load suppression, and retention in care. Secondary outcomes include quality of life and HIV-related knowledge. Outcomes were measured over time with all observations from the 12-, 24-, and 48-week visits considered as outcomes.

Key variables were defined as follows:

- Adherence: At each study visit, using a visual analogue scale (VAS) participants reported the proportion of ART doses taken in the prior 30 days as 0–100%. This continuous variable was converted into a binary variable with those reporting 95% or greater were categorised as adherent.
- Viral load suppression: A binary variable defining suppression as HIV viral load lower than detectable limit of lab assay (<50 copies/ml). All viral load tests were conducted as routine standard of care (not provided by the study) and all available test results were extracted from patient files. Only viral load tests that were collected at least three months after treatment initiation were included.
- Retention in care: Proportion of participants alive and in care ("not in care" defined as not having returned for more than 30 days after last scheduled clinic visit or refill).
- Treatment experience at enrolment: A binary variable defining treatment experience as having initiated ART more than six months prior to study enrolment date.
- Exposure to the intervention: A continuous variable defined as the total number of days the participant received one or more SMS text messages or calls from the Connect for Life platform during the study. This was then converted into a categorical variable representing level of exposure with High (96+ days of contact), Medium (48-95 days of contact), Low (12-47 days of contact), and no exposure (<12 days). These cut points serve as rough proxies for monthly, weekly, or daily contact, with the three categories of exposure (excluding no exposure) each representing at least 50 individuals.
- QOL: A continuous variable of up to a maximum of 120 points, scored as per WHOQOL-HIV BREF questionnaire.(232,276)
- Knowledge, attitudes, and practices: Knowledge was categorized as a continuous variable, based on a 16-item dichotomous response (true/false) questionnaire. The questionnaire had two additional sections about sexual activities, alcohol and drug use which included dichotomous, categorical, and continuous variables.

Statistical analysis

Demographic and clinical characteristics were described as a mean or proportion with a 95% confidence interval. Descriptive analyses of retention in care, loss to follow-up, and mortality were conducted. Descriptive analyses of adherence and viral load outcomes were performed for the entire cohort, and then according to: (1) intervention exposure category, (2) adherence above or below 95% at baseline, and (3) treatment experience of more or less than six months at enrolment. We hypothesised that higher level of exposure to the intervention could lead to greater improvements in the key outcomes. We also hypothesised that treatment-naïve participants and those with poor adherence at baseline may benefit more than others from receiving reminders to achieve adequate adherence and viral load suppression.

Adjusted odds ratios were estimated using a generalised estimating equations (GEE) model with an exchangeable correlation structure and robust variance. GEE was selected to allow for clustering of outcomes within an individual. The model included intervention exposure, treatment experience, baseline adherence, and other factors which had a *P*-value <0.1 in unadjusted univariate analyses (with some factors excluded a priori due to collinearity). For both the adherence and viral load outcomes, all observations from follow-up visits were included in outcome analyses, and the models adjusted for baseline adherence and baseline viral load, respectively. Wald tests were used to calculate *P*-values of each variable.

Several sensitivity analyses were conducted. Both univariable and multivariable analyses were reproduced using continuous variables for intervention exposure (unique number of days participant received call or SMS) and adherence (per cent adherence from 0 to 100) in place of the respective categorical and binary variables. The analyses were also reproduced using mixed-effects logistic regression models instead of GEE. Finally, the descriptive and inferential analyses were reproduced using an intention-to-treat approach, in which the dataset was updated to include data points for participants who were lost to follow-up or who died with the assumption that they were non-adherent and virally unsuppressed for the period from the time they became lost to follow-up or deceased until the date when they would have completed the study.

6.4 Results

Participants

Approximately 675 patients were receiving HIV care at the study site during the recruitment period. 485 patients were approached by the study coordinator. Of those approached 95.7% (464/485) agreed to be screened for enrolment, and 95.3% (462/485) met the eligibility criteria and consented to participate (**Figure 13**).

Reasons for refusal (21/485, 4.3%) included no need or desire for adherence support, not wanting to receive messages or calls on their mobile phone, privacy concerns, and inconsistent access to mobile phone due to frequent international travel. Of the 0.4% (2/464) of the patients who were excluded based on screening, one was ineligible because he did not speak English and the other did not have a mobile phone. Of the participants enrolled, 0.1% (3/462) withdrew, 0.1% (3/462) died, 3.7% (17/462) transferred out, 3.9% (18/462) were lost to follow-up (missed two consecutive visits), and the remaining 91.1% (421/462) completed the study.

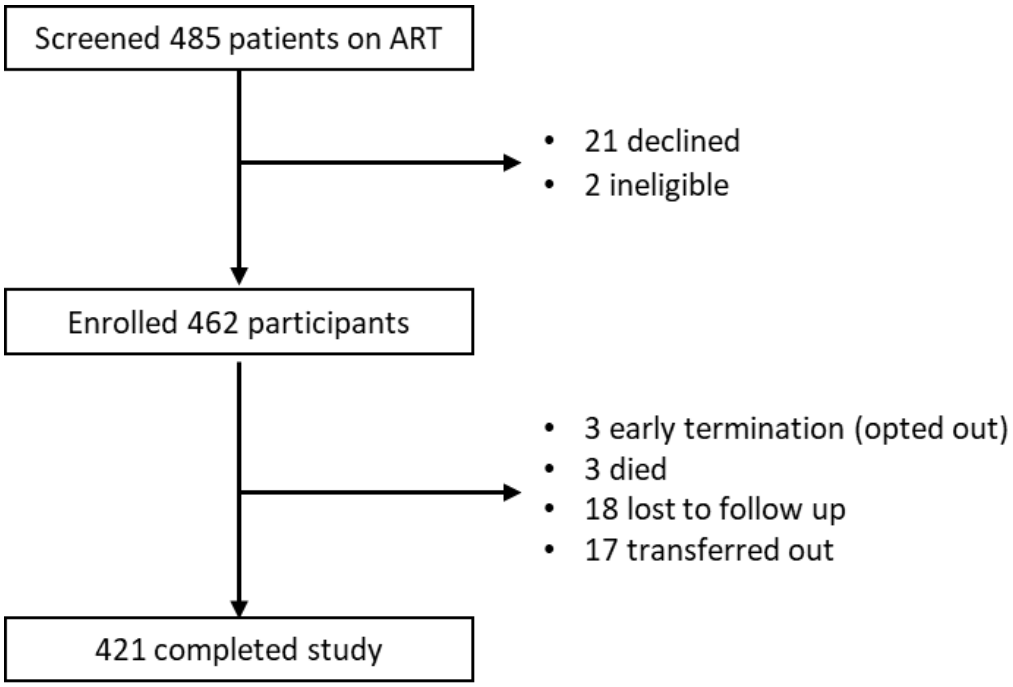

Figure 13. Recruitment and study completion of the cohort.

Demographic factors, clinical characteristics and behavioural practices of the study participants are described in **Table 18.** As the study site caters to young MSM, all but one of the participants in the study (461/462, 99.8%) were male and only 1.5% of participants (7/462) were heterosexual. Most participants were treatment experienced, with the mean time on ART among experienced participants

being 2.77 years (SD 2.0). The mean age at enrolment was 32.4 years (SD 5.7). Most participants were university graduates (397/462, 85.9%) and most were either employed or students (422/462, 91.3%).

Notably, nearly half of all participants (227/462, 49.1%) had not disclosed their HIV status to a family member or friend. Furthermore, a substantial proportion of participants (94/462, 20.4%) worked in the Business Process Outsourcing (BPO) sector, a key economic sector in which third-party vendors provide services remotely (e.g. contact centres, back-office services, data transcription, and information technology), usually to multinational corporations. Due to the variable nature of work schedules for BPO workers and lack of privacy due to working conditions in call centre settings, this group faces unique barriers to adherence.

Table 18. Baseline characteristics of study participants (N=462).

Characteristics		Number	(%)
Gender	Male	461	99.78
	Female	1	0.22
Age	18-24	23	4.98
Mean: 32.4 years (SD 5.7)	25-29	132	28.57
	30-39	262	56.71
	40+	45	9.74
Education	Elementary or less	11	2.38
	High School/Vocational	21	4.55
	College/University	345	74.68
	Postgraduate	52	11.26
	Unknown/Did not report	33	7.14
Employment	Employed	422	91.34
	Unemployed	40	8.66
Sexual Orientation	Bisexual	139	30.09
	Heterosexual	9	1.95
	Homosexual	313	67.75
	Pansexual	1	0.22
Civil Status	Married/Common-law partner	21	4.55
	Single	439	95.02
	Unknown/Did not report	2	0.43
Partner HIV Status	Not in a relationship	290	62.77
	Same-HIV-status relationship (both HIV+)	50	12.24
	Mixed-HIV-status relationship (partner is HIV-)	75	16.23
	Unknown/Did not report	47	10.17
Disclosure of HIV Status to family/friend	Disclosed	146	31.60
	Not disclosed	227	49.13
	Unknown/Did not report	89	19.26
Time on ART, years	<30 days	45	9.74
	1-6 months	30	6.49
	6 months – 1 year	39	8.44
	1-2 years	86	18.61
	2-4 years	163	35.28
	>4 years	99	21.43

Nadir CD4 (cells/mm3)	0-199	177	38.31
	200-499	253	54.76
	500+	32	6.93
ART Regimen	First Line	393	85.06
	Second/Third Line	69	14.94
Condom Usage in last 6 months	Always	184	39.83
	Sometimes/Most of the time	169	36.58
	Never	88	19.05
	N/A (not sexually active)	21	4.55
Transactional Sex	Never had transactional sex	434	93.94
	Ever had transactional sex	26	5.63
	Unknown/Refused	2	0.43
Sexual Partners in last 6 months	None	97	26.01
	One	147	39.41
	2-9	106	28.42
	10 or more	23	6.17
Alcohol Misuse*	No	388	85.84
	Yes	64	14.16
Injection Drug Use (ever)	No	406	87.88
	Yes	56	12.12
Any Drug Use (3 months preceding enrolment)	No	386	83.55
	Yes	76	16.45
Baseline Viral Load **	Detectable (>=50 copies/ml)	21	4.55
	Undetectable (<50 copies/ml)	262	56.71
	No VL data at baseline	179	38.74

**Alcohol misuse defined as two or more episodes of heavy episodic or 'binge' drinking (>five drinks) in the prior month or >14 drinks per week on average.*(230,231)

*** Conducted at the baseline visit or in six months prior to enrolment.*

Delivery of the adherence support intervention

We planned to provide daily pill reminder calls to participants who were on ART for less than six months and weekly reminder calls to those on ART for six months or longer.(183) Due to technical issues, fidelity to the intended intervention was low, with only 22.1% (102/462) of participants receiving any voice calls and most others receiving a scaled-back SMS intervention (**Figure 14**). Technical issues were first identified in the second month of the study, at which point new enrolment was paused for approximately three months while the study team assessed the cause of the issue. Ultimately, the issue was characterised as a dual tone multi-frequency DTMF malfunction – i.e. a problem with the tones not being transmitted or recognised when pressing digits on the handset to navigate interactive touch-tone menu. This was attributed to issues in the telecommunications system that neither the telecommunications provider nor the Connect for Life developers could resolve. When enrolment was resumed, participants were offered SMS text messages rather than IVRS voice call

services. Because not all participants experienced technical challenges with voice calls, those who had a strong preference for voice calls could opt in, and they were counselled about the possibility of technical challenges and how to report issues to the study team.

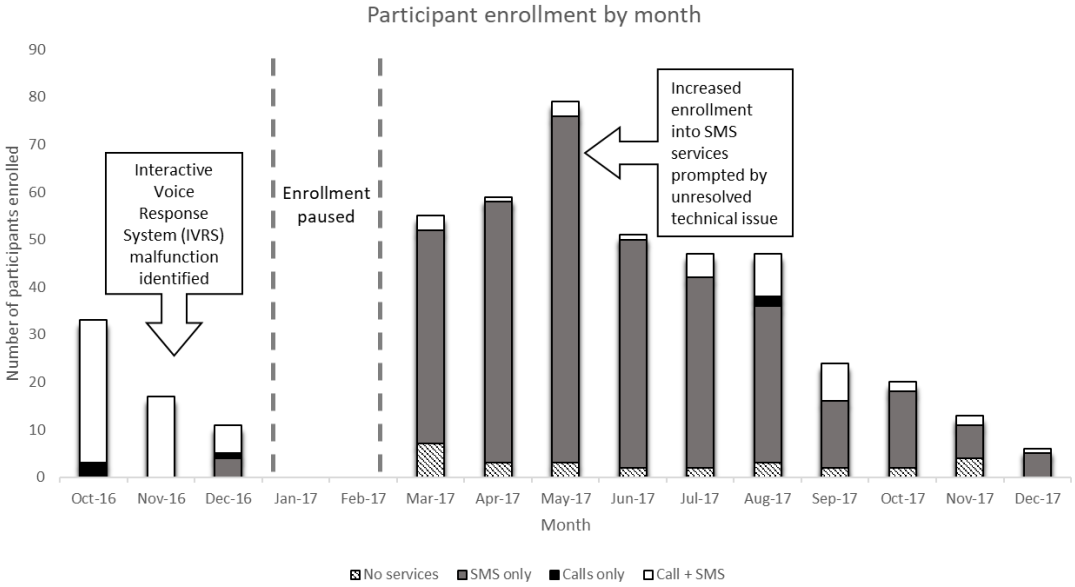

Figure 14. Participant enrolment by month and type of intervention received.

On average, study participants received contact (voice call or SMS) from the Connect for Life system on 34 separate days throughout their time on the study (min=0 and max=358 days). During the study, the Connect for Life system sent participants a total of 8,234 SMS messages. It also made 31,095 IVRS calls, of which 26% were answered. **Table 19** outlines the frequency of contact, the delivery methods used (voice or SMS), and service types that participants received. The intervention delivery is further described in a separate process evaluation paper.(185)

Table 19. Intervention level and type received by study participants (N=462).

Intervention Exposure Measure		N	%
Number of days of Contact	None	28	6.06%
	Low (12-47 days of contact)	297	64.29%
	Medium (48-95 days of contact)	53	11.47%
	High (96+ days of contact)	84	18.18%
Number of calendar quarters with Contact	None	28	6.06%
	1 quarter	7	1.52%
	2 quarters	60	12.99%
	3 quarters	145	31.19%
	4+ quarters	222	48.05%
Voice or SMS service	None	28	6.06%
	SMS only	340	73.59%
	Voice only	6	1.30%
	SMS + Voice	88	19.05%
	None	28	6.06%

	Visit reminders only	340	73.59%
	Visit reminders + pill reminders	25	5.41%
	Visit reminders + health tips	8	1.73%
Type of treatment support received	Visit reminders + health tips + pill reminders	61	13.20%

Clinical and adherence outcomes

ART experience & baseline adherence

At the time of enrolment, 83.8% (387/462) of participants had been taking ART for 6 months or more, 6.5% (30/462) had been on ART for 30 days–6 months, and 9.7% (45/462) were either treatment naïve or on ART for less than 30 days at enrolment.

At baseline among patients on ART for 30 days or more, perfect adherence of 100% of doses taken in the last 30 days was reported by 50.7% (208/410) of the participants, adherence of 95% to 99% of doses was reported by 27.3% (112/410), adherence of 90% to 94% was reported by 13.2% (54/410), and adherence of <90% was reported by 8.7% (36/410).

Retention, mortality, and treatment failure

Retention on ART at the 48-week study visit was 91.1% (421/462) and an additional 0.6% (3/462) of participants voluntarily withdrew from the study but continued receiving HIV care at the study site. Throughout the study 3.9% (18/462) became lost to follow-up, and 3.7% (17/462) transferred care to another clinic (**Figure 13**).

Clinicians changed the ART regimens of two participants due to treatment failure, the first of whom was treatment naïve and presented with opportunistic infections (PCP and TB) at the time of enrolment, and the second who was treatment experienced and reported poor ART adherence. Furthermore, three participants died during the course of the study: one death was due to an AIDS-related illness (cryptococcal meningitis), while one death was caused by a myocardial infarction, and the final participant's cause of death was not reported.

Table 20 describes the key outcomes of the cohort at each study visit and includes all available measurements at each time point.

Table 20. Primary and secondary outcomes by study visit.*

	Baseline (N=462)	**12 week (N=454)**	**24 week (N=430)**	**48 week (N=421)**
Adherence ≥95%	320/410 (78.05)	295/333 (88.59)	339/388 (87.37)	355/393 (90.33)
Treatment naïve (<30 days)	*n/a*	*31/32 (96.88)*	*34/36 (94.44)*	*35/35 (100.00)*
30 days - 6months on ART	*27/30 (90.00)*	*20/23 (86.96)*	*22/24 (91.67)*	*24/27 (88.89)*
>6 months on ART	*293/380 (77.11)*	*244/278 (87.77)*	*283/328 (86.28)*	*296/331 (89.43)*
Adherence >95% IIT (Includes LTFU and died pts as non-adherent)	*320/410 (78.05)*	*295/337 (87.54)*	*339/401 (84.54)*	*355/414 (85.75)*

VL Suppression cumulative**	262/283 (92.58)	279/299 (93.31)	294/318 (92.45)	335/364 (92.03)
VL Suppression (per VL done at each study visit)	*262/283 (92.58)*	*50/53 (94.34)*	*72/81 (88.89)*	*162/178 (91.01)*
Knowledge Score (mean)	85%	86%	87%	88%
Knowledge >90%	173/458 (37.77)	142/330 (43.03)	166/386 (43.01)	182/378 (48.15)
Quality of Life (mean, max score 120)	88.31	89.41	89.97	88.39
High QOL (≥90)	194/426 (45.54)	150/298 (50.34)	181/358 (50.56)	199/381 (52.23)
Died (cumulative)	n/a	1/462 (0.22)	3/462 (0.65)	3/462 (0.65)
Lost to Follow-up (cumulative)	n/a	3/462 (0.65)	10/462 (2.16)	18/462 (3.90)

**Denominators vary based on number of participants who completed each survey instrument at each visit, variance is due to missed visits or forms not completed. The N reported in each column reflects total number of people remaining enrolled in the study at each time point, while the denominator in each row reflects the number of data points collected for each variable.*
***Viral load at baseline is recorded for participants that had a viral load test result on file for taken at that visit or within the 6 months prior. As VL testing is conducted annually, in this table the last VL outcome is carried forward to visits where no VL was taken in order to represent the overall VL coverage and suppression rate for the cohort.*

Adherence

The 462 participants reported a total of 1,540 adherence observations. The proportion of participants with ≥95% adherence improved from 78.0% (95% CI 73.7-82.0%) at baseline to 90.3% (95% CI 87.0-93.1%) at 48 weeks. Among treatment-experienced participants, there is strong evidence of an improvement in adherence, with an increase from 77.1% (293/380) at baseline to 89.4% (269/331) at the final visit (McNemar's test = 21.88, P <0.001). Participants who were adherent at the time of enrolment continued to have higher adherence at subsequent visits, and adherence was not associated with intervention exposure level (**Figure 15**).

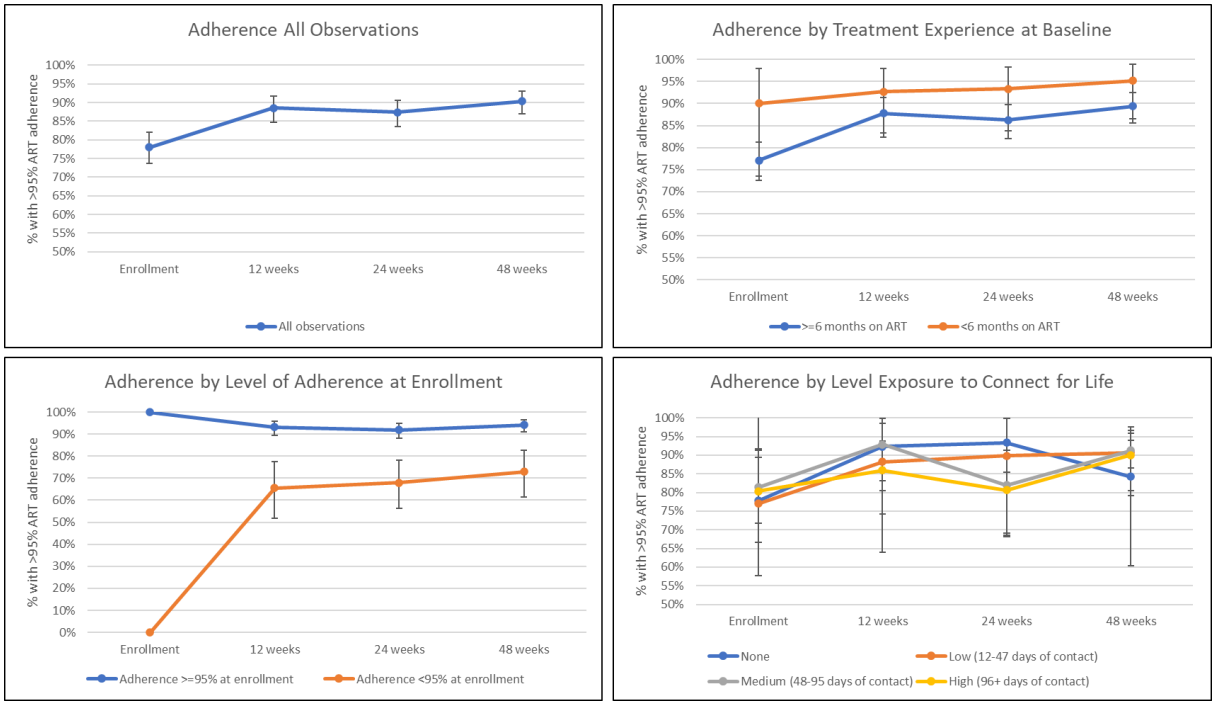

Figure 15. Adherence per study visit (includes all available data points at each study visit).

VL suppression

There were 595 routine viral load test results recorded for 374 participants. Of these, 47.6% (283/595) were recorded at the baseline visit and 52.4% (312/595) at subsequent visits (**Figure 16**). There was no change in suppression rates from baseline to end of study among treatment-experienced participants, and viral load suppression was not associated with intervention exposure level.

Viral load coverage was low, especially among the participants who were new on treatment at study enrolment. The proportion of participants who had at least one VL test done at any visit (viral load test coverage) was 81.2% (375/462) overall. However, coverage was 91.2% (353/387) among participants who were treatment experienced (≥6 months) at enrolment and only 28.0% (21/75) for participants who were new on ART (<6 months) at enrolment. Of the viral load tests done in the new on ART group, 95.2% (20/21) of these tests were recorded at the 48-week visit, which may explain the decreased suppression rate (81.0%, 17/21) at the 48-week time point (as only one viral load, which was undetectable, was reported before this time point for this group).

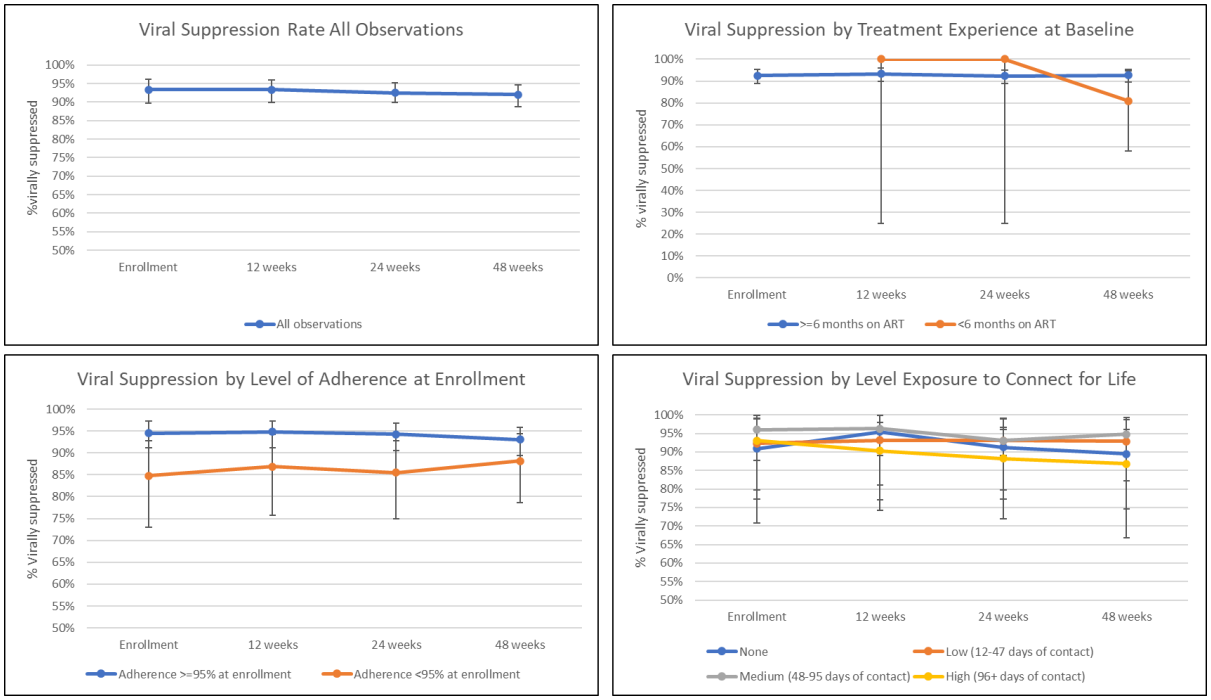

Figure 16. Viral load suppression per study visit (includes all available data points at each study visit).

Quality of Life

Among participants who were new on treatment at enrolment, the QOL score on the WHOQOL-HIV BREF scale improved from baseline to 48 weeks. Treatment-experienced participants had a higher mean QOL at baseline (89.02 of a possible 120 points) than those who were new on ART (84.6, *P* = 0.01). For the participants who were new on ART, mean QOL increased from 84.6 at baseline to 91.01 at 48 weeks (*P* = 0.025), with the largest improvement occurring in the domain related to level of independence (mobility, activities of daily living, dependence on medication or treatments, and work capacity). There was no statistical evidence for a change in QOL for treatment-experienced participants from baseline to end of study. There was no association between QOL score and level of intervention exposure.

HIV knowledge

There was a small increase in the mean knowledge score between baseline (84.5%) and 48 weeks (88.0%) (*P* <0.001). There was no difference between the experienced and new participants in knowledge scores. Nearly all participants correctly answered questions regarding how HIV can be transmitted, while most incorrect answers were on questions related to clinical topics such as whether an effective HIV vaccine exists or understanding the distinction between HIV to AIDS. Exposure to the intervention did not impact the knowledge score, regardless of whether the participants did or did not receive health tips as part of the intervention.

Factors affecting adherence and viral load

The findings from multivariable models of associations between various demographic, clinical, and behavioural factors and the outcomes of adherence and viral suppression are outlined in **Table 21** and **Table 22**, respectively. Each table includes only the variables that had an association with the respective outcome of interest with a *P*-value <0.1 in unadjusted univariate analyses.

We found that, while adherence improved over the course of the study, there was no association between intervention exposure and adherence (aOR=1.10, 0.72, 0.64 for low, medium, and high exposure, respectively; *P* = 0.28). Illicit drug use in the three months prior to enrolment was associated with non-adherence (aOR 0.56; 95%CI 0.31-1.00; CI *P* = 0.05) Participants with optimal adherence (>95%) at baseline had higher odds of optimal adherence at follow-up (aOR 5.83; 95% CI 3.60-9.46; *P* <0.001).

Viral load suppression did not change over the course of the study, and there was no association between intervention exposure and viral load suppression (aOR=1.92, 4.22, 0.96 for low, medium, and high exposure, respectively; *P* = 0.41). There was weak evidence that participants who had been on treatment for more than six months at enrolment were more likely to be virally suppressed at follow-up than those who were new on treatment at enrolment (aOR = 3.67; 95% CI 0.89-15.15; *P* = 0.07).

The 69 participants who were on second-line antiretroviral regimens (indicating previous treatment failure or intolerance) were less likely to have suppressed viral load (aOR = 0.33; 95% CI 0.14-0.78; *P* = 0.01) and were also less likely to be adherent (aOR = 0.76; 95% CI 0.43-1.37; *P* = 0.37). The viral load suppression rate among these second-line patients did not improve over the course of the study. At baseline, 77.1% (95% CI 64.8-89.4%) of second-line patients had undetectable viral load measurements as per their most recent VL test; at 48 weeks this was 80.7% (95% CI 70.53-90.76%), reflecting no significant change (McNemar's test = 0.00; *P* = 1.00).

Table 21. Factors associated with self-reported optimal adherence >95% assessed in a multivariable logistic regression model.

		% Adherent	aOR	*P*-value
Intervention Exposure	None	85.14	1.00	0.28
	Low (12-47 days of contact)	86.19	1.10 (0.41-2.94)	
	Medium (48-95 days of contact)	86.74	0.72 (0.23-2.28)	
	High (96+ days of contact)	84.31	0.64 (0.22-1.87)	
Baseline Adherence	Adherence <95% at enrolment	48.17	1.00	**<0.001**
	Adherence ≥95% at enrolment	95.02	5.83 (3.60-9.46)	

	No adherence data at baseline	96.25	9.89 (2.44-40.10)	
Treatment Experience at baseline	<6 months on ART	93.24	1.00	0.37
	6+ months on ART	84.74	0.72 (0.31-1.70)	
ART Regimen	First Line	78.75	1.00	0.37
	Second/Third Line	87.31	0.76 (0.43-1.37)	
Alcohol misuse*	No	86.85	1.00	0.23
	Yes	80.09	0.73 (0.44-1.00)	
Any Drug Use (3 months preceding enrolment)	No	86.80	1.00	**0.05**
	Yes	78.13	0.56 (0.31-1.00)	

**Alcohol misuse defined as two or more episodes of heavy episodic or 'binge' drinking (>five drinks) in the prior month or >14 drinks per week on average.*(230,231)

Table 22. Factors associated with viral load suppression assessed in a multivariable logistic regression model.

		% VL Suppressed	aOR	*P*-value
Intervention Exposure	None	87.80	1.00	0.41
	Low (12-47 days of contact)	92.47	1.92 (0.38-9.62)	
	Medium (48-95 days of contact)	93.10	4.22 (0.45-39.59)	
	High (96+ days of contact)	88.73	0.96 (0.15-6.10)	
Baseline Adherence	Adherence <95% at enrolment	86.89	1.00	0.80
	Adherence ≥95% at enrolment	92.98	1.14 (0.35-3.71)	
	No adherence data at baseline	94.12	2.32 (0.19-27.67)	
Treatment Experience at baseline	<6 months on ART	80.95	1.00	0.07
	6+ months on ART	92.16	3.67 (0.89-15.15)	
Baseline Viral Load	Detectable (≥50 copies/ml)	74.47	1.00	**0.01**
	Undetectable (<50 copies/ml)	89.29	0.44 (0.09-2.17)	
	No VL data at baseline	93.97	1.86 (0.42-8.24)	
Partner HIV Status	Not in a relationship	90.28	1.00	0.76
	Same-HIV-status relationship (both HIV+)	98.57	- (---)	
	Mixed-HIV-status relationship (partner is HIV-)	93.27	1.12 (0.34-3.69)	
	Unknown/Did not report	90.16	0.68 (0.22-2.08)	
ART Regimen	First Line	94.12	1.00	**0.01**
	Second/Third Line	80.39	0.33 (0.14-0.78)	
Adherence (post-baseline)	Adherence <95%	84.52	1.00	0.93
	Adherence ≥95%	92.84	1.07 (0.24-4.68)	

Sensitivity analyses

Both univariable and multivariable analyses were reproduced using continuous variables for intervention exposure and adherence. The analyses were also reproduced using logistic regression and mixed-effect models instead of GEE and then using an intention-to-treat approach for participants who were deceased or lost to follow-up.

For each sensitivity analysis, the direction of adjusted odds ratios did not change for any of the independent variables and the effect sizes were similar.

6.5 Discussion

Key results

The study used a personalised mobile phone adherence intervention over a 48-week period as a vehicle to improve adherence to daily ART and viral load suppression among a cohort of participants with HIV. We observed an improvement in adherence over time, with the proportion of participants taking more than 95% of their ART doses increasing from 78.6% at baseline to 90.3% at 48 weeks. The improved adherence observed in the cohort was not attributable to exposure to the mobile phone intervention as measured by number of days with any intervention contact. This may indicate that study participation alone had a positive effect on adherence. Through study participation, patients received several elements that are not standard of care: repeated adherence measurements (on the visual analogue scale questionnaire), discussions with clinicians and study staff (especially at enrolment), and SMS visit reminders. These elements may have helped improve adherence, by increasing motivation to adhere, improving on-time attendance of appointments and thereby availability of medication, or by other mechanisms.

We found that quality of life improved in the year following ART initiation. For participants in our cohort who had been on treatment for less than six months at the time of enrolment, a small increase was observed in the mean quality of life score from 84.6 points (of a possible 120) at baseline to 91.01 points at 48 weeks. This improvement was not observed among treatment-experienced participants, who already had a higher mean quality of life score at baseline. This supports the findings of previous studies conducted showing improved quality of life after starting or switching ART regimens.(220,277–279)

While adherence and quality of life improved, viral load suppression rates did not change significantly over the course of the study, with 92.6% of participants with a viral load done suppressed at baseline and 92.0% suppression at 48 weeks. The intervention did not have any observed effect on viral load suppression. An important finding was that the coverage of routine viral load testing was lower than expected, especially among participants who were new on treatment at baseline. Just 28.0% (21/75) of these participants had a viral load test done during the study period, while clinical guidelines required testing at 12 months on treatment (updated guidelines from 2018 now require a viral load assay at both 6 and 12 months).(280,281) Poor coverage of testing may have been attributed to challenges with eligibility under the Outpatient HIV/AIDS Treatment (OHAT) package provided by the Philippine Health Insurance Corporation (PhilHealth) to cover the cost of laboratory tests.

While self-reported adherence was lower in ART-experienced participants, their viral load suppression rates were still higher than participants who were new on ART at baseline. The lower viral suppression rate (81.0%) among the new-on-ART participants is not fully explained through poor adherence. This indicates the importance of monitoring drug resistance, which occurs at higher-than-expected rates in the Philippines.(242,282) Furthermore, there should be an emphasis on accelerating the use of new, more effective first-line antiretroviral regimens which may achieve faster viral suppression in patients starting ART.

The findings also highlight the need for a differentiated approach to adherence support, with a strong focus on becoming undetectable for new patients (e.g. “Undetectable=Untransmissible”/ “U=U” messaging) as well as resistance monitoring. Among more experienced patients, there should be a focus on addressing treatment fatigue. People on second-line therapy may require more intensive adherence support as we found that they continue to have poorer adherence and viral load suppression than patients on first-line regimens.

Social and family support remain important factors in successful adherence and treatment outcomes.(283,284) A substudy of 193 participants from this cohort found high rates of depression (21.8%) and anxiety (37.3%) among the cohort. However, the substudy found that these mental health factors did not impact ART adherence after factoring in low social and family support.(261) The proportion of participants in our cohort who confirmed they had disclosed their HIV status to family or friends was very low, at just 31.6%.

Another group requiring attention is people who use illicit drugs. An earlier analysis of risk factors in this cohort (184) found that injection drug use (aOR=0.54, P=0.090) and inconsistent condom use (aOR=0.50, P=0.103) were both potentially associated with reduced adherence to ART. Indicating that

these groups may be at risk of poor clinical outcomes as well as further HIV transmission to their sexual contacts. Study participants used drugs and alcohol at rates five- to 10-fold higher than the general population of the Philippines. Methamphetamine use is associated with increased sexual risk behaviour (235) and is used by MSM in chemsex or 'Partee 'n' Play' activities, posing a potential risk for HIV acquisition. Compounding these risks, evidence-based HIV prevention is not widely available in the Philippines – condom distribution has been restricted,(236,237) and pre- and post-exposure prophylaxis services are only available in select geographic areas (mostly large cities).(285,286)

In the absence of social and family support and in the context of substance use, mHealth platforms provide a mechanism for participants to be reminded about the importance of their treatment and to have more frequent contact with their health care providers.

Effectiveness of the intervention

It is difficult to draw conclusions about the effectiveness of the mobile health intervention due to the poor fidelity of the intervention delivery. We found in the process evaluation that acceptability of the intervention was high, and that the personalisable aspect of the intervention, i.e. the ability to select the desired type of and frequency of contact, was important to participants. Participant feedback was most positive regarding the health tip and visit reminder services.(185)

The SHIP clinic has continued to use the Connect for Life platform after this demonstration project. The technical issues that plagued the initial roll-out happened less frequently over time, leading to improved fidelity of the service delivery. At the time of publication, clinicians and participants report high levels of satisfaction with the intervention. In 2019, clinic staff conducted a retrospective analysis of clinic records for all scheduled visits between January 2017 and November 2019. The review found that participants receiving the SMS reminder service were more likely to attend their scheduled appointment on time than those who opted out of reminders (38% vs 30% on-time attendance, F=9.00, p=0.0028).

The intervention leveraging the Connect for Life platform in the Philippines setting was adapted from the same platform used for Call for Life Uganda as well as the mMitra and Treatment Advice using Mobile Alerts projects in India.(220,243) Studies in these other settings found improvement in patient outcomes among participants receiving the intervention.

The Call for Life study in Uganda found that viral load suppression was most improved among the group with moderate usage of the intervention, which is mirrored by our findings in the Philippine setting which suggest that medium exposure level (i.e. an average of one contact per week) was the most

effective. A systematic review and meta-analysis of studies of mHealth interventions to support ART adherence by Shah, Watson, and Free found that it is unclear if the frequency of contact (daily, weekly, scheduled) influences intervention outcomes. However, interventions that are interactive and use several behaviour change techniques more often lead to improvements in adherence. (148) While there has been substantial heterogeneity in results of mHealth adherence support interventions overall (129,148,166,265,287), these platforms should continue to be explored as part of differentiated care and treatment support services. In the context of the dual HIV and COVID-19 pandemics, a wider variety of services are being delivered virtually and community groups in the Philippines have advocated for the increased availability of mHealth and telehealth services for PLHIV.(288–291)

Strengths and limitations

The involvement of end users in the intervention design and the thorough process evaluation of the Connect for Life study were strengths that provided helpful context for understanding both the process of delivering the intervention and its results.(183,185) The delivery of the intervention in English speakers was informed by this formative research process and was appropriate for the population of Metro Manila, however, if this intervention were expanded to serve other regions of the country, translation into local languages would need to be considered.

Owing to technical issues, only 22.1% (102/462) of the participants received the IVRS pill reminder intervention and others received a scaled-back SMS text message intervention. Following this study, the frequency of technical issues decreased significantly, and the study site has continued to provide pill reminder calls as a routine service for all new patients starting ART.

This study had several weaknesses that limit the interpretation of results. It used a quasi-experimental design, which meant that exposure to the intervention was not randomised. Moreover, the participants within each of the different intervention exposure levels received a different number of messages and days of contact, and also received different types of messages (i.e. pill reminders, health tips; calls, text messages), which may have impacted the internal validity of the study when making comparisons between the exposure groups.

The intended measurement of outcomes was affected both by the poor coverage of routine viral load testing and poor quality and completeness of non-self-reported adherence measures (pharmacy refills records and interactive SMS reports). Both loss to follow-up and elevated viral load were rare, and so the study sample was underpowered to examine factors associated with these outcomes. While relying on self-report of adherence alone was not ideal, studies have shown that self-reported

adherence is useful and does correlate with clinical outcomes.(292–294) Finally, the knowledge measurement did not specifically link questions to the material in the health tips, but rather measured general HIV knowledge. A tailored knowledge, attitudes, and practices questionnaire with several versions may have been a better approach.

Conclusions

This study provides an in-depth analysis of demographic, clinical, and behavioural characteristics among a cohort of MSM living with HIV in the Philippines. We found that, by the end of the study, over 90% of the cohort reported ≥95% adherence to ART and that viral suppression rates were above 90% among those who received a test. Low coverage of viral load testing and poor suppression rates among participants who were treatment naïve at enrolment require targeted intervention. PLHIV who use illicit drugs and those on second-line treatment also require attention as they were found to be less likely to be adherent and virally suppressed, respectively.

There was no strong evidence that exposure to the mobile phone intervention conducted using the Connect for Life platform improved adherence to ART or viral load suppression. Observed improvements in adherence were not attributable to exposure to the intervention, which may be due in part to challenges in the intervention delivery during the course of the demonstration project.

Improved understanding of the factors associated with adherence and viral suppression may inform tailored prevention and treatment interventions, including those that use mHealth technologies, for MSM in the Philippines and other similar settings.

Chapter 7. Discussion

This final chapter of the thesis summarises the thesis aims and objectives, key findings, and provides a synthesis of the overall strengths and limitations of the thesis. I then discuss the challenges of conducting the outcome evaluation and key methodological considerations. Finally, I consider the thesis in the context of the current available evidence on mHealth interventions and ART adherence, the practical implications of the findings, and future directions for research.

7.1 Thesis aims and objectives

The aim of this doctoral research was to adapt an interactive voice response (IVR) mobile phone platform called Connect for Life to create an intervention suited to the needs of our patient population in the study site (people living with HIV, predominantly young bisexual and homosexual cisgender men) and to the local Philippine context, and then implement and evaluate the intervention. To achieve this aim, I set out to fulfil two distinct objectives:

Objective 1: Planning and Development. Create a locally tailored intervention using a mobile phone adherence platform for HIV patients on ART at the SHIP clinic in Metro Manila, Philippines.

Objective 2: Implementation and Evaluation. Conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to assess participant adherence, retention, and treatment outcomes at baseline and over follow-up.

The aim and objectives were achieved, with Chapter 2 detailing the intervention planning and development process and outcomes (Objective 1) and chapters 3-6 describing the evaluation methods, characteristics of the study participants, implementation process, and outcomes of the prospective cohort study (Objective 2). In brief, an intervention was designed that was acceptable to the target population and addressed a subset of factors contributing to nonadherence. Due to implementation challenges, the outcome evaluation provided limited insights into the effectiveness of the intervention. While adherence improved in the cohort, the improvement was not attributable to intervention exposure. The key findings are summarized in the section that follows.

7.2 Summary of key findings and lessons learned

Setting and context of intervention

The Philippines has one of the fastest-growing HIV epidemics in the world.(3–6) Routine surveillance finds that Filipinos' knowledge of HIV transmission, prevention, and treatment is poor.(81) Sex between males is the predominant mode of HIV transmission,(7) and chemsex is an important contributing factor in incidence among MSM.(26) Multiple stigmas surrounding HIV, drug use, homosexuality, and sex with multiple partners often serve to prevent MSM from accessing HIV prevention, testing, and treatment services.(34,35) Coverage of prevention, testing, and treatment services is insufficient, as evidenced by the fact the most new diagnoses (73.3%) happen late (with CD4 <350 copies/mm^3), reflecting a lack of routine testing.(15)

For PLHIV who are accessing care and treatment, adherence to ART is influenced by a set of complex personal and contextual factors. Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence or lack of social support, presence of mental health disorders, and time on treatment.(17,113,117–120) In addition to these factors, people may choose to not take their medications because they have negative perceptions of treatment, feel unsatisfied with healthcare facilities, for financial reasons, or because they are trying to forget about HIV. (122,123) In this study, employment in the business process outsourcing (BPO) sector (shift work) and transportation challenges emerged as important logistical challenges. In the Philippine context, issues of stigma and discrimination also emerged as a major barrier to medication adherence.(86,93,121)

The Connect for Life project was able to address a subset of the key factors driving ART adherence, the strengths and limitations of the intervention to address each individual and contextual factor is described later in this Discussion.

Intervention development

The first objective of the thesis was to create a locally tailored intervention using a mobile phone adherence platform for HIV patients on antiretroviral therapy (ART) at the SHIP clinic in Metro Manila, Philippines. This intervention development process was described in **Chapter 2**, and the key findings are summarised here.

During the intervention development process, a literature search and clinic record review were used to estimate the level of adherence in the study population. According to missed doses reported on pharmacy refill forms, 20.1% of the clinic population had suboptimal adherence (<95% of their

treatment doses), reflecting higher adherence in this group compared to global (37% non-adherent)(118,124) and regional estimates (26% non-adherent).(17)

Focus group discussions revealed that the main barriers to ART adherence in the study population were challenges around forming consistent routines and habits, low social support, stress and mental health issues, substance use, and the social stigma of living with HIV.

To create an mHealth intervention with components that would address these barriers, we applied principles from the Behaviour Change Wheel (BCW) and Capability Opportunity Motivation Behaviour (COM-B) model developed by Michie, Atkins & West.(203–205) Behaviour change techniques specifically related to ART adherence were informed by the information–motivation–behavioural skills (IMB) model of ART adherence.(206) Different components of the intervention addressed each of the three main components of the COM-B model. Capability was addressed through health tips on a variety of topics. Opportunity was addressed through pill reminders, appointment reminders, and the symptom-reporting algorithm. Motivation was addressed through health tips and adherence feedback messages. The intervention was highly personalisable, allowing users to select which features they wanted to use and whether they would receive services via SMS or voice calls.

Risk profile and adherence factors among MSM in Philippines

The second objective of the thesis was to conduct a prospective cohort study during the roll-out of the intervention to evaluate the implementation process and to describe patient adherence, retention, and treatment outcomes. The methods for this were described in detail in **Chapter 3**. A cross-sectional analysis of data collected at baseline visit described the characteristics of study participants, as detailed in **Chapter 4**.

The analysis found that adherence was not associated with clinical factors such as history of opportunistic infections or nadir CD4. Contrary to findings from previous adherence research,(17) longer time on ART was associated with lower adherence. This indicated a need in this group to identify and address treatment fatigue, which can be defined as “decreased desire and motivation to maintain vigilance in adhering to a treatment regimen among patients prescribed long-term protocols.”(295)

Relationship status emerged as an important factor in HIV adherence. Individuals in relationships, regardless of the partner’s HIV status, were more adherent to ART than those who were single. Those in relationships with HIV-negative partners were the most likely to adhere to their ART. Disclosing one’s HIV status to a trusted person was also associated with better adherence, but nearly half of participants had not disclosed.

Poor adherence to ART was also associated with substance use and inconsistent condom use, behaviours that are both linked to sexualised drug use ("chemsex"). Among the patient population at SHIP, clinicians reported that chemsex practices among MSM attending the study site were much more common than the 2% documented among MSM participants in the 2018 national Integrated HIV Behavioural and Serologic Survey (IHBSS). Concerns about the impact of chemsex on adherence was one of the initial motivations for automating daily pill reminders. Substance use in the prior three months was reported by 16% of the study participants, which is higher than the 11% reported among MSM in the IHBSS and much higher than United Nations Office on Drugs and Crime (UNODC) estimates of illicit drug use in the general population.

Reasons for non-adherence were largely situational factors like work schedules as well as habits and routines. Issues such as side effects and pill burden were rarely reported as a reason for non-adherence.

Process evaluation

The process evaluation (**Chapter 5**) used the Linnan and Steckler framework (239) and examined the fidelity, dose delivered and received, reach, usability, acceptability, and cost of the Connect for Life Philippines intervention.

After 48 weeks on the study, nearly two-thirds of participants reported they would be likely or very likely to recommend Connect for Life to a friend and more than half said they benefitted quite a bit or very much from the intervention. This was despite poor fidelity of intervention delivery, with just 22% of participants receiving any of the planned daily and weekly pill reminder calls due to problems related to the telecommunications provider.

Many mHealth evaluations have short follow-up periods, and there is limited evidence regarding the persistence of intervention effects over time or whether intervention fatigue decreases participant satisfaction over time. Intervention acceptability was not related to time on study. Those who received a higher dose of intervention were more likely to recommend the intervention to others. Patients who were on ART for less than six months at enrolment were more likely to say they benefitted.

Pill reminders, appointment reminders, and health tips were well liked by users. However, the dose delivered was affected by low call answer rates, as just 26% of outgoing calls were answered. During the intervention development stage, focus group participants were enthusiastic about receiving pill reminders as voice calls, but later expressed a preference for SMS. This was surprising, as it revealed unanticipated bias in the intervention development process. This finding emphasises the importance

of employing an iterative design and pilot-testing process, as users may not always anticipate what they will like most or what they might find irritating, until they experience it.

Participants reported that receiving calls or SMS messages made them feel more supported and connected to their health care provider and they expressed a desire for more human interaction with peers and clinic staff.

Clinicians reported that the intervention's medical record functionality facilitated easy access to laboratory results, medication history, diagnosis, and other information, which had previously been recorded in Microsoft Word documents and paper charts. Clinicians also reported that the alert function, which flagged participants with poor adherence or side effects for the clinician to follow up, was overwhelming because useful alerts were "buried" in a long list of inaccurate alerts about missed doses. Clinicians also observed an improvement in on-time attendance which saved staff time and effort by reducing the need to call participants and reschedule appointments. They attributed this to the visit reminders sent through SMS text messages.

Outcome evaluation

Participants in the prospective cohort study were followed for 48 weeks, as described in **Chapter 6**. Over the course of the study the proportion of participants who reported taking ≥95% of their ART doses increased from 78.6% (95% CI 74.4-82.4%) at baseline to 90.3% (95% CI 87.0-93.1%) at 48 weeks. Among treatment-experienced participants, adherence improved significantly between baseline and final visit (McNemar's chi-squared = 21.88, P <0.001). There was no change in viral load suppression. Small improvements were observed in HIV knowledge and in quality-of-life (QOL) scores. Improvement in QOL was associated with being new on treatment at enrolment. This finding supports existing evidence, as similar QOL improvements were previously documented in a mobile phone adherence intervention in China.(168)

Several important findings emerged throughout the course of the cohort study. Viral load testing coverage was much lower than expected, reflecting issues in clinical service delivery and laboratory capacity that require mitigation. Also, the study found that patients taking second-line ART did not have improved adherence or viral load suppression over the course of the study, and may be less adherent than first-line patients (aOR 0.76; 0.43-1.37), which supports existing evidence that this group is likely to require additional support.(173,296) Finally, participants who used illicit drugs were less likely to be adherent (aOR 0.56; 95% CI 0.31-1.00).

There was no strong evidence that the level of exposure to the mobile phone intervention improved adherence to ART or viral load suppression. However, due to the challenges in the intervention delivery during the demonstration project, it is also difficult to conclude that the intervention was not effective. Since the observed improvements in adherence were not attributable to exposure to the intervention, it is possible that regular measurement of adherence and visit reminders alone had a positive effect on adherence. There also may have been other unmeasured environmental and contextual factors that had an effect on adherence.

7.3 Strengths and limitations of thesis

Strengths

A strength of this study is that it is one of the first studies describing a cohort of people living with HIV in the Philippines, and the first to focus on MSM specifically. The literature review identified only three studies in the Philippines that focused on MSM, all of which examined HIV risk behaviours rather than care and treatment. This was also the first study of an mHealth intervention in this population and setting.

A strength of the mHealth intervention development was the user-informed design process. Young MSM in the study site were integral to each step of the process from planning to feasibility testing to implementation. Their preferences, concerns, likes, and dislikes were incorporated into the intervention design to make it more relevant to users. There were some limitations to what participant input could or could not be incorporated into the final intervention, as we were constrained by the capabilities of the Connect for Life technology.

The intervention development process was informed by behavioural theory, applying the Behaviour Change Wheel approach. I documented the 15 different behaviour change techniques that were linked to the five intervention functions (pill reminders, appointment reminders, health tips, adherence feedback scores, symptom reporting) (**Appendix 10**).(207) The mechanisms of action in promoting ART adherence involve each of the COM-B principles as described in Figure 5 of Chapter 2 and in Figure 2 of Chapter 4. Behaviour change techniques were informed by the IMB model of ART adherence.(206) This application of theory is key as, in order to facilitate the creation and implementation of more streamlined, tailored, and effective intervention approaches, researchers should systematically investigate which intervention elements are linked to the desired behaviours and their mechanisms of action. (297,298) The limitations of these theories are discussed in the next section.

It is important for mHealth interventions (and behaviour change interventions more broadly) to adequately describe the intervention content and evaluate the process of implementation. Suboptimal reporting on the details of behaviour change interventions leads to difficulty replicating interventions and poor understanding of the mechanisms supporting behaviour change.(299) A strength of this thesis is that it provides a comprehensive description of the multi-faceted intervention. The intervention development paper (**Chapter 2**) thoroughly outlines the behavioural theory informing the intervention, including the behaviour change techniques associated with each intervention element in the Connect for Life system.

In the process evaluation I applied the Linnan and Steckler framework, which defines key process evaluation components as reach, recruitment, dose delivered, dose received, fidelity. It also requires an assessment of the context (social, political, economic) in which the intervention occurs and how the environment influences implementation.(239) I added a component around acceptability/ satisfaction as this is a key mechanism of action.(251) I also used the mHealth evidence reporting and assessment (mERA) checklist to ensure the manuscript included the minimum set of information needed to support replication of the intervention. The 16-item mERA checklist guides researchers to define what the mHealth intervention is (content), where it is being implemented (context), and how it is implemented (technical features).(238) The process evaluation included a basic cost assessment that, while not a comprehensive cost-effectiveness analysis, provided a general sense of the resources required to implement Connect for Life.

While the mHealth intervention did not have the intended effects, the intervention itself had strengths. The Connect for Life platform is highly adaptable and scalable. A local IT provider can easily add or remove fields from the system, update message content, and adapt call flows. The frequency and method of contact can be quickly changed at the clinic based on each user's preference. Moreover, once the intervention is set up (i.e. the solution is hosted on a server and linked to a telecommunications provider) it is readily scalable to more sites or beneficiaries, and becomes more cost-efficient at scale.

Limitations

This thesis has a variety of limitations, which I will describe in roughly chronological order from literature review to intervention development, implementation, and evaluation. The outcome evaluation was especially challenging, and the specific issues and methodological considerations related to the outcome evaluation are described in the section that follows.

One limitation of this thesis is that the **literature review** I conducted was not a structured systematic review. At the outset of this research, I intended to conduct a systematic review of research on HIV in the Philippines. However, the demands and pace of intervention development and implementation outpaced the other aspects of the research. In 2018, Restar et al published an excellent review entitled "Trends and emerging directions in HIV risk and prevention research in the Philippines: A systematic review of the literature".(100) This review identified several publications I had not included in my literature review, but did not reveal any information that substantively changed interpretation of any aspects of the thesis. With regard to the available literature on mHealth interventions for adherence to ART, a wide variety of systematic reviews, meta-analyses, and reviews of reviews were already published at the outset of this project, and several more were published during the course of my studies, as outlined in **Chapter 1**. Due to the high quality and comprehensive nature of the existing mHealth systematic reviews available to me, I did not conduct a review as part of this thesis.

With regard to **intervention development**, a key limitation was that at the outset of the project, we already had a behaviour (adherence to ART) and an intervention technology (interactive mHealth) in mind. We did not start with a "clean slate", as we were working to adapt the Connect for Life platform to the local setting. We did not conduct any exploratory qualitative work to understand participants' priorities for a behaviour change intervention or to understand the complexity of their lives. The intervention was underpinned by priorities defined by the pharmaceutical company sponsor and by clinicians, and was therefore focused on individual behaviours of participants and providers. For this reason, the intervention did not address all of the key determinants of desired behaviour. For example, the Connect for Life platform did not increase social and family support for patients or assist with disclosing HIV status to a trusted person. If we had designed an adherence intervention without a specific technology in mind, we might have come up with an entirely different intervention. Recent literature on intervention development suggests that co-creation of intervention with stakeholders is valuable and that developers must have flexibility with regard to their own beliefs about the need for an intervention and its content and format.(300–302)

While participants were involved at key stages of intervention development and had substantial input on the content of the intervention, the development of the research protocol and research materials (e.g. questionnaires) lacked user involvement. The best practice would be to elicit and incorporate participant input into study design and local study procedures, as is often the function of community advisory boards in clinical research sites. Community input into research design ensures that research strategies acknowledge and respect participant values and the cultural differences among/between participants and researchers.

While the use of behavioural theory to inform intervention development was mentioned above as a strength of this thesis, there are also important limitations to the theory as it was applied. In the Behaviour Change Wheel, the outer ring accounts for policy and structural aspects related to a behaviour, and the Theoretical Domains Framework ring accounts for social and emotional influences; these feed into the COM-B components linked to the desired behaviour. Meanwhile, the IMB model of adherence focuses much more on individual control and responsibility, with much less consideration of contextual and social influences. As such, a weakness of this intervention design was that it put very little emphasis on environmental and social factors and focused almost entirely on individual behaviour. There were several reasons for this, the first of which was the limitation of what could be done within the functionality of the Connect for Life platform. Secondly, in the context of this study, the budget was limited to rolling out the mHealth platform and we did not have additional financial and human resources to provide a combination intervention addressing social support or environmental factors. We hoped to show the value that an mHealth intervention could add in the context of a challenging environment. Finally, we were not fully aware of the importance of social support in this cohort of patients until we analysed the baseline data. The baseline cross-sectional analysis was conducted after study completion, so the findings were not incorporated into the intervention design and implementation.

The intervention centred around reminders, with the key assumption that most people want to adhere to their medication but fail to take it because they forget. However, recent evidence from the Jackson Heart Study interrogated this assumption (albeit in a very different setting from this research), finding that, among 2,138 heart disease patients, forgetting to take medicines only accounted for 35.3% of non-adherence ("unintentional" non-adherence), 12.3% of non-adherence was the patient's choice ("intentional" non-adherence), and 52.4% was a combination of both.(303,304) People may choose to not take their medications because they have negative perceptions of treatment, feel unsatisfied with healthcare facilities, for financial reasons, or because they are trying to forget about HIV.(122,123) These factors cannot be effectively addressed via an mHealth platform like Connect for Life. This dynamic between "intentional" and "unintentional" behaviour comes through in COM-B v2 (published in 2020), in which capability and opportunity are shown as influencing the relationship between motivation and behaviour, rather than the behaviour itself.(305) Motivation may be a combination of both understanding the need to perform a behaviour and wanting to perform a behaviour. While people may have the opportunity and capability and need to take their medication, they may not have the desire to. The intervention could have been improved by a better understanding of the reasons why people intentionally choose not to take their medications.

An intervention that accounted for social environment could have combined Connect for Life health messages and reminders with support from peer coaches or digital support groups; or it could have assisted with HIV disclosure to a patient's family member or friend, training them as a treatment supporter. Emerging data has provided evidence for the feasibility and efficacy of mobile phone adherence support groups.(306–308) An intervention that better addressed the structural drivers of non-adherence (which in Manila often have to do with the difficulties of transport and travel) would prioritise virtual consults, mobile phlebotomy services, or delivery of medications to a chosen address. More recent publications in the mHealth field emphasise the importance of combination interventions,(125,149,151) as well as the superiority of less frequent messaging over daily messaging, (141,147) which could in the future be incorporated into the design of Connect for Life.

In the **process evaluation**, several participants receiving voice calls reported that they did not understand how to enter their PIN or navigate the call menus. It was also not clear to all participants that they could request clinic staff to activate or deactivate different services/functions on Connect for Life. This indicates that the intervention may have been either too complicated in terms of the call flows or not explained well enough by clinic staff at time of enrolment. To ensure call flows are easily navigable, I would recommend that intervention designers minimise the number of branches in the Interactive Voice Response System (IVRS) call flow, and they conduct thorough user experience testing during the design stages. To minimise issues around the variable quality of the description provided by study staff, I would recommend using an instructional video to orient participants on the system.

While the process evaluation methodology included qualitative feedback on the clinician-facing elements of the intervention (alerts and patient medical record), the study was not designed to evaluate the potential effects of these elements on the primary outcomes of adherence and VL suppression. In this regard, an evaluation design that compares various configurations of the intervention (i.e. with or without the clinician-facing elements) would provide a stronger basis for recommendations regarding the various aspects of the composite intervention.

Another limitation to this thesis was the low participation in focus group discussions. Recruitment for discussions was conducted by convenience sampling, and difficulties arose because a majority of participants did not want to disclose their HIV status in a group setting. Furthermore, travelling to the clinic to meet in person was inconvenient, especially in the setting of Metro Manila where traffic congestion has a significant impact on day-to-day life. The low participation in focus groups meant that the qualitative data informing intervention development and process evaluation was less rich and varied than it could have been. The perspectives represented in the groups may have been biased toward those of people who were more highly motivated to participate and those who were more

comfortable with their HIV status. When planning the research methods, I believed that groups would elicit more rich conversation about the intervention than one-on-one interviews. I did not anticipate the challenges with recruitment and participation. With hindsight, I would recommend the inclusion of individual interviews in the protocol as well as focus groups. Today, virtual interviews and virtual group meetings are more common, and would also be a good alternative to in-person focus groups. Ideally, groups and interviews would include a purposive sample of the study participants representative of age, time on ART, disclosure status, adherence, and other factors.

Despite the recruitment challenges, there were valuable learnings from the **conduct of the focus group discussions**. In the conduct of each focus group, we used two facilitators – a lead moderator and notetaker. We chose lead moderators whose positionality as Filipino men with close ties to the LGBT and PLHIV communities created opportunity for them to relate to participants on a personal level as "insiders". The notetakers in focus groups were both female health professionals (the lead investigator and the research coordinator/nurse), who were relative "outsiders" but were able to offer expertise and technical information when necessary.

The focus group discussion guides are included in **Appendices 8 and 9**, and they include guidance for the overall conduct of the groups by the moderators. This included guidance that moderators should "remain neutral, refraining from nodding/raising eyebrows, agreeing/disagreeing." It was important that the moderators did not volunteer their own opinions or reactions in a way that would bias the findings or influence the participants. The guide also suggested that the moderator should "get all participants to talk and to fully explain their answers." In practice, the moderators did an excellent job of this, managing the flow of the conversation to ensure that each participant in the focus group had an opportunity to contribute their thoughts, and prompting explanation and elaboration through effective follow-up questions. However, in retrospect I would change the wording of each of these guidelines for clarity, e.g. rather than "get all participants to talk" it would be more appropriate to say "invite all participants to talk" and rather than "remain neutral" it could say "be aware that your body language or facial expressions may convey biases." The specific instructions as originally worded could be misinterpreted by less experienced facilitators and could potentially lead to an uncomfortable or stigmatizing environment in the discussion.

An unexpected benefit of focus groups was the feedback from participants that the group setting provided a positive environment with peer support, where they experienced affirmation and validation of their experiences and challenges with treatment. While individual debriefing and counselling by a trained counsellor was available to anyone who needed it, no one reported a negative experience.

Regarding **recruitment** for participation in the study, approximately 72% (485/675) of the patients receiving HIV services at the study site were screened for participation. Patients who were not screened may have been those who attended the clinic on evenings or weekends, or patients who bypassed the waiting area for privacy reasons, which could potentially introduce some bias to the study sample. We do not know if the demographic, clinical, or behavioural characteristics of the patients who were not screened are substantively different from those who were.

The adherence measure used in analyses throughout the thesis is a self-report measure (visual analogue scale), which has a high risk of social desirability bias and recall bias. While it was not feasible to use other measures of adherence (e.g. electronic medication monitors or biomarkers), I had initially planned to triangulate self-reported adherence with other data points. The reasons for using self-report only are discussed in the next section.

Finally, the generalisability of findings is limited, as the study population had high levels of education and employment and also had higher retention and adherence rates than have been observed in other studies in the region.(17,241,242) The study population also had higher levels of substance use than observed in the general population or other MSM in the Philippines.(26,309) In order to be more generalisable the intervention would needs to be replicated and evaluated in other settings and populations. Despite these limitations, there are inferences that can be made about the wider feasibility/acceptability of the intervention. For example, the delivery of reminders and health messages by mobile phone was acceptable. Findings about the demographic, clinical, and behavioural factors affecting HIV adherence in this population, such as the importance of social support and the impact of "treatment fatigue" after longer time on ART may be useful to inform programmatic strategies in other contexts. Finally, our experience in adapting and implementing technology in a new setting may inform implementation and roll-out plans in other settings. We highlighted the need for robust pilot testing and demonstrated how an mHealth intervention may be adapted in response to contextual issues affecting intervention delivery and fidelity.

7.4 Challenges of the outcome evaluation and related methodological considerations

While at the outset of this thesis there was a clear plan about how to evaluate the impact of the Connect for Life intervention on health outcomes, along the way there were unexpected issues that added complexity to conducting the analysis, interpreting the results, and drawing conclusions about the effectiveness of the intervention.

Here I summarise the key issues that posed challenges to evaluating and drawing conclusions about the intervention, and how I approached each issue. The three most significant challenges were: (1) use of a quasi-experimental study design, (2) technical challenges that led to poor fidelity of intervention delivery, and (3) incomplete outcome data (viral load and measures of adherence).

Use of a quasi-experimental study design

We conducted an observational cohort study, which was not an optimal study design to evaluate intervention effectiveness. While a randomised controlled clinical trial would have been preferable, a stipulation of the sponsorship agreement was that the evaluation must be an observational study and not a randomised trial. A trial would have been required to undergo extensive regulatory and scientific approval processes within Janssen which were beyond the intended scope of the sponsorship agreement.

However, even in the absence of randomisation, it is possible for an evaluation to build evidence of "plausibility" of intervention impact by measuring change over time, dose response, and through qualitative data.(310) In the absence of randomised intervention and control groups, I evaluated the impact of the intervention by comparing adherence and viral load at baseline (prior to intervention exposure), with measurements at subsequent study visits. Then in models of the outcomes at follow-up visits, I adjusted for baseline adherence and viral load, and dealt with clustering of follow-up observations within patients by using Generalised Estimating Equations (GEE) models. I also adjusted for baseline demographic, behavioural, and clinical factors. However, this approach does not account for confounding by unmeasured and/or poorly understood or inaccurately measured factors, which could be accounted for through randomisation.

Another approach I used to understand the impact of the intervention was to compare subgroups within the cohort based on the dose or level of exposure to the intervention they received. The dose was based on the number of days the participant received a contact (call or SMS) from the Connect for Life system. However, this was an imperfect measure as it did not fully account for heterogeneity in the intervention. For example, a participant who received one month of daily contact and then nothing thereafter would have the same exposure level as someone who received two to three messages per month over one year. I accounted for this issue by conducting sensitivity analyses that used different exposure measures (i.e. number of days of exposure, SMS vs. phone calls, number of months/quarters with contact). The sensitivity analyses did not produce any results that differed significantly from the first model.

Poor fidelity of intervention delivery

To draw conclusions about the effectiveness of an intervention, it is necessary to have clearly categorised and defined the intervention. During the intervention development phase of the project, the study team developed a standard Connect for Life services scheme (refer to **Chapter 2, Table 5**). All participants on treatment for less than six months would be offered daily pill reminder calls for six months and weekly pill reminder calls thereafter. Participants on ART for six months or more would be offered weekly pill reminder calls for six months. All participants would be offered appointment reminders, health tips, and weekly adherence scores/motivational messages. The Connect for Life platform would allow individuals to opt into or out of each component based on their personal preferences.

The intervention delivery did not proceed as expected, as described in detail in the preceding chapters. While the study team paused enrolment to investigate the technical issues with the telecommunications provider, we could not postpone the project for an extended time and, as a result, the study team had to change the planned intervention. Of the 462 participants, 74% received only SMS appointment reminders throughout the year, while 20% received voice calls or a combination of SMS and calls, and 6% did not receive any intervention. Inevitably, this failure to deliver the intended intervention meant we did not observe a strong intervention effect on adherence and viral load suppression. However, we also cannot draw the conclusion that the planned intervention was ineffective.

A similar outcome occurred recently in a study conducted in India, where implementation of a planned IVRS adherence intervention was delayed for six months due to logistical issues. During that six-month delay, the adherence of the study participants increased from about 65% to >95%, which may have been attributable to the unplanned effects of measurement and communication about adherence at the clinic in anticipation of the study launch.(133)

The technical challenges affected user experience, which made it difficult to interpret user feedback about the acceptability and usability of the planned intervention. It is possible that user ratings were lower as a result of the technical issues than they would have been if the intervention had been delivered as intended. This is supported by the fact that the acceptability of the intervention was rated higher by the users with more exposure (it is likely that those with higher exposure were those who experienced fewer technical issues with call delivery).

Incomplete outcomes data

A key challenge of the evaluation was the incomplete measurement of the two main outcomes of interest – adherence to ART and viral load suppression.

Adherence measures: During the protocol development, I planned to measure adherence to ART using a composite measure that incorporated three pieces of information: dispensing data, adherence reports into the Connect for Life platform via the IVRS, and self-report on visual analogue scale.

The dispensing data were documented as part of standard of care on pharmacy refill forms stored in patient files. The pharmacy refill forms included basic demographic information, dispensing data, a pill count, and a field for self-report of number of doses missed in the past 30 days. Relevant data points were extracted by the study coordinator and used to calculate percentage adherence. Data quality for the forms was poor, with missing forms, fields left blank, and inconsistent/conflicting data in a large proportion of records. As a result, the adherence percentages calculated often fell outside of realistic or expected values. This measure ended up being unusable and was excluded from the analysis.

The second measure of adherence, patient reports into the interactive voice response system (IVRS), were prompted during daily pill reminder calls which asked, “If you have taken your current dose, press 1. If you have not taken the current dose yet, but are going to take it later, press 2. If you cannot take the current dose, press 3” or weekly pill reminder calls which asked “During the past seven days, have you missed any doses? Press 1 for yes, press 3 for no”, followed by a prompt to enter the number of missed doses if the user pressed 1. Per the services scheme in the protocol, all patients should have received daily or weekly pill reminders. However, due to technical issues that caused the IVRS system not to work as expected, only 82 patients reported any adherence data via IVRS (daily reports only n=14, weekly reports only n=16, combination of daily/weekly n=52). The reporting rate for those patients was just 31% for daily reminders and 36% for weekly reminders (**Table 23**). The lack of data and the poor reliability of the data we did have made this electronic adherence measure unusable. It was excluded from the analysis.

The third measure of adherence, self-reported adherence on a 30-day recall visual analogue scale, was the measure used in all analyses. While self-report approaches tend to over-estimate adherence, they are often used because they are both inexpensive and feasible in a variety of settings. Studies of self-report assessments of adherence have found them to be highly correlated with plasma HIV concentrations, dispensing measures, and electronic monitoring device measures.(120,292,294) In addition to the potential bias of the self-report measure, some measures of adherence were missing due to patients either missing study visits or leaving fields blank on the questionnaires.

Table 23. Summary of adherence reported through IVRS prompts during pill reminder calls.

	Participant response to IVRS prompt							
	Daily dose taken				Daily dose missed	No Report	% Adherence	% Calls with adherence reported
Daily Pill Reminders (N=66)	3,985				16	8,880	99.6%	31.1%
	7 doses taken	**6 doses taken**	**5 doses taken**	**1-4 doses taken**	**0 doses taken**	**No report**		
Weekly Pill Reminders (N=68)	1,003	76	16	0	2	1,934	98.4%	36.2%

Viral load: Based on clinical guidelines, all study participants should have had a viral load taken at least once during the 48-week study period as standard of care. Ideally, the study protocol would have included viral load measurements at 24 and 48 weeks. However, the cost of laboratory tests was not covered by the study sponsor. Many of the standard-of-care viral load measurements were not taken, especially for patients who were relatively new on treatment, with viral load testing provided for just 28% (21/75) of participants with less than six months on ART at enrolment compared to 87% (343/387) of those with more than six months of treatment experience. While in some cases this omission could have been clinician error, more frequently missing viral load was a result of delayed enrolment into the PhilHealth Outpatient HIV/AIDS Treatment programme, which covers the laboratory costs in the public sector.

Handling missing data: The missing outcomes data introduced additional complexity into the evaluation process. There were several key questions:

1. Do the missing outcomes data introduce bias? Are the data missing at random or is the missingness associated with the value of the outcome (missing not at random)?
2. Should the analysis be conducted using available/complete case analysis (include subjects without missing observations for analysis), or should I impute data? If I impute, should I conduct single imputation or multiple imputation? How does this affect the power of the analysis?
3. Where patients were lost to follow-up or died, should the analysis be conducted using partial data or should intention-to-treat (ITT) analysis be conducted (i.e. assuming no adherence and unsuppressed viral load until end of study)?

In order to tackle the above questions, I started by conducting an analysis of associations between missing outcome variables and other variables of interest (treatment experience, baseline adherence, intervention exposure). Of 1,819 total patient–visit records, there were 1,540 with the adherence

measure complete, 598 records with viral load complete, and just 573 records with both adherence and viral load. It is expected that viral load would be missing on most records, as it was not clinically indicated at all visits. I found that participants with lower baseline adherence were more likely to have missing data at subsequent study visits; **Table 24** below describes the reasons for missing adherence data points at follow-up visits. Viral load data were more likely to be missing for participants who were new on treatment than for those who were treatment experienced at enrolment, which would be expected as viral load testing is not clinically indicated for those new on treatment as described above.

Table 24. Missing adherence measurements at follow-up, by patient status/reason for missingness.

Baseline Adherence Reported	Total missing adherence data points*	Attended visit (incomplete questionnaire)	Missed Visit	Transferred Out	Lost to Follow Up	Early termination (opted out)	Died
No adherence data at baseline (n=52 participants)	68/156 (44%)	57/156 (37%)	6/156 (4%)	1/156 (1%)	4/156 (3%)	0/156 (0%)	0/156 (0%)
Adherence >=95% at enrolment (n=320)	161/960 (17%)	71/960 (7%)	62/960 (6%)	16/960 (2%)	8/960 (1%)	2/960 (0.2%)	2/960 (0.2%)
Adherence <95% at enrolment (n=90)	65/270 (24%)	28/270 (10%)	29/270 (11%)	0/270 (0%)	6/270 (2%)	1/270 (0.4%)	1/270 (0.4%)
TOTAL (n=462)	*294/1386 (21%)*	*156/1386 (11%)*	*97/1386 (7%)*	*17/1386 (1%)*	*18/1386 (1%)*	*3/1386 (0.2%)*	*3/1386 (0.2%)*

*As a proportion of expected observations (3 follow-up visits per participant)

The exploration of missingness showed that adherence and viral load data could potentially be missing not at random (MNAR), but it was not possible to confirm this without knowing the outcome values. When outcome data are missing not at random, all methods give biased estimates, but complete case analysis with covariate adjustment and multiple imputation each yield similar estimates, and complete case analysis with covariate adjustment is generally the analysis of choice.(311)

I conducted several sensitivity analyses in which I hardcoded the missing adherence values and/or viral load values using single imputation approach of last outcome carried forward (LOCF). Using the LOCF approach is problematic in that it assumes there is more information in the dataset than there really is, and therefore it gives confidence intervals that are too narrow and *P*-values that are too small. I further explored the impact of different assumptions about the missing visits on the results of the analysis. For example, I conducted an intention-to-treat analysis where I assumed zero adherence and viral load unsuppressed at all visits including and following an early termination of study participation (due to death or loss to follow-up), which represented a worst-case scenario.

These sensitivity analyses gave similar results to the complete case analysis, which left me fairly confident that the missing data were not a major issue for the analysis and the findings were valid.

Rationale for GEE model: In the outcome analysis I used a GEE model with robust variance. The model included the data points from follow-up visits at weeks 12, 24 and 48 in the model and adjusted for the baseline values. The advantage of the GEE model is that it accounts for correlations of observations within participants.

Other methodological considerations

In addition to the considerations around study design, intervention delivery, and missing data, there are several other aspects which could have improved the evaluation. There are several measurements I would consider adapting/adjusting in hindsight.

- Knowledge: A standardised and validated tool was used. However, the overall improvement in knowledge scores may have been due to repeated measurement using the same instrument. The knowledge measurement did not specifically link questions to the material in the health tips, but rather measured general HIV knowledge. A tailored questionnaire with several versions used in rotation may have been a better approach.
- Attendance: Clinic staff observed that on-time attendance of clinic visits improved for patients who received automated reminders from the Connect for Life system. However, the study dataset only included visit attendance in the visit window (which was a wide window); on-time attendance was not included. The inclusion of a variable for on-time visit attendance would have been beneficial. A post-hoc analysis was done to this effect, but the data were not of sufficient quality to include in the formal analysis.
- Intervention exposure: As described in Chapter 6, there were several different ways of classifying intervention exposure – number of unique days of exposure, type of intervention, time frame of exposure (quarters with contact). It would have been beneficial to more clearly define the measures of exposure at the outset and to have monitored the exposure levels throughout study implementation.
- Behavioural variables: Some of the study variables were measured only at baseline (e.g. substance use, HIV status disclosure, condom use, relationship status). It would have been beneficial to repeat these measures throughout the study to identify behavioural trends over time and to include more precise data in the multivariate model.

7.5 Research in context

In the process of developing this thesis, there were two key areas of learning that I often returned to and reflected on. The first of these was related to evaluating mHealth technologies. I found that evaluating an mHealth intervention was vastly (and unexpectedly) different to my prior experience evaluating other types of health interventions. In this section I reflect on the reasons why mHealth evaluations may require different skill sets, processes, and methods than those that are typically employed in public health evaluations. The second learning that I returned to in my reflections was the particular importance of creating a caring environment in services for key populations (who are often excluded from or experience discrimination in mainstream health services), and the role that technology can play in helping people feel cared for and attended to.

Implementing and evaluating mHealth technologies

The field of mHealth has moved rapidly in the last decade. There has been a proliferation of mHealth technologies, interventions, evaluations, and academic literature. Factors affecting the success of implementation have been well described by various groups globally.(112,312–316) Some of the main **implementation considerations** and are summarized below:

- Project/intervention design: the intervention is appropriately designed, usable, adapted to the local context.
- Technology and resources: appropriate technology and infrastructure are available, capacity building is provided to local staff and users, human resources are available to manage the project, workforce impacts have been considered (i.e. workload, workflow, division of labour).
- Context and involvement of stakeholders: the intervention is aligned with national and local policy priorities, there is involvement of multidisciplinary teams and political leadership, possibility for scalability, and interoperability/integration of intervention with other health systems.

A common theme emerging in the mHealth literature is the need for more rigorous **evaluation methods** to produce a higher quality of evidence of effectiveness. Most studies of mHealth interventions suggest positive results, but studies frequently use non-randomised designs, are underpowered, or are difficult to reproduce. These issues with quality of evidence are commonplace in mHealth interventions, suggesting that novel evaluation methods may be required.

There are several reasons why the randomised controlled clinical trial (RCT), the “gold standard” to reduce the bias in effect estimates, has limitations for evaluating mHealth technology. A large-scale RCT often takes years to complete, and requires a high level of fidelity in intervention delivery.

However, mobile phone technology is constantly evolving, which makes it difficult to develop and test interventions that are up to date and relevant. Individual mHealth interventions also evolve at a rapid pace. Implementing an mHealth intervention usually involves fixing bugs, iterating and refining content, incorporating user feedback, and improving delivery mechanisms. As I found in the Connect for Life evaluation, these changes often need to happen mid-study. And while it is possible to change the form of an intervention while maintaining the function and process of the intervention,(317) changes during the study period make it more difficult to reproduce and interpret results.

Compared to traditional RCTs, mHealth studies have a higher risk of contamination, as individuals in the control group may be exposed to content of the intervention through their social networks or their environments, even if they are not direct recipients of the intervention. In studies where adherence is a primary outcome, contamination can come in the form of other reminders like alarm clocks on cell phones. The probability of bias in mHealth evaluations may be higher due to non-randomised study designs (selection bias), lack of blinding of the investigators and participants (detection bias), participant self-reports of their behaviour (social desirability bias), and/or incomplete or selective reporting of outcomes (reporting bias). Many mHealth trials have shorter follow-up times than traditional RCTs, meaning that if an intervention effect is detected the durability of that effect is often unknown. Also, where mHealth has small effect sizes, studies are often underpowered to detect an effect. Additionally, updates to the intervention may occur more frequently in mHealth interventions, requiring frequent protocol amendments and/or deviation reports to ethics committees, which can be a barrier to conducting research on mHealth projects.

Because of the continually evolving nature of mHealth behavioural intervention technologies, it is important to develop designs that allow for iteration and refinement throughout the course of the trial. Mohr and colleagues proposed the Continuous Evaluation of Evolving Behavioural Intervention Technologies (CEEBIT) framework, which allows for refinement of mHealth interventions while retaining a high level of scientific rigour.(318) In this approach, investigators can collect data on multiple versions of behavioural intervention technology at the same time, eliminating those that demonstrate poorer outcomes, while allowing evolution of the intervention through introduction of new BITs over time. Davey and colleagues also describe four quasi-experimental design options for health communication interventions that can yield greater validity than purely observational studies. These proposed designs are all non-randomised cluster-level comparisons. The options are: non-randomised controlled comparison, interrupted time series, stepped-wedge implementation, and dose–response/implementation strength.(319) Using these more flexible approaches to evaluation may accelerate the timeline from conception to scale-up.

While limitations imposed by the funder restricted the research design to an observational study, I believe a non-randomised controlled comparison, a stepped-wedge trial (with or without randomisation), or a cluster randomised trial could each have been effective study designs for this project. Each design would have allowed us to compare outcomes between intervention control groups while reducing risk of contamination (by assigning intervention/control at a facility level rather than individual level) and allowing for more flexibility than an RCT (by enabling roll out in staged phases). Alternatively, use of the CEEBIT framework would have fostered an iterative process in which we could have made comparisons between different intervention configurations/content and introduced improvements over time. This approach fosters innovation and aligns closely with project management approaches for product development used in the technology sector.

When evaluating mHealth interventions there are many contextual variables that influence the outcome of the intervention. Failure to account for these variables in an evaluation may limit the ability to adapt the intervention to other settings and to implement at scale. Therefore it is important in mHealth to conduct mixed methods evaluations and to systematically document contextual factors.(320,321) To this end, the mERA checklist is a useful tool to ensure clarity and completeness in the reporting of research involving the use of mobile healthcare tools.(238,253) The application of mixed methods and the use of the mERA checklist were strengths of the Connect for Life evaluation in this thesis.

Prioritising Key Populations

A key learning from this thesis is the role that technology can play in holistic key populations services. The HIV epidemic in the Philippines has predominantly affected members of key populations, transitioning from a small epidemic among female sex workers to a rapidly-growing, concentrated epidemic affecting MSM and people who inject drugs, particularly in urban areas.(322,323) Among members of key populations in the Philippines, HIV knowledge is poor, condom use is low, and stigma and discrimination faced in healthcare settings is an ongoing barrier to accessing services. Targeted interventions serving key populations also benefit the general population, as infections in the general population grow primarily because of key population turnover and infections among the intimate partners of members of key populations.(324,325)

While 82% of new diagnoses in the Philippines occur in MSM, this group is not well represented in the published literature on HIV. At the outset of this thesis, I identified only three research publications from the Philippines that focused on HIV risk factors among MSM and no research evaluating interventions to serve this group. Effective, acceptable and impactful programming for MSM is hampered by the lack of robust research data. (326)

Strategies to improve access to healthcare for MSM in low- and middle-income countries include: sensitivity and competency training for health care workers; community engagement; online and social media strategies; differentiated models of care; and a targeted service package that includes comprehensive sexual health services and other services that are high priority to MSM.(326)

The study setting for this thesis is one of a handful of organisations in the Philippines spearheading innovations in HIV services for MSM, and implements nearly all of these strategies. SHIP has piloted differentiated models of care including after-hours services, telehealth consults, and motorbike courier medication delivery. The service package offered in the SHIP clinic includes HIV testing and treatment; HIV pre- and post-exposure prophylaxis; testing and treatment for other sexually transmitted infections; cryotherapy for anal and genital warts; dermatology; care for other chronic health conditions; screening and referral for substance abuse and mental health; and peer support groups. The lead clinician is active on Twitter, hosting regular online "Ask me anything" sessions where people converse with her about HIV via public tweets (usually posing questions via an alias). SHIP shares infographics, videos, and stories via various social media channels.

As education and instruction of undergraduate and postgraduate health providers and medical auxiliary staff about key populations and HIV is almost non-existent, SHIP conducts trainings for health care workers to ensure they are not just clinically competent to manage HIV, but also have the requisite knowledge and sensitivity towards the needs of MSM.

The role of social support in adherence in HIV care and treatment

Social support can play a crucial role in improving adherence to ART among people living with HIV.(327–329) Overall, social support can provide individuals with the resources, motivation, and encouragement needed to adhere to their ART medications. By providing emotional, informational, practical, and social support, friends, family, and support groups can help increase ART adherence and ultimately improve the health outcomes of people living with HIV.

Users of Connect for Life reported that, beyond the intended scope of delivery of medication reminders and health information, regular contact from Connect for Life gave the recipient a sense of care and support. The Connect for Life system was perceived by some as an extension of their relationship with their doctor. This indicates that, although automated interventions are impersonal, and increasing social support was not an planned outcome of the intervention, mHealth can be leveraged to increase social support for ART adherence. Perhaps, in the broader context of an impersonal health system, a tailored SMS or phone call can contribute to creating a sense of personal attention or belonging. Similar findings have been reported in other studies of SMS interventions, in

a pilot study of the WelTel intervention in Canada one participant stated “It was very helpful for me. Well sometimes I feel really alone, so it made me not feel so alone.”(330) To date, research of social support as an outcome of mHealth technology has been focused on interventions that are designed to directly communicate with treatment supporters of a person living with a condition.(273,331,332) Understanding the indirect impacts that an mHealth intervention may have on the participants’ perceived social support could be an important area for future research.

Richard Lester, lead investigator of the WelTel Kenya1 study, summarised this sentiment in a 2013 Letter to the Editor of the NEJM where he stated: “My experience and interpretation of the evidence support an ‘Ask, don’t tell’ approach. Although patients may eventually tire of being reminded and told things they had not specifically asked about, they do not seem to tire of being asked how they are doing. Instead, they feel cared for. Patients also do not seem to tire of having access to their health care providers in times of need; this is the true power of having their health in their own hands through their mobile phones.”(333)

If we accept that the role of mHealth extends into the realm of social support, researchers should further investigate how these interventions can facilitate peer support networks or provide counselling and coaching. By using these strategies, individuals living with HIV can feel more connected, motivated, and supported in their efforts to adhere to their medications. However, adherence interventions that require human resources are more costly than technology-based interventions, and cost-effectiveness data are limited, especially in low- and middle-income countries and in the Asia-Pacific region. Stronger evidence is still needed to justify investment in adherence promotion interventions for marginalized populations.(334)

7.6 Implications for service delivery/ future directions/ recommendations

Connect for Life Philippines continued implementation

Based on this evaluation of Connect for Life, the evidence for effectiveness is not very strong. However, the qualitative feedback from patients and clinicians was positive. Considering that the barriers to entry and costs are low, and it was not detrimental, we recommended that the clinic continue to provide the service.

Between 2018 and 2023, SHIP has scaled up clinical services, expanding from one clinic in Mandaluyong City to five clinics across Metro Manila. These clinics currently provide HIV care and treatment to more than 1,200 patients. Following the study, the technical issues that impacted delivery

of Connect for Life were resolved as the telecommunications infrastructure improved. Today, all new patients initiating ART in these clinics receive six months of daily pill reminder calls and health tips together with appointment reminders. Clinicians and patients alike have positive feedback about the intervention.

If the evaluation were to be conducted under the current conditions, in which the platform is stable and the technology is functioning, the findings would likely be different. Now that there are multiple clinic locations, a stepped-wedge trial would be feasible. At this stage, the implementers should consider updating the health tips with the more current information about treatment and adherence, reconfiguring the adherence feedback and call flows based on user feedback, and adapting the intervention to support PrEP as well as ART.

Recommendations for future research

Based on the findings that identify social support as a key driver of adherence to ART, the intervention could be adapted to increase social support. An improved intervention may involve more personal contact from the clinic, such as the ability to request a call back from a counsellor. It could also facilitate the involvement of a treatment support partner, peer supporter or coach.

Another direction would be to study the intervention in a different population. As discussed in the preceding chapters, the study participants were highly educated and had high levels of employment compared to the general population. Future research could assess the intervention effectiveness with a study population more representative of people living with HIV in the Philippines.

Finally, further research on cost-effectiveness and sustainability of the intervention could be conducted, including investigations into how the Connect for Life platform could be interoperable with electronic medical records under development by the Philippines Department of Health.

7.7 Conclusions

At the outset of this thesis, while evidence showed that the HIV epidemic was accelerating rapidly among MSM in the Philippines, there was almost no published literature about interventions to support HIV care and treatment for this group. Approaches to support adherence to ART using mHealth platforms had been studied in several trials, and the results were promising, although the evidence about effectiveness was relatively weak.

With regard to the overarching aim of this thesis, the study team successfully adapted an IVRS mobile phone platform called Connect for Life to create an intervention suited to the needs of our patient population in the SHIP clinic and to the local Philippines context. The thesis described demographic, clinical, and behavioural characteristics of the clinic population and their experiences at baseline and throughout the cohort. I found that in the target population there may be a lack of social support and there are high rates of substance use, both of which may negatively impact adherence to ART. In evaluating the intervention, we faced significant implementation challenges. The evaluation found that the intervention was acceptable to patients and clinicians. However, we did not find strong evidence of effectiveness in improving adherence or viral load suppression.

While the evidence for the effectiveness of mHealth interventions to support adherence remains mixed, the field is moving ahead at a rapid pace. In the context of the Philippines HIV epidemic, expanded coverage of ART supported by both traditional and technology-based behavioural interventions is essential.

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Appendices

1. LSHTM Research Ethics Committee approval letter
2. University of Philippines Manila Research Ethics Board approval letter
3. Informed consent form
4. Connect for Life participant information booklet
5. Study protocol
6. Case report forms
7. Questionnaires
8. Focus group discussion guide (intervention development phase)
9. Focus group discussion guide (process evaluation phase)
10. Behaviour Change Techniques
11. Health Tips
12. Publication – intervention development
13. Publication – baseline characteristics of cohort
14. Publication – process evaluation
15. Publication – outcome evaluation

Appendix 1. LSHTM Research Ethics Committee approval letter

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Ms. Cara O'Connor
LSHTM

4 July 2016

Dear Cara,

Study Title: Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines

LSHTM ethics ref: 11631

Thank you for your application for the above research, which has now been considered by the Interventions Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Protocol / Proposal	Connect for Life Evaluation Protocol v1.0 11may2016	11/05/2016	1.0
Protocol / Proposal	ART Adherence Questionnaire	11/05/2016	1.0
Protocol / Proposal	Connect for Life Patient Acceptability questionnaire	11/05/2016	1.0
Protocol / Proposal	KAP questionnaire	11/05/2016	1.0
Protocol / Proposal	Informed Consent Form Connect for Life v1.0 11may2016	11/05/2016	1.0
Investigator CV	Cara OConnor CV 415IDE	11/05/2016	1.0
Investigator CV	James Lewis CV 415IDE	11/05/2016	1.0
Investigator CV	Katerina Leyritana CV 415IDE	11/05/2016	1.0
Investigator CV	Salvana_Edsel_CV_full	11/05/2016	1.0
Information Sheet	Informed Consent Form Connect for Life v1.0 11may2016	11/05/2016	1.0
Local Approval	RGAO Certificate of Registration	17/05/2016	1.0
Local Approval	Technical Review Letter	17/05/2016	1.0

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Professor John DH Porter
Chair

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

Improving health worldwide

Appendix 2. University of Philippines Manila Research Ethics Board approval letter

University of the Philippines Manila
RESEARCH ETHICS BOARD
2nd Floor Paz Mendoza Building, College of Medicine, UP Manila
547 Pedro Gil Street, Ermita, 1000 Manila
Telephone: +63 2 5264346; *Mobile:* +63 927 3264910; *Email:* upmreb@post.upm.edu.ph

08 September 2016

DR. EDSEL MAURICE SALVAÑA
Principal Investigator
Institute of Molecular Biology and Biotechnology
University of the Philippines Manila

Re: **UPMREB 2016-265-01**
Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines

Dear DR. SALVAÑA:

We wish to inform you that the **UP Manila Research Ethics Board (UPMREB) Review Panel 1** approved the proposed amendment/s in your study entitled, **"Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines" (UPMREB 2016-265-01)** through Expedited Review. Upon review of UPMREB FORM3(A)2012: Study Protocol Amendment Submission Form and attachments, the following documents have been approved for use:

1. Protocol Amendment version 1.2 dated 04 August 2016;
2. Informed Consent Form version 1.2 dated 04 August 2016;
3. Infographic booklet; and
4. Data collection tools version 1.2 dated 04 August 2016.

Thank you.

Very truly yours,

[redacted]

JACINTO BLAS V. MANTARING III, MD, MSc
Chair, UPMREB Review Panel 1

Appendix 3. Informed consent form

Informed Consent Form

Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines

Protocol Version 1.0,

May 11, 2016

Organization: The STI/AIDS Guidance Intervention & Prevention Unit at the Philippine General Hospital (UP-PGH/SAGIP) and Sustained Health Initiatives of the Philippines (SHIP), Inc.

Sponsored By: Investigator-initiated study with support from Janssen Global Public Health

Investigators: Edsel Maurice Salvaña, MD, DTM, UP-PGH SAGIP and University of the Philippines Institute of Molecular Biology and Biotechnology; **Cara O'Connor, MPH**, Sustained Health Initiatives of the Philippines (SHIP), London School of Hygiene and Tropical Medicine; **Katerina Leyritana, MD**, Sustained Health Initiatives of the Philippines (SHIP), Inc., UP-PGH HIV Fellows Program; **James Lewis, PhD**, London School of Hygiene and Tropical Medicine

This Informed Consent Form has two parts:

1. Information Sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form.

Part 1: Information Sheet - Connect for Life Study

Introduction

Investigators from the Philippine General Hospital and Sustained Health Initiatives of the Philippines, with support from Janssen Global Public Health and the London School of Hygiene and Tropical Medicine are inviting you to participate in a study about the "Connect for Life" project.

Purpose of the research

There are many reasons that patients taking HIV medications sometimes forget or choose not to take their pills. Many studies from other countries have shown that using mobile phones to provide reminders and health information to patients can help them improve their medication adherence. There is high potential for this approach to work in the Philippines as well, because mobile phone use is very high in this country. The SHIP clinic will conduct a project called "Connect for Life," which uses a software platform to automatically send mobile phone voice messages or text messages including pill reminders, clinic visit reminders, and health tips to our patients.

The purpose of this study is to document what happens to patients' medication taking and their health when they participate in the "Connect for Life" project. The study will also try to learn if the Connect for Life platform is acceptable and if it is helpful for patients of the SHIP clinic.

Participant selection

The study will include approximately 500 participants who are patients in the SHIP clinic. You are being asked to participate in this research because you are a patient of the SHIP clinic who is 18 years or older, is currently taking or about to start taking antiretroviral therapy for HIV treatment, and who has a mobile phone.

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. Dr Katerina Leyritana is an investigator in the study and she is also the primary health care provider at the SHIP clinic. If you do join the study, you may decide to stop participating at any time and this will not affect your services at the clinic.

Procedures and Protocol

Your participation in the research will last for one year. You will continue to come to the clinic for your primary care according to the routine schedule of one visit every three months. You will be asked to fill out questionnaires at the first visit, and after 3 months, 6 months, and one year. They will take 15 to 30 minutes to complete. The questionnaires will ask you to about your adherence to your medications, about your knowledge, attitudes, and practices related to various aspects of living with HIV, and about your feedback on the Connect for Life services. The study team will also collect specific information from your clinic medical record about your medical history, and ARV regimen.

During the study, the Connect for Life platform will send you mobile phone voice or text messages that will provide you with support through tailored services. The services are:

1. pill reminders,
2. clinic visit reminders,
3. health tips,
4. and symptom reporting.

Patients who receive pill reminders will also get weekly feedback messages regarding their adherence for the week. These feedback messages will provide positive reinforcement is your adherence is high, and will provide encouragement to help you improve your pill-taking if your adherence is low. In addition, your doctor will receive an alert from the Connect for Life platform

when you report symptoms or low adherence and clinic staff may call you to provide one-on-one support.

You and your doctor will decide together which services you will receive, whether you will receive voice calls or text message, how often you will receive the messages (e.g. daily, or weekly), and the time of day you receive the calls/texts. This services the doctor recommends will depend on how long you have been taking ARVs, how often you and your doctor feel you need reminders, and your personal preferences.

Participant Responsibilities

Participants in the study will continue to receive the same routine care at the SHIP clinic. You will be responsible to allow incoming voice calls and/or SMS on your mobile phone from the Connect for Life system. You will be responsible give complete and truthful responses about your adherence or symptoms when using the Connect for Life System. You will also be responsible for completing questionnaires. You should provide complete and truthful responses to all questions.

Risks and Benefits of the Study

A risk of using mobile phones in any health project is the possibility of accidental disclosure of your HIV status via the mobile phone if someone else reads your text messages or overhears your calls. To protect your confidentiality, the Connect for Life system requires you to enter a personal PIN code before you can hear any message.

You may benefit by receiving medication reminders, clinic visit reminders, and health tips on your mobile phone. This can increase you knowledge and help you have successful treatment outcomes.

The research may have indirect benefits for communities of people affected by HIV in the Philippines and the scientific community at large. The study seeks to expand on the current body of knowledge around HIV treatment outcomes in the Philippines, a topic about which only limited information is available in peer-reviewed, academic publications. The study will also add to the growing body of knowledge about mobile phone support interventions for HIV treatment adherence, and will be the first of its kind in the Philippines context.

Reimbursements

You will not receive any financial or material incentive or reimbursement for being a part of the study.

Confidentiality

The study team will take measures to protect your confidentiality during and after the study. The collection of your personal data will be limited to only the information that is to meet the goals of the study.

By participating in the study you agree that the study staff can access your personal data your medical records. Only SHIP clinic staff or PGH staff will have access to any information that could identify you personally. Study auditors, the Research Ethics Board of UP-PGH and/or other regulatory authorities may be granted direct access to participant's medical records for purposes ONLY of verification of clinical trial procedures and data. Any study data that are transferred to the sponsor (Janssen) or to other participating organizations (LSHTM) will have all personal information removed in order to protect confidentiality.

All electronic data from Connect for Life platform will be hosted on a secure, encrypted cloud-based server. Your name and other personally identifiable information will not be included in the research database, which will use only a research ID number. All paper forms will be stored in a locked cabinet in a private and secure room in the clinic. All records with personally identifiable information will be kept confidential and will not be made publicly available, to the extent permitted by law; and your identity will remain confidential in the event the study results are published. Study staff will have training in Good Clinical Practice and Human Subjects Protection.

You have the right to request access to your personal data and the right to request that the investigator correct any data that are wrong or incomplete. Reasonable steps will be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Focus Group Discussion Subset

A subset of 20-30 patients will be invited to participate in one or more focus group discussions. Participation in the focus groups is voluntary and you can still be part of the study even if you do not want to be part of a focus group discussion.

The study team will select which patients to invite to focus groups, and will attempt to make groups representative of the clinic population and with diverse patient experiences.

The purpose of the discussions is to find out what patients do and do not like about the Connect for Life project and to learn the best ways that the SHIP clinic can help patients remember to take their medications and attend their clinic appointments. The discussions will last approximately 2 hours.

Taking part in a focus group has some additional risks and benefits. The discussion may include personal or sensitive topics that you could feel uncomfortable talking about or listening to others talk about. Also, it is not possible to be anonymous when participating in a focus group discussion. All participants will be requested to keep the identities of the participants confidential, but there is still a risk that someone could discuss the group outside of the clinic. There are no benefits for taking part in the focus group other than helping the study team learn more about ways to help serve our patients.

Those who participate in focus groups will be served snacks or a meal during the session and will receive a stipend of 200 pesos for their transportation expenses.

Sharing the Results

The knowledge that we get from doing this research will be shared with you through a written report and/or community meetings before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected. The study also may be discontinued at any time by the implementing site, the sponsors, government or regulatory authorities, or by the Research Ethics Board. You will be informed in a timely manner if any information about the study becomes available that may be affect whether you want to participate.

Who to Contact

This proposal has been reviewed and approved by the University of the Philippines Manila Research Ethics Boards (UPMREB), which is a committee whose task it is to make sure that research participants are protected from harm. It has also been reviewed by the Research Ethics Committee of the London School of Hygiene and Tropical Medicine (LSHTM). The LSHTM Ethics Review Committee can be contacted at **ethics@lshtm.ac.uk.**

If you have a concern about any aspect of the study you may contact the investigators: **Dr Edsel Salvana (02) 931-9064; Cara O'Connor, MPH (02) 209-4971; and Dr Katerina Leyritana (02) 209-4971**. If you wish to make any formal complaint, please contact:

Dr Jacinto Blas Mantaring, UPMREB Panel Chair
Address: 2/f Paz Mendoza, 547 Pedro Gil St, Ermita 1000 Manila
Email: upmreb@post.upm.edu.ph
Tel: +63 2 5222684 **Mobile:** +639273264910 or +639153080212

Part 2: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction.

I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care of legal rights being affected.

I understand that study staff and regulatory authorities may access parts of my medical record necessary for conduct of the study. I give my permission for those individuals to access my record.

I consent voluntarily to participate as a participant in this research.

I consent to be contacted to potentially participate in **focus group discussions**.

Yes _____ No _____

I consent to **receiving voice calls** on my mobile phone.

Yes _____ No _____

I consent to **receiving text messages/SMS** on my mobile phone.

Yes _____ No _____

Print Name of Participant_____

Signature of Participant _____

Date _____

Month/Day/Year

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Month/Day/Year

Appendix 4. Connect for Life participant information booklet

Any information you provide via the mobile platform will be kept private and confidential. You are free to decline to take part in Connect for Life, or to withdraw from it at any point. Your decision as to whether or not to participate will have no influence on your present status or future status as a patient.

The Connect for Life™ system is designed to help protect your confidentiality.

- You are required to enter a personal PIN code before hearing any voice message.
- You may customize the time of day and the frequency of the reminders you receive.
- You may also customize the days and times you would want to receive these reminders.
- Your account will be temporarily disabled when someone tries to login to your account using the wrong PIN. You may contact SHIP Clinic to unlock your account.

CONNECT WITH YOUR HEALTH.

Connect™ for life

For more details contact SHIP Clinic:

☎ (02) 209-4971

+63 922 854 4271

shipclinicshaw@gmail.com

CONNECT FOR LIFE SERVICES

Pill Reminders

You will receive a reminder:

- ○ Phone call
- ○ SMS
- ○ Daily at _____ (time)
- ○ Weekly on _____ (day) at _____ (time)

**Upon answering, you will hear a recognizable jingle which will continue to play until you enter your PIN to hear the voice message.*

***Stay on the line after your pill reminder in order to report symptoms if needed, and to hear your health tips.*

****You will receive a weekly adherence score by SMS, which will range from 0 to 7. This is meant to help you keep track of how you are doing and achieve your adherence goals.*

Appointment Reminders

- ○ Phone call
- ○ SMS
- ○ None

At _____ (time)

_____ days before your appointment.

Health Tips

- ○ Phone call
- ○ SMS
- ○ None

**You will receive health tips at the same time as your pill reminder.*

MOBILE PHONE SUPPORT SERVICES

AVAILABLE AT SHIP CLINIC

Powered by

Connect™ for life

Empowering Patients & Health Systems

ADHERENCE

Good adherence to HIV treatment gives the HIV medicines the chance to do their job: to prevent HIV from multiplying and destroying the immune system. HIV medicines help people with HIV live longer and healthier lives, and reduce the risk of HIV transmission.

Strict adherence to antiretroviral therapy (ART) is key to:

- Sustained HIV suppression
- Reduced risk of drug resistance
- Improved overall health, quality of life and survival
- Decreased risk of HIV transmission

*Source: https://aidsinfo.nih.gov/

WHAT IS SHIP'S MOBILE PHONE SUPPORT SERVICE?

Using SHIP's mobile phone support service, powered by Connect for Life™ you will receive information to help manage your health better and receive assistance with your treatment when required. The service will also remind you when your appointments are due. This is the first time an interactive patient mobile phone support system is being made available here in the Philippines, only at SHIP Clinic.

MOBILE PHONE SUPPORT SERVICES

REMINDERS

You will get a PIN-protected reminder phone call when it's time to take your medication or an SMS when you have an appointment at the clinic.

HEALTH TIPS

You get health tips about the topics you choose with every reminder.

SYMPTOM REPORTING

When you feel unwell, you don't have to go to the clinic right away, you can simply report your symptoms via the system. It will explain if it's serious or a normal side effect of your ART medications and gives advice on what to do.

Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines

Protocol Version 1.0

May 11, 2016

Study of:

The STI/AIDS Guidance Intervention & Prevention Unit at the Philippine General Hospital (UP-PGH/SAGIP) and Sustained Health Initiatives of the Philippines (SHIP), Inc.

Sponsored By:

Investigator-initiated study by UP-PGH SAGIP Unit and SHIP clinic with support from Janssen Global Public Health

Investigators:

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Appendix 5. Study protocol

Prospective Cohort Study of Patients in the Connect for Life Mobile Phone Adherence Demonstration Project at an HIV Satellite Clinic in Mandaluyong City, Philippines

Protocol Version 1.0

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Executive Summary

Purpose: This study will describe patient adherence, retention, and treatment outcomes, and evaluate the implementation process and the outcomes of a demonstration project of a mobile phone adherence platform for HIV patients on antiretroviral therapy (ART).

Design: Prospective Cohort Study

Population: HIV-positive patients taking ART

Study Size: 500 patients

Study Duration: 2 years

Study Site: The SHIP clinic in Mandaluyong, Metro Manila, Philippines

Primary Objective: Describe the adherence to medication, retention in care, and viral load suppression for the patient population participating in the Connect for Life demonstration project.

Secondary Objectives:

- Assess the acceptability of the Connect for Life platform among the patient population of the SHIP clinic.
- Describe the HIV-related Knowledge, Attitudes, and Practices (KAP) of the participants.
- Describe the clinical outcomes of participants including treatment failure (switch to second line), AIDS-related mortality, and CD4 recovery.
- Identify factors that affect patient adherence, retention, and treatment outcomes
- Compare the prospective cohort data to a historical control from patient records in order to describe the possible effect of the Connect for Life intervention.

This study seeks to expand on the current body of knowledge around HIV treatment outcomes in the Philippines, a topic about which only limited information is available in peer-reviewed, academic publications. The study will also add to the growing body of knowledge about mobile phone support interventions for HIV treatment adherence, and will be the first of its kind in the Philippines context.

1.0 Introduction

1.1 Background and Rationale

HIV in the Philippines: The World Health Organization announced in May 2015 that the Philippines has the fastest growing HIV epidemic in the world, with an estimated 50,000 or more cases. (3–6) Eighty-one per cent (25,896) of all the 31,911 diagnosed cases in the Philippines were reported in the past five years, from January 2011 to February 2016.(4)

The group most impacted by HIV in the Philippines is men who have sex with men (MSM), representing 85% of new sexually-acquired infections since 2011.(4) The median age of new cases is 28 years old, and more than 80% of people living with HIV/AIDS in the Philippines are under 35.(4) According to 2011 estimates, 4.5% of MSM in the National Capital Region (Metro Manila) are HIV-positive, and in some areas of Manila prevalence among MSM is as high as 11%.(5,14)

Considering how quickly the current epidemic is growing in the Philippines, it is imperative that as many HIV-infected people as possible are diagnosed, started on treatment and successfully retained in care. Achieving adequate viral suppression through the use of (ART) therapy will be one of the key tools in preventing the further spread of this epidemic in the Philippines.

Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and then ensuring high levels of adherence to ART and retention in care.(5,13,14) As in many developing countries, high rates of first-line treatment failure, loss to follow up, and sub-optimal treatment adherence lead to poor outcomes for many HIV patients in the Philippines.(16,17) An unpublished retrospective review of records from Philippine General Hospital STD/AIDS Guidance Intervention Prevention Unit (PGH-SAGIP) found that 25% of patients experienced treatment failure on their first-line regimens, indicating that many patients likely have incomplete adherence to ART. A regional cohort study found that 26% of patients self-reported sub-optimal adherence levels during their first 6 months of treatment.(17)

Demonstration Project Study Site: Within this context, Sustained Health Initiatives of the Philippines (SHIP) is one of the only public-private partnerships providing HIV treatment in the Philippines. Opened in 2012, the SHIP clinic is low-cost, private facility in Mandaluyong, Metro Manila that provides HIV primary care and wrap-around services to a growing group of nearly 700 patients as a satellite partner clinic of PGH-SAGIP.

SHIP's patient-centred approach has garnered support from community advocates, leading to collaborations with The Red Whistle, Love Yourself, AIDS Society of the Philippines, and other groups. In March 2015, UNAIDS representatives visited SHIP as part of a project to document innovative HIV programs for MSM and transgender men and women in the Philippines.

SHIP clinic's 675 HIV patients are approximately 98% MSM (with only 10 heterosexual men and one woman), with an average age of 30 at initial consult, most are employed either full-time or part-time. The patients come from all regions of Metro Manila and some live outside of Metro Manila in other provinces. SHIP currently enrols approximately 12-14 new patients each month.

During the project planning phase, study staff consulted with SHIP clinic patients to learn about their adherence challenges and to tailor the mobile phone intervention to the needs and preferences of patients in the local context.

Adherence Support for HIV Patients - the Connect for Life Platform: Mobile phone usage is very high in the Philippines and offers an e-health solution to many of the problems HIV patients face in adhering to treatment. SHIP has been working with project sponsor Janssen Global Public Health to leverage their expertise and technology to adapt and provide an innovative mobile phone service that will allow SHIP to remind patients to take their medications regularly and to return for follow-up visits, and communicate targeted health education messages underpinned by behaviour change psychology to improve their Knowledge, Attitude and Practices about HIV/ART, and to allow patients to report symptoms and get basic advice.

Connect for Life is a technology platform created by Johnson & Johnson/Janssen Global Public Health and built on the MOTECH open-source software platform. The Connect for Life platform is provided to SHIP as a free license, and the sponsor has no expectation of any commercial gain or intent to influence clinical care in any manner. The project aims to build health capacity in areas of need, and using technology facilitate access to appropriate care for HIV/AIDS/TB/Maternal and Child Health by allowing health facilities to connect to patients via their cell phones/feature phones through interactive voice response system (IVRS) or through SMS. The technology also allows the health care professionals to monitor patients' self-reported adherence in real time, track medical and visit history, and generate specific and programmable alerts on lab results, low adherence, missed appointments, etc. The alerts serve as a warning for the health care provider regarding patients that may require closer attention. The system facilitates a standardized method to capture patient details and ensure high-quality and appropriate care is provided to the patients. The platform has been piloted in both India and Uganda with positive results.(210,211)

Connect for Life provides programmable daily or weekly reminders to patients at their chosen convenient time to take their medication and logs patient responses to medication reminders (i.e. taken/not taken/will take later). Patients are also able to report their symptoms obtain first line advice via the platform and in acute situations the system can connect the patient to their physician immediately. In addition to medication reminders, patients can receive individually tailored health tips and feedback on their adherence. Finally, the platform reminds patients of their clinic appointments to help them report to the clinic on time and ensure they are properly monitored.

Mobile phone interventions have proven successful in improving ART adherence in other settings.(107,113,129,130,159,197,198) Most studies investigate medication adherence as the outcome of interest, and only a few have examined the effect of the mobile intervention on other clinical outcomes of patients.(107,159) A recent systematic review hypothesized that the most effective text messaging adherence interventions have been weekly messages with interactive elements that elicit a response from the user, but many questions remain unanswered.(107,159) This approach has potential to be successfully implemented in the Philippines, where mobile phone use is among the highest in the world with 113 mobile connections per 100 people.(335)

2.0 Study Aim and Objectives

2.1 Study Aim

This study will describe patient adherence, retention, and treatment outcomes, and evaluate the implementation process and the outcomes of a demonstration project of a mobile phone adherence platform for HIV patients on antiretroviral therapy (ART).

2.2 Primary Objectives

The primary objective of the study is to describe the adherence to medication, retention in care, and viral load suppression for the patient population participating in the Connect for Life mobile phone adherence support demonstration project.

2.3 Secondary Objectives

The secondary objectives of the study are to:

- Assess the acceptability of the Connect for Life platform among the patient population of the SHIP clinic.
- Describe the HIV-related Knowledge, Attitudes, and Practices of the participants.
- Describe the clinical outcomes of participants including treatment failure (switch to second line), AIDS-related mortality, and CD4 recovery.
- Identify factors that affect patient adherence, retention, and treatment outcomes.
- Compare the prospective cohort data to a historical control from patient records in order to describe the possible effect of the Connect for Life intervention.

3.0 Methods

3.1 Rationale for Study Design

This is a prospective cohort study, with a planned comparison to a historical control. The prospective observational design facilitates collection of reliable adherence data through both self-report and through the Connect for Life platform. In contrast, retrospective adherence data are limited in when mining clinical records. Collection of clinical information (such as diagnoses, lab results, and drug regimens), where available in routine clinical practice, will also be conducted both retrospectively at baseline, and prospectively throughout study follow up.

3.2 Study Site

Sustained Health Initiatives of the Philippines (SHIP) Clinic in Mandaluyong, Metro Manila, Philippines.

3.3 Study Population

The study will include all eligible patients initiating antiretroviral therapy (ART) for HIV as well as those who are already receiving ART at the study site who consent to take part in the Connect for Life mobile phone adherence support project. Inclusion/exclusion criteria and recruitment methods are detailed in Section 4 of the protocol, and Sample Size considerations are detailed in Section 7. During data analysis patients will be stratified into subgroups for analysis based on whether they are treatment naïve or experienced, their baseline ART adherence (for treatment experienced), and by their level of interaction/engagement with the Connect for Life platform. The stratification scheme is discussed in more detail in Section 7 of the protocol.

3.3 Study Duration

Patients will be followed up for 1 year from their enrolment in the Connect for Life project. Patient surveys and chart extraction will be conducted at 4 time points: baseline, 12 weeks, 24 weeks, and 48 weeks.

3.4 Study Activities

The study will observe and document the clinical and adherence outcomes of patients who participate in the Connect for Life demonstration project.

Patient Support: The Connect for Life platform will generate mobile phone messages that provide patients with support in the form of pill reminders, clinic visit reminders, and health tips. Patients will be able to report specific symptoms through the platform to the clinic. Patients will receive weekly feedback messages regarding their adherence for the week. These feedback messages will be designed to provide positive reinforcement to patients with high adherence, and will provide encouragement to improve pill-taking for patients with medium or low levels of adherence. In addition, the provider will receive an alert for a patient with low adherence. These alerts will be followed up with a phone call from clinic staff to provide adherence counselling.

To participate in the Connect for Life platform, the patient will need to provide a mobile phone number and consent to receiving calls on this phone number from the Connect for Life platform and the medical staff in the clinic. To ensure confidentiality, whenever a call is initiated by the Connect for Life platform, the user will need to enter a personal identification number (PIN code) into his or her phone before hearing any message from Connect for Life.

The patient and the clinician will set the frequency and time of reminders, whether they will be sent through voice or SMS, and the preferred categories for health tips. The standard Connect for Life service package is outlined in Table 1. The service scheme, which begins with daily reminders and then tapers off to weekly reminders after 24 weeks and no reminders after 48 weeks, is based on literature review of adherence programs which suggests that daily reminders can support habit forming over 2-3 months and that weekly reminders effectively support adherence.(107,161,197,201,202) It is not clear whether improvements in adherence are sustained if reminders are stopped once a habit is formed. While this is the suggested service scheme, each patient may opt out of any call or SMS services that he/she does not wish to receive, or may opt into services depending on his/her preference and the clinician's judgment. The clinician can reactivate or extend pill reminders for patients that need additional support.

Table 1. Connect for Life Services Scheme

	Pill Reminder + Adherence Feedback (voice or SMS)	**Health Tips**	**Clinic Visit Reminders (voice or SMS)**	**Symptom Reporting**
Treatment naïve and recently initiated (less than 6 months on ART)	Daily reminders from 0 to 24 weeks Weekly reminders from 25 to 48 weeks	During all Pill Reminder calls, health tips topics tailored to new patients	Yes	Yes – During all Pill Reminder calls
Treatment experienced more than 6 months with **poor adherence at baseline** (below 75%)	Daily reminders from 0 to 24 weeks Weekly reminders from 25 to 48 weeks	During all Pill Reminder calls, health tips topics selected by patient and clinician	Yes	Yes – During all Pill Reminder calls
Treatment experienced more than 6 months with **moderate to good adherence at baseline** (75% and above)	Weekly reminders from 0 to 24 weeks	By preference of clinician and patient	Yes	Yes – During all Pill Reminder calls

Provider Adherence Monitoring: The platform will serve as a tool for the clinician to monitor patient adherence over time and, while it is not a fully functional electronic medical record, it does serve as a disease specific record system securely capturing medical history, visit history, and additional clinical data (such as ART regimen, lab results, and clinic visits). The platform will alert the clinician when a patient's adherence is low or a patient reports severe symptoms. The study staff will use alerts and data from the Connect for Life platform to provide responsive care to clinic patients, such as following up an alert with a phone call to provide adherence counselling. Study staff will also actively follow up on alert outcomes with the patient during every regularly scheduled visit.

Ongoing Routine Care: Patients who participate in Connect for Life will continue to receive the same routine clinical care. In the study site, ART initiation is recommended for patients with an AIDS-defining illness, or when CD4 count is below 500. Patients have clinic visits every three months for routine safety labs and other primary care. CD4 count is performed every six months and viral load test is performed annually. No clinical procedures or tests will be performed specifically for this research study. All clinical data points will be extracted from the patient records by the study staff. At regularly scheduled visits, patients will complete study-related questionnaires.

3.5 Outcome measures

Primary Outcomes

To describe patient adherence, retention care, and treatment outcomes, the following primary endpoints will be used:

4. medication adherence: optimal adherence defined ≥95% of pills taken. Adherence will be assessed through self-report, through patient self-reports in the Connect for Life platform, and through pill count
5. retention in care: proportion of patients alive and in care (“not in care” defined as not having returned for more than 30 days after last scheduled clinic visit or refill)
6. viral load suppression: proportion of patients whose most recent HIV RNA test result was undetectable (based on the parameters of any assay performed through routine clinical care)

Secondary Outcomes

At enrolment, historical data on adherence and clinical variables will be extracted from the patient charts. This will form a historical retrospective cohort which can be compared to the prospective cohort to evaluate possible effects of the intervention. The secondary objectives of the study are to:

- Assess the acceptability of the Connect for Life platform among the patient population of the SHIP clinic.
- Describe the HIV-related Knowledge, Attitudes, and Practices of the participants.
- Describe the clinical outcomes of participants including treatment failure (switch to second line), AIDS-related mortality, and CD4 recovery.
- Identify factors that affect patient adherence, retention, and treatment outcomes
- Compare the prospective cohort data to a historical control from patient records in order to describe the possible effect of the Connect for Life intervention.

Acceptability will be determined by:

5. Quantifying the level of interaction patients have with Connect for Life platform (i.e. % of adherence reminder calls responded to, number of health tips listened to, average time listened per call, number of symptoms/side effects reported through Connect for Life and proportion of positive/negative resolution of those reports)
6. Responses to patient acceptability questionnaires
7. Participant satisfaction/concerns with Connect for Life Platform and their satisfaction with the clinic services elicited in structured interviews
8. Documenting the potential for scale to other sites via analysis of per patient cost to implement project in comparison to the overall cost of HIV primary care

Process documentation will consist of monthly narrative reports on: participant recruitment, ongoing use of the platform by patients, implementation challenges encountered, patient and health care provider feedback. Process documentation will also include contextual factors and events that may influence HIV care, such as changes in treatment guidelines or insurance coverage.

4.0 Study Population

4.1 Inclusion Criteria

1. Enrolled in HIV primary care at SHIP clinic during study recruitment period
2. Currently on ART, or plans to start ART in the next 60 days
3. Age 18 years or older
4. Has access to a Philippines mobile phone and is willing to receive calls and messages from Connect for Life
5. In order to provide consent and to understand the health tips, patient must be able to understand spoken English and read written English (Note: English is spoken fluently by all of the patients at the study site, so this criterion is not expected to systematically exclude any segment of the potential study population.)

4.2 Exclusion Criteria

1. Receives primary HIV care at a facility other than SHIP clinic
2. Has never taken ART and does not plan to start ART in the next 60 days
3. Age < 18 years
4. Has no mobile phone access
5. Unable to understand spoken or written English

4.3 Recruitment Process

All patients enrolled in care at the study site will be prospective study participants. Patients will be approached to participate in the study by a member of the study team (research analyst, clinic nurse, or doctor) either during a routine clinic visit or during a routine reminder phone call to schedule an upcoming clinic visit. New patients will be approached about participation in the study by the clinic doctor or nurse during their initial clinic visit.

500 or more patients are expected to enrol. Study recruitment will remain open for a minimum of 6 months and a maximum of 9 months from study initiation.

The investigators will recruit 20 to 30 participants for focus group sessions. Patients will indicate on the informed consent form if they wish to participate in the focus group sessions. The study team will select patients to invite to focus groups, and will attempt to make groups representative of the demographic composition of the clinic population and with diverse patient experiences.

4.4 Participant Withdrawal

Participants may voluntarily withdraw from the study for any reason at any time. The Investigator also may withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with required study procedures. In such instances, a member of the study team will document the reason for withdrawal date on the patient record, and any data entered into the patient's clinic record after the date of withdrawal from the study will not be included in the data analysis.

Participants who wish to stop receiving calls from the Connect for Life platform, but who are still willing to participate in the study, will be maintained in follow-up as originally scheduled.

5.0 Study Procedures

5.1 Screening

Screening, enrolment, and baseline visit procedures may all be conducted on the same day. The enrolment and baseline visits must be completed within a 60 days of the screening. If the subject does not enrol within 60 days from the screening visit, he or she may be rescreened .

Procedures:

3. **Approach patient** and find out if they are interested in learning about the Connect for Life (Connect for Life) demonstration project.
4. **Document inclusion/exclusion criteria and confirm eligibility**

5.2 Enrolment

For each participant, independent written informed consent for screening and enrolment will be obtained before any study procedures are initiated.

Visit Window: The enrolment and baseline visits must be completed within a 60 days of the screening. If the subject does not enrol within 60 days from the screening visit, he or she may be rescreened.

Procedures:

3. **Obtain informed consent:** Explain Connect for Life platform; Explain study
4. **Enrolment in Connect for Life:**
    a. Activate patient record in Connect for Life;
    b. Update patient contact details;
    c. Set up ART adherence reminders – based on ART regimen, patient preferred call frequency, and time of day;
    d. Set up health tips preferences – based on patient and clinician selections;
    e. Provide patient with Connect for Life information sheet and copy of informed consent form.

5.3 Baseline

At the baseline visit, historical adherence and clinical data will be extracted from the patient record. These historical data will serve as an a priori comparison for the cohort outcomes. The patient will complete self-administered questionnaires about adherence KAP and QoL.

Visit Window: The enrolment and baseline visits must be completed within a 60 days of the screening. If the subject does not enrol within 60 days from the screening visit, he or she may be rescreened.

Procedures:

5. **Demographic data including risk factors for poor adherence**
6. **HIV-specific medical History:**
    a. Opportunistic infections/STIs/TB;
    b. ART Regimen history;

c. Treatment Failure
d. CD4 count, CD4 %, and HIV RNA

7. **Patient Questionnaires:**
    a. KAP/QOL
    b. Adherence
8. **Clinical record extraction (record any new data since last visit):**
    a. Most recent laboratory values: CD4 count, CD4 %, HIV RNA level
    b. Prescription refill information (pill count)
    c. Opportunistic infections, STIs
    d. Current ART regimen
    e. Concomitant medications
    f. Treatment failure

5.4 12 Weeks and 24 Weeks

Visit windows: 12 Week target date = 12 weeks (84 days) from Baseline Visit. Window = 6 weeks - 17 weeks (7-125 days) from Baseline Visit.
24 Week target date = 24 weeks (168 days) from Baseline Visit. Window = 18 weeks - 35 weeks (126-251 days) from Baseline visit.

Procedures:

5. **Patient Questionnaires**
    d. KAP/QOL
    e. Adherence
    f. Connect for Life Feedback
6. **Clinical record extraction (see section 5.3 for details)**
7. **Connect for Life record extraction (usage data will serve as a measure of acceptability of the platform)**
    g. Connect for Life services enrolled in
    h. proportion of adherence reminder calls answered
    i. proportion of calls responded to
    j. number of health tips listened to
    k. average time listened per call
    l. number of symptom reports made and outcome of those calls
8. **Adverse events and social harms monitoring**

5.5 48 Weeks

Visit window: 48 Week target date = 48 weeks (336 days) from Baseline Visit. Window = 36 weeks – 60 weeks (252-420 days) from Baseline visit.

Procedures:

1. **Patient Questionnaires**
    a. KAP/QOL
    b. Adherence

c. Connect for Life Feedback

2. **Clinical record extraction (see section 5.3 for details)**
3. **Connect for Life record extraction (see section 5.4 for details)**
4. **Adverse events and social harms monitoring**
5. **Study termination procedures**

5.6 Schedule of Events

Table 2. Schedule of Events					
	Screening/ Enrolment	**Baseline (Week 0. Max 60 days from Screening)**	**12 Weeks (6-17 Weeks)**	**24 Weeks (18-35 Weeks)**	**48 Weeks (36-60 Weeks)**
Approach/recruit patient	X				
Document inclusion/exclusion criteria and confirm eligibility	X				
Informed Consent	X				
Enrolment in Connect for Life platform	X				
Demographic data		X			
Medical History		X			
Patient Questionnaires:					
KAP/QOL		X	X	X	X
Adherence		X	X	X	X
Connect for Life Feedback			X	X	X
Clinical record extraction (see section 5.3 for details)		X	X	X	X
Connect for Life record extraction (see section 5.4 for details)			X	X	X
Adverse events and social harms monitoring			X	X	X
Study termination procedures					X

5.7 Ongoing Monitoring & Evaluation

Ongoing monitoring and evaluation will occur to allow real-time adjustments and real-time assessment of potential weaknesses. These will include success in reaching recruitment goals through weekly reporting of number of potential participants approached, number consenting, and number enrolled.

5.8 Focus Groups

The investigators will conduct semi-structured interviews with approximately 20-30 study participants during focus group sessions to understand their assessment of the intervention (this will elicit any concerns regarding disclosure HIV status, privacy, and perceived value of the intervention). Key informant interviews will also be conducted with health care providers. As these interviews will be conducted real-time, the study team will be able to adapt to any potential concerns and tailor the program to the needs of the patients and providers.

5.9 Missed Visits

If a study participant does not come to the clinic for routine care within the specified visit window, the study team will complete a missed visit form. The team will extract any available data from the patient medical record and from the Connect for Life platform and complete the relevant fields on the eCRFs. If the patient has received treatment in a different facility, the study team may request release of medical records from other facilities with permission from the patient. The patient questionnaires will be marked as missed.

6.0 Data Management

6.1 Data Management Responsibilities

The investigators will: Provide training and guidance to staff with respect to data management issues; Oversee data quality control, including running data queries; Ensure the availability of databases to capture data from participant interview and case note abstraction from medical records; Ensure the safekeeping of data and access control; Ensure proper data management documentation is maintained;
Manage data reporting processes; Manage integration of data from different sources; Ensure processes are in place for backup and data recovery; Ensure compliance with data security and confidentiality regulations; Ensure study conduct adheres to good clinical practice standards.

The research associate will: Ensure that patients complete the questionnaires at each visit; Extract data from Connect for Life platform and paper records; Complete eCRFs.

6.2 Application and Database

Data Sources:

1) Routine data from patient medical record and the Connect for Life platform will be used to determine clinical and retention outcomes
2) Self-administered questionnaires will collect data on KAP/QOL, self-reported adherence, acceptability data on Connect for Life
3) Data from Connect for Life platform database on utilization of Connect for Life will be used as an indicator of acceptability
4) Historical program reports from the SHIP clinic and retrospective clinical data extracted from the clinical records of consenting study participants will be used to establish estimated baseline retention and adherence levels and serve as a historical control.
5) Qualitative data collection methods include purposively sampled semi-structured interviews, as well as direct observation and narrative reports of intervention activities.

Clinical data and demographic data will be collected at baseline, 12 weeks, 24 weeks, and 48 weeks. Clinical data will be extracted from each patient's medical record. Adherence data will be collected through pill counts and self-report. Data on Connect for Life platform usage will be collected automatically on an ongoing basis by the Connect for Life software platform and stored on a secure server.

6.3 Quality Control

Data will be validated on entry, using range and consistency checks. Quality control procedures will include review of paper-based and electronic case report forms (eCRFs) for completion and correctness. Logical data checks will also be performed on the data. Investigators will check for incomplete and incorrect data and send queries to the research associate for error resolution. Errors will be reviewed and corrected on an on-going basis throughout the data collection period.

Hard copies of study records (consent forms, questionnaires) will be kept in a secure location accessible only to authorized study staff, investigators, and monitors. Procedures for storage of

electronic data are described in Section 8. All records will be securely archived for at least ten years after the completion of the study.

7.0 Statistical Considerations

7.1 Study Design Considerations

Justification for observational design: The study site is implementing the Connect for Life platform as a demonstration project, with the initial goal of determining whether the platform may provide benefit to patients and whether it can be successfully implemented in real-world conditions in the setting of HIV primary care in the Philippines. For this purpose, an observational study is the most appropriate approach. An observational study design limits the ability to determine the effect of the Connect for Life intervention on patient adherence and clinical outcome. The observational study also limits the ability to control for confounding factors, although these can be controlled for through traditional regression analysis. In the future, the effect of the intervention on patient adherence levels and/or clinical outcomes may be evaluated in a randomized controlled trial (RCT). However, first establishing a strong proof of concept and demonstrating that the intervention is reasonably acceptable and feasible is an important step before undertaking a RCT. The outcomes of this observational study may inform future study design.

7.2 Sample Size Considerations

Projected Study Size: The protocol allows for all eligible patients to enrol in the study. At the time of writing, the study site provides treatment to approximately 650 patients who are eligible for participation in the study, the clinic population will continuously grow as treatment naïve patients initiate therapy throughout the course of the recruitment period. Taking into consideration the possibility of unforeseen recruitment challenges, at least 500 patients are expected to enrol. The main endpoints of the study are descriptive, not inferential. A precision estimate for a sample size of 500 is given in section 7.3.

Stratification: Subanalyses of data will be performed based on the following stratification categories

- Treatment naïve/experienced: In order to have sufficient sample size to make precise outcome measurements the study team plans to recruit at 150 treatment naïve patients
- Low/moderate/high baseline adherence level: In the region, an estimated 26% of treatment experienced patients have sub-optimal adherence.(17) Sub-optimal adherence rates are expected to be slightly lower among SHIP clinic population, approximately 15-20%, due to demographic and socioeconomic differences compared to public hospitals.
- Low/moderate/high engagement level in platform: Engagement level will be determined by the proportion of calls answered and of health tips listened to. Without any precedent for the intervention, the cut-offs for the categories/clusters cannot be determined before implementation and will be defined during interim exploratory analysis.

7.3 Endpoints

The primary endpoint for the study is <u>self-reported medication adherence</u>. Other key outcomes of interest are: retention in care, viral load suppression.

Table 3 describes projected estimates for the following Primary endpoints. Retention estimate comes from 2015 SHIP clinic data, estimates for suboptimal adherence and viral load suppression rates are based on published data from regional retrospective and prospective cohort studies and unpublished data from local programs.(4,16,17)

Table 3. Baseline Estimates for Primary Outcomes	
	Estimated Observation
Optimal Adherence (≥95%)	83%
Retention	95.4%
Viral Load Suppressed	85%

One of the secondary objectives of the study is to describe patient KAP, and the use and acceptability of the Connect for Life platform. Table 4 summarizes the key variables that will be included in the descriptive analysis. Data collection tools are included in the Appendices.

Table 4. Variables
Adherence
Self-reported % of medications taken
Connect for Life generated % of medications taken
Pill count % of medications taken
% of clinic patients with sub-optimal adherence (<95%)
Retention in Care
% of patients alive and in care (alive and in care if they are in between visits and were known to have refilled their HAART within the prior 30 days, "not in therapy" defined as not having returned for more than 30 days after last scheduled clinic visit or refill)
% of scheduled visits missed
Viral Load Suppression
% of patients whose most recent HIV RNA test result was undetectable (based on the parameters of any assay performed through routine clinical care)
Clinical Outcomes
Treatment failure (switch to second line)
AIDs-related mortality
Patient Knowledge Attitudes Practices and Quality of Life
KAP based on the topics addressed in the health tips: Adherence, ARVs, Co-infections, Drug user harm reduction, Fitness, HIV, Mental/Health Coping, Nutrition, Sexual Risk Reduction
Quality of Life score
Connect for Life Acceptability
Responses to Connect for Life questionnaire
Usage/engagement - % of adherence reminder calls responded to, number of health tips listened to, average time listened per call, number of symptoms/side effects reported through Connect for Life and proportion of positive/negative resolution of those reports

The final secondary objective is to compare the prospective cohort data to a historical control from patient records in order to describe the possible effect of the Connect for Life intervention. A power calculation concluded that in a two-sample two-sided equality test to compare proportions, a sample of 500 patients would detect the following differences between the baseline and outcome measures.(222) While the study is not designed to control for confounding factors, the exploratory analysis may be used to inform future research.

Table 4. Power Calculation		
	Estimated Baseline Observation (null hypothesis)	Per cent Increase detected with 80% power 5% type 1 error
Optimal Adherence (≥95%)	83%	6.1% (to 89.1%)
Retention in care	95.4%	3.1% (to 98.5%)
Viral Load Suppressed	85%	5.8% (to 90.8%)

7.4 Data Analysis

Since this is a demonstration project, data analysis will be conducted during at least 2 interim time points (approximately 3 months and 1 year) and at the study conclusion. Interim exploratory data analysis may identify issues that can be corrected or improved over the course of the demonstration project.

Statistical techniques: Statistical analyses will be performed by the study team, with technical advice from the study sponsor. A general description of the planned statistical methods to be used to analyse the data collected in this study is presented below. Additional details will be provided in the statistical analysis plan.

The data analysis plan includes a combination of descriptive and inferential analysis. Exploratory data analyses will be performed to analyse data quality, identify trends in the data, and identify associations between patient characteristics and outcomes. The data analysis approach will include descriptive statistics with precision estimates, chi-squared tests to compare outcomes between the different subgroups, logistic regression for categorical variables and linear regression for continuous variables as appropriate, and Cox proportional hazards as appropriate for outcomes such as loss to follow up and mortality. Sub-group analyses will compare ART-naïve to ART experienced patients, patients with poor baseline adherence to patients with already high adherence at baseline, and patients who have different levels of engagement with the platform.

Other Data Analysis Techniques: Qualitative data analysis approaches will describe themes from structured in-depth interviews and monthly narrative reports. The embedded process evaluation will use data on patient uptake and usage of the intervention to characterize for whom the intervention works, and then relate that to patient outcomes.

Possible confounders:
The outcomes of interest in this study may change over time due to aspects not related to the study intervention. These confounding influences include: individual factors related to the outcomes (e.g. Age, SES, education, employment, time on treatment, baseline adherence level, social/family support), external factors that affect adherence (e.g. health messages from other sources, availability of prescriptions, transfer in/out of treatment site, cost of care/access to PhilHealth national health insurance benefits), cyclical/seasonal changes in adherence behaviours (e.g. holiday travel, seasonal employment variations, social events like LGBT pride month, weather and natural disasters affecting ability to commute) We will also have to account for survivor bias, since those patients who have already been in treatment for some time are less likely to become nonadherent or lost to follow up over time. When conducting exploratory analyses these confounding factors will be taken into consideration wherever possible and the limitations of the analysis will be expressly stated.

8.0 Human Subjects Considerations

8.1 Vulnerability of Subjects

People living with HIV are considered a vulnerable population because they have an incurable disease and because they face significant stigma and discrimination. The investigators acknowledge that research should be conducted on vulnerable populations only when the objectives cannot be achieved through conducting the on non-vulnerable populations, and that specific considerations and augmented protections should be put will place for vulnerable groups in research. The mobile phone intervention studied in this protocol is intended to specifically benefit people living with HIV. This study is will necessarily document the outcomes of the intervention in this specific population, and will add to the body of knowledge that may benefit people living with this disease.

8.2 Regulatory Review

Ethical approval will be sought from the Research Ethics Committees of the University of the Philippines Manila and the London School of Hygiene and Tropical Medicine.

8.3 Risks and Benefits to Participants

Study participants will benefit by receiving medication reminders, clinic visit reminders, and health tips on their mobile phones. This can increase their knowledge and help them have successful treatment outcomes.

A risk of using mobile phones in any health intervention is the possibility of unintended disclosure of the patient's disease status via the mobile phone. The study team has taken a variety of measures to protect patient confidentiality and prevent unintended disclosure of HIV status, these are detailed in section 8.6. Moreover, social harms monitoring will be conducted at each study visit (see section 8.7) and in-depth interviews will be conducted throughout the demonstration project. The clinic staff will routinely identify any threats to patient confidentiality and take measures to address any perceived risks.

8.4 Informed Consent

Each participant must sign a participation agreement/ICF allowing data collection and source data verification. The participation agreement/ICF must be signed before collection of any patient data.

Before enrolment in the study, the investigator or an authorized member of the participating site personnel must explain to potential participating patients their involvement in the study and data protection. Patients will be informed that their participation in the study is voluntary and that they may withdraw consent for data collection at any time. They will be informed that choosing not to participate in this study will not affect the standard of care the patient will receive.

The patient will be given sufficient time to read the participation agreement/ICF and will be given the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the personally dated signature. After having obtained the consent, a copy of the participation agreement/ICF must be provided to the patient.

8.5 Incentives

There will be no incentives offered for study participation. Those who participate in focus groups will be served snacks or a meal during the session and will receive a stipend of 200 pesos for their transportation expenses.

8.6 Confidentiality

To participate in the Connect for Life platform, the patient will need to provide a mobile phone number and consent to receiving calls on this phone number from the Connect for Life platform and the medical staff in the clinic. To ensure confidentiality, whenever a call is initiated by the Connect for Life platform, the user will need to enter a personal identification number (PIN code) into his or her phone before hearing any message from Connect for Life. The patient and the clinician will set the frequency and time of reminders, whether they will be sent through voice or SMS, and the preferred categories for health tips.

In order to mitigate the risk of accidental disclosure of HIV status, the content of the pill reminders and clinic visit reminders will use generic language that is not specific to any particular disease or condition and they will not mention HIV specifically. The health tips, however, will be specifically tailored to people living with HIV and may contain sensitive subject matter. Health tip recordings will be initiated in the call flow only after the pill reminder is complete. Participants will be able to opt in or opt out of each service as described in section 3.4 of the protocol, so if they are concerned about someone overhearing phone calls or seeing SMS messages with HIV-specific content, they may opt out of those services.

To protect patient confidentiality in the course of clinic visits, appointments are set at specific times not in blocks, which decreases the risk that a patients confidentiality would be compromised by meeting someone in the clinic waiting room (which can be a common occurrence in crowded hospital facilities). The clinic also has a separate entrance that does not pass through the waiting room which a patient can avail of if they do not wish to use the waiting room.

The collection and processing of personal data from patients enrolled in this study will be limited to those data that are necessary to fulfil the objectives of the study. Only study staff will have access to personally identifiable data. The Connect for Life platform will be hosted locally and managed by the study site. Therefore, the study sponsor will not have access to any personally identifiable patient data.

The data will be collected and processed with adequate precautions to ensure confidentiality and compliance with data privacy protection laws and regulations. In order to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration, all personally identifiable electronic data will be stored in a secure, encrypted cloud-based server. All data extracted from clinic records will be de-identified and coded with a patient ID number. All paper forms will be keyed into the database and the hard copies will be stored in a locked cabinet in a private and secure room in the clinic. Study staff will have training in Good Clinical Practice and Human Subjects Protection.

The ICF obtained from the patient includes explicit consent for the processing of personal data and for the investigator to allow direct access to his/her original medical records (source data/documents) for audit, IRB review, and regulatory inspection as appropriate. This consent also addresses the transfer of the data to other entities and to other countries.

The patient has the right to request through the investigator access to his or her personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps will

be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

8.7 Adverse Event Reporting and Social Harms Reporting

Although study investigators will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that a social impact may result (i.e. because participants could be perceived as being HIV-infected or at "high risk" for HIV infection). For example, participants could be treated unfairly, or could have problems being accepted by their families and/or communities. A social impact that is judged by the investigator to be serious or unexpected will be reported to the IRB. Social impacts will be collected and reported on CRFs during regular visits. In the event that a participant reports a social impact, every effort will be made by study staff to provide appropriate care and counselling to the participant, and/or referral to appropriate resources for the safety of the participant.

8.8 Study Discontinuation

The study also may be discontinued at any time by the implementing site, the sponsors, government or regulatory authorities, or site IRBs.

8.9 Availability of Connect for Life After Study Conclusion

Study participants will not automatically continue receiving services from the Connect for Life platform following their final study visit. If the study team finds during interim and final analysis that the platform is acceptable and has a potential benefit for patients, the study team will make all reasonable efforts to finance and implement the Connect for Life platform beyond the end of the study and extend the product license granted by the study sponsor. Participants would be required to reconsent to participation in Connect for Life should they wish to continue receiving the service.

9.0 Administrative Procedures

9.1 Study Coordination

The investigators and site staff will be responsible for protocol implementation through study closeout, including: Facilitating successful study start-up and close-out; Recruiting study participants; Ensuring that all study procedures are completed in accordance with the protocol; Maintaining research records and regulatory documents; Managing various aspects of the research participant's experience, from recruiting participants to conducting visits; Completing case report forms and reports.

Study implementation will be directed by this protocol as well as by the study site's research SOPs. The SOPs will detail procedures for conducting study visits; data and forms processing; adverse event and social harms assessment, management and reporting; and other study operations. Study case report forms will be developed by the study team. Close coordination between protocol team members will be necessary to track study progress, rates of accrual, follow-up, and other issues in a timely manner. Study staff will have training in Good Clinical Practice and Human Subjects Protection.

9.2 Monitoring

External monitoring or auditing of the study will not be conducted. The study team will conduct continuous quality assurance checks. Social harms will be reported to the reviewing bodies. Investigators also will allow inspection of all study-related documentation by authorized representatives of regulatory authorities. A site visit log will be maintained to document all visits.

9.3 Protocol Compliance

Protocol deviations and violations identified during the course of study activities or in quality assurance checks will be documented and reported to the reviewing bodies as per each body's requirement.

9.4 Investigator's Records

All study records and regulatory documents will be archived in a secure storage facility for at least ten years after the completion of the study.

9.5 Information and Publications

The study team is responsible for the dissemination of finding to stakeholders locally and internationally. Priority stakeholders include the Philippine National AIDS and STI Prevention and Control Program (NASPCP), community based organizations, and international organizations. As applicable, the study team will published findings in academic journals in the field or present findings at regional or international conferences.

A summary of study findings will be disseminated to all participants. If the study finds strong positive outcomes as a result of the Connect for Life intervention, the study site will pursue avenues of support to continue the service.

9.6 Conflict of Interest

The Connect for Life platform is provided to the study site as a free license, and the sponsor has no expectation of any commercial gain or intent to influence clinical care in any manner. The sponsor will not have access to any personally identifiable patient data. The investigators and study staff have no financial or personal conflict of interest. Should any situation arise which would compromise, or have the appearance of compromising an investigator's professional judgment or objectivity in conducting or reporting research, the investigator is required to disclose this to the sponsor and the ERB, and disclose the conflict of interest or modify the research activities as appropriate.

10.0 References

(Removed from appendix, refer to thesis reference list above)

11.0 Protocol Appendices

Investigators' CVs

Investigators'' GCP certificates

Diagrammatic Workflow

Informed Consent form

Data collection tools:

- Screening Form
- CRFs –
    - Demographics
    - Medical History
    - Follow Up Visit
    - Connect for Life Usage
    - Missed Visit
    - Adverse Event and Social Harms Monitoring
    - Study Termination
- Questionnaires
    - KAP/QOL
    - Adherence
    - Connect for Life Acceptability
- Monthly Process Documentation Report
- Informational videos and print materials for participants

Appendix 6. Case report forms

a. Eligibility checklist
b. Demographics
c. Medical history
d. Follow-up visit form
e. Termination form
f. Missed visit form
g. Social harms report

6a. Eligibility checklist

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Month Date Year

Connect for Life Eligibility Checklist

Instructions: Use the table below to document a participant's eligibility status for Connect for Life study participation at the enrolment visit. Staff designated to confirm eligibility should initial and date the bottom of the page after reviewing all appropriate documentation. If ineligibility status is determined, the form may be stopped and the remaining questions may be left blank. Complete the Eligibility Criteria CRF for all participants once the participant's eligibility/enrolment is determined.

Inclusion Criteria		**Yes**	**No**
I1	Age of 18 or older at screening	☐	☐
I2	Currently on Anti-Retroviral Therapy (ART), or plans to start ART in the next 60 days	☐	☐
I3	Enrolled in HIV primary care at SHIP clinic during study recruitment period	☐	☐
I4	Has access to a Philippines mobile phone and is willing to receive calls and messages from Connect for Life	☐	☐
I5	Able to understand spoken English and read written English	☐	☐
Exclusion Criteria		**Yes**	**No**
E1	Age of 17 or below at screening	☐	☐
E2	Receives primary HIV care at a facility other than SHIP clinic	☐	☐
E3	Has never taken ART and does not plan to start ART in the next 60 days	☐	☐
E4	Has no mobile phone access	☐	☐
E5	Unable to understand spoken or written English	☐	☐

I certify that I have carefully reviewed all the inclusion and exclusion criteria and can attest that the patient is eligible to participate in the project.

Study Staff Signature	Date

6b. Demographics

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐
Month Date Year

Patient Demographics (Please fill out all information asked, do NOT leave any blank)			
Date of Birth: ☐☐ ☐☐ ☐☐☐☐ (Month Date Year)	Current Place of Residence Municipality/City: _____		Province: _____
Sex assigned at Birth: ☐ Male ☐ Female	Gender Identity: ☐ Male ☐ Female ☐ Transgender (specify): _____ ☐ Other: _____		Sexual Orientation: ☐ Heterosexual ☐ Homosexual ☐ Bisexual ☐ Other: _____
Highest Educational Attainment:	☐ None ☐ Elementary	☐ High School ☐ College	☐ Vocational ☐ Post-Graduate
Employment:	☐ Corporate/business ☐ BPO ☐ OFW ☐ Student ☐ Employee	☐ Service Delivery ☐ Health Worker ☐ Teacher ☐ Entertainment/media ☐ Seafarer	☐ Commercial sex worker ☐ Unemployed ☐ Other: _____
Relationship Status:	☐ Serodiscordant	☐ Seroconcordant	☐ Unknown ☐ No relationship
Disclosure Status:	☐ Disclosed	☐ Not disclosed	
Civil Status:	☐ Common-law partner	Married☐ Separat☐ Single	☐ Widowed ☐
Is the patient sexually active?	☐ Yes	☐ No	
Whom does the patient have sex with?	☐ Men	☐ Women ☐ Both	
In the past 6 months, how many partners has the patient had? (specify): _____			
Has the patient ever had sex without a condom?	☐ Yes	☐ No	
In the past 6 months, how often did the patient use a condom?	☐ Always	☐ Most of the time ☐ Sometimes	☐ Never
Has the patient ever had sex in exchange for money, gifts, goods, or other services?	☐ Yes	☐ No	
In the past 6 months, how many times did the patient trade sex for money, gift, goods, or other services? (specify): _____			
Has the patient ever used intravenous drugs?	☐ Yes	☐ No	
If yes, when did the patient last injected a drug? (specify) ☐☐ ☐☐ ☐☐☐☐			

_____ _____
Study Staff Signature Date

6c. Medical history

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Month Date Year

Medical History (record all dates as mm/dd/yyyy)

HIV

Date of diagnosis: ☐☐ ☐☐ ☐☐☐☐ | Start of treatment: ☐☐ ☐☐ ☐☐☐☐ | Age upon diagnosis:

WHO Clinical Staging Stage 1 ☐ Stage 2 ☐ Stage 3 ☐ Stage 4 ☐

CD4 and Viral Load Monitoring

Date	*CD4 Count*	*CD4 %*	*Date*	*Viral Load*
☐☐ ☐☐ ☐☐☐☐	________	________	☐☐ ☐☐ ☐☐☐☐	________
☐☐ ☐☐ ☐☐☐☐	________	________	☐☐ ☐☐ ☐☐☐☐	________
☐☐ ☐☐ ☐☐☐☐	________	________	☐☐ ☐☐ ☐☐☐☐	________
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☐☐ ☐☐ ☐☐☐☐	________	________	☐☐ ☐☐ ☐☐☐☐	________

ANTI-RETOVIRAL REGIMEN

Current ARV Medication

Drug combination	*Frequency*	*Date started*
________	________	☐☐ ☐☐ ☐☐☐☐

Initial ARV Medication (if different than current medication)

Drug combination	*Frequency*	*Date started*	*Date ended*	*Check if still ongoing*	*Reason for discontinuation*
________	________	☐☐ ☐☐ ☐☐☐☐	☐☐ ☐☐ ☐☐☐☐	☐	________

Other ARV Medications

Drug combination	*Frequency*	*Date started*	*Date ended*	*Check if still ongoing*	*Reason for discontinuation*
________	________	☐☐ ☐☐ ☐☐☐☐	☐☐ ☐☐ ☐☐☐☐	☐	________
________	________	☐☐ ☐☐ ☐☐☐☐	☐☐ ☐☐ ☐☐☐☐	☐	________
________	________	☐☐ ☐☐ ☐☐☐☐	☐☐ ☐☐ ☐☐☐☐	☐	________

Drug combination codes:
1 – EFV + 3TC + TDF (QD)
2 – AZT and 3TC (BID), EFV (QD)
3 – AZT and 3TC (BID), NVP (QD)

Frequency codes:
QD – once a day
BID – twice a day

Discontinuation codes:
1 – Treatment Failure
2 – Clinical progression/hospitalization
3 – Patient Decision/Request
5 – Drug Interaction
6 – Adverse Event (specify)
7 – Others (specify)

OPPORTUNISTIC INFECTIONS

Infections currently present (check all that apply):

	Unknown	*No History*	*Active*	*Inactive*	*Specify*
☐ Hepatitis B	☐	☐	☐	☐	________
☐ Hepatitis C	☐	☐	☐	☐	________
☐ Pneumocystis pneumonia	☐	☐	☐	☐	________
☐ Oropharyngeal candidiasis	☐	☐	☐	☐	________
☐ Syphilis	☐	☐	☐	☐	________
☐ STIs (specify)					
________	☐	☐	☐	☐	________
________	☐	☐	☐	☐	________
☐ Others (specify)					
________	☐	☐	☐	☐	________
________	☐	☐	☐	☐	________

PILL COUNT

Has the patient had any refill since the last visit? ☐ Yes ☐ No

Drug	*Last refill date*	*No. of pills dispensed*	*Total no. of pills on hand*
_____	☐☐ ☐☐ ☐☐☐☐	_____	_____
_____	☐☐ ☐☐ ☐☐☐☐	_____	_____
_____	☐☐ ☐☐ ☐☐☐☐	_____	_____

_____ _____

Study Staff Signature Date

6d. Follow-up visit

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐
Month Date Year

Follow-up Visit Form (record all dates as mm/dd/yyyy)

Visit Window: ☐12 weeks ☐ 24 weeks ☐48 weeks | Date of Visit: ☐☐ ☐☐ ☐☐☐☐

Has the patient had any ART medication changes since the last visit? ☐ Yes ☐ No
(If NO, you may skip the following questions)

NEW medications started since the last visit? ☐ Yes ☐ No
(If so, please provide the following information)

Drug Combination	***Frequency***	***Date started***
_____	_____	☐☐ ☐☐ ☐☐☐☐

DISCONTINUED medications since the last visit? ☐ Yes ☐ No
(If so, please provide the following information)

Drug Combination	***Reason for discontinuation***	***Date ended***
_____	_____	☐☐ ☐☐ ☐☐☐☐

Drug combination codes:
1 – EFV + 3TC + TDF (QD)
2 – AZT and 3TC (BID), EFV (QD)
3 – AZT and 3TC (BID), NVP (QD)
4 – Others (specify)

Frequency codes:
QD – once a day
BID – twice a day

Discontinuation codes:
1 – Treatment Failure
2 – Clinical progression/hospitalization
3 – Patient Decision/Request
5 – Drug Interaction
6 – Adverse Event (specify)
7 – Others (specify)

Has the patient collected any ARV medication refills since the last visit? Yes ☐ No ☐
(If YES, please provide the following information)

Date medication dispensed: ☐☐ ☐☐ ☐☐☐☐ ***No. of days between last prescriptions dispensed:*** _____

Drug	***No. of pills per day***	***No. of pills dispensed***	***No. of pills left***	***Total number of pills on hand***	***No. of pills missed***
_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____	_____

Has the patient had his/her viral load taken since the last visit? Yes ☐ No ☐
(If YES, please provide the following information)

Date taken: ☐☐ ☐☐ ☐☐☐☐ ***Viral Load Result:*** ***Undetectable*** ☐ ***Detectable*** ☐ ***if detectable, value:*** _____

Has the patient had his/her CD_4 count and CD_4 % taken since the last visit? Yes ☐ No ☐
(If YES, please provide the following information)

1. Date taken: ☐☐ ☐☐ ☐☐☐☐ ***CD_4 Count:*** _____ ***CD_4 %:*** _____

2. Date taken: ☐☐ ☐☐ ☐☐☐☐ ***CD_4 Count:*** _____ ***CD_4 %:*** _____

_____ Study Staff Signature

_____ Date

6e. Termination form

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Month Date Year

STUDY TERMINATION FORM		
Date of completion / early termination:	/ / (dd / mm / yyyy)	
Has the subject completed the study according to the protocol?	**Yes** ☐	**No** ☐
	(If no, please complete the rest of the page)	

Reason for early termination	
▪ Death	☐
▪ Withdrawn informed consent Reason withdrawn (if stated): _____	☐
▪ Withdrawn for other reasons, please specify:	☐
▫ Adverse event/social harm	☐
▫ Non-compliance	☐
▫ Other, specify: _____	☐

_____ _____

Study Staff Signature Date

6f. Missed visit form

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐
Month Date Year

Missed Visit (record all dates as mm/dd/yyy)
Target Visit Date: ☐☐ ☐☐ ☐☐☐☐
Reason visit was missed (Mark only one): ☐ ☐ ☐ unable to contact patient ☐ patient withdrew from the study ☐ ☐ ☐ unable to schedule appointment(s) within allowable window ☐ patient deceased ☐
ARV Medication (Mark only one): ☐ ☐ unknown ☐ _____

_____ _____
Study Staff Signature Date

6g. Social harms report

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Social Harms Report

1. Describe the social harm event:

_____

_____

☐ Patient declined to describe

2. Date of social harm onset ☐☐ ☐☐ ☐☐☐☐
Month Date Year

3. What type of social harm is this event? (Mark all that apply)

☐ Physical ☐ Emotional ☐ Financial ☐ Other (specify): _____

4. Did this event include unwanted disclosure of study participation?

☐ Yes (specify to who) : _____ ☐ Unknown/information not provided

☐ No ☐ Other (specify): _____

5. What impact did this situation have on the patient's quality of life?

☐ No disturbance ☐ A major disturbance that had a major impact

☐ A minimal disturbance that had no significant impact ☐ Other (specify): _____

☐ A moderately upsetting disturbance, but did not have a significant impact ☐ Unknown/declined to provide information

6. Other patient comments or remarks?

_____

_____

☐ None

7. Based on your discussion with the patient, do you think this situation is resolved?

☐ Yes ☐ No ☐ Other (specify): _____

8. What action, recommendation or suggestion was provided to patient to help resolve this situation?

_____

_____

_____ _____

Study Staff Signature Date

Appendix 7. Questionnaires

a. ART adherence questionnaire
b. Connect for Life patient acceptability questionnaire
c. KAP questionnaire

7a. ART adherence questionnaire

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

ART Adherence Questionnaire

1. Adherence

Please place an "X" on the line below at the point showing your best guess about how much of your current antiretroviral medication you have taken in the **past 30 days**

0% means you have **taken none of your current antiretroviral medication, 50%** means that you have **taken half of your current antiretroviral medication, 100%** means that you have **taken every single dose** of your current antiretroviral medication in the past 30 days.

2. When was the last time you missed any of your medications? Check one.
   - ☐ Within the past week
   - ☐ 1-2 weeks ago
   - ☐ 2-4 weeks ago
   - ☐ 1-3 months ago
   - ☐ More than 3 months ago
   - ☐ Never skip medications or not applicable

If you Never skip medications, please **STOP here**. Otherwise, please continue by answering the next set of questions.

3. People may miss taking their medications for various reasons. Here is a list of possible reasons why you may miss taking your medications. How often have you missed taking your medications because you: (Circle one response for each question.)

	Never	Rarely	Sometimes	Often
Were away from home?	0	1	2	3
Were busy with other things?	0	1	2	3
Simply forgot?	0	1	2	3
Had too many pills to take?	0	1	2	3

Wanted to avoid side effects?	0	1	2	3
	Never	Rarely	Sometimes	Often
Did not want others to notice you taking medication?	0	1	2	3
Had a change in daily routine?	0	1	2	3
Felt like the drug was toxic/harmful?	0	1	2	3
Fell asleep/slept through dose time?	0	1	2	3
Felt sick or ill?	0	1	2	3
Felt depressed/overwhelmed?	0	1	2	3
Had problems taking pills at specified times (with meals, on empty stomach, etc.)?	0	1	2	3
Ran out of pills?	0	1	2	3
Felt good?	0	1	2	3

_____ _____

Study Staff Signature Date

7b. Connect for Life patient acceptability questionnaire

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Connect for Life Patient Acceptability Questionnaire

We kindly ask you to answer this questionnaire about the Connect for Life service to help us understand your experience in the program.

Thank you for your participation.

Your SHIP Team

PILL REMINDERS

How many pill reminders have you listened to in the past month? (just estimate)

- ☐ None
- ☐ 1-2
- ☐ 3-4
- ☐ more than 4

If none, skip to question 4

What do you think about the frequency of pill reminders?

- ☐ Too many
- ☐ Just enough
- ☐ Too few

Please explain……

……

Do you think the Connect for Life program has helped improve your medication adherence?

- ☐ Yes
- ☐ No

Why do you think this is?.....

.....
.....

B. HEALTH TIPS

How many health tips have you listened to in the past month? (just estimate)

- ☐ None
- ☐ 1-2
- ☐ 3-4
- ☐ more than 4

If none, skip to question 10

What were the general messages in the health tips? (You can tick more than one box)

- ☐ Medical e.g. what is resistance?
- ☐ Lifestyle/Nutrition/Fitness e.g. information on working out or healthy living.
- ☐ Social/Behavioural e.g. information on mental health, sexual health, or drug & alcohol use

	Not at all	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
How **helpful** is the **information** given in the health tips?	0	1	2	3	4
How **easy to understand** is the **information** given in the health tips?	0	1	2	3	4
How **easy to understand** is the **language** used in the health tips?	0	1	2	3	4

Overall, what do you think of the health tips in Connect for Life Philippines?

.....
.....
.....

C. SYMPTOM REPORT

Over the past month, how many times have you used Connect for Life to report a symptom or health problem?

- ☐ None
- ☐ 1-2
- ☐ 3-4
- ☐ more than 4

If none, skip to question 13

	Not at all	A little bit	Some-what	Quite a bit	Very much
How helpful do you feel that using Connect for Life to report the problem was at giving you some support to manage your health problem?	0	1	2	3	4

Please explain

.....
.....

D. GENERAL

	Not at all	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
Do you find the Connect for Life system **easy to use**?	0	1	2	3	4
Do you like the **voices and tone** of the Connect for Life system messages?	0	1	2	3	4
Do you like the **music** played at the start of the call when you enter your PIN code?	0	1	2	3	4
Has the program **benefited you**?	0	1	2	3	4
	Not at all	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
Has the program **affected your privacy**?	0	1	2	3	4
How likely would you be to **recommend** the Connect for Life program to a friend?	0	1	2	3	4

Thank-you for participating in this questionnaire

Study Staff Signature	Date

7c. KAP questionnaire

Study ID No. ☐☐☐☐

Date Completed ☐☐ ☐☐ ☐☐☐☐

Connect for Life KAP Questionnaire

We kindly ask you to answer this questionnaire about your personal experience and practices related to your health and well-being. Thank you for your participation.

Your SHIP Team

QUALITY OF LIFE ASSESSMENT

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

		Very poor	Poor	Neither poor nor good	Good	Very good
1	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last two weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3	To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4	How much are you bothered by any physical problems related to your HIV infection?	1	2	3	4	5
5	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
6	How much do you enjoy life?	1	2	3	4	5
7	To what extent do you feel your life to be meaningful?	1	2	3	4	5
8	To what extent are you bothered by people blaming you for your HIV status?	1	2	3	4	5
9	How much do you fear the future?	1	2	3	4	5

10	How much do you worry about death?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
11	How well are you able to concentrate?	1	2	3	4	5
12	How safe do you feel in your daily life?	1	2	3	4	5
13	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about **how completely** you experience or were able to do certain things in the last two weeks.

		Not at all	A little	Moderately	Mostly	Completely
14	Do you have enough energy for everyday life?	1	2	3	4	5
15	Are you able to accept your bodily appearance?	1	2	3	4	5
16	Have you enough money to meet your needs?	1	2	3	4	5
17	To what extent do you feel accepted by the people you know?	1	2	3	4	5
18	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
19	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
20	How well are you able to get around?	1	2	3	4	5

The following questions ask you how good or satisfied you have felt about various aspects of your life over the last 2 weeks.

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
21	How satisfied are you with your sleep?	1	2	3	4	5
22	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
23	How satisfied are you with your capacity for work?	1	2	3	4	5
24	How satisfied are you with yourself?	1	2	3	4	5

25	How satisfied are you with your personal relationships?	1	2	3	4	5
26	How satisfied are you with your sex life?	1	2	3	4	5
27	How satisfied are you with the support you get from your friends?	1	2	3	4	5
28	How satisfied are you with the conditions of your living place?	1	2	3	4	5
29	How satisfied are you with your access to health services?	1	2	3	4	5
30	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to **how often** you have felt or experienced certain things in the last two weeks.

		Never	Seldom	Quite often	Very often	Always
31	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

HIV INFO

	True	False	Don't Know
HIV and AIDS are the same thing.	T	F	DK
There is a cure for AIDS.	T	F	DK
HIV can be spread by mosquitoes.	T	F	DK
A person can be infected with HIV for 5 years or more without getting AIDS.	T	F	DK
There is a vaccine that can stop adults from getting HIV.	T	F	DK
People are likely to get HIV by deep kissing, putting their tongue in their partner's mouth, if their partner has HIV.	T	F	DK
Using Vaseline or baby oil with condoms lowers the chance of getting HIV.	T	F	DK
Taking antiretroviral therapy (ART) greatly reduces the risk of opportunistic infections like pneumonia, thrush, and tuberculosis.	T	F	DK
A person with HIV has AIDS when his or her CD4 (T-cell) count falls below 800 cells/mm	T	F	DK
A person can get HIV by sharing a glass of water with someone who has HIV.	T	F	DK

Washing drug use equipment/"works" with cold water kills HIV.	T	F	DK
Taking a test for HIV one week after having sex will tell a person if she or he has HIV.	T	F	DK
Pulling out the penis before a man climaxes/cums means the partner cannot get HIV during sex.	T	F	DK
A person cannot get HIV by having oral sex, mouth-to-penis, with a man who has HIV.	T	F	DK
If a person tests positive for HIV, then the test site will have to tell all of his or her partners.	T	F	DK
A person can get HIV through contact with saliva, tears, sweat, or urine.	T	F	DK

SEXUAL ACTIVITY

	Never	**Rarely**	**Sometimes**	**Often**	**Every time**	
How often have you used condoms when having sex with your regular partner(s) in the last 3 months?	1	2	3	4	5	N/A
How often have you used condoms when you had sex with casual partners in the last 3 months?	1	2	3	4	5	N/A
If you had sex with any new partners in the last 3 months, how often did you talk with those partners about HIV before having sex?	1	2	3	4	5	N/A
How often did you drink alcohol or use drugs before you had sexual intercourse in the last 3 months?	1	2	3	4	5	N/A
How many sexual partners have you had in the last 3 months?	_____					

ALCOHOL AND DRUG USE

1. **How often have you had a drink containing alcohol – a glass of beer, wine, a mixed drink, or any kind of alcoholic beverage – in the last 30 days?**

Never	Once a Month	2 or 3 times a month	Once or Twice a Week	3 or 4 times a Week	Nearly every day	Daily
□	□	□	□	□	□	□

If Never, skip ahead to question #4.

2. **On days when you drank any alcoholic beverages in the last 30 days, how many drinks did you usually have altogether? By a drink we mean a can or glass of beer, a 4-ounce glass of wine, a 1-1/2 ounce shot of liquor, or a mixed drink with 1-1/2 ounces of liquor?**

Check one.

1 or 2 drinks per day	3 or 4 drinks per day	5 or 6 drinks per day	7 or 8 drinks per day	9 to 11 drinks per day	12 or more drinks per day
□	□	□	□	□	□

3. **During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a couple of hours (e.g. 2-4 hours)?**

Check one.

Never	Once a Month	2 or 3 times a month	Once or Twice a Week	3 or 4 times a Week	Nearly every day	Daily
□	□	□	□	□	□	□

In the past 3 months have you…	**Yes**	**No**
4. Used marijuana?	□	□
5. Used methamphetamine (shabu, ice)?	□	□
6. Used inhalants (rugby)?	□	□
7. Used prescription drugs to get high (e.g. Nubain, Valium)?	□	□
8. Injected drugs or been injected by someone else?	□	□
9. Shared used needles or equipment (syringes, cookers, cotton, water, etc…) to inject yourself or someone else?	□	□

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE!

_____ _____

Study Staff Signature Date

Appendix 8. Focus group discussion guide (intervention development phase)

Focus Group Discussion Guide
Connect for Life

Moderator Checklist

 The focus group moderator has a responsibility to adequately cover all prepared questions within the time allotted. S/he also has a responsibility to get all participants to talk and fully explain their answers. Some helpful probes include:

- "Can you talk about that more?"
- "Help me understand what you mean"
- "Can you give an example?"

 It is good moderator practice to paraphrase and summarize long, complex or ambiguous comments. It demonstrates active listening and clarifies the comment or everyone in the group.

 Because the moderator holds a position of authority and perceived influence, s/he must remain neutral, refraining from nodding/raising eyebrows, agreeing/disagreeing, or praising/denigrating any comment made.

 A moderator must tactfully deal with challenging participants.
Here are some appropriate strategies:

- Self-appointed experts: "Thank you. What do other people think?"
- The dominator: "Let's have some other comments."
- The rambler: Stop eye contact; look at your watch; jump in at their inhale.
- The shy participant: Make eye contact; call on them; smile at them.
- The participant who talks very quietly: Ask them to repeat their response more loudly.

 When the focus group is complete the moderator thanks all participants and distributes the transportation allowance.

 Immediately after all participants leave, the moderator and assistant moderator debrief while the recorder is still running and label all tapes and notes with the date, time (if more than one group per day), and name of the group.

FOCUS GROUP INTRODUCTION
(5 Minutes)

Once everyone has completed the Consent Form and the Questionnaire the moderator may begin with the introduction.

WELCOME
Thanks for agreeing to be part of the focus group. We appreciate your willingness to participate.

INTRODUCTIONS
Moderator (Renier); assistant moderator/note taker (Cara)

PURPOSE OF FOCUS GROUPS
We have been asked by Dr. Kate Leyritana to conduct the focus group.

The reason we are having these focus groups is to find out about the challenges patients face with taking their medications and possible ways to support our patients.

We need your input and want you to share your honest and open thoughts with us.

GROUND RULES

1. WE WANT YOU TO DO THE TALKING.
We would like everyone to participate.
I may call on you if I haven't heard from you in a while.

2. THERE ARE NO RIGHT OR WRONG ANSWERS
Every person's experiences and opinions are important.
Speak up whether you agree or disagree.
We want to hear a wide range of opinions.

3. WHAT IS SAID IN THIS ROOM STAYS HERE
We want folks to feel comfortable sharing when sensitive issues come up.

4. WE WILL BE RECORDING THE GROUP
We want to capture everything you have to say.
We don't identify anyone by name in our report. You will remain anonymous.

5. REMINDER: TURN OFF CELL PHONES IF POSSIBLE

6. HAVE FUN

“Does anyone have any questions? (answers). OK, let’s begin”

FOCUS GROUP DISCUSSION

<<<START THE RECORDING>>>

A. WARM UP
(3 minutes)

First, I'd like everyone to introduce themselves. Can you tell us your name? If you don't want to share your name for privacy reasons, then you can feel free to use a different name for this discussion.

B. ADHERENCE
(15 minutes)

I am just going to give you a couple of minutes to think about your experience of taking your daily medications? What works well and what doesn't for you when it comes to taking your medications? Would anyone be willing to start by sharing his experience?

Probing questions (as needed, to keep the conversation going):

- *What aspects have a positive effect or a negative effect on your taking your meds?*
- *What about coming to the clinic regularly for your follow ups?*
- *What would help you or what would you find useful to support taking your meds?*

C. MOBILE PHONES
(15 minutes)

I am interested to find out about what ways do you use your cell phone in your health care?

Probing questions:

- *For example, do you use any alarm function on your phone to remind you about your meds? Do you use any apps related to your health care? Do you text or email your doctors from your phone?*
- *Would you be open to using your phone in your health care? Why or why not?*

D. INTRODUCE THE CONCEPT OF "CONNECT FOR LIFE"
(3 minutes)

SHIP clinic has been working on developing a mobile phone support system to help us better support our patients in taking their medications and staying in care.

The project we are working on would use interactive voice response (IVR) to provide a variety of services and information to patients. The platform could remind you when to take your pills, and record and track your adherence to your medication schedules and let the doctor know how you are doing. It can remind you about upcoming appointments. It also can play short audio messages on HIV related information spanning from nutrition, lifestyle advice, or family dynamics. Patients could also call into the system to report symptoms, receive personalized instructions, or connect directly with their doctor.

This project has been tried out in India and in Uganda and has been well-received there.

I would like to ask you some questions specifically related how you think it would work here in the Philippines, and specifically in the SHIP clinic.

E. REMINDERS
(10 minutes)

Firstly, would you find it useful to receive phone calls or text messages reminding you to take your medication? Why or why not?

Probing questions:
- *Would you have any concerns? What are they?*
- *Would you prefer SMS or voice recording?*

F. VOICE
(20 minutes)

I have some samples of different kinds of voices that I would like you to listen to. I would like to know which of the voices would be most appealing to you if he or she were giving you an adherence reminder or some health tips. After we listen to them all we can discuss.

PLAY SAMPLES

What did you think? Who did you like and who didn't you like? Why?

Probing questions:
- *Do you think the reminders or health tips would come across the same in English and Tagalog? Do you have a preference?*
- *Do you think it is better to have a formal tone or a friendly tone?*
- *Do you think it is better to have male voice or a female voice?*

G. HEALTH TIPS CONTENT
(15 minutes)

If you were to get a regular call that included a recorded health message, what kinds of topics would you want to those messages to cover?

Probing questions:
- *What topics related to your health do you want to know more about? What information do you feel you need?*
- *For example, the health tips could cover anything -- it could be about basic HIV info, HIV medications, managing side effects, nutrition, mental health, sexual health, harm reduction for recreational drug use and addiction, etc.*
- *I have some samples of health tips from other countries. What are your thoughts about these tips? (SHOW OR READ SAMPLES)*

H. FEEDBACK APPROACH
(10 minutes)

We are interested in learning about how we could give extra motivation for people to take their meds. One thing that the phone system could do for patient would be to provide them with instant feedback on how they are doing with their adherence.

For example, if someone took all of his doses in the last week, he could get a message that says: "Congratulations! Your performance score for the last week was 7 out of 7. This places you among our top performers!! Don't lose your spot at the top. Take your pills every day this week to keep your perfect score of 7/7"

Whereas if he had missed a certain number of doses the message might say: "Your performance score for the last week was X out of 7. Most other patients like you have a performance score of at least 6. Take your pills every day this week to meet your performance score goal"

What do you think of a feedback system regarding your adherence? What kinds of messages would make you the most motivated to take care of yourself and take all of your meds?

Probing questions:

- *Do you think this feedback would me more or less helpful depending on an individual patient's situation? Who could benefit? Who would be less likely to benefit?*

I. FINAL QUESTION
(5 minutes)

Of all the things we've discussed today, what would you say are the most important issues you would like to express about this topic?

J. CONCLUSION
(2 minutes)

Thank you for participating. This has been a very successful discussion. Your opinions will be a valuable asset to the project. We hope you have found the discussion interesting.

If there is anything you are unhappy with or wish to complain about, please contact Dr. Kate or speak to me later.

I would like to remind you that we will keep your identities and what was discussed completely anonymous. We request that you also respect confidentiality of all the participants as well.

Before you leave, please hand in your completed questionnaire.

Appendix 9. Focus group discussion guide (process evaluation phase)

Focus Group Discussion Guide
Connect for Life

Moderator Checklist

 The focus group moderator has a responsibility to adequately cover all prepared questions within the time allotted. S/he also has a responsibility to get all participants to talk and fully explain their answers. Some helpful probes include:

- "Can you talk about that more?"
- "Help me understand what you mean"
- "Can you give an example?"

 It is good moderator practice to paraphrase and summarize long, complex or ambiguous comments. It demonstrates active listening and clarifies the comment or everyone in the group.

 Because the moderator holds a position of authority and perceived influence, s/he must remain neutral, refraining from nodding/raising eyebrows, agreeing/disagreeing, or praising/denigrating any comment made.

 A moderator must tactfully deal with challenging participants.
Here are some appropriate strategies:

- Self-appointed experts: "Thank you. What do other people think?"
- The dominator: "Let's have some other comments."
- The rambler: Stop eye contact; look at your watch; jump in at their inhale.
- The shy participant: Make eye contact; call on them; smile at them.
- The participant who talks very quietly: Ask them to repeat their response more loudly.

 When the focus group is complete the moderator thanks all participants and distributes the transportation allowance.

 Immediately after all participants leave, the moderator and assistant moderator debrief while the recorder is still running and label all tapes and notes with the date, time (if more than one group per day), and name of the group.

FOCUS GROUP INTRODUCTION
(5 Minutes)

Once everyone has completed the Consent Form and the Questionnaire the moderator may begin with the introduction.

WELCOME
Thanks for agreeing to be part of the focus group. We appreciate your willingness to participate.

INTRODUCTIONS
Moderator (Ed); assistant moderator/note taker (Kris)

PURPOSE OF FOCUS GROUPS
We have been asked by Dr. Kate Leyritana to conduct the focus group.

The reason we are having these focus groups is to find out about the challenges patients face with taking their medications and possible ways to support our patients.

We need your input and want you to share your honest and open thoughts with us.

GROUND RULES

1. WE WANT YOU TO DO THE TALKING.
We would like everyone to participate.
I may call on you if I haven't heard from you in a while.

2. THERE ARE NO RIGHT OR WRONG ANSWERS
Every person's experiences and opinions are important.
Speak up whether you agree or disagree.
We want to hear a wide range of opinions.

3. WHAT IS SAID IN THIS ROOM STAYS HERE
We want folks to feel comfortable sharing when sensitive issues come up.

4. WE WILL BE RECORDING THE GROUP
We want to capture everything you have to say.
We don't identify anyone by name in our report. You will remain anonymous.

5. REMINDER: TURN OFF CELL PHONES IF POSSIBLE

6. HAVE FUN

“Does anyone have any questions? (answers). OK, let’s begin”

FOCUS GROUP DISCUSSION

<<<START THE RECORDING>>>

K. WARM UP
(3 minutes)

First, I'd like everyone to introduce themselves. Can you tell us your name? If you don't want to share your name for privacy reasons, then you can feel free to use a different name for this discussion.

L. THE CONCEPT OF "CONNECT FOR LIFE"
(3 minutes)

SHIP clinic has been working on developing a mobile phone support system to help us better support our patients in taking their medications and staying in care.

The plan was to use interactive voice response (IVR) to provide a variety of services and information to patients. The platform could remind you when to take your pills, and record and track your adherence to your medication schedules and let the doctor know how you are doing. It can remind you about upcoming appointments. It also can play short audio messages on HIV related information spanning from nutrition, lifestyle advice, or family dynamics

I would like to ask you about your experience using Connect for Life.

M. ADHERENCE
(15 minutes)

I am just going to give you a couple of minutes to think about your experience of taking your daily medications? What works well and what doesn't for you when it comes to taking your medications? Would anyone be willing to start by sharing his experience?

Probing questions (as needed, to keep the conversation going):

- *What aspects have a positive effect or a negative effect on your taking your meds?*
- *What about coming to the clinic regularly for your follow ups?*
- *What would help you or what would you find useful to support taking your meds?*

N. MOBILE PHONES
(10 minutes)

How was it having Connect for Life contact you on your mobile phone? What do you like or dislike about using your mobile phone for health care?

Probing questions:

- *Would you prefer SMS? Calls? App? All of the above?*

O. REMINDERS
(10 minutes)

Was the Connect for Life experience receiving pill reminders helpful or not helpful? Visit reminders?

Probing questions:

- *Do you have any concerns? What are they?*
- *Did you prefer SMS or voice recording?*

P. HEALTH TIPS CONTENT
(10 minutes)

How was the Connect for Life experience with receiving health tips by voice call or SMS? Were the topics relevant?

Probing questions:

- *What topics related to your health do you want to know more about? What information do you feel you need?*
- *For example, the health tips could cover anything -- it could be about basic HIV info, HIV medications, managing side effects, nutrition, mental health, sexual health, harm reduction for recreational drug use and addiction, etc.*

Q. FEEDBACK APPROACH
(10 minutes)

Connect for Life was able to provide adherence feedback by SMS, for example: "Congratulations! Your performance score for the last week was 7 out of 7. This places you among our top performers!! Don't lose your spot at the top. Take your pills every day this week to keep your perfect score of 7/7"

What do you think of the feedback system regarding your adherence? Does it have an effect on your motivation to take care of yourself and take all of your meds?

Probing questions:

- *Do you think this feedback would me more or less helpful depending on an individual patient's situation? Who could benefit? Who would be less likely to benefit?*

R. TECHNICAL ISSUES
(15 minutes)

Did you experience any technical issues with the Connect for Life System? What were they? How were they resolved? Did you continue or discontinue using the platform?

S. THE FUTURE
(5 minutes)

After the end of the study, should we continue Connect for Life? If yes, which parts of the service and in what modality (SMS, voice, other)? If no, what would be a better way to support our patients?

T. FINAL QUESTION
(5 minutes)

Of all the things we've discussed today, what would you say are the most important reflections you have about your experience on Connect for Life?

U. CONCLUSION
(2 minutes)

Thank you for participating. This has been a very successful discussion. Your opinions will be a valuable asset to the project. We hope you have found the discussion interesting.

If there is anything you are unhappy with or wish to complain about, please contact Dr. Kate or speak to me later.

I would like to remind you that we will keep your identities and what was discussed completely anonymous. We request that you also respect confidentiality of all the participants as well.

Before you leave, please hand in your completed questionnaire.

Appendix 10. Behaviour change techniques

In their 2008 article describing a taxonomy of 26 behaviour change techniques, Michie & Abraham ask: "Do differences in the content of behaviour change interventions have an impact on effectiveness? If so, which techniques or combinations of techniques enhance effectiveness?"(207)

I used the taxonomy to map out the BCTs used in the Connect for Life intervention. This exercise will help identify which parts of the intervention may be responsible for any effects observed.

Method	Applied in the Connect for Life intervention?	Parameters
1. Provide information about behaviour health link	✓	Health tips, Adherence feedback score/messages
2. Provide information on consequences	✓	Health tips
3. Provide information about others' approval	✓	Adherence feedback score/messages
4. Prompt intention formation	✓	Pill reminders, Health tips, Visit reminders
5. Prompt barrier identification	✓	Symptom management, Health tips
6. Provide general encouragement	✓	Health tips, Adherence feedback score/messages
7. Set graded tasks		
8. Provide instruction	✓	Health tips
9. Model or demonstrate the behaviour		
10. Prompt specific goal setting	✓	Health tips
11. Prompt review of behavioural goals		
12. Prompt self-monitoring of behaviour	✓	Health tips
13. Provide feedback on performance	✓	Adherence feedback score/messages
14. Provide contingent rewards		
15. Teach to use prompt or cues	✓	Pill reminders
16. Agree on behavioural contract		
17. Prompt practice		
18. Use follow up prompts	✓	

Method	Applied in the Connect for Life intervention?	Parameters
19. Provide opportunities for social comparison	✓	Adherence feedback score/messages
20. Plan social support of social change	✓	Health tips
21. Prompt identification as role model		
22. Prompt self-talk		
23. Prevent relapse		
24. Stress management	indirectly	Health tips
25. Motivational interviewing		
26. Time management	✓	Pill reminders, Visit reminders, Health tips

Appendix 11. Health Tips

Number	Topic	Subtopic	Title	Tip script
1	Medical	Adherence	Missed dose	Q: What should I do if I miss a dose? A: ARVs work best when you are 100% adherent and take them as the doctor has instructed, even if you experience side effects. Unless your health care provider tells you otherwise, take the medicine you missed as soon as you realize you skipped it. But if it's almost time for the next dose of the medicine, don't take the missed dose and instead just continue on your regular medication schedule. Don't take a double dose of a medicine to make up for a missed dose.
2	Medical	Adherence	Pill box	To help you remember if you've taken your dose for the day, use a 7-day pill box. Once a week, fill the pill box with your ARVs for the entire week.
3	Medical	Adherence	Resistance 1	ARVs prevent the HIV virus from multiplying in the body. It is important that you maintain a steady amount of ARVs in the blood, or else the virus will be able to mutate and become resistant to your meds. This means that your ARVs will no longer work effectively, and you may have to change to a higher, and possibly more complicated, set of ARVs. Avoid missing your meds.
4	Medical	Adherence	Resistance 2	Q: Whether I take my ART doses or miss them, I don't feel any difference. Why is it still important to take my ART? A: ART is a long-term therapy. The people who take at least 95% of their doses are the most likely to stay healthy over the long-term. If you miss a dose, it does have an effect, though you may not notice it immediately. Each missed dose gives a chance for the HIV virus to develop resistance to the drug. This can weaken your immune system and may be evident only when you develop infections that occur 6 to 8 months after skipping multiple doses. Remember to take your medicines exactly as directed by your doctor.
5	Medical	Adherence	Routine setting	To keep from forgetting your daily doses, associate your ART with a routine activity, like lunch, dinner, a TV show, or a radio program. Some people take their morning pills with their breakfast or when they leave for work. Others take their night pill just before going to bed or set the alarm on their mobile phones to remind them of their daily dose. It is helpful to have a treatment buddy who will encourage you to stick to your ARV schedule. Remember, adherence to your ART is your key to a healthier life.
6	Medical	ARVs	Access to care - Accessing ARVs	Q: Where do I get ARVs? A: ARVs are dispensed by the designated treatment hubs. There are main hubs and satellite hubs all over Manila, and others throughout Luzon, Visayas, and Mindanao. ARVs and some laboratory tests important for HIV are free under the PhilHealth Outpatient HIV Package. It is best to be an active member and contributor of PhilHealth, to enjoy your medical benefits.
7	Medical	ARVs	Access to care - HMOs	Many patients want to know whether their HMO will cover the costs for HIV testing and medications. Most HMOs in the Philippines do not cover any services related to HIV or sexually transmitted diseases. Make sure you enroll in PhilHealth so that you will have benefits to help cover the costs of HIV care and other services in PhilHealth accredited facilities. Talk to your doctor about which services may be covered under your HMO plan.
8	Medical	ARVs	Alternative medicine	Some patients prefer to treat their symptoms with alternative and traditional methods such as herbs, acupuncture and other non-traditional methods. Studies have shown that these treatments alone are not effective in prolonging the life of an HIV positive individual. ARVs are still the most effective way to manage HIV, but non-traditional forms of medicine are also welcome forms of treatment if they provide comfort for HIV symptoms and improve your overall well-being, and do not have significant drug interactions with your ARVs. Give your doctor your full medication list, including any alternative treatments, in addition to your ARVs.

9	Medical	ARVs	ART definition	Antiretroviral therapy, or ART, is a combination of medications taken by people living with HIV. These medications prolong life expectancy of HIV positive people, but they do not cure HIV. ART boosts the immune system of an HIV positive person so he or she can fight infections better than if they don't take the medications. It is important to take your ART every day without fail.
10	Medical	ARVs	First-line and second-line	When a person with HIV starts on ARVs, the first combination of medicines they take is called "first line treatment." If the first line drugs stop working, or if you develop severe reactions to the first line drugs, your clinician may decide to change your medications to other drugs in the first line regimen or switch "second line treatment." First line drugs may stop working If you miss too many doses, if you get infected with a resistant virus, or if you have been on treatment for a very long time. Taking 100% of your doses is the best way to make sure you won't have to switch to second line treatment.
11	Medical	ARVs	How ARVs work	Medicines to treat HIV are called antiretrovirals, or ARVs. They work by reducing the amount of the virus in your blood and help the immune system fight infections. ARVs do not cure HIV, but taking your meds daily can help control the virus, enabling you to live a healthier life.
12	Medical	ARVs	Initiation	Q: When can a person with HIV start taking ARVs? A: Earlier initiation of ARVs is associated with better outcomes across the board, but several factors need to be considered before starting on treatment. These considerations include the patient's CD4 count, symptoms, presence of other diseases, and his willingness and ability to adhere to treatment. Treatment should be started as soon as possible if a patient has AIDS-defining illnesses, is pregnant, has another active Tuberculosis, Hepatitis B needing treatment, or if the CD4 count falls below 500. Effective ART depends on taking HIV medicines properly. So before starting ART, it's important to address any issues that can make adherence difficult.
13	Medical	ARVs	Medication interactions	Once you start ARVs, you need to be careful about taking other medicines together with them. Other medications and even herbal remedies may have interactions with your ARVs. It is best to inform your doctor everything you're taking, to check for drug interactions.
14	Medical	ARVs	Recreational drug interactions	Taking recreational drugs can affect your HIV medications. Taking drugs may either shorten or prolong the availability of the ARVs in your blood stream. Regularly taking recreational drugs affects the amount of ARVs that your body gets and may cause damage to your other organs in the long run. It is always best to refrain from taking drugs while taking ARVs, or at least reduce your drug use. Tell your doctor about your drug use, to check for important interactions, and for tips to reduce risk.
15	Medical	ARVs	Resistance	If an HIV-positive person's viral load continues to increase despite taking ARVs, then the doctor may consider the possibility that the patient is not responding properly to the medications. This could be a sign of medication resistance, and the physician may opt to change the medications or do additional tests to investigate further. It is important to have your viral load checked annually.
16	Medical	ARVs	Side effects	Q: Can I stop taking the ARVs because of severe side effects? A: If your ARVs cause side effects, DO NOT stop or change your treatment on your own, as this can lead to drug resistance. Side effects that are not life threatening do not require discontinuation of ARV intake. Most side effects usually resolve after 2 weeks. Possible ARV side effects include rash, dry skin and lips, loss of appetite, difficulty sleeping and pain in the lower extremities. Report all adverse effects to your doctor. If the clinic is closed and you need urgent medical attention, proceed to the nearest emergency room.
17	Medical	ARVs	HAART	Q: What is "HAART"? A; For lifelong treatment, you must take a combination of 3 different ARV medicines together. This is called HAART, or highly active antiretroviral therapy. Some patients take one pill containing all 3 ARV's once or twice a day, but often patients are on regimens that have more than one pill. Always follow your doctor's instruction about how you should take your medication.

18	Medical	Co-infections	Bloody stool	Patients sometimes see blood when they pass stools. One explanation could be hemorrhoids. This means that there is weakening of the walls of your lower intestine, causing it to protrude. Because of the delicate nature of the tissue of your intestinal lining, bleeding is possible when stools pass. If you have blood in your stool, you should drink plenty of water, eat high-fiber foods like vegetables and whole grains, and avoid straining while passing stool. If symptoms persist, talk to your doctor about medications or procedures that can help. If you think that you need urgent medical care, go to your clinic ASAP or the nearest emergency room.
19	Medical	Co-infections	CMV Retinitis	CMV, or cytomegalovirus, is a serious viral infection of the retina that can affect your eyesight and if not treated early can lead to blindness. It can also cause chronic diarrhea if it affects your gut. It is more common in people with weakened immune systems. If you are HIV positive and you notice that your eyesight is getting worse, go to an eye doctor as soon as possible.
20	Medical	Co-infections	Fungal infections	Several fungal infections that don't usually affect people with healthy immune systems can occur in a patient with AIDS. Systemic fungal infections generally affect more than one area of the body, and they can be difficult to treat. Fungi can cause meningitis, pneumonia, and thrush. The symptoms of a fungal infection can be non-specific like cough, headache, fever, and fatigue. Most invasive fungal infections require treatment with medications given through the vein, but some mild ones can be treated with creams or ointments or with oral meds. Tell your doctor about new symptoms to ensure early detection and treatment.
21	Medical	Co-infections	Fungal skin infections	Fungal infections of the skin are very common and include athlete's foot, jock itch, ringworm, and yeast infections. They are contagious. Fungal infections of the skin can affect any part of your body – from the face to the feet. You should avoid sharing towels, articles of clothing or other materials that come in contact with the infected areas.
22	Medical	Co-infections	Fungal skin infections	Q: Can you treat fungal skin infections with sulfur soap? A: Sulfur soap can make skin dry. These may help some fungal infections but may sometimes be too harsh for the skin. Sulfur does not cure the fungus. It only deprives the fungus of the moist environment in which it thrives. Fungal infections are still best treated with oral or topical antifungals.
23	Medical	Co-infections	Hepatitis	Viral Hepatitis, or Hep for short, is a virus that damages the liver. Hep A, B, and C are the most common types of viruses that cause hepatitis. Hep A is caused by bad food or poor sanitation or sewage disposal. Hep B and C are passed by sharing blood and bodily fluids. They can be passed by sex and by sharing needles and syringes. If you have HIV, you will need to get tested for Hepatitis before starting your ARVs. Ask your doctor about vaccines, advice for safe sex and safe injection practices to avoid Hepatitis.
24	Medical	Co-infections	Kaposi's sarcoma	Q: What is Kaposi's sarcoma? A: Often patients report skin lesion that appear like big red to purple skin patches that may be elevated or flat. These lesions are seen on the chest, arms or the face, and more commonly the legs. These lesions can sometime also cause swelling of the affected areas. It is important to determine whether these lesions are of Kaposi's Sarcoma, which may occur in HIV. Inform your doctor of your skin issues.
25	Medical	Co-infections	Opportunistic Infections 1	Q: What are opportunistic infections? A: HIV weakens a person's immune system, which means people with HIV may get some illnesses that don't usually affect people with healthy immune systems. These are called 'opportunistic infections'. Common opportunistic infections include tuberculosis, PCP, thrush, and fungal meningitis. ARVs do not treat these diseases. You have to take other medicines to treat them. However, taking your ARVs will strengthen your immune system and reduce the risk of infections, so take your medicines regularly.
26	Medical	Co-infections	Skin conditions	Most of the kinds of skin lesions that occur in HIV positive patients are also seen in HIV negative patients. Dry, scaly, and itchy skin caused by psoriasis, seborrheic dermatitis, and eczema, for example, can be more common in HIV positive patients. Skin problems can cause a lot of distress for patients, Rest assured that skin lesions usually improve with creams or ointments or with

				oral medications, in conjunction with taking your ARVs. So, continue taking your ARVs and seek help from your clinic if you are experiencing skin problems.
27	Medical	Co-infections	STDs	Sexually transmitted infections, or STIs, affect HIV transmission. The risk of transmitting HIV during sex is increased when either person has an STI, especially if it's an ulcer. Ulcers and wounds can bleed or cause discharge, which makes it easier for HIV to enter into the bloodstream. Get tested regularly for STIs and if you do contract an STI, see your doctor to get treated right away. Remember, condoms can prevent STIs, so use them even if you're having sex with someone who is also HIV-positive, to prevent STIs.
29	Medical	Co-infections	STDs - Chlamydia	Chlamydia is a type of Sexually Transmitted Infection. Having a Chlamydia infection makes someone 5 times more likely to get HIV. Common symptoms include discharge from your penis or anus, burning sensation when urinating, and anal bleeding. Chlamydia is easy to treat but you can be infected for a long time without having symptoms. When you get treated for Chlamydia, it is important that your sex partner or partners are all treated AS WELL, or else you will get infected again.
30	Medical	Co-infections	STDs - gonorrhea	Gonorrhea is a Sexually Transmitted Infection. Symptoms include a white to yellowish opaque discharge from the penis or vagina, painful urination or occasionally a swollen lymph node in the groin area. Once you develop symptoms of gonorrhea, it is important to seek medical attention. Remember, condoms can prevent STIs, so use them even if you're having sex with someone who is also HIV-positive, to prevent STIs.
31	Medical	Co-infections	STDs - Herpes simplex 1	Herpes is a type of viral infection that can occur in the mouth or genital area and is frequently among people with HIV. Herpes tends to remain hidden in a person who is infected, and recurring ulcers are common, especially when the immune system is weak. Herpes is highly contagious, so whenever ulcers are present you should abstain from sex or kissing to prevent passing on the infection to others. If abstaining from sex is not possible, then at least use condoms to reduce the risk of infection. If you have herpes or experience frequent outbreaks of herpes, inform your doctor immediately.
32	Medical	Co-infections	STDs - Herpes simplex 2	Q: Is it true that once I have herpes, it will never go away? A: You get herpes by having oral or penetrative sex with an infected person. Condoms reduce the risk of getting it. There is no cure for herpes; it comes and goes over time. Go to a clinic for medicine to ease the symptoms. If you have symptoms of ANY STI it's important not to have sex as you may infect others. If you have herpes, you are more at risk of getting HIV. If you have ANY sores on your mouth or genitals, DO NOT have sex until you are treated and wounds are gone. Even then, virus can still be transmitted. Always use a condom to reduce the risk of infecting your partner.
33	Medical	Co-infections	STDs - HPV	The human papillomavirus, or HPV, is a very common sexually transmitted infection. HPV is the main cause of genital warts, and it can cause cervical cancer in women, anal cancer in men who have sex with men, and oral and throat cancers. If you have warts on your genitals or anus, these can be treated in the clinic by a dermatologist. The HPV vaccine is recommended for gay, bisexual, and other men who have sex with men up to 26 years of age. Remember condoms can prevent STIs, so carry them with you and practice safe sex.
34	Medical	Co-infections	STDs - syphilis	Many people who have syphilis don't know it, as primary syphilis usually goes undiagnosed. It presents with a painless ulcer on the genital area. Most patients don’t know that they have syphilis until they develop symptoms of secondary syphilis which include a red rash, occasionally with fine scaling over the palms and soles, and sometimes the back. The rash may or may not be itchy. If you experience this kind of rash, you should consult your physician immediately. You should get regular tests for syphilis and other STDs at the clinic. Practice safe sex and use condoms
35	Medical	Co-infections	Tuberculosis co-infection	Q: How is TB treated in an HIV positive patient? A: A common opportunistic infection among people with HIV is tuberculosis, or TB. Unlike HIV, TB can be cured. TB treatment uses a combination of drugs and takes 6 to 12 months, with a combination of drugs. Like ARVs, TB medicines must be taken every day exactly as prescribed by the doctor to ensure they work. You MUST complete the entire treatment, even if you feel better. If

				not, your TB could return and be much harder to treat. If you're being treated for TB and not getting better, consult with your doctor.
36	Medical	Co-infections	Tuberculosis risk	Q: Does an HIV positive person have a higher risk for TB? Tuberculosis, or TB, is a mycobacterial infection that often occurs in the lungs but can also develop in the brain and other parts of the body. HIV positive people are 5 to10 times more likely to get TB because HIV weakens the immune system. Go to a clinic for a TB test if you've been losing weight, if you've had chills, fever, night sweats or coughing for more than 2 weeks, or if you have aches in the joints, kidneys, stomach or spine. For people with HIV, getting on treatment for TB as soon as possible can sometimes be a matter of life and death.
37	Medical	Co-infections	Warts	Q: How often should I get my checked for anal warts? A: It is best to consult with your doctor yearly to check for warts. If you recently had warts removed, it is recommended that you see your doctor every 2 weeks until there are no more lesions, then every 6 months until there are no recurrences.
38	Medical	Co-infections	Warts	Q: I've had my anal warts removed several times. They still keep coming back! What does this mean? A: One factor that affects the recurrence of genital warts is your CD4 count. Your immune system is very important in combating recurrences of anogenital warts. If your CD4 count is too low, recurrence rates will be higher. Take your ARV medications daily and have regular checkups.
39	Medical	HIV	Acute infection	A few days or weeks after getting infected with HIV, some people experience a flu-like illness with fever, muscle aches and fatigue. This is called acute HIV infection, or acute retroviral syndrome, and symptoms will resolve on their own. Other people have no symptoms at all for many years. The reactions of an individual to HIV vary from person to person. If someone suspects that he or she has HIV, it is always best to get tested immediately and see your friendly doctor.
40	Medical	HIV	AIDS definition	Not everyone who has HIV also has AIDS. The diagnosis of AIDS happens when HIV has severely weakened the immune system. This is when a person has a CD4 cell count of less than 200 or if he or she develops an AIDS-defining illness. These illnesses include several types of fungal infections, cancers, and recurrent bacterial or viral infections. Treatment with antiretroviral medications is very effective at helping the immune system recover. Don't forget to take your medication on time every day.
41	Medical	HIV	Blood test	A person's HIV status can be determined by a blood test to check for antibodies. An HIV rapid test is a quick and easy test that uses a drop of blood from a finger prick, with results available in a few minutes.
42	Medical	HIV	HIV cure	Q: Is there a cure for HIV? A: There is no cure for HIV and AIDS yet. However, antiretroviral therapy can control HIV and enable you to live a long and healthy life. Researchers remain hopeful that they're heading in the right direction to find a cure for HIV and AIDS, and they are testing new approaches all the time. Remember to take your ART regularly without fail.
43	Medical	HIV	HIV definition	HIV is the Human Immunodeficiency Virus. If left untreated, HIV can progress to acquired immunodeficiency syndrome, or "AIDS". But not all people who are infected with HIV automatically have AIDS. An HIV-infected person has AIDS when he or she has a CD4 count below 200 or develops any of the AIDS-defining illnesses. Taking antiretroviral medication can help control HIV and stop progression towards AIDS. Please always take your medications as prescribed daily.
44	Medical	HIV	HIV doctors	Q: What kind of doctor should I go to if I have HIV? A: A doctor who specializes in care for patients with HIV is usually an infectious diseases specialist. You can receive care from infectious diseases doctors at HIV treatment hubs. There are many treatment hubs in the Philippines – 5 of them are in Manila, and there are also hubs in the Visayas, Mindanao, and other parts of Luzon. Social hygiene clinics and satellite clinics also provide HIV healthcare. At the treatment hubs, the doctors and the other members of the HIV and AIDS treatment team are ready to help you.

45	Medical	HIV	HIV vaccine	Q: Is there a vaccine for HIV? A: There have been many attempts to develop a vaccine against HIV, but unfortunately there still isn't a truly effective vaccine available. Vaccines stimulate the body's immune system to provide protection against infection or disease, but HIV has unique ways of evading the immune system, and so the human body seems unable to mount an effective immune response against it. Researchers are still working to develop vaccines against HIV, and they are in various stages of clinical trials. Currently ARVs are the best defense against HIV so please take your medicines without fail.
46	Medical	HIV	Immune system - CD4 cells	CD4 stands for "cluster of differentiation 4". It is a marker that measures the strength of your immune system. A high CD4 means that you have a strong immune system, and a low CD4 means that your immune system is weak. The CD4 of someone with a robust immune system is above 500. For a person living with HIV, having a low CD4 count can increase the risk of catching infections and make those infections more severe. Remember to have your CD4 count monitored every 6 months to check on your immune system, and to monitor your therapy.
47	Medical	HIV	Immune system - effects of HIV	When a person gets infected with the HIV virus it reproduces and destroys white blood cells called CD4 T-cells. These CD4 T-cells form part of the body's immunity. This means that people with HIV have lower immunity, so they may catch infections more easily than people who are HIV-negative. These illnesses are called 'opportunistic infections'. Taking your medications every day will help increase your CD4 T-cells and improve your immune system.
48	Medical	HIV	Life span	Q: How long can a person live with HIV or AIDS? A: Being diagnosed with HIV or AIDS is not a death sentence. A person who takes Antiretrovirals, or "ARVs" can have a nearly normal life span, once taken early in the course of HIV. However, without treatment, life expectancy can shorten significantly. Continue to take your medicine daily
49	Medical	HIV	Testing - antibody test	Q: What is an antibody test? A: When you are get any kind of infection, your immune system produces antibodies to fight off the organism that is infecting you and serves as a marker of having had that infection. If someone gets HIV, after several weeks their body begins to produce the HIV antibody. A blood test for the presence of the HIV antibody can be done to determine the presence of HIV.
50	Medical	HIV	Testing - mandatory testing	Q: Is it mandatory to take an HIV test? A: HIV testing should be voluntary, No one should ever be forced to get tested. However, blood and organ donors are automatically tested for HIV and other blood-borne diseases in order to protect the person receiving the donation from any possible infection. It is still best for each of us to know our HIV-status so that we may start taking medications, if necessary, and also so that we may protect our partners and other people from getting infected.
51	Medical	HIV	Testing - rapid test	Q: What test can I do to know my HIV status? A: The fastest results are achieved using the Rapid Test. In this test, a person has his or her finger pricked for a sample of blood. Blood is dropped in the well of the test strip, and then a reagent is applied. A 5–10-minute wait for the results will show a positive or negative result. This test is not 100% accurate, so if it comes back positive, a confirmatory test will be needed. Ask your clinic for more information.
52	Medical	HIV	Testing - where to go	Q: Where can someone go to get tested for HIV? A: Social hygiene clinics and public hospitals can provide free HIV counseling and testing services. Many private clinics and hospitals provide testing for a fee. There are also free HIV testing sites and events run by HIV advocacy groups and community organizations. A person must consent to the test prior to its administration. All results are kept confidential. Self-testing through home test kits deprives the person of counseling support and medical advice to help him interpret the result. If someone needs a test, go to the local clinic or check online for details about other testing sites.

53	Medical	HIV	Testing - who need testing	Q: Who needs HIV testing? A: Ideally, everyone should get tested and know their HIV status. Pregnant women, health care professionals and people who are at high-risk for HIV should get tested regularly. Those at high risk include men who have sex with men, people who inject drugs and who have shared needles or syringes, individuals with an HIV-positive sexual partner, people who have exchanged sex for money, or those who have had a history of other sexually transmitted diseases. It is important and it should be considered our personal responsibility to know our HIV status. Knowing our status enables us to take care of not only ourselves, but others as well.
54	Medical	HIV	Testing - window period	Q: When should I get tested for HIV after unprotected sex? A: After someone is exposed to HIV, he or she won't test positive right away. Each person's body reacts to the virus differently. It can take anywhere from 9 days up to 3 months for the immune system to make HIV antibodies, which is how HIV tests diagnose the infection. The time between the initial infection and the appearance of detectable antibodies is called the "window period" It is therefore best to get a test one month after unprotected sex and to repeat this test 3 months after the sexual encounter. To avoid worrying, always practice safe sex using a condom.
55	Medical	HIV	Transmission - anal sex	One of the highest risks for HIV transmission is having unprotected anal sex with an HIV positive person or with someone whose HIV status is unknown. There are many blood vessels in the walls of the anus and rectum, and these may rupture during anal sex, making it easier for the virus to enter into your bloodstream. This is why you should always use condoms when having sex so you can reduce the risk of transmitting the virus. Be safe, always use condoms
56	Medical	HIV	Transmission - biting	Q: If an HIV positive person bites me, will I get infected? A: It is technically possible -- though very, very, unlikely -- for somebody to get HIV by biting or being bitten. Saliva does not carry HIV. Special attention is warranted in cases where the biter has blood in his or her mouth and where the bite breaks the skin. If you do get bitten, it is best to wash of the bitten area and to consult your physician.
57	Medical	HIV	Transmission - blood and organs	Q: If I get a blood transfusion, how will I know that the blood is safe? A: All blood and organ donors since 1986 have been routinely screened for HIV and other blood-borne diseases. If donated blood is positive for any blood-borne disease, the collected blood is discarded, and the donor is notified of his or her disease. If you need a transfusion or transplant, it is important that you only get blood or organs from reputable medical facilities.
58	Medical	HIV	Transmission - health workers 1	Q: Are health care professionals at risk for HIV transmission from their patients? A: All health care professionals should practice standard precautions, regardless of HIV status of their patients. This means that they should always use personal protective equipment when dealing with blood, blood products, and bodily fluids. They should always wash or disinfect their hands before and after contact with all patients.
59	Medical	HIV	Transmission - health workers 2	Q: How do health care professionals decrease the risk of getting infected? A: If a health care professional is working in a high risk environment, he or she should receive the necessary vaccines and also get tested regularly for blood-borne diseases, including Hepatitis, B, C, and HIV. Post exposure prophylaxis, which is the intake of medications after coming in contact with infective bodily fluids, is also a practice for health care professionals to decrease the risk of infection.
60	Medical	HIV	Transmission - healthy appearance	Q: Can a person with HIV pass the virus to someone else even if he or she has no symptoms? A: A person who has no symptoms of HIV still carries the virus and is still capable of infecting others even if he or she is otherwise healthy. If someone with HIV is taking antiretrovirals consistently and has an undetectable viral load, the risk of transmission is lower. This is called treatment as prevention. Get your viral load checked every year to make sure you are undetectable. Also remember to always carry and use condoms.

61	Medical	HIV	Transmission - hugging	Q: I just found out I'm positive. I've been hugging my niece who is just 2 months old. Is she at risk? A: Hugging a baby is one of the best experiences in the world. The risk of infecting anyone with HIV by hugging, regardless of age, is almost impossible. You should be careful if you ever have an open, bleeding wound. If blood comes into contact with a break in the skin of someone else, only then there is a possibility of infection. Hugging poses no risk to your loved ones.
62	Medical	HIV	Transmission - Kissing	Q: Can kissing transmit HIV? A: Kissing is a very low risk activity. HIV is not transmitted through saliva. There has been only one case of a woman who may have been infected with HIV by deep kissing. The virus was transmitted through sores and cuts in the woman's mouth when he kissed her male partner who had a habit of brushing his teeth vigorously, which may have ruptured blood vessels inside the mouth. You should always be mindful of your oral hygiene – and if you have mouth sores or other lesions, postpone deep kissing.
63	Medical	HIV	Transmission - mosquitoes	Q: Can mosquitoes transmit HIV? A: When a mosquito or other insect bites an HIV infected person and then bites you, there is no risk of transmission. Mosquitoes only inject their saliva into the person that they bite, so no infected blood comes into contact with the person bitten by the mosquito. Mosquitoes' saliva contains an enzyme that lyses the HIV virus. However, mosquitoes do transmit several other infectious diseases like dengue fever and malaria. If a person bitten by a mosquito develops a high fever, he should seek consult from a physician immediately.
64	Medical	HIV	Transmission - mother to child	An infected mother can pass HIV to her baby during pregnancy and delivery. Antiretroviral medications can be taken during and after pregnancy to reduce the risk of transmitting the virus to the unborn child. Exclusive breastfeeding until 12 months of age is recommended when both mother and baby are taking ARVs. At four to six weeks old, all infants who are born to HIV-positive mothers should be given an early infant diagnosis. Another HIV test should be done at 18 months or when breastfeeding ends to provide the final infant diagnosis.
65	Medical	HIV	Transmission - non-sexual	Q: If you have never had unprotected sex, could you still get HIV? A: Sex is not the only way to get HIV. Sharing needles with an infected person can also transmit the virus. Blood in the needle may carry the virus and if the needle is used again on a different person, that person may be exposed to the virus. It is important that needles be disposed of properly and safely once used. Do not share needles, and practice safe sex.
66	Medical	HIV	Transmission - oral sex	Q: Can HIV be spread through oral sex? A: Oral sex is less risky than anal or vaginal sex – but it is still possible for HIV to enter through open cuts and sores in the mouth or on the genitals. Once semen gets past the mouth, stomach acid and enzymes in the esophagus kill the virus. The safest way is to always use condoms or dental dams for oral sex.
67	Medical	HIV	Transmission - possible routes	Q: How does a person get infected with HIV? A: A person can get infected if he or she comes in contact with infected blood, semen, vaginal fluids or breast milk. HIV is not transmitted by saliva, sneezing, coughing, eating or drinking from the same plates, glasses or utensils. You also cannot get infected by hugging, shaking hands, using toilets, hot tubs, drinking fountains, or swimming pools.
68	Medical	HIV	Transmission - shared household items	Q: If a child accidentally uses a razor of an infected member of the family, what should we do? A: If the child cuts him or herself with a razor or any sharp object used by an HIV positive member of the family, you must bring the child to your physician to determine the need for post-exposure prophylaxis and an HIV test.
69	Medical	HIV	Transmission - sharing utensils	Q: Can I share utensils, plates and the like with my family members? A: Saliva does not carry the HIV virus, hence utensil sharing poses no risk to your family members. However, you should make sure to never share shaving blades or needles.

70	Medical	HIV	Transmission - single exposure	Q: If someone gets exposed to the virus, do they automatically get infected? A: HIV infection depends on how the virus enters the body, the amount of the virus that enters, and the health of the immune system of the person exposed to the virus. Someone may get infected after a single exposure to the virus, some don't. If someone suspects they have been exposed to the virus, they should get a test as soon as possible.
71	Medical	HIV	Transmission - STDs	Having a sexually transmitted infection, or STI, increases the risk of getting HIV. STIs, especially the types that cause ulcers, like herpes, can make the mucosal membranes in the genitals more vulnerable to HIV and allow the virus to enter the bloodstream more easily. Studies have shown that treating existing STIs lowers the risk of transmission of HIV. It is important to get tested for STIs, get them treated, and to use condoms when having sex, in order to reduce the risk of transmitting both HIV and STIs.
72	Medical	HIV	Transmission - tattoos and piercings	Q: Can people get HIV from tattooing or piercings? A: Tattooing and piercing involve the use of needles to pierce the body, providing risk of blood-borne virus transmission like hepatitis B and C and HIV, unless infection control measures are taken. Tattoo artists and piercers should always use new, single-use, disposable needles to eliminate the possibility of infection.
73	Medical	HIV	Transmission - women and girls	Q: Are menopausal women at lower risk of getting HIV through vaginal sex? No. Menopausal women and teenage girls are in fact, at higher risk of getting HIV through unprotected vaginal sex. The mucosal membranes of the vagina of these women and girls are more fragile, and so small tears during intercourse are more likely. These tears in the vaginal wall make it easier for the virus to enter into the bloodstream. Condom use is advised.
74	Medical	HIV	Universal precautions	Q: What are health care workers supposed to do to? A: All health care workers can reduce their risk of infection by practicing standard precautions when handling bodily fluids. Using gloves, masks and goggles protects the worker from being inadvertently exposed to infectious fluids. In addition to this, proper disposal of needles, syringes and other sharp objects should always be observed. Receptacles for sharps should be available for proper disposal.
75	Medical	HIV	Vaccinations and HIV	Q: Can a person with HIV get all kinds of vaccines? A: In general, it is very important for people with HIV to be protected from illness through routine vaccinations. However, there are certain vaccines which are MUST HAVEs and those that are unsafe in HIV. Ask your doctor about what vaccines you should take. Hepatitis, pneumococcal, and flu vaccines are MUST HAVE vaccines if applicable.
76	Medical	HIV	Viral Load test	A viral load test is a lab test that measures the number of HIV virus particles in a milliliter of your blood. A viral load test helps provide information on your health status and how well your treatment with HIV medications is controlling the virus. The more HIV there is in your blood -- and therefore the higher your viral load-- then the faster your CD4 cell count will fall, and the greater your risk of becoming ill because of HIV. Taking your ARVs every day will help reduce your viral load and increase your CD4 count.
77	Medical	HIV	Who can get HIV	Any person, regardless of age, sexual preference, ethnicity, or status in life can get HIV. People who have unprotected sex with a person who has HIV can get infected. People who share needles or syringes with a person who has HIV when using drugs can also get infected. Children born to mothers with HIV, or those who breastfeed from an HIV-infected mother are also at risk. As are health care workers who may be exposed to blood or bodily fluids while working.
78	Nutrition/Fitness/Lifestyle	Fitness	Cardiovascular exercise	Cardiovascular exercise means increasing your heart rate while moving your body continuously for at least 30 minutes. Activities such as brisk walking, jogging, dancing, bicycling or swimming can be considered cardiovascular exercise. You should get an average of at least 30 minutes of exercise per day. Walk your dog, park your car far away, use the stairs, and get creative about ways not to remain sedentary. The quality of your old age depends on this!

79	Nutrition/Fitness/Lifestyle	Fitness	Exercise	Regular exercise makes you feel more alert, helps to relieve stress and stimulates the appetite. Exercise is the only way to strengthen and build up muscles. The body uses muscles to store energy and protein that the immune system can draw upon when required. Exercise is therefore especially important for people with HIV. If your everyday work does not involve much exercise, you should find an enjoyable exercise like walking, running, swimming, dancing, or playing a sport that can be part of your daily life.
80	Nutrition/Fitness/Lifestyle	Fitness	Exercise and depression	Depression, stress, and anxiety can be difficult to overcome and are very common for people living with HIV. Exercise is one of the best things you can do to help yourself feel better mentally -- it's not just about physical fitness. Exercise is beneficial because we produce hormones that help calm us down when we exercise. Aim for at least 30 minutes of physical activity every day.
81	Nutrition/Fitness/Lifestyle	Fitness	Fitness for a busy schedule	When you're busy and under a lot of stress, it can be hard to find the time to exercise. Remember exercise is a gift that you give yourself. The mood-enhancing benefits of exercise and its effects on the immune system are well documented. Find a friend who can become your "exercise buddy." Or start with short 10-minute sessions and build up from there.
82	Nutrition/Fitness/Lifestyle	Fitness	Fitness supplements	When it comes to sports supplements and their potential interactions with HIV meds, research is scarce and inconclusive. Some common supplements like glutamine have no reported adverse effects. However, other supplements such as Saint-John's-wort, can have significant interactions with some HIV medications. It's best to avoid products that have documented interactions and to communicate with your doctor about all the supplements you're using.
83	Nutrition/Fitness/Lifestyle	Fitness	Gym risks - bacterial and fungal infections	People with HIV are at higher risk for bacterial and fungal infections, which can be easily spread in the typical gym or fitness center. At the gym, be very careful to cover or bandage any broken skin since this is one common way for bacteria to get inside you. Use a clean towel during your workout to create a barrier between you and the weight bench or mat. After your workouts, wash your towels in hot water and always dry them in a hot dryer. Many gyms provide hand-sanitizer dispensers and alcohol-based sprays or wipes for equipment. Make use of them before and after your training.
84	Nutrition/Fitness/Lifestyle	Fitness	Peripheral neuropathy	Some people with HIV experience peripheral neuropathy, or the loss of sensation in their fingers or toes. Walking and weight training are great ways to improve overall muscle strength and they may help slow down neuropathy. But if you have neuropathy, you should avoid high-impact exercises like running on a treadmill or jumping up and down, as this can result in foot injuries.
85	Nutrition/Fitness/Lifestyle	Fitness	Risks of exercise	Working out is key to improving your fitness. However, if you are HIV-positive, your body is already under a lot of stress – don't push beyond certain limits. Exercise should be enjoyable. If you are terribly exhausted or you get muscle cramps or other aches and pains, you could be overdoing things. Exercising every other day will give your body time to rest and also time to adjust to a new exercise routine. If you plan to embark on a new routine, talk to your doctor about your fitness plans.
86	Nutrition/Fitness/Lifestyle	Fitness	Weight loss	People with HIV have extra nutrient needs, however, for some patients it is important to avoid trending towards obesity and overweight. To control your weight, eat more vegetables and smaller portions of rice and other carbs. Eating small healthy snacks like fruits and veggies between meals can go a long way to help you to feel full, meet your nutrient and energy requirements, and help your body fight off infections.
87	Nutrition/Fitness/Lifestyle	Fitness	Weight training	Weight training is one of the best ways to increase muscle mass and bone density that may be lost through HIV disease and aging. Working out three times a week for an hour should be enough if done well. Doing weight training followed by 30 minutes of cardiovascular exercise may be the best way to improve body composition and keep your blood cholesterol and sugar down.
88	Nutrition/Fitness/Lifestyle	Fitness	Working out while ill	Q: I have a cold. Should I continue working out, or is it better to wait until I'm feeling better? A: As a general rule - listen to your body. If your symptoms are minor, then working out is probably not out of the question, but never work out with a cough, sore throat, or fever. When you are sick, you should avoid pushing yourself while your body is recovering.

89	Nutrition/Fitness/Lifestyle	Fitness	Yoga	Yoga improves immune function, high blood pressure, anxiety, depression — even irritable bowel syndrome. It also increases strength and flexibility. It's accessible and inexpensive, with many community classes free of charge. The benefits of yoga become more evident if you do it regularly. It's a good idea to add some yoga into your fitness routine.
90	Nutrition/Fitness/Lifestyle	Lifestyle	Healthy Living	Q: How can I keep healthy after being diagnosed with HIV? A: Living with HIV means you will have to be conscious about living a healthy lifestyle and taking care of your body in order to strengthen your immune system. Eat small, healthy meals throughout the day. Limit the amount of caffeine, nicotine, alcohol, and recreational drugs you use. Hydration and regular exercise are also necessary to keep healthy.
91	Nutrition/Fitness/Lifestyle	Lifestyle	Mental exercise	HIV can have long-term effects on the brain and mental function. Mental exercise — doing a daily crossword puzzle or playing brain-challenging games — can help maintain your cognitive health. Exercise your memory, concentration, and attention, all of which can be affected by HIV.
92	Nutrition/Fitness/Lifestyle	Lifestyle	Sex life	Q: I have HIV and I am afraid of having sex with other people. A: Having HIV does not stop you having a normal life or stop your sexual desire. People with HIV can have healthy sex lives by practicing safe sex. It is important that you take your medications every day and that you use condoms every time you have sex to prevent infecting other people. Condoms also protect you from other sexually transmitted infections. Even if the person you have sex with is also HIV-positive, you should still use condoms since it is possible that you could re-infect each other with drug-resistant types of HIV.
93	Nutrition/Fitness/Lifestyle	Lifestyle	Tattoos and piercings	Q: Can I get a tattoo or a piercing even if I am HIV-positive? A; The process of getting a tattoo or piercing is an invasive procedure that breaks the skin and introduces foreign material into the skin's surface. This can cause major issues with a patient's immune system. For those who have the HIV virus under control, the ability to get a tattoo or piercing is fine as long as you have doctor's approval. You may have a harder time finding a tattoo artist that is willing to work with an HIV-positive client. To protect yourself from infection, it is important that you go to a reputable artist who uses disposable single-use needles, wear gloves, and practices universal precautions.
94	Nutrition/Fitness/Lifestyle	Nutrition	Appetite	Q: What do I do if I lose my appetite? People with HIV often lose their appetites when they are sick. Early on, HIV medicines can decrease your appetite, or make food taste bad. Sometimes having oral thrush can also decrease taste. You can improve your appetite by eating smaller meals throughout the day. If you are ill, you still need energy and nourishment from food, so make sure you eat enough. If you are vomiting, drink small amounts of water, soup and tea, eat dry foods such as crackers, drink clean water after eating and do not lie down until one or two hours after eating. Relieve diarrhea by drinking enough oral rehydration solutions to replace volume losses. If symptoms persist or if you notice the presence of oral thrush, consult your doctor at the earliest time.
95	Nutrition/Fitness/Lifestyle	Nutrition	Balanced diet	Q: Does being on ART affect what I should eat? A: ART does not stop you from eating anything. You can eat everything that others eat, as long as it is clean, well-cooked, and hygienic. To help increase your immunity, make sure you get all the necessary nutrients. Cook your food properly, meats should be well done. Always wash the vegetables and fruits thoroughly in running water to avoid infection. Remember teat a balanced diet, eat healthy, and eat right.
96	Nutrition/Fitness/Lifestyle	Nutrition	Diabetes	If you have HIV and diabetes, you should meet your nutritional needs as advised by your diabetes healthcare provider. Never miss any meal. A well-distributed meal helps to keep the level of glucose in blood low. Avoid sugary drinks like tea and soda and avoid sugary sweets as much as possible. Eat high-fiber food like whole grain breads, brown rice, vegetables, and fruits. Try to go for a walk every day. Take your diabetes medicines and your ARVs on time.

97	Nutrition/Fitness/Lifestyle	Nutrition	Diarrhea	Q: I have diarrhea from my ARVs. What can I do? A: Relieve diarrhea by drinking fluids to replace losses, volume-per-volume. You can make oral rehydration salts with water, salt and sugar; or purchase the prepared ones at the pharmacy. You can also eat bananas, rice and apples to help make more formed stools. Avoid oily food.
98	Nutrition/Fitness/Lifestyle	Nutrition	Food hygiene	Q: Is there anything that I should avoid or not eat at all? A: ART does not stop you from eating anything in particular. But it is important to avoid food poisoning. Eat food from a reputable, dependable food source to avoid risk of other bacterial or viral infections that can be transmitted by improper handling of food. Also, try to avoid oily or greasy foods, and processed food as far as possible as they can be more difficult to digest.
99	Nutrition/Fitness/Lifestyle	Nutrition	Foods for immunity	Q: Will certain food improve my immune system? A: People with HIV, whether or not they take ARVs, need to eat well to give the immune system the energy it needs to fight the virus. There is NO food that is known to treat AIDS, not garlic or sweet potato. Eat normal, healthy foods at least 3 times a day. Abstain or refrain from smoking, consuming alcoholic beverages or using recreational drugs. These vices may weaken the immune system and interact with your ARVs.
100	Nutrition/Fitness/Lifestyle	Nutrition	HIV and the gut	HIV may reduce food absorption. As your food is digested - nutrients pass through the gut walls into the bloodstream and are transported to the organs and tissues in the body where they are needed. One of the consequences of HIV is that it damages the gut wall, which means the body does not absorb nutrients as efficiently as it would have before you were HIV-positive, causing malnutrition. This problem is made worse by diarrhea, which is a common occurrence for people who have HIV. Make sure you are getting the right nutrition by eating a variety of nutrient-rich foods.
101	Nutrition/Fitness/Lifestyle	Nutrition	HIV's effect on nutrition	When infected with HIV the body must work harder in order to fight the virus. This increases energy and nutrient requirements. Other infections and fevers also increase the body's demand for food. People with HIV, and especially those whose HIV has progressed to AIDS, need to eat more to meet these extra energy and nutrient needs.
102	Nutrition/Fitness/Lifestyle	Nutrition	Hypertension	If you have hypertension, a low salt diet is best for you. You should try to increase your intake of vegetables and fruits and eat rice and meat in moderation. You should also limit caffeinated drinks and sugary drinks.
103	Nutrition/Fitness/Lifestyle	Nutrition	Malnourishment	Malnutrition occurs when a person's body is not getting enough food or is not getting the right food for proper nourishment. People with HIV, cancer, diarrhea, difficulty swallowing, and alcoholism or drug abuse all stand the chance of becoming malnourished. Early on, HIV medicines can decrease your appetite, or make food taste bad. To stay well-nourished and healthy, eat small, healthy meals throughout the day. And limit the amount of caffeine, nicotine, alcohol, and recreational drugs you use.
104	Nutrition/Fitness/Lifestyle	Nutrition	Sore mouth	If you have sores in your mouth, eating can be painful. Eat soft foods that are easy to chew, such as avocado, pumpkin, bananas and yogurt. Do not eat acidic foods like oranges, lemons, pineapples or tomatoes. And soften dry food by dipping it in liquids. Improve your appetite by eating smaller meals throughout the day.
105	Nutrition/Fitness/Lifestyle	Nutrition	Vitamin A	Vitamin A is important for boosting your immune system, it is also required for vision and gene transcription. If you want to increase your vitamin A intake naturally, eat foods rich in vitamin A including calabaza, sweet potato, carrots, dark green leafy vegetables, romaine lettuce, dried apricots, cantaloupe, sweet red peppers, tuna, and mango.
106	Nutrition/Fitness/Lifestyle	Nutrition	Vitamin B	Vitamin B12 is important for the function of your brain and nervous system, and it helps in the formation of red blood cells. It is only found naturally in animal products such as shellfish, beef liver, mackerel, crustaceans, red meat, low fat dairy milk, cheese, eggs. For vegetarians, fortified soy products and fortified all bran cereals contain significant amounts of Vitamin B12. Synthetic forms are also available in supplements for those who prefer not to consume animal products.

107	Nutrition/Fitness/Lifestyle	Nutrition	Vitamin C	The recommended daily allowance of for vitamin C is 75mg for women and 90mg for men. Vitamin C helps protect against colds and flu. If you want to increase your vitamin C intake naturally, the foods that have the highest vitamin C content include guava, kiwi, oranges, grapefruit, strawberries and cantaloupe. Vegetables that have high vitamin C content are red and green bell peppers.
108	Nutrition/Fitness/Lifestyle	Nutrition	Vitamin D	Vitamin D is actually a hormone produced by your body when you are exposed to the sun. It helps you absorb calcium and maintains bone strength. You can get more vitamin D by eating salmon, tuna, sole, flounder, milk, cereal, pork, eggs, mushroom, beef liver and ricotta cheese.
109	Nutrition/Fitness/Lifestyle	Nutrition	Vitamin E	Vitamin E prevents stress to the body, protects tissues from damage, and helps keep the immune system strong. It also protects against heart disease, cancer and age-related eye damage. Foods rich in vitamin E are dark leafy green vegetables, almonds, hazelnuts, pistachios, pecans, walnuts, sunflower seeds, avocados, shrimp, oysters, smoked salmon, wheat germ, canola and corn oil, broccoli, squash and kiwi.
110	Nutrition/Fitness/Lifestyle	Nutrition	Weight gain	If you need to gain weight to get your weight back to a normal level, you will need to eat more food, either by eating larger portions or by eating meals more frequently, using a variety of foods. Eat plenty of starchy foods like rice, potatoes, bread, and bananas. Increase your intake of protein including beans, nuts, and peas, as well as meat, poultry fish and eggs. Add healthy snacks in between meals. High fat foods may be more difficult to digest, so slowly add fats and oils into your diet as you can tolerate them in order to help you gain weight.
111	Nutrition/Fitness/Lifestyle	Nutrition	Weight loss	HIV can lead to unintended weight loss. An HIV-positive person may have less appetite due to feeling ill, or as a side-effect of the HIV medications. And for people with HIV, the food that they eat is poorly absorbed. This can cause the body to draw on its reserve stores of energy from body fat and protein from muscle. As a result, the person loses weight because body weight and muscles are lost. Weight can be regained once the underlying problem is addressed, coupled with proper nutrition and continuing improvement of immune status.
112	Social/Behavioral	Drug use harm reduction	Addiction	When people use drugs or alcohol on a regular basis, the mind and body can begin to feel an overpowering need for the drug. When the mind feels like this, it is called dependence. When the body feels like this, it is called physical addiction. Not all people who use drugs are addicted, but if you find yourself turning toward alcohol or drugs to avoid bad feelings, if you have built up a higher tolerance, or if your drug use or drinking is interfering in other aspects of your life and relationships, these can be signs of dependence or addiction. Seek out counseling or drug addiction therapy.
113	Social/Behavioral	Drug use harm reduction	Alcohol	Drinking alcohol, particularly binge drinking, can increase your risk for HIV. Being drunk affects your ability to make safe choices and lowers your inhibitions, which may lead you to take risks you are less likely to take when sober, such as having sex without a condom. Alcohol use and abuse can also make the effects of HIV worse if you already have HIV. Alcohol use may make it difficult for you to follow your HIV treatment plan and it can contribute to health conditions such as liver disease that have an impact on the progression of HIV infection.
114	Social/Behavioral	Drug use harm reduction	alternatives to injecting	If you are using drugs—including injection drugs, meth, alcohol, or other drugs—the best way to reduce your risk of getting or passing on HIV is to stop taking drugs. Substance abuse treatment programs can help you do this. If you believe you cannot stop using yet, try alternative ways of using drugs rather than injecting. And do not share used needles with other people.
115	Social/Behavioral	Drug use harm reduction	drugs/alcohol and sexual risk	Reducing drug and alcohol intake is important when you have HIV in terms of both your physical health and your sexual health. Using drugs and alcohol increases the risk of HIV transmission because when using these people are more likely to have sex without a condom, have more sex partners, engage in riskier kinds of sexual activities, and inject drugs. Talk to your doctor or a counselor about your drug or alcohol use.

116	Social/Behavioral	Drug use harm reduction	HCV coinfection for injecting drug users	You can get some forms of viral hepatitis the same way you get HIV—through unprotected sexual contact and injection drug use. In fact, the majority of HIV-infected injection drug users are also infected with the Hepatitis C virus. Hep C infection is more serious in people living with HIV because it leads to liver damage more quickly. Co-infection with Hep C may also affect the treatment of HIV infection. Therefore, it's important to find out if you have Hep C. Ask your doctor to test your blood. Hep C can be treated successfully, even in people who have HIV.
117	Social/Behavioral	Drug use harm reduction	Methamphetamine	Methamphetamine is a very addictive stimulant that can be snorted, smoked, or injected. It has many street names, including crystal, ice, shabu, and more. Meth can reduce your inhibitions and interfere with your judgment about your behavior, which may make you less likely to protect yourself or others. Meth use can also increase your sexual behavior. This increases your risk of getting or transmitting HIV infection, both through sex and through injecting. Meth use can also make the effects of HIV worse for people who already have HIV. Avoid using meth or talk to a drug counselor to plan ways to reduce your use.
118	Social/Behavioral	Drug use harm reduction	Nubain	In the Philippines, injecting the prescription narcotic Nalbuphine, or Nubain, is known to have a very high risk for HIV transmission. It is common for people to share needles or use "service needles" provided by the seller to inject Nubain. Nubain is highly-addictive, so avoid using it. If you are using Nubain, talk to your doctor or to a counselor about drug addiction treatment.
119	Social/Behavioral	Drug use harm reduction	Partners of injecting drug users	The partners of people who inject drugs are at increased risk for sexual transmission of HIV and Hepatitis. It's important who people who inject drugs and also for their partners to get tested for HIV every 3 months. Use condoms every time you have sex to protect yourself and your partners from HIV.
120	Social/Behavioral	Drug use harm reduction	Planning ahead	If you are going to party, set limits for yourself before you head out. Think about what kinds of alcohol or drugs you plan to use, how much you will have, how much money you will spend, and what kinds of sexual activities you want to do. Party with a friend that you trust and tell him what your limits are. If you make a plan ahead of time, it can help keep you from taking too many risks in the moment.
121	Social/Behavioral	Drug use harm reduction	safe injecting	It's best to avoid injecting drugs, but if you are going to inject you will need to prepare your hit safely. Wash your hands with soap and water before preparing your hit, use STERILE water to mix the hit and make sure the powder is completely dissolved, filter the hit through a piece of clean cotton as you draw it into the syringe. ALWAYS use a new, sterile needle and syringe, and don't share. To avoid abscesses you should clean the injection spot with alcohol or with soap and water before you insert the needle. Rotate which spot you use for injecting, but it can be dangerous to inject in your legs hands or neck. Finally, dispose of your used needle and syringe in a solid, non-puncture-prone bottle, and in the trash can, not on the ground.
122	Social/Behavioral	Drug use harm reduction	Safer drug use	The best way for drug users to reduce HIV infection is to stop using drugs or to at least minimize using drugs that are injected. If the urge to use drugs is too much, it is better to take the drug through smoking or another route other than injecting. If you do inject, always use new sterile needles and syringes. Needle sharing most definitely increases the risk of infection, so bring your own equipment. If new needles and syringes are not available, cleaning them with bleach and sterile water before and after each use can reduce the of infection.
123	Social/Behavioral	Drug use harm reduction	Sterilizing needles and syringes	If you are injecting drugs, to avoid HIV transmission you will need to use a new needle and syringe each time you inject. Never share equipment with other people. If you don't have access to new unused needles and syringes, soak your old ones in bleach for three minutes and rinse them with clean water before using them again. Bleach is very likely to kill HIV but is it not effective against Hep C.
124	Social/Behavioral	Mental Health	Anti-discrimination laws	There is no national law in the Philippines yet that protects people living with HIV from discrimination. Several cities have passed laws to protect LGBT people from discrimination, these include Cebu, Quezon City, Angeles, Antipolo, Bacolod, Davao, and Vigan, among others. The AIDS Prevention and Control Act, or Republic Act 8504, protects the privacy and confidentiality of people living with HIV and guarantees access to health care. There are community groups that help advocate for patients who

				experience discrimination in health facilities, employment, or other aspects talk to your doctor or counselor if you have a legal or personal issue that you need help to resolve, they may be able to refer you to helpful resources.
125	Social/Behavioral	Mental Health	Anxiety 1	Q: I get so nervous around other people because I think they know I have HIV. What do I do? It is normal to feel anxious when you are newly diagnosed with HIV. Feelings of rejection and fear may be overwhelming. Keep in mind that people react differently to HIV positive individuals. Some may be accepting, and others may not. You have very little control over how others react to you, but on the other hand, you can control your reaction to their behavior. Choose to think and act positively. Talk to your doctor about medicines for anxiety if your anxious feelings don't lessen with time or if they get worse.
126	Social/Behavioral	Mental Health	Anxiety 2	Q: Sometimes, I can't cope with my feelings of anxiety? What can I do? A: Fear and anxiety may be caused by not knowing what to expect after you've been diagnosed with HIV, or by not knowing how others will treat you if they find out you have HIV. You also may be afraid of telling people that you are HIV positive. Fear can make your heart beat faster or make it hard for you to sleep. Anxiety also can make you feel nervous or agitated. To help control your anxiety you should learn as much as you can about HIV and HIV treatments, talk to a loved one, a counselor or a support group, volunteer to help others who are also experiencing the same situation. Talk to your doctor about medicines for anxiety if your anxious feelings don't lessen with time or if they get worse.
127	Social/Behavioral	Mental Health	Coping strategies	It is completely normal for people living with HIV to experience anxiety, anger, or depression. These feelings do not last forever. There are many things that you can do to help take care of your emotional needs. A few ideas are to: Find activities that relieve your stress, such as exercise or hobbies. Be sure to get enough sleep each night to help you feel rested. And learn relaxation methods such as meditation, yoga, or deep breathing.
128	Social/Behavioral	Mental Health	Depression	If you are coping with depression, you can take control of this. Monitor changes in your mood; develop a list of personal warning signs. Develop a support system; isolating yourself can bring on depression. If you are having a good day, share your joy with others. If you are having a bad day, share it with others and accept their help.
129	Social/Behavioral	Mental Health	Depression 1	Q: What should I do if I feel depressed? A: Others with HIV will understand what you are experiencing, so consider joining a support group where you can talk about living with HIV. Choose someone in your life to be your treatment supporter to help remind you to take your medicines and attend your doctor's visits. However, if you have trouble sleeping, eating or concentrating, or if you have thoughts of suicide, tell your doctor. If you are depressed or feel anxious, treatment can also help you feel better.
130	Social/Behavioral	Mental Health	Depression 2	Q: I feel sad. But does this mean I am depressed? A: It is normal to feel sad when you learn you have HIV. If, over time, you find that the sadness doesn't go away or is getting worse, talk with your doctor or someone else you trust. You may be depressed. Symptoms of depression can include: Feeling hopeless, gaining or losing weight, changes in your sleep habits, losing interest in things you enjoy, feeling tired, and feeling worthless or guilty, and thinking about death or giving up. Talk to your doctor if you have these symptoms, especially if they last for more than 2 weeks. Depression can be treated with counseling and with medication.
131	Social/Behavioral	Mental Health	Depression or substance abuse	If you are dealing with mental health or substance abuse problems, you are not alone. It's important for you to stick to your treatment plan; take your medication as prescribed and keep your appointments. Make a list of 5 people you can call if you are struggling. Make sure you carry their numbers with you all the time.
132	Social/Behavioral	Mental Health	Disclosure 1	If you have tested positive for HIV, there are some people that will need to know. You should tell your past and present sexual partners. They should get tested too. You will need to tell any future sexual partners that you have tested positive for HIV. If you are now in a relationship, your doctor can help advise you on how to explain your positive test results to your partner.
133	Social/Behavioral	Mental Health	Disclosure 2	Being able to be open and honest with someone in your life about your HIV status and your feelings can be really powerful. It can make you feel closer to the person, and they may offer you emotional and practical support when you need it. It's up to you to

				decide who you tell. You may decide you want to be completely open about your HIV status, or you may decide to only tell a small number of people close to you – it's your choice. You don't have to decide right away. Take your time to take in the news that you have HIV.
134	Social/Behavioral	Mental Health	Disclosure 3	Q: I haven't told my partner about my HIV status yet. What can I do? A: Because HIV can be passed on during sex, telling someone who is a current or previous sexual partner can be particularly difficult and emotional. Getting the HIV test together with your partner is a sure way to let your partner know about your HIV status. If you take the test It does not matter who brought HIV/AIDS, the most important thing is to know whether you have got it so you can live a positive life together and get treatment to live a longer and healthier life with HIV.
135	Social/Behavioral	Mental Health	Disclosure 4	Q: I want to tell someone close to me about my status, but I don't know how to start the conversation. What can I do? A: It's worth thinking ahead about how you will tell someone. It can help to have some information on hand to share with them. They may not know about how HIV is passed on, or about HIV treatment. They may assume that you don't have long to live, or that you won't be able to have relationships or have a family. If you can help them to understand the facts about HIV, they are less likely to react negatively. It's a good idea to find a time when you are unlikely to be interrupted, and you can take your time, and to talk in a setting where it's quiet and you can sit comfortably together. Give them time to process what you're saying, and check they understand.
136	Social/Behavioral	Mental Health	Disclosure 5	Q: Should I disclose my HIV status to my family? A: Support from family is the best support you can get in your fight against HIV. People who disclose to family have better adherence to their medications. Family members can also give financial and emotional support and can help you in an emergency. Often, family members may not know about how HIV is passed on, or about HIV treatment. At first, they may react negatively. The doctor and the counselor in your HIV clinic are experienced in handling such situations. If you have not yet disclosed your status to your family members, you can always take the help of doctor or counselor. If necessary, they can also counsel your family members.
137	Social/Behavioral	Mental Health	Marriage and family	Q: I have HIV. Does that mean I should not get married? A: Many HIV positive men and women get married – to partners who are either HIV positive or HIV negative. Even if your partner is HIV-negative it is still possible to have children. Since the advent of ART medication, many HIV-positive people have started living long and healthy lives. Make sure that you do not hide your HIV status from your spouse. Your doctor or counselor can guide you about how to tell someone about your diagnosis.
138	Social/Behavioral	Mental Health	New diagnosis 1	Q: What do I do when I find out that I am HIV positive? A: If you recently tested positive for HIV, you may feel shock, anger, fear or guilt. Strong feelings are normal. It could take time for you to accept your HIV status. Try to remember that HIV is not a death sentence. With a healthy lifestyle and antiretroviral medications, you can live a long life. When you feel ready, talk to someone you trust who can give you support like a family member or friend, counselor or a doctor.
139	Social/Behavioral	Mental Health	New diagnosis 2	Q: How can I cope with my HIV diagnosis? A: HIV changes your life, but if you live healthily and take medication when you need to, you can live a good, long life. If you're in shock about your diagnosis, one way to fight your fear is to learn as much as you can about the disease. Knowing about HIV and AIDS will help you take the best care of yourself. Try to stay active and busy – see friends, play sport, cook food. Talk to friends, family and your sexual partner, even if it's hard. Seek counseling, getting support sooner will help you to live a healthy life with HIV.
140	Social/Behavioral	Mental Health	New diagnosis 3	Q: I feel like HIV is a death sentence. A: Being diagnosed with HIV is not a death sentence. Today, many people have survived for years with the help of ARVs. Not

				everyone is going to die of AIDS once diagnosed with HIV. You need to become proactive with regards to your health – a balanced, healthy diet, exercise and enough rest along with your ARVs and regular visits to your doctor will prolong your life.
141	Social/Behavioral	Mental Health	Parents educating kids	Q: Should parents tell their kids about HIV? Keeping kids sheltered from information about sex and sexual health does not necessarily protect them in the long run. Kids who receive comprehensive sex education actually have lower rates of STDs and unplanned pregnancies. Parents are the primary educators of children. They can access and share accurate information about HIV by visiting websites such as www.cdc.org. In addition to the medical details, it is important for parents to also educate their children about to how they can help reduce stigma toward people living with HIV. Encourage other parents you know to share accurate information about HIV with their children.
142	Social/Behavioral	Mental Health	Sleep	Q: I have been experiencing difficulty falling asleep since my diagnosis. How do I deal with this? Sleep hygiene helps you stay healthy by keeping the mind and body rested and strong. Some habits that can improve your sleep include: having a routine that helps you relax each night before bed, going to bed when you feel sleepy, avoiding naps, getting up and going to bed the same time every day, making your bedroom quiet, dark and cool, using the bed only for sleep and not for watching TV or using your computer--- avoiding large meals just before bedtime, and avoiding caffeine, smoking and alcohol too close to bedtime.
143	Social/Behavioral	Mental Health	SOGIE - general	Transgender women and men often have a harder time starting and adhering to HIV treatment because they may experience discrimination or a poor understanding about transgender health issues in health care settings. Regardless of your gender identity or expression, it is important to adhere to your antiretroviral therapy in order to stay alive and healthy. Seek out a doctor or counselor who understands your needs, community advocacy groups may be able to help to refer you to more sensitive health care providers.
144	Social/Behavioral	Mental Health	SOGIE - hormone therapy	For transgender men and women, hormone therapy is often a personal priority. Cross-gender hormone therapy is not contraindicated for HIV-positive people on antiretroviral therapy, you CAN take both hormones and ARvs. However, many health care providers may still be wary, because there is very little medical literature on interactions between hormone therapy and ARVs or the impact of hormones on the immune system for transgender people. There is some evidence that certain HIV medications do impact hormone levels and visa versa, so make sure to discuss this with your doctor.
145	Social/Behavioral	Mental Health	Staying busy	Staying busy can really help if you are feeling down. Being busy increases happiness generally. So, do fun stuff. Spend time with people you like. And don't procrastinate on important tasks.
146	Social/Behavioral	Mental Health	Stigma	Unfortunately, in many communities, there is stigma attached to HIV, and it may be that some people you know do not really understand what it means to have HIV. They may not understand how it is passed on, be afraid, or judgmental. Stigma causes many people living with HIV to feel ashamed about their HIV positive status and to hide it, which can have a negative impact on living positively. Dealing with stigma is hard, so seek support from someone you trust, a support group, a counselor, and your doctor.
147	Social/Behavioral	Mental Health	Stress	If you are HIV infected, you and your loved ones constantly have to deal with stress. Stress is unique and personal to each of us. When stress does occur, it is important to recognize the fact and deal with it. Some key approaches to handle stress are to try physical activity, it helps release tension and keeps your body healthy. Try to take care of yourself, by eating well and getting enough sleep. And finally, talk about it. It can help to talk about your worries and concerns with a friend, counselor or doctor.
148	Social/Behavioral	Sexual risk reduction	Abstinence	What is the surest way to avoid getting infected or passing HIV to a partner? The answer is that abstinence is the only 100% guarantee for preventing the transmission of HIV. Abstinence from oral, anal, and vaginal sex, abstinence from sharing of needles or syringes or abstinence in general from coming into contact with any infectious material is the only 100% guarantee of not getting HIV. Other measures can reduce the possibility of infection, but can't prevent it 100%.

149	Social/Behavioral	Sexual risk reduction	Alternatives to penetrative sex	To reduce the risk of HIV, you can enjoy different kinds of sex that don't include penetration. Kissing, cuddling, masturbation, mutual masturbation and massage are safe, so is ejaculating on unbroken skin. Oral sex and using your fingers have some risk, but the risk is quite low. Agree on ways of sexual expression that fit with the level of risk you are comfortable with.
150	Social/Behavioral	Sexual risk reduction	Anal health	Anal sex can be a pleasurable experience for gay men, but there are a few things you should do to take care of your health. Friction from anal sex can cause fissures or hemorrhoids. Using plenty of water-based lubricant can help prevent this, but if you do experience it, see a doctor. You may also be at risk for anal warts and anal cancer caused by the common sexually transmitted HPV virus. So you should have a doctor's exam every year to check on your anal health.
151	Social/Behavioral	Sexual risk reduction	Condoms 1	Q: If I use a condom, am I completely safe from getting infected or passing HIV to my partner? A: Latex condoms significantly reduce the risk of HIV and other sexually transmitted diseases, but they do not guarantee 100% against HIV infection. Condoms are most effective when they are stored in a cool dry place, removed from the package without being damaged, and correctly put on and removed from the penis. Never reuse a condom. Use water-based lubricants rather than oil-based lubricants, since oils can cause condom breakage. Proper condom use means no penetration without it.
152	Social/Behavioral	Sexual risk reduction	Condoms 2	Condoms should be stored in a cool, dry place away from sunlight. The expiration date on the package should be strictly followed. Opening the package should be done with care, as carelessly ripping the package or using one's teeth to open it may cause breaks in the condom. You should pinch the tip of the condom while rolling it onto the penis to allow space for sperm to collect after ejaculation. Make sure the penis is erect before putting on the condom, otherwise it may slip off during intercourse. After sex, hold the base of the condom as you pull out to avoid slippage or leakage. Latex condoms stop HIV and STDs, however if the condom breaks or spills occur during sexual intercourse, infection may be possible.
153	Social/Behavioral	Sexual risk reduction	Condoms 3	Prevent transmitting HIV to others or re-infecting yourself by using a condom every time you have sex. Remember to check that the package is sealed, and the expiry date has not passed. Heat and strong sun can damage condoms. They should be stored in a cool dry place. Condoms can break if they are poorly stored, expired, damaged or incorrectly used. Check the expiry dates before you unwrap the condom from the package.
154	Social/Behavioral	Sexual risk reduction	Condoms 4	For condoms to be effective, they need to be used correctly. Do not unroll the condom before putting it on the penis. If the penis is not circumcised pull back the foreskin before putting on the condom. Make sure to tear the packet carefully so as not to damage the condom. Only put on the condom when the penis is fully erect. Make sure the condom is put on the right way up. Hold the tip of the condom with one hand and roll down with the other hand. When you are finished, unroll the condom immediately. Do not spill the contents of the used condom. Tie the condom and discard in the trash can.
155	Social/Behavioral	Sexual risk reduction	Disclosing to new partners	If you are living with HIV, you will need to talk to any new partners about your status or about safe sex. This can be difficult because you may not know the person well or know how to gauge their reaction. You may favor a direct approach and simply inform your potential new partner that you have HIV. Or you may want to initiate a discussion about safer sex. However, you approach it, informing potential partners of your status before you have sex is important.
156	Social/Behavioral	Sexual risk reduction	HIV-positive partners	Even when both partners are HIV positive, it is still recommended that you use condoms. Apart from HIV infection, condoms also protect you from other sexually transmitted diseases. Condoms can also protect you from acquiring a different strain of HIV, which is called “reinfection”. Reinfection with a new strain of HIV can have a serious impact on the progression and severity of the disease. So, it’s best to always use a condom.
157	Social/Behavioral	Sexual risk reduction	HPV vaccine	Q: Should I get the HPV vaccine? The HPV vaccine is recommended for sexually active individuals under age 26, to prevent the possibility of getting genital warts and cancer brought about by some strains of the *human papillomavirus* or HPV. The HPV vaccine is given as a three-dose series

				over six months. It is best to be vaccinated before your first sexual contact, but later vaccination may still protect you if you have not already been exposed to HPV.
158	Social/Behavioral	Sexual risk reduction	Lube	For men having sex with men, you can reduce the risk of HIV transmission by using plenty of lubricant any time you have anal sex. Water-based lubes can be used with latex condoms, but oils, lotions, and conditioner can cause latex condoms to break. Lube reduces the amount of tearing in the rectum and anus. Tearing exposes blood and helps HIV transmission happen, so using plenty of lube can help protect you and your partners.
159	Social/Behavioral	Sexual risk reduction	Oral sex	Q: Is oral sex less risky than vaginal or anal sex? A: Oral sex is much less risky than anal or vaginal sex – but it is still possible for HIV to enter through open cuts and sores. Use of a non-lubricated or flavored condom when performing oral sex on a male is the best way to reduce the risk of HIV and other STDs. Using a lubricated condom is fine, but not ideal as the taste can be bad. A condom that is cut open can be used to cover the vagina or anus for performing oral sex on a female or for oral-anal sex.
160	Social/Behavioral	Sexual risk reduction	Oral sex 2	Q: I know it's best to use a condom but is there any way to make oral sex without a condom safer? A: Oral sex is much less risky than anal or vaginal sex – but it is still possible for HIV to enter through open cuts and sores. To reduce your risk even more, make sure you keep the mucous membranes in your mouth healthy – don't perform oral sex for about 45 minutes after you brush your teeth or floss, and not at all when you or your partner have open sores on your mouth or genitals. The safest approach for orals sex is to use a condom, preferably non-lubricated or flavored one.
161	Social/Behavioral	Sexual risk reduction	Oral sex and STDs	Q: If a person has a wart or a cold sore in his mouth and performs oral sex on me, can I get them too? Yes, skin to skin contact is the primary mode of transmission of HPV, the virus that causes genital warts, and also of Herpes simplex, of the virus that causes herpes sores. This does not mean, however, that after a single contact, you will get infected. The transmission depends on the amount of virus in the lesion and the immune system. It is always best to use condoms when engaging in oral or anal sex to protect yourself from STDs.
162	Social/Behavioral	Sexual risk reduction	Partners	A lot of people are into the hook up and dating scene these days. One way to reduce your HIV risk when on the dating and hook up scene is to try to have one regular sex partner instead of one-night-stands or anonymous partners. Whenever you are having sex with someone whose HIV status you don't know, you should use a condom.
163	Social/Behavioral	Sexual risk reduction	PEP	If someone is accidentally pricked by a needle previously used by a person who is HIV positive, or if someone has had unprotected sex with an HIV positive individual, it is important to seek medical consult immediately. The physician may start post-exposure prophylaxis, or "PEP", which is a combination of medications that can help prevent HIV infection after exposure.
164	Social/Behavioral	Sexual risk reduction	PrEP	PrEP, or pre-exposure prophylaxis, is an HIV prevention method for people who are HIV-negative. It involves taking a daily anti-HIV medication to reduce the risk of becoming infected with HIV. Several studies have shown that, when taken as directed, PrEP dramatically reduces the risk of becoming infected when combined with other prevention services. PrEP is not yet widely available in the Philippines, but some Filipinos have travelled to other countries to access it.
165	Social/Behavioral	Sexual risk reduction	Pulling out	Condoms are always recommended, but some guys don't use condoms, or don't use them all the time. If condoms are not part of the picture, there are other ways you can still make sex less risky. During sex, the partner who is topping should always pull out before he ejaculates to reduce the risk of passing on HIV. Pulling out is not considered safe sex, because the pre-ejaculate does contain HIV, but it is still a better alternative to ejaculating inside without a condom. Pulling out is not considered safe sex, because the pre-ejaculate DOES contain HIV, but it is still a slightly better alternative to ejaculating inside without a condom. This advice is the same for anal sex, vaginal sex, or for oral.
166	Social/Behavioral	Sexual risk reduction	Seropositioning	Condoms are always recommended, but some guys don't use condoms, or don't use them all the time. If condoms are not part of the picture, there are other ways you can still make IT less risky. One way is to have sex only with guys of the same HIV status as

				you, this is called serosorting. Or, if you don't have the same HIV status, it's safer for the HIV-negative person to top and for the HIV-positive person to bottom, this is called seropositioning.
167	Social/Behavioral	Sexual risk reduction	Sex toys	Using sex toys can be an enjoyable and less risky alternative to penetrative sex. However, if sex toys are shared between more than one person, then there is a risk that they can spread STDs or HIV. Use a toy on only one person at a time and wash it with hot water and soap between uses. You can also use condoms on a sex toy and change the condom between uses.
168	Social/Behavioral	Sexual risk reduction	Sex with undetectable VL	People often ask if it is safe for someone who has undetectable viral load to have unprotected sex. Undetectable viral load means that the tests that are used to check for the amount of virus in the blood cannot detect any virus. It does not mean that someone is HIV negative. As for having unprotected sex, you will need to discuss the risks with your partner before you make up your mind about it. Having an undetectable viral load makes it much less likely to pass on HIV, but there is still a chance that it could be transmitted. Regardless of viral load, it is recommended that if you have HIV, you should always use a condom.
169	Social/Behavioral	Sexual risk reduction	Spermicides	Did you know that while spermicides reduce the risk of pregnancy, they may actually increase the rate of HIV transmission? Compounds present in spermicides may irritate the vaginal lining and increase the risk of infection. Latex condoms and water-based lubricants are still the most effective means of preventing HIV and other STDs.
170	Social/Behavioral	Sexual risk reduction	STD exposure	If you've had unprotected oral sex with an HIV negative individual who was recently diagnosed with an STD, your physician may choose to give you post-exposure treatment for the specific STD that your sexual partner had. It is important for you to disclose this to your doctor or to seek consult immediately.
171	Social/Behavioral	Sexual risk reduction	STDs - HPV	Did you know that it's possible to get anal warts and other STDs from sharing sex toys? Warts are transmitted by skin-to-skin contact and by sharing inanimate objects that contain viral particles. *Human papillomavirus* or HPV, the virus that causes warts, is very hard to kill, and the viruses may remain on moist inanimate objects. This is why you should use a clean condom on sex toys every time they will be used by a different person.

Original Paper

Interactive Mobile Phone HIV Adherence Support for Men Who Have Sex With Men in the Philippines Connect for Life Study: Mixed Methods Approach to Intervention Development and Pilot Testing

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Abstract

Background: The HIV epidemic in the Philippines is one of the fastest growing epidemics globally, and infections among men who have sex with men are rising at an alarming rate. The World Health Organization recommends the use of mobile health (mHealth) technologies to engage patients in care and ensure high levels of adherence to antiretroviral therapy (ART). Existing mHealth interventions can be adapted and tailored to the context and population served.

Objective: This study aims to create a locally tailored intervention using a mobile phone platform to support treatment adherence for HIV patients on ART in the Philippines.

Methods: A mixed methods approach guided by the Behavior Change Wheel framework was used to adapt an existing mHealth adherence support platform for the local setting and target population. A literature review, retrospective clinical record review, and focus group discussions with patients were conducted to understand the drivers of ART adherence and tailor the intervention accordingly. The resulting intervention was pilot-tested for 8 weeks, followed by focus group discussions with patients who received the intervention to assess the acceptability of the design.

Results: Key issues contributing to nonadherence included side effects, lack of behavioral skills for pill taking, social support, mental health, and substance use. Patients identified mHealth as an acceptable mode of intervention delivery and wanted mHealth services to be highly personalizable. The study team, clinicians, and software developers integrated these findings into the intervention, which included a menu of services as follows: pill reminders, health tips, adherence feedback, appointment reminders, and symptom reporting. During the pilot phase, technical issues in the interactive voice response system (IVRS) were identified and addressed. Patients who participated in the pilot phase expressed a preference for SMS text messaging over the IVRS. Patients responded positively to the appointment reminders and health tips, whereas patient feedback on daily and weekly pill reminders and adherence feedback was mixed.

Conclusions: The mobile phone–based SMS text messaging and IVRS intervention was acceptable to men who have sex with men in Manila, the Philippines, and qualitative analysis suggested that the intervention helped promote ART adherence and appointment attendance.

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KEYWORDS

mHealth; adherence; HIV; antiretroviral therapy; intervention development; mobile phone

Introduction

HIV on the Rise in the Philippines

The Philippines has the fastest growing HIV epidemic in the Asia-Pacific region [1-3]. National surveillance data show that the number of new HIV cases in the Philippines has increased at an alarming rate during the past decade, with an increase from 311 cases identified in 2007 to 12,778 cases identified in 2019—a 41-fold increase in new HIV diagnoses [4]. According to the surveillance reports by the Joint United Nations Program on HIV/AIDS, the Philippines' progress toward reaching HIV/AIDS 90-90-90 goals has been slow, with 73% of people living with HIV being aware of their status, 44% on treatment, and low coverage of viral load testing (<50%) [5,6].

The group most impacted by HIV in the Philippines is men who have sex with men (MSM), representing 84% of new diagnoses since 2015. The median age of new cases is 28 years, and >80% of people living with HIV/AIDS in the Philippines are aged <35 years [4,7]. In 2015, a national surveillance survey found that HIV prevalence among MSM who practiced anal sex was 6%—an increase from 3.3% in 2013 [4-6,8-10].

As the burden of HIV increases, it is imperative that as many HIV-infected people as possible are diagnosed, started on treatment, and successfully retained in care. Achieving adequate viral suppression through the use of antiretroviral therapy (ART) will be one of the key tools in ending the HIV epidemic in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and ensuring high levels of adherence to ART and retention in care [8,10,11]. As in many low- and middle-income countries, high rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence led to poor outcomes for many HIV patients in the Philippines [12,13].

Evidence-based public health interventions are required. However, a 2015 report by the World Health Organization highlights that the body of HIV research conducted in the Philippines has been limited [14], and a systematic review of HIV risk studies in the Philippines through April 2018 found only 3 publications that included data about the group most affected by HIV—MSM [15].

Mobile Health for Adherence

As mobile phone technologies have become widespread in low- and middle-income countries, mobile phone interventions have become increasingly popular in the global health and development sectors as a potentially inexpensive and efficient way to communicate with and deliver services to people.

Mobile phones are multifunctional tools that can be used for a variety of functions that range from simple alarm functions, SMS text messaging, calls, interactive voice response systems (IVRSs), and complex apps and games. People usually have their mobile devices with them; therefore, using mobile technologies allows the timing of the intervention delivery to be synchronized with the most relevant time to claim the attention of the recipient [16]. Moreover, mobile phones can be used almost anywhere. As wireless coverage is improving globally, mobile communications can be provided even in remote areas.

In the Philippines, 99% of the population is reached by mobile cellular network coverage and mobile phone use is among the highest in the world, with 155 mobile connections per 100 people [17,18]. Although the coverage of mobile networks is high, smartphone coverage and mobile internet (Long-Term Evolution) speeds are lower in the Philippines than in other countries in the region [19], which limits the potential reach of mobile internet and app-based solutions.

The 2016 World Health Organization Consolidated Guidelines on the Use of ART for the Treatment and Prevention of HIV Infection promoted the use of SMS text messaging to improve adherence to therapy [20]. Research has shown that mobile health (mHealth) interventions have potential benefits for a wide variety of health issues, including antiretroviral adherence, smoking cessation, diabetes control, maternal health, and vaccination programs [16,21].

Mobile phone interventions have proven successful in improving ART adherence in Africa, South Asia, and Latin America [22-28]. Several systematic reviews have been published regarding mHealth for ART adherence specifically [29,30]. A variety of mHealth approaches to improve adherence to antiretroviral medications have been studied globally, including daily and weekly short text messages [22,31-33], weekly long text messages [31], weekly voice messages [34], and fortnightly phone calls [35,36]. The outcome measures of ART adherence interventions vary; outcome measures include self-reported adherence, objective measures of adherence (ie, pill count, pharmacy refill, and medication monitors), biological end points (ie, viral load suppression), and quality-of-life measures.

In Kenya, 2 important examples of successful ART adherence interventions were implemented. At the WelTel Kenya1 multisite randomized clinical trial of HIV-infected adults initiating ART, adherence to ART was reported in 61.5% (168/273) of patients receiving the SMS text messaging intervention compared with 49.8% (132/265) of patients in the control group (relative risk for nonadherence 0.81; P=.006). Suppressed viral loads were reported in 57.1% (156/273) of

patients in the SMS text messaging group and 48.3% (128/265) of patients in the control group (relative risk for virologic failure 0.84; *P*=.04) [22].

Another randomized trial of 131 adult patients who had initiated ART less than 3 months before enrollment found that 53% of participants receiving weekly SMS text messaging reminders achieved adherence of ≥90% during the 48 weeks of the study, compared with 40% of participants in the control group (*P*=.03). Participants in groups receiving weekly reminders were also significantly less likely to experience treatment interruptions exceeding 48 hours during the 48-week follow-up period compared with participants in the control group [31].

Multiple reviews of the literature on adherence programs suggest that mobile phones are a feasible, acceptable, and effective mode of delivery for HIV interventions targeting young MSM [37-40]. There is also evidence that daily reminders can support habit forming over 2-3 months and that weekly reminders effectively support adherence [23,25,29,41,42]. It is not clear whether improvements in adherence are sustained if reminders are stopped once a habit is formed. Some evidence suggests that weekly messages with interactive elements that elicit a response from the user may be the most effective SMS text messaging adherence interventions, but many questions remain unanswered [23,24].

Aim and Objective

The investigators aim to create a locally tailored intervention using a mobile phone platform to support treatment adherence for HIV patients on ART at the study clinic in Metro Manila, Philippines.

The objective of the formative research phase of the study is to adapt an existing technology platform (Connect for Life) for the local context. We seek to answer the following questions:

- What is the level of adherence in the study clinic population and similar populations in the country and region?
- What are the barriers to and determinants of ART adherence among the study clinic population?
- What components should an mHealth intervention include to address these barriers and determinants?

Methods

Setting

The Sustained Health Initiatives of the Philippines (SHIP) Clinic is a public-private partnership that opened in 2012. It is a low-cost, private facility in Metro Manila, a city of approximately 13 million people in the predominantly Catholic country of the Philippines and the most densely populated city in the world. As of April 2021, the SHIP clinic provided HIV primary care and wraparound services to approximately 900 patients. Between 2012 and 2018, SHIP was a satellite partner clinic of the Sexually Transmitted Infection/AIDS Guidance Intervention and Prevention Unit at the Philippine General Hospital, the largest public hospital in the country.

Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at the initial consultation. Most are employed full time or part time. The patients come from all regions of Metro Manila, and some live outside of Metro Manila in other provinces. SHIP currently enrolls approximately 4 new patients each month.

Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All patients provided written consent before inclusion in the study.

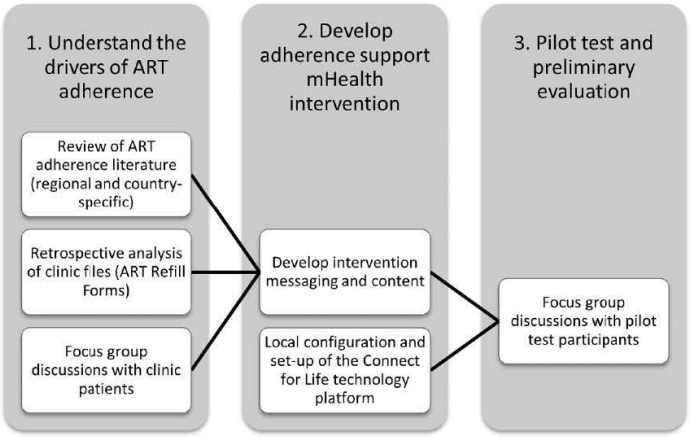
Intervention Development Approach

Overview

To determine the best configuration of mobile phone support services for patients in the study site, we used the following methodology (Figure 1):

1. Formative research to understand the drivers of ART adherence: literature review of factors associated with ART adherence (global, regional, and country-specific data), retrospective analysis of clinic files (ART refill forms), and focus group discussions (FGDs) with patients in the SHIP clinic.
2. Development of mHealth intervention: we adapted an existing mHealth adherence support platform, tailored it to the setting and target population, and pilot-tested the platform, guided by the Behavior Change Wheel (BCW) approach.
3. Pilot test and preliminary evaluation: we piloted the intervention with a subset of clinic patients for 8 weeks and then conducted FGDs with patients who received the intervention in the pilot phase.

Figure 1. Intervention development process. ART: antiretroviral therapy, mHealth: mobile health.



Formative Research to Understand the Drivers of ART Adherence

Review of ART Adherence Literature

A literature review of regional, country-specific, and site-level routine clinical data on ART adherence was conducted by the investigators. The literature provided point estimates for adherence that could serve as a comparison with our study population and outline some of the main facilitators of and barriers to adherence in the Philippines context.

Retrospective Analysis of Clinic Files

A record review of all pharmacy refill forms from the study clinic was conducted. Data were captured from 3381 pharmacy refill forms collected during routine clinical care for 682 patients between May 2012 and August 2016. The pharmacy refill forms included basic demographic information, dispensing data, pill count, and self-report of the number of doses missed in the past 30 days. Data quality for these forms was poor, with missing forms, fields left blank, and inconsistent or conflicting data in a large proportion of the records. Owing to these limitations in data quality, only the most recent refill form for each patient was included in the analysis, as data were much more complete in the recent forms. The estimate of adherence was calculated as follows:

> Adherence percentage = 1 − (number of pills reported missed since last visit/number of pills dispensed at the last visit) **(1)**

FGDs With Clinic Patients

During the formative research stage, the study team conducted FGDs to explore adherence challenges and possible approaches to support adherence. The specific topics covered during the discussions were adherence challenges, use of mobile phones, attitudes toward receiving adherence reminders, priority health education topics for mHealth tips, and acceptability of receiving an adherence score as a feedback mechanism.

Focus group participants were recruited through convenience sampling of clinic patients as identified by the SHIP clinic physician. Patients were eligible to participate if they were aged ≥18 years, HIV-positive and on ART at the SHIP clinic, and willing to participate in a group discussion setting. Privacy around HIV-positive status was the biggest barrier to recruitment, and only patients who were publicly open about their HIV-positive status participated in FGDs.

Each FGD was facilitated by a qualified HIV test counselor who was experienced in qualitative methods. A second staff member took detailed notes throughout the session, and immediately after the discussion, the notetaker and facilitator debriefed and recorded their initial observations. The FGDs were conducted in a mix of English and Filipino, which is common in Metro Manila. The discussions were held in a hired conference room located in the building next to the SHIP clinic, selected for the convenience of the participants. Before the discussion, the participants completed the informed consent process and provided demographic data and ART adherence data using a short questionnaire. The FGDs were audio recorded on 2 devices, and the discussions ranged from 60 to 105 minutes.

The FGDs were transcribed, and a framework-guided rapid analysis was conducted. Transcripts were manually coded using a deductive coding methodology in which initial coding grouped responses into overarching themes as per the topic areas included in the FGD guide. Following initial coding, line-by-line coding was used to assign the subthemes. Qualitative data were consolidated in a structured template based on the a priori research questions. The template enabled the consolidation of data into matrices by each category to identify salient themes.

Develop Adherence Support mHealth Intervention

Develop Intervention SMS Text Messaging and Content

The intervention development process was broadly guided by the BCW developed by Michie et al [43-45]. Behavior change techniques (BCTs) related specifically to ART adherence were informed by the information-motivation-behavioral skills (IMB) model of ART adherence [46].

The BCW is a method for characterizing and developing behavior change interventions based on a comprehensive causal analysis of behavior (Figure 2) [45]. In the BCW approach, the intervention design process consists of 3 stages.

The first stage of intervention development is to understand the behavior. In this case, the specific target behavior is optimal adherence to ART, defined as taking at least 95% of the prescribed ART doses on time. To understand behavior, the BCW approach starts with the question, *What conditions internal to individuals and in their social and physical environment need to be in place for a specific behavioral target to be achieved?* On the basis of the formative research findings, the components of capability, opportunity, and motivation that interact to account for behavior in the BCW approach were summarized [43-45]. Using the capability, opportunity, motivation, behavior (COM-B) model, we aimed to understand the challenges faced by patients and identify opportunities to address specific behaviors through the provision of BCTs.

The second stage of intervention development in the BCW model is to identify the intervention options. In this case, we planned to use an mHealth platform that would be tailored to the setting and population.

The third stage is to identify the content and implementation options, including BCTs and mode of delivery. To better understand the most appropriate BCTs, we referenced the BCW taxonomy of BCTs [47] and IMB skills model of ART adherence (Figure 3) [46]. IMB is a useful behavioral theory for exploring factors that lead to adherence and is supported by robust evidence [46,48,49]. It posits that adherence-related information, motivation, and behavioral skills are the fundamental determinants of adherence to ART. The model's mediational assumption asserts that ART adherence information and motivation generally work through ART adherence behavioral skills to affect adherence behavior. We used the IMB skills model to identify the aspects of motivation, information, and behavioral skills that our intervention might target.

The intervention services were tailored based on input from the IMB skills model, input by SHIP patients during FGDs, and information from clinical service providers at the study site. The study team and clinicians worked together to write 210 health tips, script the reminder messages, and map the call flows. The lead clinic physician created a symptom-reporting algorithm. A local voice talent agency was engaged to record the content. Figure 4 provides examples of tips in each of the health tip categories.

Figure 2. The Behavior Change Wheel [45].

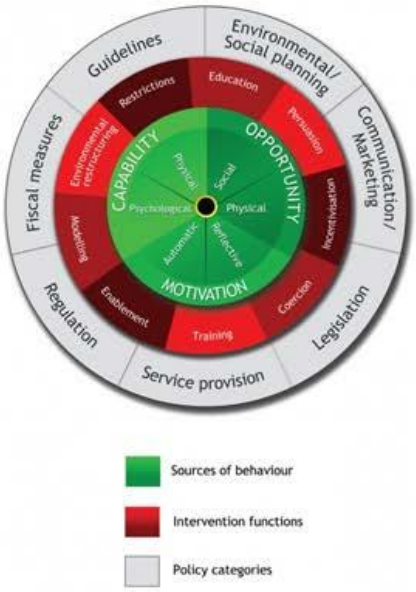


Figure 3. The information-motivation-behavioral skills model of highly active antiretroviral therapy adherence [46]. HAART: highly active antiretroviral therapy.

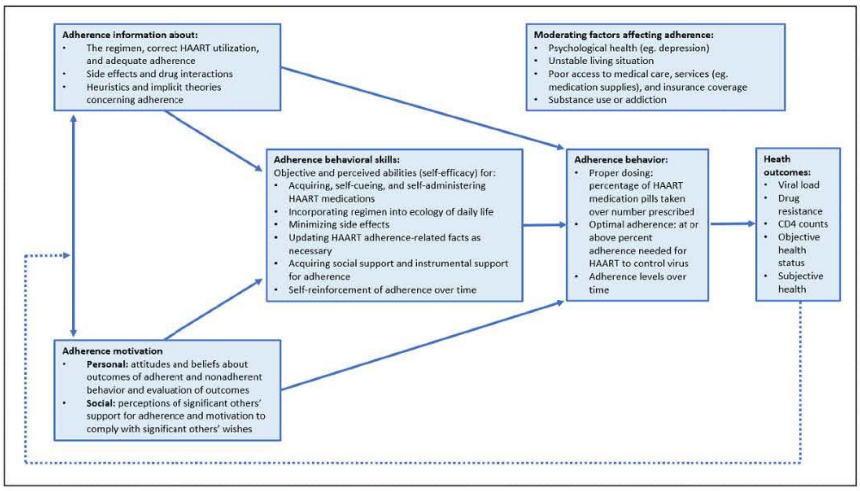
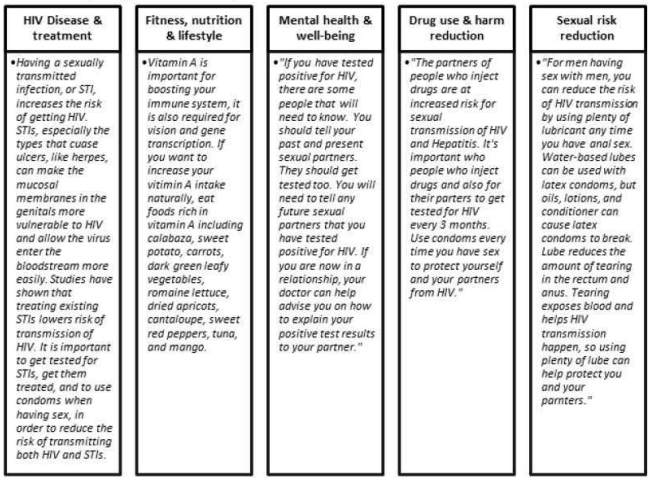


Figure 4. Health tip topic areas and sample tips. STI: sexually transmitted infection.



Local Configuration and Setup of Connect for Life Technology Platform

From 2015 to 2016, SHIP staff worked with internet technology specialists and public health professionals from the study sponsor Janssen Global Public Health to adapt the Connect for Life platform for use at the SHIP clinic. Connect for Life is a technology built on the Mobile Technology for Community Health (MOTECH) open-source software platform [50]. It enables health facilities to connect to patients via their cell phones or feature phones through IVRS or SMS text messaging. It was piloted in India and Uganda before roll out in the Philippines [51,52].

The platform has the following functionalities: pill reminders, visit reminders, symptom reporting, health tips, and adherence feedback messages. The study team collaborated with clinic physicians and software developers to adapt the various functions of the Connect for Life platform to align with the needs of the patients, as documented in the formative research phase.

Pilot Test and Preliminary Evaluation

Overview

During the first 8 weeks of piloting the intervention, 62 patients were enrolled in the study. These patients received adherence reminder calls and health tips and reported their adherence via IVRS. During this pilot test phase, the feasibility and

acceptability of the intervention were analyzed before moving to a larger scale implementation phase.

Feasibility

To assess the feasibility of the intervention, use data from the Connect for Life platform were analyzed. This included the number of calls generated from the platform, the number of calls answered by the participants, and the outcomes of those calls.

Acceptability

To assess acceptability, 2 FGDs were held to assess user experience. All eligible study participants were invited to participate in the focus groups, of which only 5 agreed to participate in a FGD (the major barrier to participation in these FGDs was the difficulty of transport owing to the traffic congestions in Metro Manila). Participants discussed their experience with Connect for Life; their reactions to the reminders, health tips, and adherence feedback; their feedback on the call length and call frequency; and their suggestions for improving the system.

Results

Understanding Drivers of ART Adherence

Review of ART Adherence Literature (Regional and Country-Specific)

Globally, approximately 40% of patients report suboptimal adherence to ART [53,54]. In the regional Therapeutics, Research, Education, and AIDS Training (TREAT) in Asia cohort (which includes 12 clinical sites from Thailand, Hong Kong, Malaysia, the Philippines, and Indonesia) of the 1316 patients, 421 (31.99%) self-reported suboptimal adherence of <100% [13]. Similar to our Connect for Life study cohort, majority of the TREAT Asia group comprised a male (67%) population and was aged <40 years (66%); however, most participants of the TREAT Asia cohort were exposed to HIV via heterosexual contact (69%), whereas our study group was primarily homosexual. The study found that the adherence rate was the lowest during the first 6 months on ART and the rate improved the longer the patient was on treatment [13].

Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence of social support, and time spent on treatment [13,28,54-57]. In the Philippines context, issues of stigma and discrimination also emerged as a major barrier to medication adherence [1,58,59].

Retrospective Analysis of Clinic Files

On the basis of the pharmacy refill forms for SHIP clinic patients, 67.7% (317/468) of patients reported perfect adherence in the 30 days before their most recent refill, 31.8% (149/468) reported suboptimal adherence <100%, and 20% (94/468) reported adherence <95%. A retrospective review of pharmacy refill data is summarized in Table 1.

Table 1. Sustained Health Initiatives of the Philippines clinic adherence data from pharmacy refill forms (N=682).

	Value
Demographic information (n=542), median (IQR; range)	
Age (years)	32 (28.6-35.9; 21-72)
HIV history (years)	
Time since diagnosis	3 (1.8-5; 0-25)
Time from diagnosis to antiretroviral therapy initiation	0.2 (0.1-0.9; 0-21)
Time on antiretroviral therapy	2.4 (1.5-3.9; 0-10)
Adherence estimates for patients with 30-day adherence reported at the last pharmacy refill (n=468), n (%)	
100% adherence	317 (67.7)
Missed 1 dose—adherence (95%-100%)	55 (11.8)
Missed ≥2 doses—suboptimal adherence (<95%)	94 (20.1)

FGDs With Clinic Patients

We also conducted FGDs with 1.8% (12/682) of the participants regarding their adherence challenges. All participants were male, 75% (9/12) were homosexual, 25% (3/12) were bisexual, and 67% (8/12) had full-time employment. The time patients had been on ART ranged from 5 months to 6 years, with a median time of 4 years. Overall, 83% (10/12) of the participants reported that they sometimes forgot to take their medications and 42% (5/12) had missed a dose within the past 2 weeks.

FGD findings on the causal factors for ART adherence are summarized in Table 2.

Table 2. Causal analysis of antiretroviral therapy adherence behavior.

Reason for nonadherence	Illustrative quotes from FGD[a] participants
Inconsistent daily routines, change in habits, behavioral skills, or difficulties with timing of dose	
Common reasons that patients report missing doses include simply forgetting, being busy, being away from home, and changes in routine [57].	• "You usually...take it at home, not in the office; there are some instances when you calculated the time...so you have to be in the office to take it properly. Then when you are there, you forget to take it, it's because you're busy already working." • "The challenge that I faced with ARV[b]...I think it's very essential for those working in BPO [business process outsourcing], is adjusting the time when your schedule shifts, because it has to be taken during your sleeping time...And, you know, you can't disclose, 'I was late because I overslept because I was really high with my ARVs'."
Low social support	
Patients who have a treatment support person are more likely to be adherent [60]. Having a good relationship with the HIV primary care physician and clinic staff was an important factor.	• "My partner is really helping me a lot to adhere to the schedule in taking the medications...When my partner gets too busy, the tendency is that we both forget that I need to take the medications." • "The reason why most of the patients are lost to follow up is because they feel like they are treated like patients in other [HIV treatment] hubs. The reason why we continue going to SHIP is because we feel welcome, we feel like it's like an extension of our family. Unlike in other hubs – they feel they have to wait, they don't know if they are going to die on that day or that hour. They feel that they are not that important."
Medication side effects or type of regimen	
Experiencing an adverse drug reaction is associated with poor adherence [61]. Furthermore, a large cohort study in Southeast Asia found that patients taking an NRTI[c] + NNRTI[d] regimen had poorer adherence than those who initiated on an NRTI + protease inhibitor regimen [13]. This is most likely because of difficulty tolerating the central nervous system side effects of efavirenz, a theme that was noticed throughout our focus groups.	• "If we open a fresh bottle of ARV sometimes it feels kind of strong...It's like the first time. You feel all the side effects of the ARV." • "For me it really is the headache, especially this first few weeks." • "Especially when I was having a pneumonia, especially with interactions with antibacterials – It's really hard to actually take the ARV together with the other medicines because you will be getting a really, really painful stomach, even if you ate something. So sometimes in order for me to finish the whole course of the meds that's been described I have to skip if I really can't tolerate anymore."
Shorter time on ART	
Some studies show that longer duration on ART[e] is associated with better adherence [13]. Treatment-experienced FGD participants insisted that *newbies* would benefit most from the intervention.	• "For the newbies this would be a big help because for a while it's a way for them to adjust. Not all of them are still open in discussing their status with people, and this is a first step for them to accept the fact that they have this situation that they need to cope with. And to do that, it's like the IVR is helping [them]. So, it's a big help."
Substance use or abuse	
Patients who use illicit drugs or abuse alcohol may be less likely to adhere to their medication regimen [54,62]. Among our focus group participants, use of methamphetamine in the context of *Partee n Play* emerged as a theme.	• "[When you are high on drugs] You tend to delay it more and more. When you are high you are more carefree, it's like 'I'll take it later, then later, then later'…" • "I make it a point of, I have been with my friends taking drugs, and then I know that some of them have that schedule of taking the ARV. So I make it a point that I remind them to take ARV. It's like a sisterly bond, like 'Friend, it's your time…' You have to insist. It's like a responsibility within friends."
Stress, coping abilities, or poor mental health	

Reason for nonadherence	Illustrative quotes from FGD[a] participants
People living with HIV are more likely to be affected by depression and anxiety [54,55]. Focus group participants stated that coping with a new diagnosis can be overwhelming. Interruptions in treatment for patients who have been in care for several years may be caused by episodes of depression.	• "The only reason why we really skip for days is like when you are really depressed. And drugs, with your serotonin and dopamine levels really low and you're really emotional. You tend to be like 'my life sucks and I don't want to take my meds.'" • "You mentioned harm reduction – okay, yes. Could be. Another thing we are not really addressing is mental wellness...It's one reason why we consciously skip our medication, is our mental wellness."
Stigma	
Many people living with HIV are fearful of the repercussions of disclosing their status (or having it disclosed inadvertently) to family, friends, or employers [33,55,63,64]. Focus group participants shared their fears and their experiences that disclosing their diagnosis could result in personal rejection, losing their housing (multi-generation family homes are the norm in Philippines), or being dismissed from their jobs. They do not want to be seen taking medicines around other people. The psychological challenges of coping with and accepting an HIV diagnosis during the early stages is a major factor for nonadherence.	• "For me I've been battling this on my own for 6 years. None of my relatives know that I'm positive. The only people that know that I'm positive are my friends. So, I think this reminder thing...the IVR thing, the health tips, is really good." • "I think there is one point that I when I consciously, not really skipped, but delayed it 4 to 6 hours, just because when that alarm went really crazy everyone was looking at me...There's this thing now that gay people are being judged when we take our meds in public...That's why it's hard to have that really loud alarm now."

[a]FGD: focus group discussion.

[b]ARV: antiretroviral.

[c]NRTI: nucleoside reverse transcriptase inhibitor.

[d]NNRTI: nonnucleoside reverse transcriptase inhibitor.

[e]ART: antiretroviral therapy.

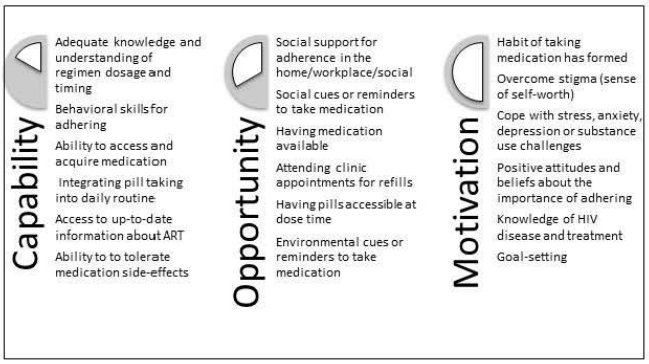
Development of the mHealth Intervention

Overview

The intervention services were tailored based on the input from SHIP patients and clinicians during formative research.

On the basis of the formative research findings, the various components of the COM-B framework were summarized, incorporating the aspects of the IMB skills model of adherence (Figure 5).

Figure 5. Summary of the components contributing to optimal antiretroviral therapy adherence based on the capability, opportunity, motivation, and behavior and information, motivation, and behavioral models. ART: antiretroviral therapy.



The focus group findings suggested that mobile phones would be an acceptable mode of delivery for HIV interventions targeting young MSM in the Philippines. During the FGDs, participants provided detailed input about the acceptability of various intervention aspects, including pill reminders, health tips, visit reminders, adherence feedback, and symptom reporting.

mHealth Intervention Preferences

Patients reported that they would like mHealth services to be personalizable. For example, patients requested to be able to select whether they receive pills and visit reminders via SMS text messages or via calls, as well as to determine the frequency and the time of the day that they receive reminders. Participants believed that newer patients who recently started ART would benefit most from daily pill reminders and experienced patients

would prefer less frequent reminders. They stated that it would be important to be able to opt in or out of any call or SMS text messaging services at any time.

Patients expressed a strong interest in health tips that covered a variety of topics, not strictly HIV disease, and they wanted to personally select which categories of health tips they would hear.

In summary, patients suggested that an ideal mHealth service should be personalized based on the following factors: (1) call or SMS text messages, (2) timing of calls or messages, (3) frequency of calls or messages, and (4) content or topic areas for health education messages.

mHealth Intervention Configuration

The investigators created a standard service scheme (Table 3) that could be adjusted at the patient's request. The recommended service scheme included *pill reminders* for all patients. As focus groups and literature review suggested that more intensive adherence support is required in the early stages of HIV treatment while forming of habits, ART-naïve patients and patients in their first 24 weeks of ART received reminders daily for the first 24 weeks and weekly for the next 24 weeks. Patients who were experienced with ART received weekly reminders for 24 weeks and no reminders after 48 weeks.

During IVRS pill reminder calls, patients were prompted to *report symptoms or side effects* of medications using an IVRS touch-tone menu. The patients received SMS text message recommendations for over-the-counter medications and advice depending on the algorithm outcome. The system automatically generated an alert for the clinician of any symptom reports that required urgent attention.

All patients received SMS *appointment reminders* at 2 set times in advance of their scheduled clinic visit date.

All patients who received IVRS calls for their pill reminders could receive a weekly *adherence feedback* message informing them of their *score*—from 0 to 7—based on the number of days they reported taking their doses in the prior week via the IVRS platform. The adherence feedback score was followed by a short motivational message to encourage improvement among patients with low adherence or support continued good adherence among patients with high adherence scores.

Patients would automatically receive audio *health tips* when they received pill reminder calls, or they could opt to receive health tips via SMS text messages. For patients new on ART, there was a tailored set of health tips that explained the basics of HIV and ART. In addition, we created tips on a variety of other health topics based on the suggestions of patients from the FGDs. The following five broad categories were selected for health tips: (1) HIV disease and treatment, which include tips about HIV testing and diagnosis, transmission of HIV, coinfections, and laboratory tests for people living with HIV; (2) fitness, nutrition, or lifestyle, which included tips for exercise and eating healthy; (3) mental health or well-being, which included tips on acceptance and disclosure of HIV status, and approaches for understanding and dealing with depression, anxiety, and stress; (4) drug use and harm reduction, which included medical information about common recreational drugs, safer injection, and hepatitis C; and (5) sexual risk reduction, which included tips on condoms and lubricants and tips on leading a healthy sex life with HIV.

The investigators worked with 2 clinic providers and a local voice talent agency to write and record 210 health tips that related to the common questions and issues raised by patients and tips that incorporated the themes that emerged from the focus groups. The messages were crafted ensuring that they not only provided didactic information related to the health topic but also ended with a specific action or behavior that the patient could adopt to improve or to minimize the impact of a specific behavior.

The system was configured to protect patient privacy and prevent unintended disclosure of health information. Upon answering any call from the system, the patient would immediately hear a *jingle*, a song that was associated with the Connect for Life system. Upon hearing the *jingle*, they would enter a personal identification number to advance to the next step of the call. No health-related information would be transmitted unless the personal identification number was keyed in, to protect patient privacy and confidentiality.

Services in the intervention package address the 3 main components of the COM-B model. Capability is addressed through health tips, which aim to improve knowledge regarding ART and HIV disease and improve behavioral skills. Opportunity is addressed through the pill reminder service, which provides an external prompt or cue for pill taking and supports habit forming through the appointment reminder service, which prompts attendance at the clinic for refill, thereby increasing accessibility and availability of medications; and through the symptom-reporting algorithm, which addresses the medical barriers to pill taking by expediting a response to side effects or medication reactions. Motivation is addressed through health tips (eg, messages designed to help with stress, overcome stigma, and inform positive attitude toward pill taking) and adherence feedback messages, which reward and reinforce high adherence and encourage improvement for low adherence.

Table 3 presents the proposed service scheme. However, the services were flexible and a patient could opt out of any call or SMS text messaging service that they did not wish to receive or opt into services depending on their preference and the clinician's judgment. The clinician could reactivate or extend the pill reminders for patients who needed additional support.

Table 3. Connect for Life services scheme.

Patient characteristics	Pill reminder and adherence feedback messages (voice or SMS text messages)	Health tips (voice or SMS text messages)	Appointment reminders (voice or SMS text messages)	Symptom reporting (voice calls only)
Treatment naïve and recently initiated (<6 months on antiretroviral therapy), or treatment experienced more than 6 months with adherence <80% in the 30 days before enrollment	• Daily reminders from 0 to 24 weeks • Weekly reminders from 25 to 48 weeks	Health tips play during all pill reminder calls; health tips topics tailored to new patients	Yes	Yes (during all pill reminder calls)
Treatment experienced >6 months with adherence ≥80% in the 30 days before enrollment	• Weekly reminders from 0 to 24 weeks • No reminders from 24 to 48 weeks	Health tips frequency and topics selected based on the preference of clinician and patient	Yes	Yes (during all pill reminder calls)

Pilot Test and Preliminary Evaluation Findings

A pilot test phase was conducted from October 2017 to January 2018, in which 62 patients were enrolled in the service. During the pilot test period, we received reports of several technical issues that affected the functionality of the system. In all, 2 FGDs were held in January and February 2018, after approximately 3 months of the pilot project implementation. There were 5 participants—3 in one discussion and 2 in the next. FGD findings on the themes that emerged from the pilot test are summarized in Table 4.

On the basis of the findings from the pilot phase FGDs, enrollment in the study was suspended because of pending solutions to technical issues. The study team worked with software developers to trace the source of the technical issues. It was determined that the platform was functioning well and that the technical failures were because of issues within the local telecommunications infrastructure (ie, poor call quality). After the team addressed all the technical issues on the software development side, enrollment continued with SMS text messaging services only.

Since mid-2019, we have found that as telecom services improved in the Philippine setting, voice calls in the Connect for Life system can now be delivered with fewer technical issues. Following the initial pilot study, the intervention was scaled up at the SHIP clinic and currently serving 1491 patients at 2 HIV clinics. The platform is being further developed to move from the MOTECH base to open medical record system. We plan to pilot test the new version in several HIV treatment sites across the Philippines.

Table 4. Themes emerging from the pilot test evaluation.

Themes	Illustrative quotes from FGD[a] participants
CfL[b] technical issues or functionality	
• PIN[c] issues: DTMF[d] is the signal to the phone company that is generated when a user presses a telephone's touch keys. All FGD participants reported instances in which they attempted to enter their PIN code and the code was not recognized. The frequency of DTMF problems varied widely among the participants. • Call origin: Calls are generated from an interactive voice response platform using a United States–based telecom provider. The interactive voice response service provider sets the incoming call number to be displayed as the patient's own phone number. However, patients reported that this was inconsistent and that some of the incoming calls from the CfL system that they answered displayed phone numbers originating in different countries.	• "Actually, I just experienced that issue last night [DTMF malfunction]. Sometimes I have been able to enter [my PIN code] and sometimes I haven't. The jingle kept going on, so I kept entering the PIN again and nothing happened, so I just hung up." • "In my case, I think I received thrice already from various locations an unknown number that's why I didn't bother answering. One from South Korea, one from US and one from China. The problem is if the number is unknown basically I don't answer it. I'm just guessing that the number came from CfL."
SMS vs voice call preferences	
• There was mixed feedback about whether SMS text messages or voice calls were more effective or acceptable. Some participants said that the frequency and length of voice calls were too much. Several FGD participants requested to be changed from voice calls to SMS text messages, as texting is more convenient and less intrusive. Others preferred to stay on voice calls as they are more difficult to ignore.	• "I think SMS would be nice to have as an option. If at the time the program calls you but you didn't answer an SMS reminder would be good just to keep in touch." • "I hated the call because I've been receiving the calls especially when I'm on my way home in an Uber. If I mistakenly answer it without the headset, the voice will be loud and basically everyone in the Uber would know." • "If you are going to put the schedule of the consultation, I'd rather those to be in text because there's too much information that I need to remember." • "I think it's also cultural when people don't like answering calls. Mostly Asians I know don't like answering calls. I'm not good at answering calls and most of the people I know don't also like answering calls especially if the number is unknown and overseas and then you hear this very gloomy guy voice."
Adherence feedback *gamification*	
• Participants did not like receiving adherence feedback scores because it was inaccurate and made them feel stressed.	• "[The adherence feedback score] has no effect. It has no significance to me." • "For me I don't even care about it because it just stresses me out."
Pill reminders	
• Daily pill reminder calls were not as used as expected by the study team based on the findings from the first 2 focus groups. After the pilot phase, patients reported that, although they like the idea of regular reminder calls, in practice, they are often too busy to answer the calls and report their adherence. • The issue of poor uptake of pill reminder calls was further compounded by the technical issues with the entering their PIN code (DTMF issue). • Some participants said that the pill reminders did not make a big difference for them as they already had other systems in place to remind them to take their medications.	• "It helped. Sometimes I would forget but it would help to remind me because I usually take my pill after work, and after work I'm just so tired, I don't check the time and sometimes I almost forget because I'm so sleepy." • "I hate to be reminded that I have this condition every single day. I know I need to take it but I don't need to be reminded every single day that I have to." • "If you call seven times a week that's a bit irritating for the patient. What the patient can do is have the option to get reminded through text."
Health tips	
• The content of the health tips was useful and informative. All participants wanted to continue to receive health tips. • Some participants would prefer SMS text messages rather than voice recordings for the health tips. Some thought the voice recording spoke too slowly; therefore, they would prefer to read it by SMS text messages. • One technical issue reported was that sometimes the same health tips were received for multiple days instead of receiving a new tip each day, as intended.	• "The health tips are super helpful. Those are the tips about alcohol, and that say you can have sex, you are not prevented but protected. There are even those great tips on eating and what you should eat." • "Just the voice. The girl answering the questions in the health tips is okay. The guy is very depressing."

Themes	Illustrative quotes from FGD[a] participants
Other findings	
• Participants were enthusiastic about receiving the automated reminders for their clinic appointments. • Participants stated they would have liked a more in-depth orientation or onboarding process at the outset of the intervention. They emphasized the importance of onboarding, setting expectations, and a thorough explanation of the intervention. • Not all participants understood they could change or adapt the service model. • Peer support: Participants mentioned that they found participating in a FGD with other people living with HIV very helpful and asked if there could be an opportunity for the clinic to organize in person support groups.	• "But what I noticed was that it helped with the appointment. That was a big help as I was reminded that I had to go to the clinic. That's a big deal to me. But about missing the meds, it's still human." • "I think the program's good. I could recommend that for the newbies. I think the program should be laid on properly. For example, scheduling, the time, reminders, and the tips. Maybe after a month if the patient has already established a routine so maybe it could lessen the reminders." • "Besides, the importance of the support group is for patients who have not disclosed to family members. There you can get support or have conversations like this. If there were a support group now, I'd want to be a part of it because I would like to share what I have experienced before with others."

[a]FGD: focus group discussion.

[b]CfL: Connect for Life.

[c]PIN: personal identification number.

[d]DTMF: dial tone multifrequency.

Discussion

Principal Findings

The intervention development approach resulted in an mHealth intervention tailored to the information needs and communication preferences of MSM in the Philippines. The intervention was designed to address various aspects of capability, opportunity, and motivation to achieve optimal adherence to ART.

The formative research found that mobile phone use is widespread in the Philippines and that mobile phones are an acceptable mode of communication for health information and adherence support. The literature review and FGDs revealed that in our patient population, key behavioral barriers to adherence included challenges around forming consistent routines and habits, low social support, stress and mental health issues, substance use, and social stigma of living with HIV. Focus group participants strongly emphasized the need for social and family support to enable and encourage good adherence to ART. Key clinical issues affecting adherence included medication side effects (especially among efavirenz-based regimens) and shorter duration on ART.

Following the pilot test, recipients of the intervention reported that the tone, frequency, and content of the voice messages were acceptable and appropriate. In the prepilot focus groups, participants preferred the male voice actor whose voice sounded more "attractive" according to several participants, whereas in the postpilot groups, several participants mentioned that they preferred the female voice actor because her tone was warmer and she came across as a trusted friend. This finding indicates that more iterations of recording should be tested in future implementations before a full-scale roll out and that budgets and project work plans should allow for several rounds of recording. The accounts of the focus group participants indicated that the intervention increased their knowledge and adherence behaviors. However, a large-scale cohort is needed to assess the intervention's effectiveness.

In the prepilot focus groups, participants were enthusiastic about receiving voice reminders via phone calls, following their experience of participating in the pilot most participants expressed a preference for SMS text messaging over voice calls. This preference may have been related to the inconvenience of answering phone calls, and it may also have been related to the technical problems experienced with the IVRS. These technical challenges posed a significant challenge to the feasibility of the intervention, and delivery would need to be adapted to allow for SMS text messaging options to achieve full-scale implementation.

Strengths and Limitations

The strength of the intervention development process was the participatory approach, which included the beneficiaries or users of the potential intervention, clinical service providers, and developers of the technology platform. The views of the target audience were collected during focus groups, which informed the tone, style, frequency, duration, and content of the intervention.

The BCW is a robust intervention development approach that provides a comprehensive understanding of the sources of a behavior, spectrum of intervention functions, and environment in which the behavior occurs. A strength of this approach is the COM-B model at the hub of the BCW. By identifying the capabilities, opportunities, and motivations behind a behavior, we can clearly identify the most relevant intervention approaches and BCTs. This approach allowed us to develop a solid intervention plan that described the technique, mode, and content to address each identified barrier to or enabler of ART adherence.

A weakness of our approach was the sampling and recruitment strategy for the participants in the focus groups. It was a challenge to identify patients who were willing to participate

in a group where everyone had a HIV-positive status because many patients were not publicly *out* as people living with HIV, indicating that individual interviews may be an option in future studies. The patients who agreed to participate may not be representative of the wider patient population, introducing a degree of selection bias to the process. The study only included patients >18 years and the patients were almost exclusively male; thus, the findings do not address the distinct needs and challenges of adolescents and women living with HIV. In addition, there was low attendance among those who confirmed their intention to participate in the focus groups. This is reflective of the larger need to provide differentiated models of care in the Philippines, as transportation to the clinic site is not easy in Metro Manila because of traffic congestion.

Another weakness of our approach was that we had an intervention mode in mind—mobile phone—at the outset of the intervention development process. Although there are several key determinants of adherence that the Connect for Life platform can address (ie, knowledge, habit forming, and environmental cues to take medication), there are other factors that the mHealth approach does not address (ie, physical availability of medication and social support).

Notably, the technical challenges experienced in delivering the intervention during the pilot phase made it difficult to assess the true acceptability and feasibility of the planned intervention. Feedback received after the pilot phase focused largely on the mobile phone functionality issues, which then limited the discussion regarding the content and design of the intervention as it was intended to be delivered. Conducting a small pilot phase with a few participants allowed us to identify the problems with functionality and adapt the intervention before scaling up the intervention to the larger cohort; however, a more iterative process with several pilot stages would have been advantageous if budget and timeline had allowed us to do so.

Comparison With Prior Work

Research on ART adherence has shown that less time on ART is associated with an increased risk of poor adherence [13,65-67]. With this in mind, the intervention was designed with more frequent (daily) pill reminders for patients during their first 6 months on ART and less frequent (weekly) reminders for patients with longer than 6 months on ART. However, after the intervention design was completed and pilots, an analysis of the Philippine cohort found a different trend within the study population, observing that, even before receiving the intervention, newer patients in the Connect for Life cohort tended to be more adherent compared with patients who had taken ART for longer and showed signs of *treatment fatigue* [68]. This highlights the importance of the ability of clinicians to tailor the reminder frequency and other intervention functions based on individual patient needs.

Before this study, 2 other projects using the same technology that the Connect for Life program was built on were implemented and evaluated in India and Uganda. First, a program called Treatment Advice by Mobile Alerts (TAMA), provided people living with HIV in India with daily or weekly pill reminders, adherence feedback, automated algorithms for managing clinical events for patients being initiated on ART, health tips, appointment reminders, and real-time reporting to the clinics of patient interaction with TAMA. Evaluation of the TAMA pilot found that patients gave the platform a high system usability score and gave generally positive feedback about their experience with using the technology. In TAMA, patients could call a toll-free number to access health tips and a clinical event algorithm. Health tips were used by 76% (42/55) of the patients, and automated clinical advice was accessed by 64% (35/55) of the participants in the pilot study. In the Philippines, these functions were available only through outgoing system-generated calls and SMS text messaging because of the prohibitive cost of toll-free inbound telephone lines in the Philippine setting [51,69].

The second project, the Call for Life Uganda program, also found good uptake, acceptability, and positive response to the system. In Uganda, there was a strong preference for interactive voice response over SMS text messages, which was different from the Philippines where participants preferred SMS text messages [70,71].

Conclusions

Our research found that a mobile phone–based SMS text messaging intervention and IVRS intervention were acceptable to MSM in Manila, the Philippines, and the FGDs suggested that it helped promote ART adherence and appointment attendance. A randomized controlled trial is required to establish the effects of the intervention on the clinical outcomes of HIV care and treatment.

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Conflicts of Interest

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Abbreviations

ART: antiretroviral therapy
BCT: behavior change technique
BCW: Behavior Change Wheel
COM-B: capability, opportunity, motivation, behavior
FGD: focus group discussion
IMB: information-motivation-behavioral skills
IVRS: interactive voice response system
mHealth: mobile health
MOTECH: Mobile Technology for Community Health
MSM: men who have sex with men
SHIP: Sustained Health Initiatives of the Philippines
TAMA: Treatment Advice by Mobile Alerts
TREAT: Therapeutics, Research, Education, and AIDS Training

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Risk factors affecting adherence to antiretroviral therapy among HIV patients in Manila, Philippines: a baseline cross-sectional analysis of the Philippines Connect for Life Study

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Abstract. ***Background*:** The Philippines HIV epidemic is one of the fastest growing, globally. Infections among men who have sex with men (MSM) are rising at an alarming rate, necessitating targeted evidence-based interventions to reach epidemic control. Treatment as prevention is a key strategy to end AIDS, making it a priority to explore novel approaches to retain people living with HIV (PLHIV) in care, support adherence, and reach viral suppression. ***Methods*:** This cross-sectional analysis describes HIV-related risk behaviours and adherence to antiretroviral therapy (ART) in a population of HIV-positive patients at a clinic in Metro Manila, Philippines participating in the Philippines Connect for Life™ cohort study. ***Results*:** Among 426 HIV-positive adults taking ART, 79% reported ≥95% adherence over the prior 30 days. Longer time on treatment was associated with reduced adherence to ART (adjusted odds ratio (AOR) = 0.87 per year, $P = 0.027$). Being in a serodiscordant relationship, in which the subject's primary partner was HIV negative, increased adherence (AOR = 3.19, $P = 0.006$). Inconsistent condom use (AOR = 0.50, $P = 0.103$) and injection drug use (AOR = 0.54, $P = 0.090$) are potentially associated with reduced adherence to ART. Patients used drugs and alcohol at significantly higher rates than the general population. ***Conclusions*:** The study found that patients in this setting require intervention to address treatment fatigue. Interventions to improve social support of PLHIV, as well as harm-reduction approaches for drug and alcohol use, could improve adherence in this population, strengthening the test-and-treat strategy to control the epidemic.

Keywords: adherence, antiretroviral therapy, Asia, evidence-based policy, harm reduction, HIV/AIDS, men who have sex with men, people living with HIV, Philippines.

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Introduction

The Philippines has the fastest growing HIV/AIDS epidemic in the Asia–Pacific region.[1–3] National surveillance data show that the number of new HIV cases in the Philippines has risen at an alarming rate during the past decade, with an increase from 311 cases identified in 2007 to 11 427 cases identified in 2018 – a 36-fold increase in new HIV diagnoses.[4] According to the Joint United Nations Programme on HIV/AIDS (UNAIDS)'s surveillance reports, the Philippines' progress towards reaching HIV/AIDS 90–90–90 goals is slow, with 67% of people living with HIV (PLHIV) aware of their status, 48% of those who know their status on treatment, and low coverage of viral load testing (<50%).[5]

Young men who have sex with men (MSM) are the key population in this emerging epidemic. Early in the HIV epidemic, most diagnoses were among heterosexual females,

especially sex workers. Today, 85% of new cases are in MSM, the median age of new cases in the Philippines is 28 years, and more than 80% of people living with HIV/AIDS in the Philippines are aged under 35 years.[4] In 2015, a national surveillance survey found that HIV prevalence among MSM who practice anal sex was 6%, an increase from 3.3% in 2013.[6–8]

As the burden of HIV increases, it is imperative that as many HIV-infected people as possible are diagnosed, started on treatment and successfully retained in care. Achieving adequate viral suppression through the use of antiretroviral therapy (ART) will be one of the key tools in ending the HIV epidemic in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and then ensuring high levels of adherence to ART and retention in care.[6,8,9] As in many developing countries, high rates of first-line treatment failure, loss to follow up, and suboptimal treatment adherence lead to poor outcomes for many HIV patients in the Philippines.[10,11]

Evidence-based public health interventions are needed. However, a 2015 report by the World Health Organization (WHO) highlights that the body of HIV research conducted in the Philippines has been limited,[12] and a systematic review of the HIV risk studies in the Philippines through April 2018 found only three publications that included data about the group most affected by HIV, MSM.[13]

This study aims to describe the demographic profile, clinical characteristics, HIV-related risk behaviours, quality of life (QOL), and ART adherence levels in a population of HIV-positive individuals comprised primarily of MSM receiving treatment at the Sustained Health Initiatives of the Philippines (SHIP) Clinic in Metro Manila, Philippines.

Methods

Study design, participants, and setting

A cross-sectional analysis was conducted using data from the baseline visit of a cohort study of patients at the SHIP clinic. The purpose of the larger cohort study was to evaluate the Connect for Life™ mobile phone adherence support intervention. Data were collected from October 2016 to December 2018.

The SHIP Clinic is a public–private partnership, low-cost, fee-for-service facility in Mandaluyong, Metro Manila, which has provided HIV treatment and a comprehensive package of primary healthcare services to more than 900 patients since it opened in 2012. SHIP is a satellite partner clinic of the STI/AIDS Guidance Intervention & Prevention Unit at the Philippine General Hospital.

All patients starting or continuing on ART at the SHIP clinic who had a mobile phone and who spoke English (one of the two official languages in the Philippines and spoken fluently by nearly all of the patients from the study site) were eligible to participate in the study. Mobile phones were required because all patients who were enrolled would receive a mobile phone adherence intervention. The study coordinator approached patients during their routine clinic visits to provide information about the study and complete the informed consent process.

Measures

At the baseline study visit, the study coordinator collected demographic data and extracted medical history from the patient charts. Each participant completed a questionnaire on HIV-related knowledge, attitudes and practices (KAP) that was specific to the mobile phone adherence intervention and the WHO HIV Quality of Life questionnaire (WHOQOL-HIV BREF; https://www.who.int/mental_health/publications/whoqol_hiv_bref.pdf). Patients who had taken ART before also completed an adherence questionnaire that was adapted from the AIDS Clinical Trials Group tools. All questionnaires were in English. The questionnaires were self-administered, with assistance from the study coordinator as requested.

The self-reported adherence measure used a visual analogue scale (VAS) in which patients reported the proportion of ART doses taken in the prior 30 days from 0–100%. For ART to be effective, it should be taken consistently, and early studies reported that ≥95% adherence to ART was required to achieve and maintain viral suppression.[14,15] More recent studies have shown that virological suppression may be achieved with adherence levels <95%; however, this is dependent on the duration of treatment and the ART regimen.[16–18] Therefore, in this analysis, those who took ≥95% of their ART doses were considered adherent, and <95% as non-adherent.

Statistical analysis

Descriptive data analysis was conducted to categorise the study population. Categorical variables were described with proportions and continuous variables were described with means and confidence intervals (CIs). We examined which characteristics of individuals were associated with adherence to ART of >95%. Crude odds ratios (ORs) were calculated with logistic regression to examine which demographic, behavioural, and clinical factors are related to self-reported adherence. Factors significant at P-value <0.1 on univariate analysis were included in a multivariate logistic regression analysis. Clinical variables were excluded from the multivariate if there was plausible reverse causality between ART adherence and the clinical characteristics (i.e. viral load suppression). Where possible, continuous variables were used in the multivariate model, whereas categorical variables were used for illustrative purposes in the crude OR descriptive analyses. Data analysis was conducted in Stata 15 (StataCorp LLC).

Ethics

Ethical clearance was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016–265–01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All patients provided written consent before inclusion in the study.

Results

The cross-sectional analysis included 426 individuals. Variables were included in the following categories:

Demographics, Clinical Characteristics, HIV Knowledge, Risk Behaviours, QOL, Adherence/Reasons for Missing Medication.

At the time study enrolment began, the clinic had ~600 active patients. The study coordinator screened 485 patients as they presented during routine clinic visits, of whom 483 were eligible to participate in the study (one did not speak English, one did not have a Philippine mobile phone), and 462 patients provided consent and were enrolled (of the 21 who declined, the most common reason was that they did not want to receive calls or SMS related to the intervention). Of 462 people enrolled in the Connect for Life intervention study, 31 were either ineligible to fill out the adherence questionnaire (initiated ART at the study baseline visit and had not started taking pills) or had missing questionnaires; as a result 426 individuals reported ART adherence, and are included in this analysis. All but one of these 426 subjects were male (99.8%), and almost all were MSM (419/426 or 98.4%). The mean age was 32.4 years. University or post-graduate studies had been completed by 86% of participants (365/426), and 91% were employed (389/426), which reflects the higher socioeconomic status of patients who access private fee-for-service care.

Perfect adherence of 100% of doses taken in the past 30 days was reported by 52.1% (222/426), 95–99% was reported by 26.6% (113/426), adherence of 90–94% was reported by 12.7% (54/426), and adherence of <90% was reported by 8.7% (37/426) of patients.

Medical history was extracted from patient files and included time on ART, nadir CD4 count, history of opportunistic infections (OIs), current and past ART medications and regimen changes, viral load suppression, and CD4 recovery. Various sociodemographic and clinical factors and their association with self-reported adherence to ART at ≥95% are reported in Table 1.

Patient demographic and clinical characteristics

Demographics

There is evidence to suggest that low education level is associated with non-adherence (OR = 0.20, $P = 0.031$). There was no strong evidence of associations between employment/profession or age and adherence.

Patients working in the Business Process Outsourcing (BPO) sector had lower adherence than other professions; this may be due to the varying shift times worked by call centre agents in this sector. Health workers had the highest adherence of any profession, followed by self-employed individuals. However, overall, there was no strong evidence of association between employment/profession and adherence.

Relationship status appears to be an important factor in ART adherence. Of the 27.9% of subjects (119/426) who were in a relationship, most were in a serodiscordant relationship in which their primary partner was HIV negative. Those in serodiscordant partnerships had improved odds of adherence to ART compared with individuals who were not in a relationship (OR = 2.49). The evidence suggests that being in seroconcordant relationships (both HIV positive) and disclosure of HIV status to a trusted person may be also be factors that improve adherence; however, the sample size in this study was insufficient to reach these conclusions with confidence.

Adherence and viral suppression

Self-reported adherent patients were more likely to be virally suppressed (OR = 3.1, $P = 0.016$).

Time on ART and virological failure

Having been on ART for a longer time led to decreased adherence (0–6 months: OR = 1.00; 6 months–1year: OR = 0.36; 1–2 years: OR = 0.43; 2–4 years: OR = 0.32; ≥4 years: OR = 0.25; $P = 0.013$), which indicates that patients may be experiencing treatment fatigue over time.

In total, 27.9% of patients (119/426) had changed their ART medications at least once. Of those who changed regimens, 17.7% (21/119) had to change due to virological failure, whereas the remaining 98 people changed for other reasons such as intolerance/side-effects or depression worsened by efavirenz (EFV). Only 7.5% of patients (32/426) were on second-line lopinavir/ritonavir (LPV/r) or multiple resistance ART regimens, whereas 92.5% (394/426) were on efavirenz, nevirapine, or rilpivirine-based first-line ART regimens.

CD4 and opportunistic infections history

Most patients had a nadir CD4 count in the range of 200–350 cells/mm^3, indicating that they were diagnosed and started on ART before disease progression to AIDS. However, 74 patients (17.4%) had nadir CD4 count <50 cells/mm^3, indicating that they did not receive HIV diagnosis and treatment until they were already severely immune-compromised. Only 51.5% (206/400) of patients who had a nadir CD4 count <500 cells/mm^3 had reached CD4 recovery back to levels <500 cells/mm^3.

History of OI was common, with 61% of patients (260/426) having one or more potential OIs recorded in their complete medical history. Pnuemocystis pneumonia (PCP) history was recorded in the medical history of 6% of patients (27/426), and 5% had a history of thrush (20/426). Hepatitis B at 11% (46/426) and tuberculosis (TB) history at 18% (76/426) are similar to the overall population rates of these diseases, which are endemic to the Philippines.[19,20] Hepatitis C prevalence was 0.7% in our cohort (3/426), which is also similar to the general population rate.[19] Over 13% of patients (57/426) had a history of syphilis and 39% (166/426) had had another sexually transmissible infection (STI). There was no evidence of an association between ART adherence and nadir CD4, CD4 recovery, or OI history.

Risk behaviours

The association between risk behaviours and ART adherence is outlined in Table 2.

Sexual partners and condom use

The mean number of sex partners for participants in the past 6 months was 2.73. Among participants, 21.8% reported zero partners (93/426), 32.2% reported one partner (137/426), 23.2% reported between two and nine partners (99/426),

Table 1. Patient characteristics
*$P < 0.05$. –, no observations

Patient characteristics	Total (n = 426)		Adherent ≥95%[A] (n = 335)		Non-adherent <95%[A] (n = 91)		Crude OR (95% CI)	P-value
	n	(%)	n	(%)	n	(%)		
Gender								
Male	425	99.77	334	78.59	91	21.41	–	
Female	1	0.23	1	100.00	0	0.00	–	
Age (years)								
18–24	19	4.46	17	89.47	2	10.53	1.00	0.498
25–29	119	27.93	95	79.83	24	20.17	0.47 (0.10–2.16)	
30–39	245	57.51	188	76.73	57	23.27	0.39 (0.09–1.73)	
≥40	43	10.09	35	81.40	8	18.60	0.51 (0.10–2.69)	
Education								
Elementary or less	10	2.35	4	40.00	6	60.00	0.20 (0.05–0.72)*	0.010*
High school/vocational	19	4.46	15	78.95	4	21.05	1.11 (0.36–3.44)	
College/University	316	74.18	244	77.22	72	22.78	1.00	
Postgraduate	49	11.50	44	89.80	5	10.20	2.60 (0.99–6.79)	
Unknown/Did not report	32	7.51	28	87.50	4	12.50	2.07 (0.70–6.08)	
Employment								
Business Process Outsourcing (BPO)	88	20.66	66	75.00	22	25.00	1.00	0.406
Self-employed/other	38	8.92	34	89.47	4	10.53	2.83 (0.90–8.89)	
Health worker	16	3.76	15	93.75	1	6.25	5.00 (0.62–40.06)	
Professional[B]	234	54.93	182	77.78	52	22.22	1.17 (0.66–2.07)	
Student	13	3.05	10	76.92	3	23.08	1.11 (0.28–4.41)	
Unemployed	37	8.69	28	75.68	9	24.32	1.04 (0.42–2.53)	
Sexual orientation								
Bisexual	128	30.05	96	75.00	32	25.00	1.00	0.467
Heterosexual	7	1.64	6	85.71	1	14.29	2.00 (0.23–17.25)	
Homosexual	290	68.08	232	80.00	58	20.00	1.33 (0.81–2.18)	
Pansexual	1	0.23	1	100.00	0	0.00	–	
Civil status								
Married/Common-law partner	21	4.93	19	90.48	2	9.52	1.00	0.282
Single	404	94.84	315	77.97	89	22.03	0.47 (0.11–2.10)	
Unknown/Did not report	1	0.23	1	100.00	0	0.00	–	
Serodiscordant								
Not in a relationship	262	61.50	199	75.95	63	24.05	1.00	0.030*
Seroconcordant relationship (both HIV+)	48	11.27	41	85.42	7	14.58	1.85 (0.79–4.34)	
Serodiscordant relationship (partner is HIV–)	71	16.67	63	88.73	8	11.27	2.49 (1.13–5.48)*	
Unknown/Did not report	45	10.56	32	71.11	13	28.89	0.78 (0.39–1.58)	
Disclosure of HIV status to family/friend								
Disclosed	137	32.16	113	82.48	24	17.52	1.00	0.181
Not disclosed	207	48.59	155	74.88	52	25.12	0.63 (0.37–1.09)	
Unknown/Did not report	82	19.25	67	81.71	15	18.29	0.95 (0.47–1.93)	
Time on ART, years (mean)	2.77 years (95% CI 2.58–2.96)		2.61 (2.40–2.82)		3.35 (2.90–3.79)			
0–6 months	46	10.80	42	91.30	4	8.70	1.00	0.078
6 months–1 year	38	8.92	30	78.95	8	21.95	0.36 (0.10–1.3)	
1–2 years	83	19.48	68	81.93	15	18.07	0.43 (0.13–1.39)*	
2–4 years	162	38.03	125	77.16	37	22.84	0.32 (0.11–0.96)*	
>4 years	97	22.77	70	72.16	27	27.84	0.25 (0.08–0.75)*	

(*continued next page*)

Table 1. (*continued*)

Patient characteristics	Total (n = 426)		Adherent ≥95%[A] (n = 335)		Non-adherent <95%[A] (n = 91)		Crude OR (95% CI)	P-value
	n	(%)	n	(%)	n	(%)		
Nadir CD4 (cells/mm^3) (Mean)	245 (95% CI 229–260)		246 (227–263)		244 (212–275)			
0–200	163	38.26	132	80.98	31	19.02	1.00	0.065
200–499	237	54.76	179	75.53	58	24.47	0.72 (0.44–1.18)	
500+	26	6.93	24	92.31	2	7.69	2.82 (0.63–12.56)	
Viral suppression								
Undetectable	257	92.45	207	80.54	50	19.46	3.11 (1.24–7.77)	0.020*
Detectable (>500 copies)	21	7.55	12	57.14	9	42.86	1.00	

[A]Adherence is self-reported over the past 30 days.
[B]'Professional' is a broad category that includes patients who work as corporate or government employees, and workers in the education, IT, science, engineering, media, and sales and marketing sectors.

Table 2. Association between risk behaviours and antiretroviral therapy adherence
*P < 0.05

	Total (n = 426)		Adherent ≥95% (n = 335)		Non-adherent <95% (n = 91)		Crude OR (95% CI)	P-value
	n	(%)	n	(%)	n	(%)		
Condom usage in past 6 months								
Always	176	41.31	146	82.95	30	17.05	1.00	0.043*
Sometimes/Most of the time	151	35.45	106	70.20	45	29.80	0.48 (0.29–0.82)*	
Never	78	18.31	66	84.62	12	15.38	1.13 (0.54–2.35)	
N/A (not sexually active)	21	4.93	17	80.95	4	19.05	0.87 (0.27–2.78)	
Transactional sex								
Never had transactional sex	399	93.66	314	78.70	85	21.30	1.00	0.662
Ever had transactional sex	25	5.87	20	80.00	5	20.00	1.08 (0.39–2.97)	
Unknown/Refused	2	0.47	1	50.00	1	50.00	0.27 (0.02–4.37)	
Drug use in past 3 months								
No	356	83.57	282	79.21	74	20.79	1.00	0.519
Yes	70	16.43	53	75.71	17	24.29	0.82 (0.45–1.50)	
Injection drug use ever								
No	374	87.79	301	80.48	73	19.52	1.00	0.018*
Yes	52	12.21	34	65.38	18	34.62	0.46 (0.25–0.86)*	
Heavy alcohol use								
No	363	86.43	289	79.61	74	20.39	1.00	0.201
Yes	57	13.57	41	71.93	16	28.07	0.66 (0.35–1.23)	
QOL	88.68 (95% CI 87.46–89.89)		89.45 (88.13–90.76)		85.85 (82.97–88.73)			
High (90–120)	183	46.45	148	80.87	35	19.13	1.00	0.427
Medium (60–89)	206	52.28	159	77.18	47	22.82	0.80 (0.49–1.31)	
Low (0–59)	5	1.27	3	60.00	2	40.00	0.35 (0.06–2.20)	
HIV knowledge score (mean, %)	85.01% score (95% CI 83.74–86.29)		85.01% (83.53–86.49)		85.03% (82.54–87.51)			
<80	95	22.35	80	84.21	15	15.79	1.00	0.044*
80–89	163	38.35	118	72.39	45	27.61	0.49 (0.26–0.94)*	
≤90	167	39.29	136	81.44	31	18.56	0.82 (0.42–1.62)	

and 4.2% reported >10 partners (18/426), whereas 20.9% (89/426) of participants did not provide an answer on the questionnaire. Only 6% (25/426) of the patients reported having ever engaged in transactional sex, and of those, only two participants had had transactional sex within the past 6 months. In the study population, 41.3% (176/426) reported they always use condoms and 35.4% (151/426) use them some of the time or most of the time. This inconsistent condom use was associated with non-adherence to ART (OR = 0.48, P = 0.007); however, individuals who reported never using condoms did not have reduced odds of ART adherence.

Drug and alcohol use

In our study population, 9.4% (40/426) used 'shabu' (methamphetamine hydrochloride), 8.0% (34/426) used cannabis, 4.5% (19/423) used prescription drugs for non-medical use, and 1.4% (6/426) used inhalants (e.g. 'rugby' or 'poppers') within the past 3 months, and 0.7% (3/426) of respondents did not complete the substance use portion of the questionnaire. Injecting drug users (IDU) were 12.2% (52/426) of the study population; 52 who had ever injected drugs and 28 who had done so within the past 3 months. Among IDUs, the odds of ART adherence were lower (IDU ever OR = 0.46, P = 0.015; IDU in past 3 months OR = 0.38, P = 0.019). Only two individuals reported ever having shared needles for injecting drugs. There was no association between adherence and non-injecting drug use.

Although 30.5% (130/426) of patients abstained from alcohol, 37.3% (159/426) engaged in heavy episodic drinking in the past 30 days. Problem drinking, defined as two or more episodes of heavy episodic or 'binge' drinking (>five drinks) in the past month or >14 drinks per week on average,[21,22] was prevalent in 13.4% (57/426) of the study population. Alcohol use did not have an association with ART adherence.

Quality of life

The WHOQOL-HIV BREF scores QOL in six domains, a maximum of 20 points per domain and a total score of 120. The mean for each of the six domains and the total WHOQOL-HIV BREF score are as follows: Physical 15.21; Psychological 15.04; Level of Independence 15.54; Social Relationships 15.01; Environmental 13.43; and Spirituality 14.44. The domain with the lowest overall score was Environment, which measures aspects such as safety and security; access to health care; financial resources; opportunities for learning and for leisure; and physical environment (pollution/noise/traffic/climate).[23]

The mean QOL score in the cohort was 88.68 (95% CI 87.46–89.89). Just under half (46.5%) of the 426 participants had an overall QOL score of ≥90, which represents a high QOL, and 52.3% percent had a medium QOL with a score between 60 and 89. Only five patients (1.3%) had a QOL score <60. One patient did not complete the QOL questionnaire. There was no significant association between ART adherence and overall QOL (Table 2) or individual QOL domains (data not shown).

Knowledge of HIV

There was evidence of an association between knowledge of HIV, as scored on a 16-item questionnaire, and ART adherence. There is an association between scoring 80% and 89% on the HIV knowledge questionnaire and lower adherence (OR = 0.49, P = 0.044). This association does not hold for those scoring >90% and the reason for the association is unclear, warranting further investigation.

Adherence/reasons for missing medication

There were 228 study participants who reported having missed medications at any point in the past; the reasons they reported for ever missing medications are detailed in Figure 1. The most common reasons for missing medications were that that the patient was busy, they forgot, fell asleep, was away from home, or had a change in their daily routine. Stigma is also a factor affecting adherence, as 44% of patients who had skipped a pill at some point did so because they did not want to be seen taking medications. Issues around side-effects, toxicity, and pill burden were the least likely contributors to non-adherence.

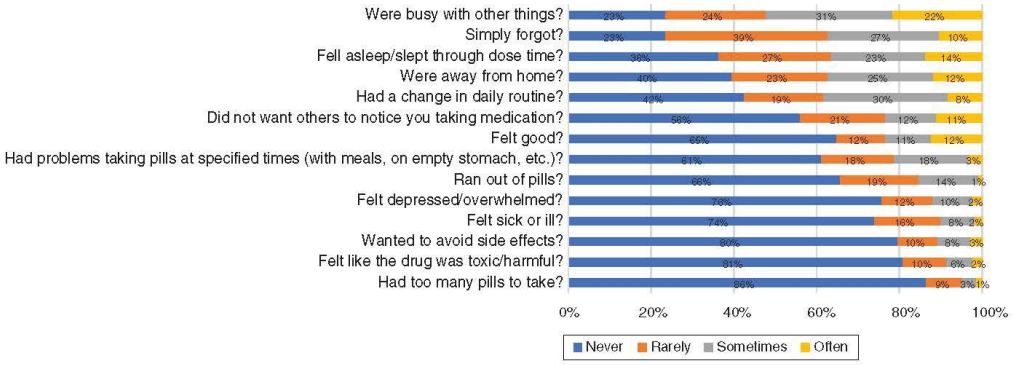

Fig. 1. Reasons for missing medication (n = 228).

Multivariate logistic regression model for adherence to antiretroviral therapy

In the final multivariate logistic regression model (Table 3), time on ART (adjusted OR (AOR) = 0.87 per year, P = 0.027 seroconcordant/serodiscordant relationship status (P = 0.006)), and knowledge score (P = 0.047) were associated with ART adherence. Injection drug use and inconsistent condom use (using condoms sometimes or most of the time) may also be related to adherence, whereas the study sample may have been too small to evaluate these factors.

Table 3. Multivariate logistic regression analysis of factors associated with antiretroviral therapy (ART) adherence
*$P < 0.05$

Variable	Adjusted OR	95% CI	P-value
Education			
Elementary or less	0.42	(0.10–1.75)	0.084
High school/vocational	1.16	(0.36–3.82)	
College/University	1.00		
Postgraduate	2.40	(0.87–6.63)	
Unknown	2.57	(0.81–8.16)	
Serodiscordant			
N/A (not in a relationship)	1.00		0.006*
Seroconcordant relationship (both HIV+)	2.37	(0.95–5.93)	
Serodiscordant relationship (partner is HIV–)	3.19	(1.39–7.35)	
Unknown	0.81	(0.37–1.79)	
Time on ART, years	0.87	(0.77–0.98)	0.027*
Nadir CD4 (cells/mm^3)			
0–200	1.00		0.1334
200–499	0.78	(0.46–1.33)	
500+	2.87	(0.60–13.61)	
Condom usage (in past 6 months)			
Always	1.00		0.103
Sometimes/Most of the time	0.50	(0.28–0.89)	
Never	0.81	(0.24–2.75)	
N/A (not sexually active)	0.94	(0.43–2.06)	
Injection drug use (in past 3 months)	0.54	(0.27–1.09)	0.090
HIV knowledge score (mean, %)			
<80	1.00		0.047*
80–89	0.47	(0.23–0.94)	
≤90	0.81	(0.39–1.67)	

Discussion

Twenty-one percent (91/426) of the study participants reported suboptimal adherence. By comparison, ~37% of patients globally report suboptimal adherence to ART,[17,24] and in the regional Therapeutics Research, Education, and AIDS Training in Asia (TREAT Asia) cohort (which includes a large treatment site in the Philippines), 32% of 1316 patients reported suboptimal adherence of <100%.[11] As expected, self-reported adherent patients were more likely to be virally suppressed, which indicates that patient self-report of adherence or non-adherence accurately reflects their pill-taking behaviour.

The study found that people who had been on treatment longer were less likely to be adherent to their ART. This finding is contrary to the TREAT Asia regional cohort study, which found 26% of patients self-reported suboptimal adherence levels during their first 6 months of treatment, and that adherence improved over time from initiation to 24 months.[11] These contradictory findings warrant further investigation. Reasons for non-adherence in this study were largely situational factors, habits, and routines, whereas clinical issues such as side-effects and pill burden were less likely to impact adherence in this population.

Condom use in this study population was comparable to the general MSM population in the Philippines – 41.3% (146/405) of the sexually active SHIP population study participants always use condoms and 35.5% (151/405) use condoms most or some of the time, whereas the 2013 surveillance data showed 40.7% condom use at last anal sex among MSM.[8,25] Inconsistent condom use (using condoms sometimes or most of the time) may be associated with ART non-adherence, which suggests that motivating factors and abilities that enable a patient to adhere to ART could also be the same factors that lead to consistent condom use. The average total number of sex partners in the past 6 months was 2.14, which is lower than has been reported in other surveillance of MSM in the Philippines;[8,25] this may indicate that MSM reduce their sexual activity after becoming HIV positive and starting ART, a question that warrants further investigation.

Relationship status appears to be an important factor in ART adherence. Patients in serodiscordant relationships were more likely to adhere to ART. The data suggest that being in a relationship, whether seroconcordant or serodiscordant, is better than being single when it comes to ART adherence, and that disclosure of one's HIV-positive status to a trusted person can also lead to better outcomes. These findings emphasise the important role of partner, family and social support for HIV patients in order to achieve good clinical outcomes.

Another key finding in this study is that the study participants used drugs and alcohol at rates five- to 10-fold higher than the general population. In the Philippines general population, 44.7% of males abstain from alcohol and 3.5% of males engage in heavy episodic drinking,[26] whereas in our study population, only 30.5% abstained and 37.3% had engaged in heavy episodic drinking in the past 30 days. According to the United Nations Office on Drugs and Crime, 1.1% of Filipinos use 'shabu' (methamphetamine hydrochloride) and 1.6% use cannabis.[27] In our study population, 9.9% had used 'shabu' and 7.7% used cannabis within the past 3 months. Methamphetamine use is strongly associated with high-risk sexual behaviour and HIV acquisition,[28] and is commonly used by MSM in chemsex or 'Partee 'n' Play' activities. Compounding these risks, evidence-based HIV prevention services are not widely available in the Philippines – condom distribution is restricted,[29,30] pre- and post-exposure prophylaxis are not widely available, except through very limited pilot projects,

and syringe exchange is illegal under the current administration's interpretation of the Philippines' Dangerous Drugs Act of 2002.

Limitations

This study is limited by several factors. First, adherence and risk behaviours were self-reported, and the responses are subject to social desirability bias. However, adherence was strongly associated with viral load suppression, and risk behaviours were not significantly lower than the general population (and in many cases much higher), which suggests that the self-report method was generally accurate. Furthermore, the generalisability of study data from the SHIP clinic population is limited. Due to the higher socioeconomic status and education levels of the SHIP clinic patients, and due to the fact that it is a fee-for-service clinic, the cohort may not be representative of MSM in the Philippines more broadly. Apart from employment, education, and high HIV knowledge levels, other demographic factors (age, clinical outcomes, risk profile) align with other published data on MSM and people living with HIV from the country.[7,8,25,31] Ongoing follow up of the SHIP Connect for Life study cohort will provide further details about incidence of OIs, retention in care, and ART adherence.

Conclusions

This study provides an in-depth analysis of demographic, clinical, and behavioural characteristics of MSM living with HIV in the Philippines, which can improve understanding of the country's epidemic and may be used to inform tailored prevention and treatment interventions.

Factors found to be associated with adherence to HIV treatment were time on ART, being in a serodiscordant relationship in which the person's main partner is HIV negative, and HIV knowledge level.

The issue of treatment fatigue warrants further investigation and should be addressed through implementation of tailored adherence interventions. Clinicians and other service providers should prioritise counselling and interventions to improve family and social support for HIV patients. There is also an unexplored opportunity for harm-reduction interventions among HIV-positive and HIV-negative MSM who use drugs and alcohol.

Conflicts of interest

Sustained Health Initiatives of The Philippines (SHIP) received project funding from Johnson & Johnson Global Public Health to conduct this study.

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Original Paper

Delivering an mHealth Adherence Support Intervention for Patients With HIV: Mixed Methods Process Evaluation of the Philippines Connect for Life Study

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Abstract

Background: The Philippines HIV epidemic is one of the fastest growing epidemics globally, and infections among men who have sex with men are increasing at an alarming rate. Connect for Life Philippines is a mobile health (mHealth) intervention that supports antiretroviral therapy (ART) adherence in this key population through individualized voice calls and SMS text messages.

Objective: The objective of this process evaluation is to assess the intervention reach, dose delivered and received, fidelity, and acceptability and to describe contextual factors affecting the implementation of an mHealth adherence support intervention for patients on ART in a clinic in Metro Manila, Philippines.

Methods: A mixed methods process evaluation approach was used in an observational cohort study. Quantitative data sources for the process evaluation were call and SMS text message logs obtained from the mHealth platform and questionnaires collected at 12-, 24-, and 48-week study visits. Qualitative data were collected from process reports and through a series of focus group discussions conducted with a subset of participants during the intervention development phase, after an initial 8-week pilot phase, and at the end of the study.

Results: The 462 study participants received 31,095 interactive voice calls and 8234 SMS text messages during the study. Owing to technical issues, intervention fidelity was low, with only 22.1% (102/462) of the participants receiving reminders via voice calls and others (360/462, 77.9%) receiving only SMS text messages during the intervention. After 48 weeks in the study, 63.5% (293/462) of the participants reported that they would be quite likely or very likely to recommend the program to a friend, and 53.8% (249/462) of the participants reported that they benefited quite a bit or very much from the intervention. Participants who were on ART for <6 months at the beginning of the study and those who received the daily or weekly pill reminders were more likely to report that they benefited from the intervention (P=.02 and P=.01, respectively).

Conclusions: The Connect for Life intervention had high participant satisfaction and acceptability, especially among those who received high dose of the intervention. However, poor reliability of local telecommunication networks had a large impact on the intervention's usability, fidelity, and dose received.

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KEYWORDS

mobile health; mHealth; adherence; HIV; antiretroviral therapy; process evaluation; Philippines; men who have sex with men; MSM; mobile phone

Introduction

Background

The HIV epidemic in the Philippines is one of the fastest growing epidemics globally, with 207% increase in new HIV infections and 388% increase in AIDS deaths from 2010 to 2020. In 2020, an estimated 73% of people living with HIV in the Philippines knew their status and 44% of people living with HIV were on antiretroviral therapy (ART) [1-4]. In 2 studies of cohorts of patients with HIV in Manila, 84% to 90% of patients who started ART had achieved viral suppression [4,5]. Most new and existing HIV infections occur among men who have sex with men (MSM) [3]. Improving treatment coverage, retention, adherence, and viral suppression are key to slowing the spread of HIV in the Philippines. Unfortunately, widespread stigma, lack of knowledge, and barriers to accessing care pose a challenge to engaging patients in testing and ensuring high levels of adherence to ART and retention in care [6-8]. High rates of first-line treatment failure, loss to follow-up, and suboptimal treatment adherence lead to poor outcomes in many patients with HIV in the Philippines [9,10].

This paper describes the process evaluation of a mobile phone technology for health (mobile health [mHealth]) intervention for people living with HIV in Metro Manila, Philippines. To support ART adherence, the intervention, Connect for Life, provided patients with HIV with individualized voice calls and SMS text messages, pill reminders, appointment reminders, symptom reporting, health tips, and adherence feedback.

The Connect for Life platform was developed by Janssen Global Public Health, and before adaptation for the Philippines, its versions were piloted in India and Uganda. The mMitra (mobile friend) project in India aimed to improve maternal health outcomes through health messages to pregnant women [11,12]. The Treatment Advice using Mobile Alerts project in India [13,14] and Call for Life Uganda [15,16] supported ART adherence among people living with HIV.

Process Evaluation of mHealth Interventions

As mHealth technologies have become widespread in low-income and middle-income countries, mobile phone interventions have become increasingly popular in the global health and development sectors as an inexpensive and efficient way to communicate and deliver services. Several trials have shown that mHealth approaches show potential for improving self-management of chronic diseases, including adherence to HIV medications [17-21], whereas systematic reviews show mixed outcomes of mHealth interventions and highlight the need for more rigorous evaluation methods and longer follow-up periods in mHealth studies [22-31].

Trials assessing mHealth adherence interventions for HIV often do not include process evaluations to examine the fidelity and quality of the intervention delivery, causal mechanisms for the health outcomes, contextual factors affecting the delivery, and costs to implement [29,32,33]. For mHealth interventions, current guidance suggests that practitioners should also include a minimum set of information about the content, context, and technical features of the intervention, including aspects such as ease of use, content quality, privacy and security, service quality, personalization, and perceived enjoyment [34-37].

Process evaluations of SMS text messages and interactive voice response systems (IVRSs) have examined fidelity, reach, dose delivered, and user satisfaction for projects ranging from water and sanitation to prevent diarrheal disease [38]; airline pilot fatigue [39]; and prevention of weight gain, smoking, or HIV among young people [40-42]. A systematic review of mHealth projects in Africa found that in projects where acceptability and usability of mHealth technology among participants was measured, it was generally high. However, infrastructure issues (unreliable network and internet and electricity access) were frequently cited as key challenges in delivery [24].

The success of mHealth projects in achieving the intended health outcomes is almost entirely dependent on the adaptation and delivery of the intervention in local contexts. Having a complete understanding of the implementation process of an mHealth intervention can enable practitioners to interpret the outcomes and replicate the intervention in other contexts. Therefore, we performed a process evaluation alongside the Connect for Life Philippines prospective cohort study. The process evaluation examined the fidelity, dose delivered and received, reach, usability, acceptability, and cost of the Connect for Life Philippines intervention.

Methods

Recruitment

The study was conducted at the Sustained Health Initiatives of the Philippines (SHIP) Clinic, a low-cost, private facility in Metro Manila, a city with approximately 13 million people in the predominantly Catholic country of the Philippines.

SHIP Clinic provides HIV primary care and wraparound services to approximately 900 people living with HIV. Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at initial consultation. Most are full-time or part-time employees. The clients come from all regions of Metro Manila, and some live in other provinces.

Recruitment into the Connect for Life study occurred in person at the study site between October 2016 and December 2017. As patients checked in for their routine clinic visits, the study coordinator approached all patients seated in the clinic waiting room, briefly introduced the study following a recruitment script, elicited their interest in participating, screened them for

eligibility, completed the informed consent process, and provided a brief orientation to the intervention.

Connect for Life Mobile Phone ART Adherence Support Intervention

The study team worked with IT specialists and public health professionals from Jannsen Global Public Health, University of the Philippines, and local IT companies to develop the content and functionality of the Connect for Life mHealth platform (Figure 1). Connect for Life is a technology built on the Mobile Technology for Community Health (MOTECH; Grameen Foundation) open-source software platform [43]. It enables health facilities to connect to patients via their mobile phones through IVRS call flows or SMS text messages. As Connect for Life works through phone calls and SMS text messages, it does not require the user to have a smartphone, install an app, or have mobile internet connection. This makes it accessible to a wide range of users in the Philippines, where, in 2015, mobile phone penetration was high, but smart phone coverage and internet access were low (with 113 mobile subscriptions per 100 people, 99% of the population reached by network coverage, and 22% of the population owning a smart phone) [44-46].

The study team tailored the Connect for Life platform for the Philippine context. Some existing features were retained, such as reminders sent on the recipient's preferred days and times, health tips, and symptom screening. New features were developed, such as medical record functionality and adherence feedback scores. Clinicians at the study site developed new content for the voice and SMS text messages, which were recorded by a local voice talent agency. During the formative study and intervention development stage, a series of focus groups were conducted to engage with patients at the clinic about their adherence behaviors and preferences for configuration and content, and their feedback was incorporated to ensure that the intervention was tailored to the target population [47-49].

The Connect for Life system was installed in a secure cloud server environment and linked to a local telecom provider through application programming interface integration to execute calls and SMS text messages. A local IT service provider was contracted to monitor server functionality, install software updates, and troubleshoot technical issues. The Connect for Life software developers provided in-depth technical training and software documentation to the local IT provider and training for the clinical staff on how to use the Connect for Life web-based platform.

The intervention development process was guided by the Behavior Change Wheel and the Capability Opportunity Motivation–Behavior model developed by Michie, Atkins, and West [50-52]. Behavior change techniques related specifically to ART adherence were informed by the information-motivation-behavioral skills model of ART adherence [53]. Each service in the intervention package was designed to address ≥1 of the 3 main components that drive behavior in the Capability Opportunity Motivation–Behavior model, as outlined in Figure 2 [47,48].

Figure 1. Connect for Life Philippines mobile health intervention functions. ART: antiretroviral therapy; IVRS: interactive voice response system; PIN: personal identification number.

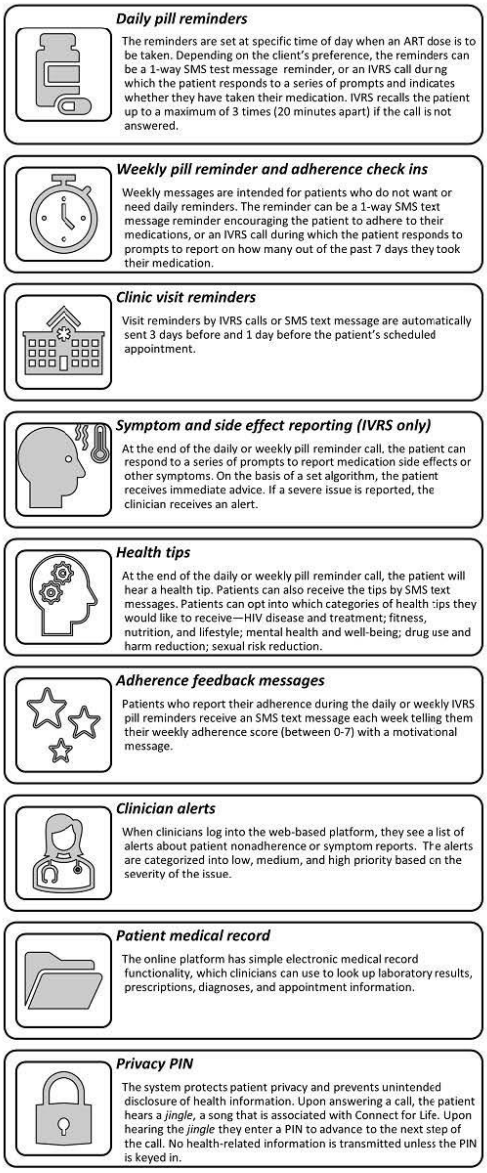
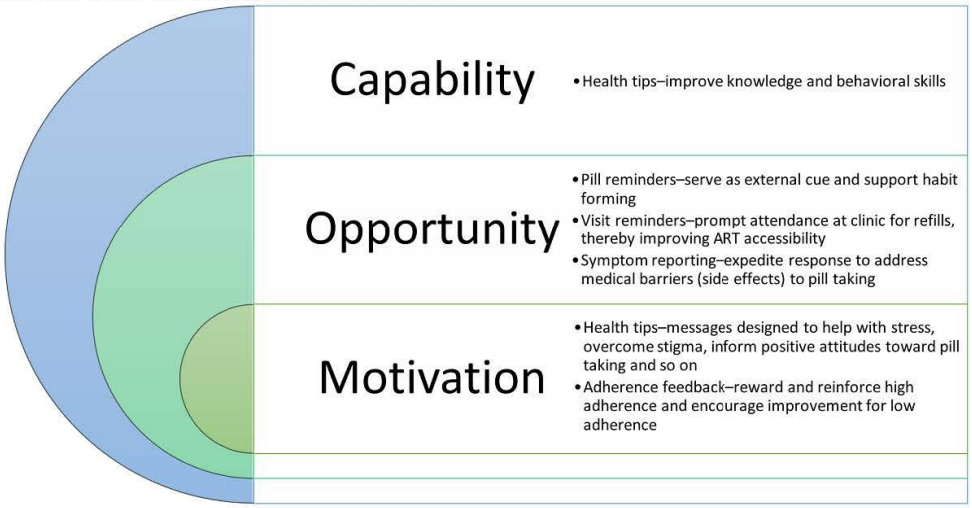


Figure 2. Intervention theory of change. ART: antiretroviral therapy.



Data Collection and Analysis

A mixed methods approach was used with qualitative data embedded in the experimental design of the 48-week prospective cohort study [54]. The design allowed us to assess participants' use of and experience with the system and use quantitative and qualitative analyses to generate complementary data about acceptability, usability, and the impact of contextual factors on the intervention.

The process evaluation measures were based on the framework proposed by Linnan and Steckler [55], which defines the approach to adequately describe the context, reach, dose (delivered and received), acceptability, and fidelity of the intervention. Additional aspects related to reporting on mHealth technology were included based on guidance from the mHealth Evidence Reporting and Assessment checklist [36].

The process evaluation questions, tools, methods, and data sources are described in Multimedia Appendix 1.

To measure the fidelity and dose of intervention delivery, records from the mHealth platform detailing the services received by each participant were exported. To understand the usability and acceptability of the intervention, participants completed self-administered paper-based questionnaires at 3 time points during the study. Where questionnaires had blank or missing fields, all available data points were included in the analysis. Data distributions were explored to categorize the responses to the questionnaires. Associations between acceptability of the intervention and independent variables (time point, treatment experience, and reminder frequency) were calculated using chi-square tests. Data analysis was conducted using Stata 15.

Qualitative feedback was collected in several ways: routine monthly process reports from clinicians to document implementation successes and challenges, comments recorded on the acceptability questionnaires, and a series of focus group discussions (FGDs). The study team conducted 2 FGDs with a total of 12 participants during the intervention development phase in 2016. In early 2017, a total of 2 additional FGDs were conducted with 5 participants after an 8-week pilot phase. Finally, in 2018, during the final 2 months of the study, 3 FGDs were conducted with 15 participants. The FGDs were transcribed, transcripts were manually coded using a deductive coding methodology to group responses by topic areas in the FGD guide, subtopics were assigned through line-by-line coding, and data were consolidated in a structured template that enabled identification of salient themes. Results from the FGDs in the formative and pilot phases informed the content and structure of the intervention and helped to identify implementation issues early in the project [47].

Ethics Approval

Ethics approval for the study was obtained from the University of the Philippines Manila research ethics board (protocol number 2016-265-01) and the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent before inclusion in the study.

Results

Study Population and Intervention Delivery

Process Evaluation Questions 1 and 2: Reach and Recruitment

Of approximately 675 patients receiving ART services at the study site during the recruitment period, 485 (71.9%) were approached by the study coordinator while attending a routine visit at the clinic, 464 (68.7%) were interested in learning about the study, and 462 (68.4%) met the eligibility criteria and consented to participate.

Reasons for refusal (21/485, 4.3%) included no need or desire for adherence support, not wanting to receive messages or calls on their mobile phone, privacy concerns, and frequent travel

out of the country. Of the 0.4% (2/464) of the patients who were excluded, one was ineligible because he did not speak English and the other did not have a mobile phone.

All but 1 of the participants in the study (461/462, 99.8%) identified as male, and 98.5% (455/462) were MSM. The mean age at enrollment was 32.4 (SD 5.7) years. University or postgraduate studies had been completed by 85.9% (397/462) of the participants, and 91.3% (422/462) were employed or enrolled in university, which reflects the higher-than-average socioeconomic status of patients at the study site, a private fee-for-service clinic.

At the time of enrollment, 92.2% (426/462) of the participants were already taking ART and 7.8% (36/462) had not yet started. Of those already taking ART, perfect adherence of 100% of doses taken in the last 30 days was reported by 52.1% (222/426) of the participants, 95% to 99% adherence was reported by 26.6% (113/426), 90% to 94% adherence was reported by 12.7% (54/426), and adherence of <90% was reported by 8.7% (37/426).

Participants were followed for 48 weeks, during which time 91.1% (421/462) of the participants were retained for the study duration and active on ART at the study site, 0.6% (3/462) had withdrawn from the study but were still in care, 0.6% (3/462) had died, 3.9% (18/462) had defaulted from treatment, and 3.7% (17/462) had transferred to another clinic.

Process Evaluation Question 3: Fidelity

The process evaluation found that the fidelity of the intervention was low. The planned intervention consisted of daily IVRS pill reminder calls for all participants in the first 6 months of ART and weekly IVRS calls for those on ART for >6 months. During the study, only 22.1% (102/462) of the participants received the IVRS intervention, whereas 72.7% (336/462) received a scaled-down SMS text message version of the intervention. The reasons for the small proportion of participants receiving the voice calls were technology-related challenges described in the *Usability and Context* section.

Process Evaluation Questions 4 and 5: Dose Delivered

Of the 462 participants, 95 (20.6%) participants received a combination of voice calls and SMS text messages, 336 (72.7%) received SMS text messages only, 7 (1.5%) received voice calls only, and 24 (5.2%) received neither.

The 22.1% (102/462) of the participants who opted for IVRS services received a total of 30,940 calls during their study enrollment period (Table 1). During the calls, participants listened to 3980 health tips. Only 2 symptom or side effect reports were made. An average of 303 calls were made per participant, which included repeat reminder calls (up to 3 calls per day) if the initial call was unanswered. Of all the scheduled outgoing IVRS calls by the Connect for Life system, only 0.14% (44/31,095) of the calls failed to initiate owing to a software or platform issue.

The 93.3% (431/462) of the participants who opted for SMS text messages received 8234 messages in total: 2468 (29.97%) adherence feedback, 417 (5.06%) health tips, 2272 (27.59%) pill reminders, and 3077 (37.37%) visit reminders.

Table 1. IVRS[a] and SMS text message services provided.

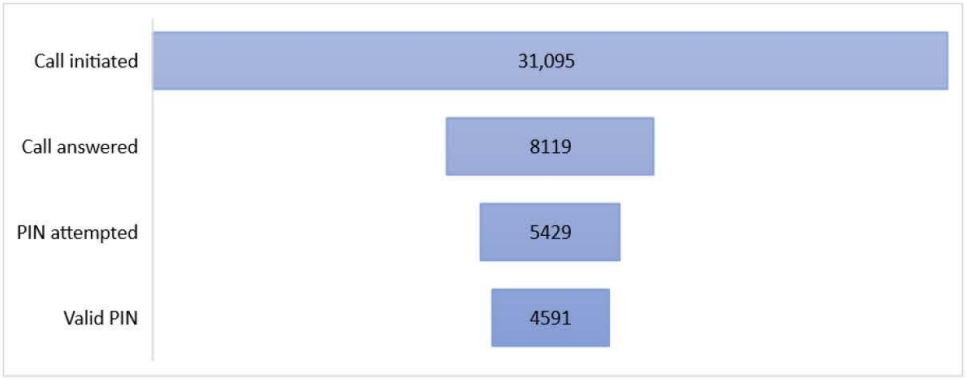
Services	Participants who received the service (N=462), n (%)	Total number of calls and messages delivered after enrollment (N=30,940 calls; N=8234 SMS text messages), n (%)	Number of calls and SMS text messages per participant, mean (SD)
IVRS calls (n=102)			
Any	102 (22.1)	30,940 (100)	303 (324.3)
Listened to health tip	69 (14.9)	3980 (12.86)	58 (80.1)
Reported symptoms or side effects	2 (0.4)	2 (0.01)	1 (0)
SMS text messages (n=431)			
Any	431 (93.3)	8234 (100)	19 (49)
Adherence feedback	70 (15.2)	2468 (30)	35 (17.3)
Health tip	11 (2.4)	417 (5.1)	38 (45.7)
Pill reminder	10 (2.2)	2272 (27.6)	227 (187.3)
Visit reminder	428 (92.6)	3077 (37.4)	7 (4)

[a]IVRS: interactive voice response system.

Process Evaluation Question 6: Dose Received

Including setup calls during the visits, of the 31,095 outgoing calls made by the Connect for Life system, 8119 (26.11%) were answered by the participants. To listen to the message, the participant had to enter their personal identification number (PIN). A PIN attempt was recorded for 66.87% (5429/8119) of the calls that were answered, and the PIN was entered successfully in 84.56% (4591/5429) of the PIN attempts (Figure 3).

Figure 3. Interactive voice response system calls made and outcomes. PIN: personal identification number.



Of the 2690 calls that were answered and no PIN was entered, an estimated 1846 (68.62%) went to voicemail. This estimate was based on the number of seconds the call was connected before it was automatically terminated by the software (approximately 140 seconds).

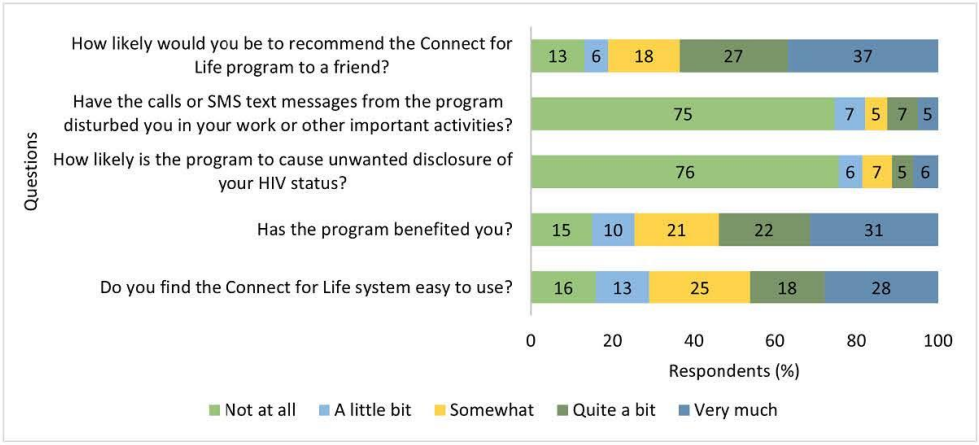
Experiences of Participants and Providers

Process Evaluation Questions 7 and 8: Usability and Context

The biggest technology challenge that the project faced was frequent dial tone multifrequency (DTMF) malfunction during IVRS calls. This was reported by study participants and observed by the study staff during the process of activation of the IVRS service. During the DTMF malfunction, the system was unable to recognize the tones as users pressed number keys on their phones, resulting in invalid PINs or inability to navigate the IVRS menus. DTMF failure was suspected during an estimated 32.08% (2605/8119) of calls that were answered by participants (1767/2605, 67.83% of the answered calls where no PIN was entered and 838/2605, 32.17% calls where an invalid PIN was entered). Enrollment was temporarily suspended, and an investigation of the issue found that the DTMF malfunctions were related to the telecommunication infrastructure rather than the Connect for Life platform; therefore, it was not possible for the study team to correct the issues.

Only 46.1% (159/345) of the participants reported that they found the Connect for Life system quite easy or very easy to use (Figure 4), indicating that ease of use can be improved.

Figure 4. Intervention acceptability after 48 weeks (n=392 respondents).



The provider's experience with the system was largely positive. In monthly process reports, clinicians reported that the medical record functionality facilitated easy access to laboratory results, medication history, diagnosis, and other information, which had previously been recorded in Microsoft Word documents and paper charts. Clinicians also reported that the alert function, which flagged patients with poor adherence or side effects for the clinician to follow up, was overwhelming to use. The symptom reporting alerts were useful, but these alerts were "buried" in a long list of alerts about missed doses and missed

clinic visits. This occurred when participants failed to answer calls and responded to the IVRS prompts, which triggered alerts for nonadherence, resulting in high numbers of inaccurate alerts for missed doses. Clinicians recommended reviewing and updating the criteria for generating alerts.

Clinic staff also observed that across the clinic, participant compliance with attending appointments on the scheduled date and time improved from 17% before the study to >30% after the implementation of Connect for Life. They attributed this improvement to the visit reminders sent through SMS text messages. The improved on-time visit attendance saved staff time and effort by reducing the need to call patients and reschedule appointments.

Process Evaluation Question 9: Acceptability and Satisfaction

Acceptability

Acceptability questionnaires were collected at 3 time points (426/462, 92.2% completed at the 12-week visit; 335/462, 72.5% at the 24-week visit; and 392/462, 84.8% at the 48-week visit). Acceptability levels are summarized in Figure 4.

After 48 weeks in the study, 63.5% (221/348) of the participants reported that they would be quite likely or very likely to recommend the program to a friend, and 53.9% (187/347) of the participants reported that they benefited quite a bit or very much from the intervention.

Some participants reported concern over privacy and inconvenience, with 12.4% (43/347) of the participants reporting that the messages and calls disturbed them quite a bit or very much during their work or other important activities and 11.3% (39/345) of the participants stating it was quite likely or very likely that the intervention could cause unwanted disclosure of HIV status. Social harm monitoring was conducted at each study visit and no instances of disclosure were reported.

Associations between acceptability and several independent variables were explored.

Time on Study

There was no strong evidence of difference in the acceptability indicators at different time points after enrollment. The proportion of participants who reported that the intervention benefited them quite a bit or very much was 45.2% (128/283) at the 12-week study visit, 54.3% (188/346) at the 24-week visit, and 53.9% (187/347) at the 48-week visit (P=.51)

Time on Treatment

Among participants who had started ART <6 months before enrollment in the intervention, after 48 weeks, 65% (39/60) reported that the intervention benefited them quite a bit or very much, compared with only 51.6% (148/287) of the more experienced participants who had been on ART for >6 months at the time of enrollment (P=.02).

Frequency of Service

People who received daily or weekly pill reminders were much more likely to report that the intervention benefited them compared with those who did not receive pill reminders. This trend was consistent across all time points. At the 48-week visit, 70% (21/30) of the participants who received weekly pill reminder and 64% (9/14) of those who received daily pill reminder reported that they benefited quite a bit or very much from the intervention compared with only 51.5% (157/305) of those who received no reminders (P=.01).

There was no evidence of difference between those receiving daily and those receiving weekly pill reminders in terms of acceptability of the frequency of pill reminders or participants' likelihood to recommend Connect for Life to a friend. Of those who received daily pill reminder, 14% (11/78 observations) said that there were "too many" reminders, whereas 7% (4/58 observations) of those who received weekly pill reminder said that there were "too many" reminders (P=.29). At week 48, a total of 80% (24/30) of the participants who received weekly pill reminders were quite likely or very likely to recommend to a friend, compared with 64% (9/14) of those who received daily pill reminders and 61.4% (188/306) of those who received no reminders (P=.30).

Other Factors

No association was observed between viral load suppression or HIV knowledge score and intervention acceptability.

Qualitative Feedback From FGDs and Adherence Questionnaires

Qualitative data were collected to facilitate better understanding of participants' experiences with the system and the contextual and motivating factors influencing the use, acceptability, and usability of the intervention.

The key findings from the acceptability questionnaires and the FGDs at the end of the study were that the intervention was received positively, and participants believed that the intervention should continue after the study ended. Several main themes emerged—the importance of personalized reminders, technical challenges and usability issues, desire for health tips, and importance of social support as part of HIV care (Textbox 1).

Textbox 1. Main themes from focus group discussions (FGDs).

Personalized reminders

- Participants liked that the intervention was highly personalizable, enabling them to select the frequency and time of calls or SMS test messages and the topics of health tips. Preferences for voice calls and SMS text messages varied. Participants also reported that they found the visit reminders and pill reminders to be helpful for their adherence; however, most patients were using their own alarms or pill boxes as adherence tools. Several participants who only received the visit reminder service expressed interest in trying the pill reminders and health tips after hearing the feedback from participants who received those components of the service:

It is an advantage being reminded at work especially when you get busy so you would not miss to take your medicine on time.

Receiving pill reminder call on a weekly basis made me more aware of the time and I think it is more beneficial to those who has tight schedule. But in my end, I never forget a dose with the aid of alarm clock.

For me, the two times [visit] reminder is fine. Actually, it is very helpful on reminding me on my next visit. There are times that I got surprised receiving the text because I already forgot that I have a follow-up visit.

Technical challenges

- Participants who received the calls described challenges with entering their personal identification number and with navigating the interactive voice response system (these challenges were owing to failure of the dial tone multifrequency technology) and more broadly about the hassle of responding to the prompts in the calls. Even when the call went unanswered, it still served as a prompt to take medication:

In the evening, I don't know how to use the PIN so whenever I received the call (usually an international number) and hear the music, I already know that it is the pill reminder call. I actually can't go through the IVR because I don't know exactly when I need to enter the PIN... On the other hand, the call itself serves as an alarm to take my meds though I was not able to answer or enter my PIN.

Health tips

- Participants expressed that although they use the internet to find health information, they trusted health tips from Connect for Life more, because the information was vetted by their health care provider. They liked that the health tips included information on a range of related health topics, such as nutrition and mental health, in addition to the HIV basics. However, some participants were unwilling to receive tips via SMS text message because of concerns about privacy, and some stated that they knew someone who they could ask for health information:

In general, I think it is better that the health tips are coming from Sustained Health Initiatives of the Philippines and recommended by health care professionals. It would be more reliable as compared to information in the Google.

It's like trivia for today, even you are on meds for a long time already.

Social support

- Almost all FGD participants mentioned the importance of human connection. Several participants mentioned that they would prefer to connect to a live person in addition to electronic information, especially regarding symptom management. Participants stressed the role of support from their health care providers or other patients in helping them to understand more about living with HIV:

I would like to suggest having someone to reach to answer a not so relevant question like if I have stomach-ache and I want to know if it is connected to my meds or a side effect versus to searching in Google which is sometimes inaccurate.

Exchange of experiences [is important] especially to the new patient so they would know what to do. They would feel that they are not alone, because you won't know how to avoid feeling self-pity. At least with a support group they have someone to communicate with.

Process Evaluation Question 10: Cost

A description of the types of expenses involved in the implementation and the approximate costs from the Philippines setting are shown in Table 2.

Table 2. Costs involved in the intervention.

Aspect	Description	Cost
Cloud hosting of solution	The database and software require hosting on RDS[a] and EC2[b] server instance. The cost of a monthly or yearly subscription depends on the amount of storage needed and payment schedule. Our database includes data for approximately 700 patients.	US $50 per month
VOIP[c] provider	This may be the local telecommunications company (eg, Vodacom and Globe) or a specialist service provider.	PHP 0.50 (US $0.01) per SMS text message or PHP 5 (US $0.10) per minute for voice calls
Local service provider IT support	IT support monitors the server, VOIP functionality, and software updates and manages users' log-ins. Our local IT support provides up to 20 hours of support monthly and charges an hourly rate for additional support.	PHP 10,000 (US $200) per month
Staff	An administrative clerk, counselor, or other cadre of staff will allocate time and effort to enroll patients on the system, activate their services, monitor alerts, and update details.	Cost varies (0.1-0.5 FTE[d] of administrator)

[a]RDS: relational database service.

[b]EC2: Elastic Compute Cloud.

[c]VOIP: voice over IP.

[d]FTE: full time equivalent.

Discussion

Principal Findings

During the study, >31,000 IVRS calls and 8000 SMS text messages were sent to 462 study participants. The Connect for Life system was acceptable to both participants and providers. Participants liked that the intervention was highly personalizable, enabling them to select the frequency and time of calls or SMS text messages and the topics of health tips. Feedback on the pill reminders, visit reminders, and health tips was very positive. Participants appreciated that health tips covered a variety of topics beyond HIV basics. The FGDs revealed that acceptability of the weekly adherence scores and symptom reporting functionalities of the intervention was low, as these 2 functions required lengthy navigation of the IVRS menu.

Owing to technical issues, the intervention was not implemented as originally intended, with only 22.1% (102/462) of the participants receiving the IVRS pill reminder intervention and others receiving a scaled-back SMS text message intervention. When the technical issues were first identified, enrollment in the study was paused for 3 months, while the study team assessed the cause of the issue. Ultimately, the issue of DTMF malfunction was attributed to issues in the telecommunications system that neither the telecommunications provider nor the Connect for Life developers could resolve. When enrollment was resumed, participants were provided SMS text messages rather than IVRS services. Despite the technical challenges, acceptability remained high, and only 0.6% (3/462) of the participants withdrew from the study. Following the study, the frequency of technical issues has decreased significantly, and the study site has continued to provide the service. Currently, pill reminder calls are a routine service for all new patients undergoing ART.

Notably, the technical challenges experienced in delivering the intervention were related to navigating the IVRS menu and made it difficult to distinguish whether the issues raised with ease of use or overall satisfaction were related to the technical challenges (ie, the dial tones were not recognized when keyed in) or to the product design (ie, IVRS menus were very complicated). The accuracy of the adherence scores in the weekly feedback SMS text messages was dependent on successful navigation of the IVRS process. This type of feedback may have been better delivered via a smart phone app rather than an IVRS setup. The interactive component of the IVRS system was an important aspect of the study design, which was not effectively evaluated in this study owing to the low number of participants who received this part of the service, warranting ongoing monitoring and future studies.

The scaled-back intervention provided everyone with visit reminders, which addressed part of the theory of change by improving medication accessibility through timely refills, but did little to prompt pill-taking, habit forming, and improvements in health knowledge. Individuals who received a high dose of the intervention (daily or weekly pill reminders) were more likely to recommend the intervention to others, suggesting that the planned intervention was more acceptable than the scaled-back version.

Our analysis of dose received shows that the call answer rate was low, with only 26.24% (8119/30,940) of outgoing calls answered, which is reflective of a preference for SMS text messages and chat services among the target population. The requirement of a PIN reduced exposure to the intervention, which was mostly owing to technological challenges. After experiencing technical difficulties several times, many participants stopped answering the calls. However, some mentioned that the phone ringing at the set time each day served as an effective adherence reminder.

Privacy considerations were paramount, with 11% (51/462) of the participants reporting that they had concerns about the potential for disclosure of their HIV status. Therefore, in situations where entering a PIN is a barrier to intervention exposure, practitioners can consider adapting the content to

eliminate potentially sensitive health information and delivering the service with no PIN requirement.

Ultimately, the study showed the importance of choosing technologies that can function in local contexts. In low-resource settings, it may take time to scale-up technologies that will be quick to roll out in high-resource settings. Practitioners must identify service providers with appropriate capacity and ensure that patients have the skills and motivation to use the intervention. Conducting an iterative process with several pilot stages is advantageous, as it enables practitioners to identify the problems with functionality and adapt the intervention before scaling up.

An important aspect of the intervention was that, through this regular contact from the clinic, participants felt cared for and felt that their health care provider was concerned about their well-being. This social support was a key motivator for adherence. Participants requested to be able to speak to someone about side effects or for social support, suggesting that an intervention that links calls to counselors more effectively may be an area for future evaluation.

Comparison With Previous Studies

The Connect for Life Philippines intervention was adapted from the same platform used for Call for Life Uganda and mMitra and Treatment Advice using Mobile Alerts in India. Acceptability was high in all 3 settings [11,16]. However, there were differences in the preferences and use patterns of the participants in the Philippines setting compared with those in Uganda and India. The Philippines had a high preference for SMS text messages over voice calls and a low call answer rate. The Connect for Life Philippines and Call for Life Uganda projects experienced similar challenges with network instability issues in the early stages [16].

Similar to Connect for Life and Call for Life, other mHealth interventions for people living with HIV have shown improvements in ART adherence, even where participant response rates (ie, dose received) are low [29,31,56]. For example, the PositiveLinks app used by people living with HIV in Virginia, United States, had response rates of <40% to most app prompts, but participant retention in care, CD4 results, and viral suppression improved significantly [57]. There is an important distinction between adherence to the intervention (ie, calls, app prompts, and device use) and adherence to medication.

Strengths and Limitations

A strength of the Connect for Life platform is its scalability; the project can easily be expanded to cover a large number of sites and patients with great cost efficiency, if those facilities have access to computers and internet connectivity. To deliver the project at scale, creation of content in regional languages will be an important consideration. The platform is adaptable, as the local IT provider can add and remove new data fields and update the SMS text message content, voice files, and call flows. However, changes to the functionality of the software or interoperability with other systems will require support from the software developers at Johnson and Johnson Global Public Health. The Philippines Department of Health has plans to implement electronic reporting systems for HIV services at an aggregated level. If the department is ever to implement a patient-level electronic medical record, interoperability with Connect for Life will be an important consideration to ensure delivery at scale.

A strength of this process evaluation study is the mixed methods and participatory approach. The study used prospectively collected quantitative data on participants' responses to the intervention and qualitative feedback from questionnaires, monthly process reports, and FGDs. The evaluation included the users of the intervention, clinical service providers, and developers of the technology platform.

The methodology addressed all key components in process evaluation for public health interventions and studies (context, reach, dose delivered, dose received, fidelity, implementation, and recruitment) [55]. Furthermore, the study included information on the technology platform, infrastructure, security, and cost, as guided by the mHealth Evidence Reporting and Assessment checklist developed by the World Health Organization mHealth Technical Evidence Review Group [35].

A limitation of our approach was that the evaluation was conducted by the same study team responsible for planning and implementing the intervention, rather than by independent evaluators. Other limitations included the convenience sampling strategy for participants in the FGDs and the low participation in the focus groups. Although the study team approached many individuals to participate, it was a challenge to identify those who were willing owing to reluctance to disclose their HIV status in a group. Furthermore, owing to transportation challenges, there was low attendance among those who confirmed their intention to participate in the groups.

Incomplete data may have affected the interpretation of the results. Of the 462 participants in the study, 440 (95.2%) attended the final study visit at week 48, and 89.1% (392/440) of them completed the questionnaire during the final visit. There may be differences in the experiences of participants who transferred out, died, withdrew from the study or were lost to follow-up, attended but did not complete the questionnaire, and completed the questionnaire.

This study focused on MSM in Metro Manila, and the study population was urban and highly educated. Participants may have had alternative adherence reminders, including self-set phone alarms and email alerts. Therefore, the results are not broadly generalizable to other contexts.

Conclusions

mHealth interventions are useful to support adherence, as they have low replication costs and are highly adaptable to specific cultural contexts. On the basis of the findings of this process evaluation, we can guide practitioners implementing mHealth interventions to support medication adherence to consider the following recommendations:

1. The intervention should allow the participant to personalize the service based on their preferences for delivery by SMS text message or voice calls, timing of messages and calls, and selection of content.

2. Limit the complexity of the IVRS menus to reduce the "hassle" factor and likelihood of technical failures. If the navigation of menus is a key aspect of the intervention, consider using an app or a chatbot instead of, or in addition to, an IVRS system.
3. Consider how to use the mHealth intervention to facilitate human interaction. For example, certain responses to the intervention may prompt counselor-, clinician-, or peer support.
4. Ensure that the roll out of an existing mHealth technology in a new setting is an iterative process that includes robust process evaluation methods. Rigorous pilot-testing is needed to ensure technical function. Work plans should include ample time and budget for adaptation of the technology.

The Connect for Life mHealth intervention to support adherence to ART had high participant satisfaction and acceptability. However, the feasibility of the intervention was dependent on the reliability of local telecommunications networks, and poor reliability of the local mobile networks had a large impact on the intervention's usability, fidelity, and dose received.

The process evaluation allowed us to better understand the preferences and use patterns of mHealth services by MSM in the Philippines. This will enable the effective scale-up of mHealth services for this key population, which is essential in the context of the dual HIV and COVID-19 pandemics, where more services must be delivered virtually.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Process evaluation methodology.
[DOCX File , 19 KB-Multimedia Appendix 1]

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Abbreviations

ART: antiretroviral therapy
DTMF: dial tone multifrequency
FGD: focus group discussion
IVRS: interactive voice response system
mHealth: mobile health
MOTECH: Mobile Technology for Community Health
MSM: men who have sex with men
PIN: personal identification number
SHIP: Sustained Health Initiatives of the Philippines

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ORIGINAL PAPER

Changes in Adherence and Viral Load Suppression Among People with HIV in Manila: Outcomes of the Philippines Connect for Life Study

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Abstract
The Philippines HIV epidemic is among the fastest growing globally. Infections among men who have sex with men are rising at an alarming rate, necessitating targeted evidence-based interventions to retain people living with HIV in care, support adherence, and reach viral suppression. We conducted a 48-week prospective cohort study of 462 participants in which we provided a mobile health (mHealth) adherence support intervention using the Connect for Life platform. We observed an improvement in adherence, with the proportion of participants taking more than 95% of their antiretroviral therapy (ART) doses increasing from 78.6% at baseline to 90.3% at 48 weeks. Among treatment experienced participants, adherence improved significantly (McNemar's test = 21.88, P < 0.001). Viral load suppression did not change, with 92.6% suppression at baseline and 92.0% at 48 weeks. Illicit drug use was associated with reduced adherence (aOR = 0.56, 95%CI 0.31–1.00, P = 0.05) and being on second-line therapy was associated with poor viral load suppression (aOR = 0.33, 95%CI 0.14–0.78, P = 0.01). Quality of life improved following ART initiation, from a mean of 84.6 points (of a possible 120) at baseline to 91.01 at 48 weeks. Due to technical issues, fidelity to the intended intervention was low, with 22.1% (102/462) of participants receiving any voice calls and most others receiving a scaled-back SMS intervention. The mHealth intervention did not have any observed effect on adherence or on viral load suppression. While evidence of effectiveness of mHealth adherence interventions is mixed, these platforms should continue to be explored as part of differentiated treatment support services.

Keywords mHealth · Adherence · HIV · Antiretroviral therapy · Philippines

Background

The HIV epidemic in the Philippines is one of the fastest growing HIV epidemics globally, with a doubling of the number of new HIV infections and the number of AIDS deaths increasing nearly by 400% from 2010 to 2020 [1, 2]. Most new and existing HIV infections in the Philippines occur among men who have sex with men (MSM) [2].

To slow the spread of HIV, the Philippines must continue to progress toward the Joint United Nations Program on HIV/AIDS (UNAIDS) 95-95-95 goals within all subpopulations and age groups. Currently, in the Philippines 64% of people living with HIV (PLHIV) know their status, 41% of those who are HIV positive are on antiretroviral therapy (ART), and the proportion of PLHIV with suppressed viral loads is unknown [3–5]. HIV care and treatment is freely available through the government-funded Philippine Health Insurance Corporation (PhilHealth) Outpatient HIV/AIDS Treatment (OHAT) package [6].

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mHealth for Medication Adherence Support

To achieve viral suppression, patients on ART must take their treatment consistently. However, in clinical practice achieving and maintaining optimal ART adherence is challenging [7, 8]. Early clinical studies reported that ≥ 95% adherence to ART was required to achieve and maintain viral suppression [9, 10]. More recent studies have shown that virologic suppression may be achieved with adherence levels < 95%, however this is dependent on the duration of treatment and the ART regimen [11–13]. ART non-adherence has been linked to the development of ART resistance [14, 15], progression to AIDS [16], and death [17].

Several key factors influencing ART adherence are well documented in the literature, including medication side effects, substance abuse, presence of social support, and time on treatment [7, 8, 18–21]. In the Philippine context, issues of stigma and discrimination have also been documented as a major barrier to medication adherence [22–25].

As mobile phone technologies for health (mHealth) have become increasingly popular in the global health and development sectors, clinical trials have shown that mHealth approaches have promise in improving self-management of chronic disease including adherence to HIV medications [26–30]. A 2017 systematic review and meta-analysis assessing interventions to improve adherence to ART found that SMS interventions were superior to standard of care (OR 1.48, CrI 1.00–2.16), and that multiple interventions had additive affects [31]. Systematic reviews show mixed outcomes of mHealth interventions and highlight the need for more rigorous evaluation methods and longer follow-up periods [32–38].

The WHO Consolidated Guidelines on ART recommend using mHealth approaches to support HIV care and treatment and improve adherence. The 2016 guidelines endorsed mobile phone text messages as low-cost interventions that have demonstrated benefit in improving adherence and viral suppression and are backed by "moderate evidence" [39].

During this study, we provided participants with an mHealth adherence support intervention using a platform called Connect for Life. The platform is able to send automated messages to participants via their mobile phones through interactive voice response system (IVRS) call flows or through SMS text messages [40]. Participants received varying levels of exposure to the intervention, with the frequency of contact and types of messaging received being dependent on a combination of personal preference and contextual factors.

Prior to roll out in the Philippines, the Connect for Life platform was piloted for use in maternal health and HIV programs in India and Uganda [41–44]. To adapt the intervention for the local setting and target population in the Philippines, we applied a mixed methods approach guided by the Behavior Change Wheel (BCW) framework and the information, motivation, and behavioral skills (IMB) model of adherence [25, 45, 46]. The BCW is a method for characterizing and developing behavior change interventions based on a comprehensive causal analysis of the behavior, while the IMB model includes three primary constructs that influence behavior changes: information and knowledge about the behavior; the individual's motivation to perform the behavior; and the behavioral skills necessary to perform the behavior.

In the context of the emerging HIV crisis among MSM in the Philippines, there is an imperative to expand options for tailored HIV prevention and treatment support. While other studies have found high levels of feasibility and acceptability of SMS interventions targeted toward HIV-positive MSM in the United States, in Peru, and in Asia [47–50], there is a lack of data on interventions to improve adherence and treatment outcomes among HIV-positive MSM. Furthermore, few mHealth interventions for MSM have been evaluated in Asia and none in the Philippines. In this paper we present the outcomes of a prospective cohort study of HIV patients in the Philippines, describing adherence to medication, retention in care, and viral load suppression. We examine various factors affecting these outcomes including the mHealth adherence support intervention received.

Methods

We conducted a prospective cohort study, collecting data at four time points: baseline, 12-, 24-, and 48-weeks. The study was conducted at the Sustained Health Initiatives of the Philippines (SHIP) clinic, a low-cost, private facility providing HIV care and treatment to people in Metro Manila, Philippines. Approximately 98% of SHIP's clients are MSM, with an average age of 30 years at initial consultation.

Recruitment into the Connect for Life study occurred in-person at the SHIP clinic from October 2016 to December 2017. Eligible participants were HIV-positive, receiving ART at the study site, could speak and read English, and had a mobile phone. The study coordinator approached patients attending their routine visits while they were in the clinic waiting room. Patients were not approached or screened on days the study coordinator was not available, or if they bypassed the waiting room.

During the study, participants received a personalized combination of services, including automated pill reminders, appointment reminders, health tips, and adherence feedback messages delivered by voice call or SMS on the patient's preferred time and day. Based on findings from

formative stages of the project, we planned to provide daily pill reminder calls to participants who were on ART for less than 6 months and weekly reminder calls to those on ART for 6 months or longer [25].

Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631). All participants provided written consent prior to inclusion in the study.

Objectives

The primary objective of this observational, single-arm study was to describe the adherence to medication, viral load suppression, and retention in care of the patient population participating in the Connect for Life mobile phone adherence support demonstration project. The secondary objectives were: to describe the Quality of Life and the HIV-related Knowledge, Attitudes, and Practices of participants; to describe the clinical outcomes of participants including treatment failure (switch to second-line), and AIDS-related mortality; and to identify factors that affected patient adherence and treatment outcomes.

Data Sources/Measurements

Laboratory results, diagnoses, dispensing, and other clinical information were extracted from patient charts by the study coordinator. Each participant completed three questionnaires at each visit: HIV-related Knowledge, Attitudes and Practices (KAP) adapted from the Brief HIV Knowledge Questionnaire (HIV-KQ-18) [51]; the WHO HIV Quality of Life questionnaire (WHOQOL-HIV BREF) [52, 53]; and an adherence questionnaire that was adapted from the AIDS Clinical Trials Group adherence instrument [21]. All questionnaires were in English. The questionnaires were self-administered, with assistance from the study coordinator as requested. Where questionnaires had blank or missing or incomplete fields, all available data points were included in the analysis.

Outcomes

The main outcomes of interest were adherence, viral load suppression, and retention in care. Secondary outcomes included quality of life and HIV-related knowledge. Outcomes were measured over time with all observations from the 12-, 24-, and 48-week visits considered as outcomes.

Key variables were defined as follows:

- Adherence: At each study visit, using a visual analogue scale (VAS) participants reported the proportion of ART doses taken in the prior 30 days as 0–100%. This continuous variable was converted into a binary variable with those reporting 95% or greater categorized as adherent.
- Viral load suppression: A binary variable defining suppression as HIV viral load lower than detectable limit of lab assay (< 50 copies/ml). All viral load tests were conducted as routine standard of care (not provided by the study) and all available test results were extracted from patient files. Only viral load tests that were collected at least 3 months after treatment initiation were included.
- Retention in care: Proportion of participants alive and in care ("not in care" defined as not having returned for more than 30 days after last scheduled clinic visit or refill).
- Treatment experience at enrollment: A binary variable defining treatment experience as having initiated ART more than 6 months prior to study enrollment date.
- Exposure to the intervention: A continuous variable defined as the total number of days the patient received one or more SMS text messages or calls from the Connect for Life platform during the study. This was then converted into a categorial variable representing level of exposure with High (96+ days of contact), Medium (48–95 days of contact), Low (12–47 days of contact), and no exposure (< 12 days). These cut points serve as rough proxies for monthly, weekly, or daily contact, with the three categories of exposure (excluding no exposure) each representing at least 50 individuals.
- QOL: A continuous variable of up to a maximum of 120 points, scored as per WHOQOL-HIV BREF questionnaire [52, 53].
- KAP: Knowledge was categorized as a continuous variable, based on a 16-item dichotomous response (true/false) questionnaire. The questionnaire had two additional sections about sexual activities, alcohol and drug use which included dichotomous, categorical, and continuous variables.

Statistical Analysis

Demographic and clinical characteristics were described as a mean or proportion with a 95% confidence interval. Descriptive analyses of adherence and viral load outcomes were performed for the entire cohort, and then according to: (1) intervention exposure category, (2) adherence above or below 95% at baseline, and (3) treatment experience of more or less than 6 months at enrollment. We hypothesized that higher level of exposure to the intervention could lead to greater improvements in the key outcomes. We also hypothesized that treatment naïve participants and those with poor adherence at baseline may benefit more than others from receiving reminders to achieve adequate adherence and viral load suppression.

Adjusted odds ratios were estimated using a generalized estimating equations (GEE) model with an exchangeable correlation structure and robust variance. GEE was selected to allow for clustering of outcomes within an individual. The model included intervention exposure, treatment experience, baseline adherence, and other factors which had a P-value < 0.1 in unadjusted univariate analyses (with some factors excluded a priori due to collinearity). For both main outcomes, all observations from follow-up visits were included in outcome analyses, and the models adjusted for baseline adherence and baseline viral load, respectively. Wald tests were used to calculate P-values of each variable.

Several sensitivity analyses were conducted. Both univariable and multivariable analyses were reproduced using continuous variables for intervention exposure (unique number of days participant received call or SMS) and adherence (percent adherence from 0 to 100) in place of the respective categorical and binary variables. The analyses were also reproduced using mixed-effects logistic regression models instead of GEE. Finally, the descriptive and inferential analyses were reproduced using an intention to treat approach, in which the dataset was updated to include data points for participants who were lost to follow-up or who died with the assumption that they were non-adherent and virally unsuppressed for the period from the time they became lost to follow-up tor deceased until the date when they would have completed the study.

Results

Participants

Approximately 675 participants were receiving HIV care at the study site during the recruitment period. 485 patients were approached by the study coordinator. Of those approached 95.7% (464/485) agreed to be screened for enrollment, and 95.3% (462/485) met the eligibility criteria and consented to participate (Fig. 1).

Reasons for refusal (21/485, 4.3%) included no need or desire for adherence support, not wanting to receive messages or calls on their mobile phone, privacy concerns, and inconsistent access to mobile phone due to frequent international travel. Of the 0.4% (2/464) of the patients who were excluded based on screening, one was ineligible because he did not speak English and the other did not have a mobile phone. Of the participants enrolled, 0.1% (3/462) withdrew, 0.1% (3/462) died, 3.7% (17/462) transferred to another clinic for their care, 3.9% (18/462) were lost to follow-up (missed two consecutive visits), and the remaining 91.1% (421/462) completed the study.

Demographic factors, clinical characteristics and behavioral practices of the study participants are described in

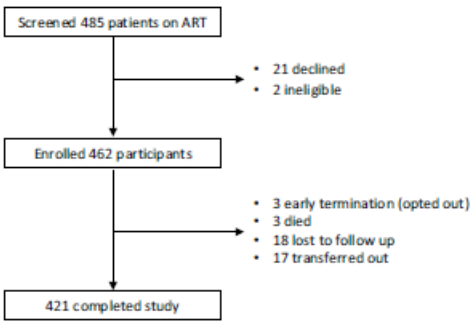

Fig. 1 Recruitment and study completion of patient cohort

Table 1. As the study site caters to young MSM, all but one of the participants in the study (461/462, 99.8%) were male and only 1.5% of participants (7/462) were heterosexual. Most participants were treatment experienced, with the mean time on ART among experienced participants being 2.77 years (SD 2.0). The mean age at enrollment was 32.4 years (SD 5.7). Most participants were university graduates (397/462, 85.9%) and most were either employed or students (422/462, 91.3%).

Notably, nearly half of all participants (227/462, 49.1%) had not disclosed their HIV status to a family member or friend. Furthermore, a substantial proportion of participants (94/462, 20.4%) worked in the Business Process Outsourcing (BPO) sector, a key economic sector in which third-party vendors provide services remotely (e.g. contact centers, back-office services, data transcription, and information technology), usually to multinational corporations. Due to the variable nature of work schedules for BPO workers and lack of privacy due to working conditions in call center settings, this group faces unique barriers to adherence.

Delivery of the Adherence Support Intervention

The intended intervention would provide daily pill reminder calls to participants who were on ART for less than 6 months and weekly reminder calls to those on ART for 6 months or longer [25]. Due to technical issues, fidelity to the intended intervention was low, with only 22.1% (102/462) of participants receiving any voice calls and most others receiving a scaled-back SMS intervention (Fig. 2). Technical issues were first identified in the second month of the study, at which point new enrollment was paused for approximately three months while the study team assessed the cause of the issue. Ultimately, the issue was characterized as a dual tone multi-frequency (DTMF) malfunction—i.e., a problem with the tones not being transmitted or recognized when

Table 1 Baseline characteristics of study participants (N=462)

Characteristics		Number	(%)
Gender	Male	461	99.78
	Female	1	0.22
Age	18–24	23	4.98
Mean: 32.4 years (SD 5.7)	25–29	132	28.57
	30–39	262	56.71
	40+	45	9.74
Education	Elementary or less	11	2.38
	High school/vocational	21	4.55
	College/university	345	74.68
	Post-graduate	52	11.26
	Unknown/did not report	33	7.14
Employment	Employed	422	91.34
	Unemployed	40	8.66
Sexual orientation	Bisexual	139	30.09
	Heterosexual	9	1.95
	Homosexual	313	67.75
	Pansexual	1	0.22
Civil status	Married/common-law partner	21	4.55
	Single	439	95.02
	Unknown/did not report	2	0.43
Serodiscordant relationship	Not in a relationship	290	62.77
	Seroconcordant relationship (both HIV+)	50	12.24
	Serodiscordant relationship (partner is HIV−)	75	16.23
	Unknown/did not report	47	10.17
Disclosure of HIV status to family/friend	Disclosed	146	31.60
	Not disclosed	227	49.13
	Unknown/did not report	89	19.26
Time on ART, years	<30 days	45	9.74
	1–6 months	30	6.49
	6 months–1 year	39	8.44
	1–2 years	86	18.61
	2–4 years	163	35.28
	>4 years	99	21.43
Nadir CD4 (cells/mm^3)	0–199	177	38.31
	200–499	253	54.76
	500+	32	6.93
ART regimen	First line	393	85.06
	Second/third line	69	14.94
Condom usage in last 6 months	Always	184	39.83
	Sometimes/most of the time	169	36.58
	Never	88	19.05
	N/A (not sexually active)	21	4.55
Transactional sex	Never had transactional sex	434	93.94
	Ever had transactional sex	26	5.63
	Unknown/refused	2	0.43
Sexual partners in last 6 months	None	97	26.01
	One	147	39.41
	2–9	106	28.42
	10 or more	23	6.17

Table 1 (continued)

Characteristics		Number	(%)
Problem alcohol use[a]	No	388	85.84
	Yes	64	14.16
Injection drug use (ever)	No	406	87.88
	Yes	56	12.12
Any drug use (3 months preceding enrollment)	No	386	83.55
	Yes	76	16.45
Baseline viral load[b]	Detectable (≥ 50 copies/ml)	21	4.55
	Undetectable (< 50 copies/ml)	262	56.71
	No VL data at baseline	179	38.74

[a]Problem alcohol use defined as two or more episodes of heavy episodic or 'binge' drinking (> five drinks) in the prior month or > 14 drinks per week on average [54, 55]

[b]Conducted at the baseline visit or in six months prior to enrollment

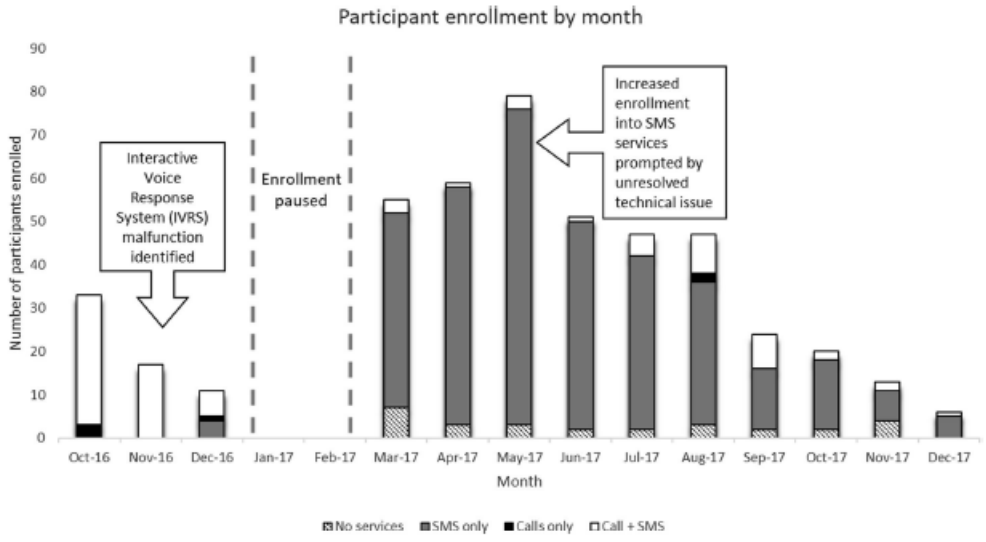

Fig. 2 Participant enrollment by month and type of intervention received

pressing digits on the handset to navigate interactive touch-tone menu. This was attributed to issues in the telecommunications system that neither the telecommunications provider nor the Connect for Life developers could resolve. When enrollment was resumed, participants were offered SMS text messages rather than IVRS voice call services. Because not all participants experienced technical challenges with voice calls, those who had a strong preference for voice calls could opt in, and they were counselled about the possibility of technical challenges and how to report issues to the study team.

On average, study participants received contact (voice call or SMS) from the Connect for Life system on 34 separate days throughout their time on the study (min = 0 and max = 358 days). During the study, the Connect for Life system sent participants a total of 8234 SMS messages. It also made 31,095 IVRS calls, of which 26% were answered. Table 2 outlines the frequency of contact, the delivery methods used (voice or SMS), and service types that participants received. The intervention delivery is further described in a separate process evaluation paper [40].

Table 2 Intervention level and type received by study participants (N = 462)

Intervention exposure measure		N	%
Number of days of contact	None	28	6.06
	Low (12–47 days of contact)	297	64.29
	Medium (48–95 days of contact)	53	11.47
	High (96+ days of contact)	84	18.18
Number of calendar quarters with contact	None	28	6.06
	1 quarter	7	1.52
	2 quarters	60	12.99
	3 quarters	145	31.19
	4+ quarters	222	48.05
Voice or SMS service	None	28	6.06
	SMS only	340	73.59
	Voice only	6	1.30
	SMS + voice	88	19.05
Type of treatment support received	None	28	6.06
	Visit reminders only	340	73.59
	Visit reminders + pill reminders	25	5.41
	Visit reminders + health tips	8	1.73
	Visit reminders + health tips + pill reminders	61	13.20

Clinical and Adherence Outcomes

ART Experience & Baseline Adherence

At the time of enrollment, 83.8% (387/462) of participants had been taking ART for 6 months or more, 6.5% (30/462) had been on ART for 30 days-6 months, and 9.7% (45/462) were either treatment naïve or on ART for less than 30 days at enrollment.

At baseline among participants on ART for 30 days or more, perfect adherence of 100% of doses taken in the last 30 days was reported by 50.7% (208/410) of the participants, adherence of 95–99% of doses was reported by 27.3% (112/410), adherence of 90–94% was reported by 13.2% (54/410), and adherence of < 90% was reported by 8.7% (36/410).

Retention, Mortality, and Treatment Failure

Retention on ART at the 48-week study visit was 91.1% (421/462) and an additional 0.6% (3/462) of participants voluntarily withdrew from the study but continued receiving HIV care at the study site. Throughout the study 3.9% (18/462) became lost to follow-up, and 3.7% (17/462) transferred care to another clinic (Fig. 1).

Clinicians changed the ART regimens of two participants due to treatment failure, the first of whom was treatment naïve and presented with opportunistic infections (PCP and TB) at the time of enrollment, and the second who was treatment experienced and reported poor ART adherence. Furthermore, three participants died during the course of the study, one death was due to an AIDS-related illness (cryptococcal meningitis), while one death was caused by a myocardial infarction, and the final participant's cause of death was not reported.

Table 3 describes the key outcomes of the cohort at each study visit and includes all available measurements at each time point.

Adherence

The 462 participants reported a total of 1540 adherence observations. The proportion of participants with ≥ 95% adherence improved from 78.0% (95% CI 74.4–82.4%) at baseline to 90.3% (95% CI 87.0–93.1%) at 48 weeks. Among treatment experienced participants, there is strong evidence of an improvement in adherence, with an increase from 77.1% (293/380) at baseline to 89.4% (269/331) at the final visit (McNemar's test = 21.88, P < 0.001). Participants who were adherent at the time of enrollment continued to have higher adherence at subsequent visits, and adherence was not associated with intervention exposure level (Fig. 3).

VL Suppression

There were 595 routine viral load test results recorded for 374 participants. Of these, 47.6% (283/595) were recorded at the baseline visit and 52.4% (312/595) at subsequent visits (Fig. 4). There was no change in suppression rates from baseline to end of study among treatment experienced participants, and viral load suppression was not associated with intervention exposure level.

Table 3 Primary and secondary outcomes by study visit

	Baseline (N = 462)	12 week (N = 454)	24 week (N = 430)	48 week (N = 421)
Adherence ≥ 95%	320/410 (78.05)	295/333 (88.59)	339/388 (87.37)	355/393 (90.33)
Treatment naïve (< 30 days)	n/a	31/32 (96.88)	34/36 (94.44)	35/35 (100.00)
30 days–6 months on ART	27/30 (90.00)	20/23 (86.96)	22/24 (91.67)	24/27 (88.89)
> 6 months on ART	293/380 (77.11)	244/278 (87.77)	283/328 (86.28)	296/331 (89.43)
Adherence > 95% IIT (includes LTFU and died pts as nonadherent)	320/410 (78.05)	295/337 (87.54)	339/401 (84.54)	355/414 (85.75)
VL suppression cumulative[a]	262/283 (92.58)	279/299 (93.31)	294/318 (92.45)	335/364 (92.03)
VL suppression (per VL done at each study visit)	262/283 (92.58)	50/53 (94.34)	72/81 (88.89)	162/178 (91.01)
Knowledge score (mean)	85%	86%	87%	88%
Knowledge > 90%	173/458 (37.77)	142/330 (43.03)	166/386 (43.01)	182/378 (48.15)
Quality of life (mean, max score 120)	88.31	89.41	89.97	88.39
High QOL (≥ 90)	194/426 (45.54)	150/298 (50.34)	181/358 (50.56)	199/381 (52.23)
Died (cumulative)	n/a	1/462 (0.22)	3/462 (0.65)	3/462 (0.65)
Lost to follow-up (cumulative)	n/a	3/462 (0.65)	10/462 (2.16)	18/462 (3.90)

Denominators vary based on number of participants who completed each survey instrument at each visit, variance is due to missed visits or forms not completed. The N reported in each column reflects total number of people remaining enrolled in the study at each time point, while the denominator in each row reflects the number of data points collected for each variable

[a]Viral load at baseline is recorded for participants that had a viral load test result on file for taken at that visit or within the 6 months prior. As VL testing is conducted annually, in this table the last VL outcome is carried forward to visits where no VL was taken in order to represent the overall VL coverage and suppression rate for the cohort

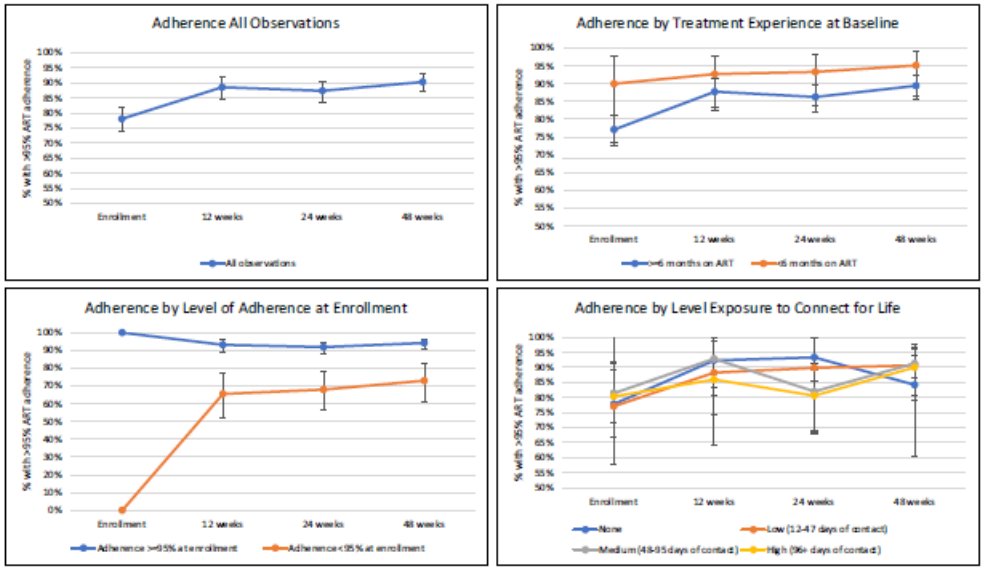

Fig. 3 Adherence per study visit (includes all available data points at each study visit)

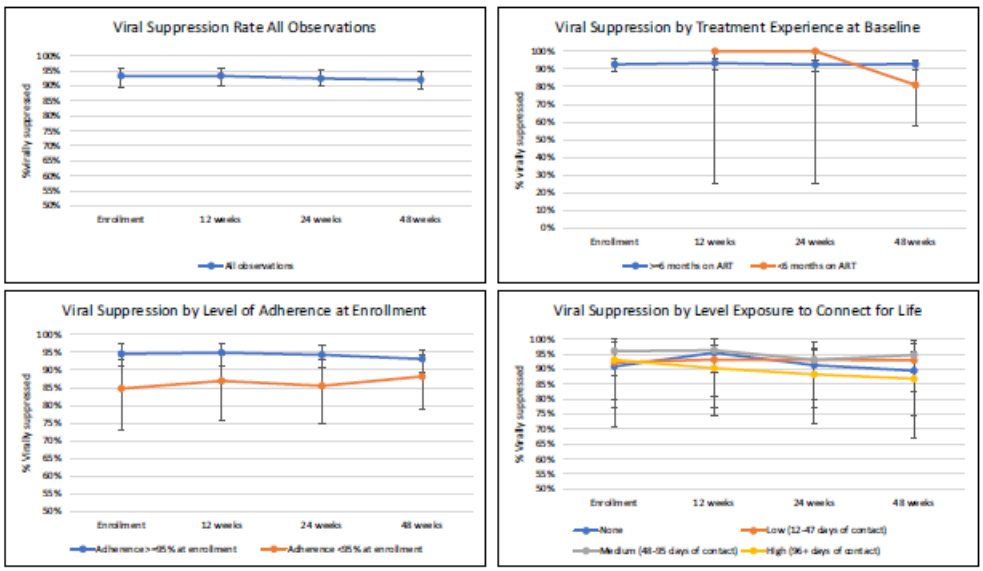

Fig. 4 Viral load suppression per study visit (includes all available data points at each study visit)

Viral load coverage was low, especially among the participants who were new on treatment at study enrollment. The proportion of participants who had at least one VL test done at any visit (viral load test coverage) was 81.2% (375/462) overall. However, coverage was 91.2% (353/387) among participants who were treatment experienced (≥ 6 months) at enrollment and only 28.0% (21/75) for participants who were new on ART (< 6 months) at enrollment. Of the viral load tests done in the new on ART group, 95.2% (20/21) of these tests were recorded at the 48-week visit, which may explain the decreased suppression rate (81.0%, 17/21) at the 48-week time point (as only one viral load, which was undetectable, was reported before this time point for this group).

Quality of Life

Among participants who were new on treatment at enrollment, the QOL score on the WHOQOL-HIV BREF scale improved from baseline to 48 weeks. Treatment experienced participants had a higher mean QOL at baseline (89.02 of a possible 120 points) than those who were new on ART (84.6, P = 0.01). For the participants who were new on ART, mean QOL increased from 84.6 at baseline to 91.01 at 48 weeks (t = − 2.2491, P = 0.025), with the largest improvement occurring in the domain related to level of independence (mobility, activities of daily living, dependence on medication or treatments, and work capacity). There was no statistical evidence for a change in QOL for treatment experienced participants from baseline to end of study. There was no association between QOL score and level of intervention exposure.

HIV Knowledge

There was a small increase in the mean knowledge score between baseline (84.5%) and 48 weeks (88.0%) (t = − 4.6825, P < 0.0001). There was no difference between the experienced and new participants in knowledge scores. Nearly all participants correctly answered questions regarding how HIV can be transmitted, while most incorrect answers were on questions related to clinical topics such as whether an effective HIV vaccine exists or understanding the distinction between HIV and AIDS. Exposure to the intervention did not impact the knowledge score, regardless of whether the participants did or did not receive health tips as part of the intervention.

Factors Affecting Adherence and Viral Load

The findings from multivariable models of associations between various demographic, clinical, and behavioral factors and the outcomes of adherence and viral suppression are outlined in Tables 4 and 5, respectively. Each table includes only the variables that had an association with the respective

Table 4 Factors associated with self-reported optimal adherence (≥95%) assessed in a multivariable logistic regression model

	% Adherent	aOR	P value
Intervention exposure			
None	85.14	1.00	0.28
Low (12–47 days of contact)	86.19	1.10 (0.41–2.94)	
Medium (48–95 days of contact)	86.74	0.72 (0.23–2.28)	
High (96+ days of contact)	84.31	0.64 (0.22–1.87)	
Baseline adherence			
Adherence < 95% at enrollment	48.17	1.00	**< 0.001**
Adherence ≥ 95% at enrollment	95.02	5.83 (3.60–9.46)	
No adherence data at baseline	96.25	9.89 (2.44–40.10)	
Treatment experience at baseline			
< 6 months on ART	93.24	1.00	0.37
6+ months on ART	84.74	0.72 (0.31–1.70)	
ART regimen			
First line	78.75	1.00	0.37
Second/third line	87.31	0.76 (0.43–1.37)	
Problem alcohol use[a]			
No	86.85	1.00	0.23
Yes	80.09	0.73 (0.44–1.00)	
Any drug use (3 months preceding enrollment)			
No	86.80	1.00	**0.05**
Yes	78.13	0.56 (0.31–1.00)	

Bold values indicate statistical significance ($P \leq 0.05$)

[a]Problem alcohol use defined as two or more episodes of heavy episodic or 'binge' drinking (> five drinks) in the prior month or > 14 drinks per week on average [54, 55]

outcome of interest with a P-value < 0.1 in unadjusted univariate analyses.

We found that, while adherence improved over the course of the study, there was no association between intervention exposure and adherence (aOR = 1.10, 0.72, 0.64 for low, medium, and high exposure, respectively; P = 0.28). Illicit drug use in the 3 months prior to enrollment was negatively associated with adherence (aOR 0.56; 95% CI 0.31–1.00; P = 0.05). Participants with optimal adherence (> 95%) at baseline had higher odds of optimal adherence at follow-up (aOR 5.83; 95% CI 3.60–9.46; P < 0.001).

Viral load suppression did not change over the course of the study, and there was no association between intervention exposure and viral load suppression (aOR = 1.92, 4.22, 0.96 for low, medium, and high exposure, respectively; P = 0.41). There was weak evidence that participants who had been on treatment for more than 6 months at enrollment were more likely to be virally suppressed at follow-up than those who were new on treatment at enrollment (aOR = 3.67; 95% CI 0.89–15.15; P = 0.07).

The 69 participants who were on second-line antiretroviral regimens (indicating previous treatment failure or intolerance) were less likely to have suppressed viral load (aOR = 0.33; 95% CI 0.14–0.78; P = 0.01) and may also less likely to be adherent (aOR = 0.76; 95% CI 0.43–1.37; P = 0.37). The viral load suppression rate among these second-line patients did not improve over the course of the study. At baseline, 77.1% (95% CI 64.8–89.4%) of second-line patients had undetectable viral load measurements as per their most recent VL test; at 48 weeks this was 80.7% (95% CI 70.53–90.76%), reflecting no significant change (McNemar's test = 0.00; P = 1.00).

Sensitivity Analyses

Both univariable and multivariable analyses were reproduced using continuous variables for intervention exposure and adherence. The analyses were also reproduced using logistic regression and mixed effect models instead of GEE and then using an intention-to-treat approach for participants who were deceased or lost to follow-up.

For each sensitivity analysis, the direction of adjusted odds ratios did not change for any of the independent variables and the effect sizes were similar.

Table 5 Factors associated with viral load suppression assessed in a multivariable logistic regression model

	% VL suppressed	aOR	P value
Intervention exposure			
None	87.80	1.00	0.41
Low (12–47 days of contact)	92.47	1.92 (0.38–9.62)	
Medium (48–95 days of contact)	93.10	4.22 (0.45–39.59)	
High (96+ days of contact)	88.73	0.96 (0.15–6.10)	
Baseline adherence			
Adherence < 95% at enrollment	86.89	1.00	0.80
Adherence ≥ 95% at enrollment	92.98	1.14 (0.35–3.71)	
No adherence data at baseline	94.12	2.32 (0.19–27.67)	
Treatment experience at baseline			
< 6 months on ART	80.95	1.00	0.07
6+ months on ART	92.16	3.67 (0.89–15.15)	
Baseline viral load			
Detectable (≥ 50 copies/ml)	74.47	1.00	**0.01**
Undetectable (< 50 copies/ml)	89.29	0.44 (0.09–2.17)	
No VL data at baseline	93.97	1.86 (0.42–8.24)	
Serodiscordant relationship			
Not in a relationship	90.28	1.00	0.76
Seroconcordant relationship (both HIV+)	98.57	– (–)	
Serodiscordant relationship (partner is HIV−)	93.27	1.12 (0.34–3.69)	
Unknown/did not report	90.16	0.68 (0.22–2.08)	
ART regimen			
First line	94.12	1.00	**0.01**
Second/third line	80.39	0.33 (0.14–0.78)	
Adherence (post-baseline)			
Adherence < 95%	84.52	1.00	0.93
Adherence ≥ 95%	92.84	1.07 (0.24–4.68)	

Bold values indicate statistical significance ($P \leq 0.05$)

Discussion

Key Results

The study used a personalized mobile phone adherence intervention over a 48-week period as a vehicle to improve adherence to daily ART and viral load suppression among a cohort of participants with HIV. We observed an improvement in adherence over time, with the proportion of participants taking more than 95% of their ART doses increasing from 78.6% at baseline to 90.3% at 48 weeks. The improved adherence observed in the cohort was not attributable to exposure to the mobile phone intervention as measured by number of days with any intervention contact. This may indicate that study participation alone had a positive effect on adherence. Through study participation, participants received several elements that are not standard of care: repeated adherence measurements (on the visual analogue scale questionnaire), discussions with clinicians and study staff (especially at enrollment), and SMS visit reminders. These elements may have helped improve adherence, by increasing motivation to adhere, improving on-time attendance of appointments and thereby availability of medication, or by other mechanisms.

We found that quality of life improved in the year following ART initiation. For participants in our cohort who had been on treatment for less than 6 months at the time of enrollment, a small increase was observed in the mean quality of life score from 84.6 points (of a possible 120) at baseline to 91.01 points at 48 weeks. This improvement was not observed among treatment experienced participants, who already had a higher mean quality of life score at baseline. This supports the findings of previous studies conducted showing improved quality of life after starting or switching ART regimens [44, 56–58].

While adherence and quality of life improved, viral load suppression rates did not change significantly over the course of the study, with 92.6% of participants with a viral load done suppressed at baseline and 92.0% suppression at 48 weeks. The intervention did not have any observed effect on viral load suppression. An important finding was that

the coverage of routine viral load testing was lower than expected, especially among participants who were new on treatment at baseline. Just 28.0% (21/75) of these participants had a viral load test done during the study period, while clinical guidelines required testing at 12 months on treatment (updated guidelines from 2018 now require a viral load assay at both 6 and 12 months) [59, 60]. Poor coverage of testing may have been attributed to challenges with eligibility under the Outpatient HIV/AIDS Treatment (OHAT) package provided by the Philippine Health Insurance Corporation (PhilHealth) to cover the cost of laboratory tests.

While self-reported adherence was lower in ART experienced participants, their viral load suppression rates were still higher than participants who were new on ART at baseline. The lower viral suppression rate (81.0%) among the new on ART participants is not fully explained through poor adherence. This indicates the importance of monitoring drug resistance, which occurs at higher than expected rates in the Philippines [61, 62]. Furthermore, there should be an emphasis on accelerating the use of new, more effective first-line antiretroviral regimens which may achieve faster viral suppression in patients starting ART.

The findings also highlight the need for a differentiated approach to adherence support, with a strong focus on becoming undetectable for new patients (e.g., "Undetectable = Untransmissible"/"U = U" messaging) as well as resistance monitoring. Among more experienced patients, there should be a focus on addressing treatment fatigue. People on second-line therapy may require more intensive adherence support as we found that they continue to have poorer adherence and viral load suppression than those on first-line regimens.

Social and family support remain important factors in successful adherence and treatment outcomes [63, 64]. A substudy of 193 participants from this cohort found high rates of depression (21.8%) and anxiety (37.3%) among the cohort. However, the substudy found that these mental health factors did not impact ART adherence after factoring in low social and family support [65]. The proportion of participants in our cohort who confirmed they had disclosed their HIV status to family or friends was very low at just 31.6%.

Another group requiring attention is people who use illicit drugs. An earlier analysis of risk factors in this cohort [66] found that injection drug use (aOR = 0.54, P = 0.090) and inconsistent condom use (aOR = 0.50, P = 0.103) were both potentially associated with reduced adherence to ART. Indicating that these groups may be at risk of poor clinical outcomes as well as further HIV transmission to their sexual contacts. Study participants used drugs and alcohol at rates five to tenfold higher than the general population of the Philippines. Methamphetamine use is strongly associated with high-risk sexual behavior and HIV acquisition [67], and is commonly used by MSM in chemsex or 'Partee 'n' Play' activities. Compounding these risks, evidence-based HIV prevention is not widely available in the Philippines—condom distribution has been restricted [68, 69], and pre- and post-exposure prophylaxis services are only available in select geographic areas (mostly large cities) [70, 71].

In the absence of social and family support and in the context of substance use, mHealth platforms provide a mechanism for participants to be reminded about the importance of their treatment and to have more frequent contact with their healthcare providers.

Effectiveness of the Intervention

It is difficult to draw conclusions about the effectiveness of the mobile health intervention due to the poor fidelity of the intervention delivery. We found in the process evaluation that acceptability of the intervention was high, and that the personalizable aspect of the intervention, i.e. the ability to select the desired type of and frequency of contact, was important to participants. Participant feedback was most positive regarding the health tips and visit reminder services [40].

The SHIP clinic has continued to use the Connect for Life platform after this demonstration project. The technical issues that plagued the initial rollout happened less frequently over time, leading to improved fidelity of the service delivery. At the time of publication, clinicians and participants report high levels of satisfaction with the intervention. In 2019, clinic staff conducted a retrospective analysis of clinic records for all scheduled visits between January 2017 and November 2019. The review found that patients receiving the SMS reminder service were more likely to attend their scheduled appointment on time than those who opted out of reminders (38% vs 30% on-time attendance, F = 9.00, P = 0.0028).

The intervention leveraging the Connect for Life platform in the Philippines setting was adapted from the same platform used for Call for Life Uganda as well as the mMitra and Treatment Advice using Mobile Alerts projects in India [41, 44]. Studies in these other settings found improvement in patient outcomes among participants receiving the interventions.

The Call for Life study in Uganda found that viral load suppression was most improved among the group with moderate usage of the intervention, which is mirrored by our findings in the Philippine setting which suggest that medium exposure level (i.e., an average of one contact per week) was the most effective. A systematic review and meta-analysis of studies of mHealth interventions to support ART adherence by Shah, Watson, and Free found that it is unclear if the frequency of contact (daily, weekly, scheduled) influences intervention outcomes. However, interventions that

are 'interactive' and use several behavior change techniques more often lead to improvements in adherence [36].

While there has been substantial heterogeneity in results of mHealth adherence support interventions overall [36, 72–75], these platforms should continue to be explored as part of differentiated care and treatment support services. In the context of the dual HIV and COVID-19 pandemics, a wider variety of services are being delivered virtually and community groups in the Philippines have advocated for the increased availability of mHealth and tele-health services for PLHIV [76–79].

Strengths and Limitations

The involvement of end users in the intervention design and the thorough process evaluation of the Connect for Life study were strengths that provided helpful context for understanding both the process of delivering the intervention and its results [25, 40].

Owing to technical issues, only 22.1% (102/462) of the participants received the IVRS pill reminder intervention and others received a scaled-back SMS text message intervention. Following this study, the frequency of technical issues decreased significantly, and the study site has continued to provide pill reminder calls as a routine service for all new patients starting ART.

This study had several weaknesses that limit the interpretation of results. It used a quasi-experimental design, which meant that exposure to the intervention was not randomized. Moreover, the participants within each of the different intervention exposure levels received a different number of messages and days of contact, and also received different types of messages (i.e. pill reminders, health tips; calls, text messages), which may have impacted the internal validity of the study when making comparisons between the exposure groups.

The intended measurement of outcomes was affected both by the poor coverage of routine viral load testing and poor quality and completeness of non-self-reported adherence measures (pharmacy refill records and interactive SMS reports). Both loss to follow-up and elevated viral load were rare, and so the study sample was underpowered to examine factors associated with these outcomes. While relying on self-report of adherence alone was not ideal, studies have shown that self-reported adherence is useful and does correlate with clinical outcomes [80–82]. Finally, the knowledge measurement did not specifically link questions to the material in the health tips, but rather measured general HIV knowledge. A tailored KAP questionnaire with several versions may have been a better approach.

Conclusions

This study provides an in-depth analysis of demographic, clinical, and behavioral characteristics among a cohort of MSM living with HIV in the Philippines. We found that, by the end of the study, over 90% of the cohort reported ≥ 95% adherence to ART and that viral suppression rates were above 90% among those who received a test. Low coverage of viral load testing and poor suppression rates among participants who were treatment naïve at enrollment require targeted intervention. PLHIV who use drugs and those on second-line treatment also require attention as they were found to be less likely to be adherent and virally suppressed, respectively.

There was no strong evidence that exposure to the mobile phone intervention conducted using the Connect for Life platform improved adherence to ART or viral load suppression. Observed improvements in adherence were not attributable to exposure to the intervention, which may be due in part to challenges in the intervention delivery during the course of the demonstration project.

Improved understanding of the factors associated with adherence and viral suppression may inform tailored prevention and treatment interventions, including those that use mHealth technologies, for MSM in the Philippines and other similar settings.

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Data Availability The datasets generated during and/or analyzed during the current study are not publicly available until after the study outcome evaluation is complete, but are available from the corresponding author upon reasonable request.

Declarations

Competing Interests The authors declare that they have no competing interests. The study was funded through a sponsorship agreement with Johnson & Johnson Global Public Health (J&J), the developer of the Connect for Life™ platform. Per the licensing agreement all platform content and data are owned solely by the licensee (SHIP). While J&J had a collaborative role in the intervention development phase, all data collection and analysis herein were conducted by the study team at Sustained Health Initiatives of the Philippines.

Ethical Approval Ethical clearance for the study was obtained from the University of the Philippines Manila Research Ethics Board (protocol number 2016-265-01) and from the London School of Hygiene and Tropical Medicine (reference number 11631).

Consent to Participate All participants provided written consent prior to inclusion in the study. All data collection and reporting is compliant with national privacy laws, and no report will allow an individual participant to be identified.

Consent for Publication Not applicable.

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