TEXT MESSAGING FOR ADHERENCE TO ANTIRETROVIRAL THERAPY

MOBILE PHONE TEXT MESSAGING FOR ADHERENCE TO ANTIRETROVIRAL THERAPY: APPROACHES TO EVIDENCE GENERATION AND SCALE UP

By

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ABSTRACT

Background and Objectives:

HIV in a major public health problem in many countries of the world. Recent advances in care for people living with HIV such as the use of antiretroviral medication have reduced the mortality and morbidity associated with HIV infection. However, many people receiving antiretroviral therapy do not take it as prescribed and still experience sub-optimal health outcomes. Mobile phone text messaging is emerging as an important tool in health care, and HIV in particular. Our objectives were to explore the determining factors for adherence to antiretroviral therapy, test text messaging as an adherence enhancement tool, develop a framework for community ownership of a text messaging program and describe strategies for transfer of evidence in HIV to other conditions.

Methods:

This research is primarily based in Yaoundé, Cameroon, and employs a variety of methodologies, including a systematic review, two cross- sectional surveys, a randomized controlled trial, an individual patient data meta-analysis, a mixed methods study and a systematic review of systematic reviews.

Results and Conclusions:

Two-way weekly text messaging is an effective strategy in improving adherence to antiretroviral therapy and enhancing provider-client communication. People living with HIV in Yaoundé, Cameroon like receiving text messages, and are willing to own and run a text messaging program. Text messaging interventions may be transferred to other conditions by integrating services or by copying what works in HIV. Further research on potential harms, cost effectiveness and text messaging for other chronic conditions is warranted.

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DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis is a sandwich thesis which combines six individual projects prepared for publication in peer-reviewed journals. The first four have been published. The following are contributions of L. Mbuagbaw in all the papers included in this dissertation: developing the research questions, writing the protocols and statistical analyses plans, data extraction and management, conducting the statistical and qualitative analyses; designing the figures; writing all the manuscripts; submitting the manuscripts and responding to reviewers' comments. My co-authors contributed in acquiring, managing and analysing data; and preparing the manuscripts for publication. The work in this thesis was conducted between Fall 2011 and Fall 2014.

CHAPTER 1

INTRODUCTION

A brief overview of HIV:

Currently, more than 35 million people are living with human immunodeficiency virus (HIV)(UNAIDS, 2013). Most of these people live in sub-Saharan Africa and Southern Asia (UNAIDS, 2013). In 2012, about 1.6 million people died from HIV worldwide. This represents a drop from 2.3 million in 2005, but since the beginning of the pandemic more than 25 million lives have been claimed (Simon, Ho, & Abdool Karim, 2006). Even though the highest rates of HIV are located in specific regions of the world, with southern Africa as the epicentre, there is no region of the world that has not been touched by the epidemic (Simon et al., 2006). The peculiarities of this epidemic include the disproportionate burden borne by females, especially in Africa, where more than 70% of infected females reside (Simon et al., 2006); the diversity of the virus, due to rapid replication and development of new strains; and evolving management strategies that incorporate prevention, detection, and lifelong multidisciplinary therapy.

HIV is contracted by sexual or parenteral contact with HIV-containing fluids (Volberding & Deeks, 2010). Heterosexual transmission is responsible for approximately 85% of infections. In Europe and Asia, a third of the infection are caused by injection drug use (Simon et al., 2006). Once infection has occurred, the virus attacks the CD4 T-lymphocytes and these lymphocytes progressively deplete as the virus multiplies. Acute infection often goes unrecognised, but some patients may experience an acute retroviral syndrome, with flu-like symptoms like fever, malaise, lymph node swelling and rash (Volberding & Deeks, 2010). During this period, plasma HIV RNA may be high (Simon et al., 2006), and the infected individuals are very likely to transmit infection

if they continue to engage in unprotected sexual acts. After this stage, the infected person may go into an asymptomatic phase. This phase may last for many years or progress rapidly into Acquired Immune Deficiency Syndrome (AIDS). As the CD4 T-lymphocyte counts drop AIDS-defining illnesses occur, such as Kaposi's sarcoma, *Pneumocystis carini* pneumonia and cytomegalovirus retinitis. Even though a few so-called "elite controllers" naturally control their HIV infection, untreated patients usually die (Volberding & Deeks, 2010). HIV infection is monitored by frequent measurement of viral load to access viral replication, CD4 T-lymphocyte counts to access immune system changes and drug resistance testing, to ensure that antiretroviral therapy is still potent (Volberding & Deeks, 2010).

As the epidemic stabilises, the number of new infections is also reducing (Simon et al., 2006). Despite progressive drops in the number of new infections, the number of people living with HIV remains high because they are living longer, due in part to the widespread use of antiretroviral therapy (UNAIDS, 2013).

The management of HIV:

The cornerstone of HIV management is combination antiretroviral therapy. There are five classes of antiretroviral drugs: nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors and entry inhibitors (Broder, 2010). Various combinations of these from at least two classes are required to suppress viral load and subsequently morbidity and mortality (Ickovics & Meade, 2002; Simon et al., 2006). Treatment should be started as soon as CD4 T-lymphocyte cell counts drop to the 350 cells/mm threshold, as research has shown that there are mortality benefits (Hammer, 2005; Volberding & Deeks, 2010). Providing antiretroviral therapy is not without challenges of its own. Not only is it a life-long

treatment that is costly, but it also comes with side-effects and toxicities that reduce quality of life (Simon et al., 2006). Other issues such as high pill burdens and dietary restrictions make it even more challenging for patients to take medication (Mills et al., 2006). In addition, life style changes, psychosocial support, nutritional support and sometimes home-based care are often needed, especially for patients who are too ill to go to health facilities.

HIV control is hampered by suboptimal levels of adherence to medication:

The WHO seeks to ensure that all those who are eligible for antiretroviral therapy can have access to treatment. Despite considerable efforts and strong international commitment, only 34% of people eligible for treatment actually receive it (UNAIDS, 2013). The situation is aggravated by the fact that up to two-thirds of those who are receiving antiretroviral therapy may not be taking it as prescribed (WHO, 2003). They are not adherent. Adherence is defined as the "extent to which patients take medications as prescribed by their health care providers"(Osterberg & Blaschke, 2005).

Adherence is a major predictor of success in the management of HIV; without which morbidity and mortality are high (Bangsberg, 2006; Garcia de Olalla et al., 2002; Ickovics & Meade, 2002). In addition, non-adherent patients are more likely to transmit the virus (Kalichman et al., 2010). It was previously thought that very high levels of adherence are required to maintain supressed viral load (Paterson et al., 2000), but recent evidence suggests that viral suppression may be achieved at lower levels of adherence (Apisarnthanarak & Mundy, 2010; Bangsberg, 2006).

Adherence to antiretroviral therapy is multifactorial, and includes patient factors, medication factors; the client-provider relationship; disease characteristics, the clinical setting and health

system (Chesney, 2000; Ickovics & Meade, 2002; Roberts, 2002). These factors are addressed in detail in the second chapter. In light of the numerous factors that affect adherence, it is challenging to maintain appropriate levels of adherence to antiretroviral therapy without support. Support for adherence to antiretroviral therapy may require modifications to one of more of these determining factors, for example, enhancing communication between clients and providers can strengthen their relationship, clarify issues regarding complex regimens, dietary restrictions and side-effects; and therefore foster adherence. In addition the clinical and public health benefits and adequate adherence, economic models have demonstrated that adherence enhancing interventions result in cost savings (Munakata et al., 2006). In light of the critical need for optimal levels of adherence to be respected and the quest to explore further adherence enhancing strategies in a more technology oriented world, text messaging, using the short messages service (SMS) of the mobile phone has emerged as a potentially useful tool.

Text messaging for HIV:

Africa has the highest uptake of mobile phone technology (Lester, Gelmon, & Plummer, 2006). This is no surprise, since they are more reliable and require less infrastructure than land lines (Sinha & Barry, 2011). They are now available in both cities and villages, and are used for communication and banking (Lester & Karanja, 2008). This technology has been shown to improve health outcomes in low resource settings, when used for provider or client support. Text messaging can enhance drug supply management, adherence to medication and attendance at appointments. (Barrington, 2010; Hardy et al., 2011; Lester et al., 2010; Mukund Bahadur, 2010; Pop-Eleches et al., 2011) The bulk of text messaging research in Africa is on HIV, as an effective adherence enhancement tool (Lester et al., 2010; Pop-Eleches et al., 2011). Despite these promising results, there is still much to be learned on how text messaging works. Information is

lacking on the required length, content, frequency and duration to achieve optimal results. It is also unclear if text messaging may be more useful in some subgroups or whether messages should be two-way or one-way. We also query the thresholds of adherence that clients receiving text messaging interventions can achieve. More so, we need an in-depth understanding of how clients perceive text messaging and what would be the best approaches for scaling up and transfer. Current thinking has evolved from using mobile phones merely as reminders, but more as a communication enhancement device, and this raised questions as to how often messages should be sent.

As a simple non-invasive tool that can be used to encourage adherence, improve provider-client communication and support the delivery of other services such as booking appointments and delivering results of lab tests, text messaging holds enormous potential to relieve health systems burdened by human resource shortages and chronic illnesses.

The research setting:

This thesis is primarily focused on Cameroon, yet draws on evidence and lessons learnt in other parts of the world. Cameroon is a Central African bilingual country (French and English). It has one of the highest rates of HIV in west and central Africa, with 4.5 percent of the adult population infected in 2012 (UNAIDS, 2013). In the past decade, a progressive reduction in the cost of antiretroviral therapy and decentralization of HIV treatment centres to all health districts in the country have improved access to treatment. Yet, other constraints such as distance from treatment centres and poor communication with health workers still abide (Mosoko et al., 2011; Roux et al., 2011).

In Chapters 2 to 6, patients were recruited from the Yaoundé Central Hospital HIV treatment Centre. This is a largest HIV management centre in Cameroon, and is located in Yaoundé, the capital city.

Thesis objectives and outline:

The general objective of this thesis is to *investigate the role of text messaging in HIV care with a focus on adherence, patient perspectives, messaging characteristics, community ownership and transfer of technology, using appropriate study designs.*

This thesis is a "sandwich" of six papers. (Chapters 2 to 7) exploring the use of text messaging in HIV care and beyond. We explore the factors linked to poor adherence in Cameroon; text messaging as an adherence and communication enhancement strategy using data from Cameroon and Kenya; we delve into the implications of this novel method of communication; the messaging characteristics that provide the best outcomes; scale-up through community ownership and a framework for transfer of evidence from HIV to other diseases. More specifically, we address the following research questions:

1. What factors determine adherence to antiretroviral therapy?
2. Is text messaging effective in improving adherence to antiretroviral therapy?
3. What are client perceptions regarding the use of text messages for HIV care?
4. In what subgroups are text messages most effective?
5. What types of text messages are the most effective?
6. Are communities ready to own and run a text messaging programme?
7. How can a text messaging program be transferred to the community?

8. What is the state of the evidence on text messaging technology?
9. How can text messaging technology be transferred from HIV to other conditions?

The responses to these questions should lead to a compelling body of evidence than will inform clinicians, researchers, decision makers and community members of the role of text messaging in HIV care.

Chapter 2 is divided into two parts. The first part is a systematic review of studies reporting adherence to antiretroviral therapy in Cameroon, detailing the factors associated with adherence and trends in adherence over time. In the second part, we used baseline data from the Cameroon Mobile Phone SMS (CAMPS) trial to investigate the factors associated with optimal adherence and the effects of changing the measure of adherence on these factors (Mbuagbaw, Thabane, Ongolo-Zogo, Yondo, et al., 2012).

In the third Chapter, we report the findings from the CAMPS trial. The goal of the CAMPS trial was to test the efficacy of motivational weekly text messages compared to no messages for improving adherence to antiretroviral therapy. The CAMPS trial was a parallel group, single-blinded randomized trial. Two-hundred participants were recruited and randomized to either the control or the intervention arm in a 1:1 allocation ratio. Data was collected at baseline, at 3 months and at 6 months. The primary outcomes for this trial at 6 months were adherence (measured using the visual analogue scale, self-report and pharmacy refill data). The secondary outcomes were weight, body mass index, occurrence of a new opportunistic infection, mortality, retention in care, viral load, CD4 T- lymphocyte count and quality of life (Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2011).

For Chapter 4, we retrieved data from the participants in the intervention arm of the CAMPS trial and analysed the nature and content of their responses to text messages, and comment on the implications for health care providers (Mbuagbaw, Thabane, & Ongolo-Zogo, 2013).

The fifth chapter is an individual patient data meta-analyses of three randomized controlled trials investigating the use of text messaging to improve adherence to antiretroviral therapy. In this paper we explore participant and messaging characteristics that are associated with better adherence, and the efficacy of text messaging in improving adherence to antiretroviral therapy under different analytical assumptions (Mbuagbaw, van der Kop, Lester, Thirumurthy, Pop-Eleches, Ye, et al., 2013).

Having established the efficacy of text messaging in improving adherence to antiretroviral therapy and communication between health care providers and clients, we sought to investigate avenues for scale up. In Chapter 6, with used the sequential exploratory mixed methods design to investigate community ownership of a text messaging program among clients at the Yaoundé Central Hospital in Cameroon. The objectives of this paper were to gauge acceptability and readiness in the community of people living with HIV to own a text messaging programme and to develop a framework for initiating ownership.

Our next approach to scale- up is covered in the seventh Chapter. Using systematic overview methodology we mapped the scope of text messaging research worldwide. The goal of this paper was to summarise the state of the evidence of text messaging for health outcomes, to identify knowledge gaps and avenues for transfer of evidence to other chronic conditions, and to develop a framework for transfer.

Methodological issues addressed in this paper:

This thesis uses a variety of research methods to address our research questions, each with specific challenges. Chapter two is a systematic review and regression analyses for different definitions of adherence and the effect of changing these definitions on the identified determinants. Chapter 3 is a randomized controlled trial using multiple imputation to replace missing data and analysed according to the intention-to-treat principle. Chapter 5 is an individual patient data meta-analyses using hierarchical linear models to estimate the effect of text messaging on adherence while taking into account the clustering effect within trials using different statistical methods. Chapter 6 is an exploratory sequential mixed methods study using qualitative and quantitative methodologies to develop a concrete framework. We also developed an innovative approach to displaying qualitative and quantitative data in the same graphical tool. The final chapter is an overview (systematic review of systematic reviews).

Overlap in material covered:

Chapters 2 to 7 were developed as independent stand-alone manuscripts from the same data set and therefore there is some overlap in their introductory sections, description of study setting and participants. As such, we wish to highlight the specific instances where this occurred. The CAMPS trial generated three distinct data sets: 1) baseline characteristics of the participants randomized, 2) outcome data for the trial and 3) feedback from participants in the intervention arm. The first data set was used in Chapter 2 to determine the factors associated with adherence to antiretroviral therapy (Mbuagbaw, Thabane, Ongolo-Zogo, Yondo, et al., 2012). The second data set was used in Chapters 3 for the report of the CAMPS trial (Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012), and in Chapter 5 (Mbuagbaw, van der Kop, Lester, Thirumurthy, Pop-Eleches, Ye, et al., 2013), for the individual patient data meta-analyses alongside data from two other trials (Lester et al., 2010; Pop-Eleches et al., 2011). The third data set was used in Chapter 4 to describe

communication opportunities that arose with the text messaging intervention (Mbuagbaw, Thabane, et al., 2013). The mixed methods study in Chapter 6 was conducted in the same clinic on different participants three years later.

Research context:

This piece of work was carried out in tandem with other related pieces of work, which though not a part of this thesis, may be integral to understanding the whole body of evidence. Prior to conducting the CAMPS trial, we conducted a qualitative study to appraise potential participants' perceptions on text messaging as a reminder and communication tool (Mbuagbaw, Bonono-Momnougui, & Thabane, 2012). The findings from this study informed the design of the trial. During the trial, we faced some administrative, methodological and ethical challenges. We described these challenges and the solutions we employed (Mbuagbaw, Thabane, Ongolo-Zogo, & Lang, 2011). After the trial, we conducted a cross-sectional survey amongst the staff of the trial centre (Mbuagbaw, Thabane, Ongolo-Zogo, & Karanja, 2012). Finally, the design, conduct and analysis of the trial (Chapter 3), individual patient data meta-analyses (Chapter 5) and mixed methods study (Chapter 6) were informed by published protocols (Mbuagbaw, Ongolo-Zogo, & Thabane, 2013; Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2011; Mbuagbaw, van der Kop, Lester, Thirumurthy, Pop-Eleches, Smieja, et al., 2013).

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AIDS RESEARCH AND THERAPY

RESEARCH Open Access

Trends and determining factors associated with adherence to antiretroviral therapy (ART) in Cameroon: a systematic review and analysis of the CAMPS trial

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Abstract

Background: The benefits of antiretroviral therapy (ART) cannot be experienced if they are not taken as prescribed. Yet, not all causes of non-adherence are dependent on the patient. Having to pay for medication reduces adherence rates. Non- adherence has severe public health implications which must be addressed locally and globally. This paper seeks to describe the trends in adherence rates reported in Cameroon and to investigate the determinants of adherence to ART in the Cameroon Mobile Phone SMS (CAMPS) trial.

Methods: We conducted a systematic review of electronic databases (PubMed, Google Scholar, Web of Science, CINAHL, EMBASE and PSYCINFO) for publications on adherence to ART in Cameroon (from January 1999 to May 2012) and described the trend in reported adherence rates and the factors associated with adherence. Data were extracted in duplicate. We used multivariable analyses on the baseline data for 200 participants in the CAMPS trial to determine the factors associated with adherence in four models using different measures of adherence (more than 90% or 95% on the visual analogue scale, no missed doses and a composite measure: 100% on the visual analogue scale, no missed doses and all pills taken on time).

Results: We identified nine studies meeting our inclusion criteria. Adherence to ART in Cameroon has risen steadily between 2000 and 2010, corresponding to reductions in the cost of medication. The factors associated with adherence to ART in Cameroon are grouped into patient, medication and disease related factors. We also identified factors related to the health system and the patient-provider relationship. In the CAMPS trial, education, side effects experienced and number of reminder methods were found to improve adherence, but only using multiple reminder methods was associated with better adherence in all the regression models (Adjusted Odds Ratio [AOR] 4.11, 95% Confidence Interval [CI] 1.89, 8.93; p<0.001; model IV).

Conclusions: Reducing the cost of ART is an important aspect of ensuring adequate adherence rates. Using multiple reminder methods may have a cumulative effect on adherence to ART, but should be investigated further.

Keywords: Adherence, Antiretroviral therapy, Cameroon, Reminder methods, CAMPS

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Background

The advent of antiretroviral medication as a treatment for HIV is one of the most celebrated advances in medicine [1]. Antiretroviral therapy (ART) reduces viral loads to undetectable levels, and dramatically decreases morbidity and mortality. Decreasing serum viral load with antiretroviral medication also reduces mother to child transmission rates [2,3]. However, viral replication still occurs in reservoirs like lymph node or gastrointestinal T-cells even when viral loads are undetectable [4,5]. As such, good adherence is necessary to maintain prolonged viral suppression [5]. Non-adherence to HIV medication is a major reason for treatment failure, the development of resistant strains, and increased costs [6]. It is also one of the key predictors or determinants of success in the management of HIV/AIDS and the progression to AIDS and death [7,8]. Non-adherence reduces the immunologic potential of ART and is associated with drops in CD4-positive-T-lymphocyte counts [9-11]. Non-adherence has also been found to be associated with increased hospitalisations and longer hospital stays [10,12]. Initial worries in the scientific community about non-adherence in sub-Saharan Africa were dispelled when research findings demonstrated similar or higher rates of adherence than in the developed world [13]. However, only a third of people living with HIV (PLHIV) take their medication as prescribed [1]. Non-adherence leads to increased viremia which might lead to increased transmissibility and consequently a higher incidence of HIV. High risk activity may also lead to the transmission of resistant strains to newly infected individuals, thereby reducing their therapeutic options [14,15]. Adherence to ART has clinical and public health implications, and should therefore be addressed on global and local levels.

Defining adherence

Adherence can be narrowly defined as the "extent to which patients take medications as prescribed by their health care providers" [16], or more broadly as the "the extent to which a person's behaviour—taking medication, following a diet, or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" [1]. The former definition refers to compliance with medication as prescribed by the provider while the latter goes beyond medication to include all the recommendations jointly agreed upon by both provider and client to improve health care. The latter definition also highlights or acknowledges additional factors such as diet or lifestyle which may affect adherence. It also recognises that the client may not agree with the recommendations of the health care provider. Such factors are even more relevant in HIV where dietary restrictions are required for the uptake of certain medications [17,18] and that certain lifestyles (e.g. substance abuse) can lead to non- adherence to ART [19]. In this paper, all degrees of adherence which are not optimal are referred to as non-adherence.

The factors associated with adherence to ART exist in many categories, defined in literature [1,16,19]:

Patient factors such as substance abuse, being male (i.e. gender), depression, lower levels of education, lack of self efficacy, extreme anxiety, extreme pain, no change in health status despite ART and non-white race are significantly associated with non-adherence [1,19].
Medication factors like dose frequency, pill burden, type of drug, inability to take medication when away from home, food requirements, side effects are also responsible for less than optimal adherence [1,19]. In other words the complexity of the regimen and its side-effects are associated with non-adherence.
Provider-related factors such as a poor patient-health care provider relationship can affect the patient's overall satisfaction and trust in the provider. The quality of these relationships is significantly associated with better adherence [1,20,21].
Disease characteristics, notably stage and duration of HIV infection, symptoms experienced and the presence of opportunistic infections play a role in adherence to ART. HIV related symptoms like nausea may impede a patient from swallowing pills. Some studies report that patients who have experienced an opportunistic infection tend to be more adherent than those who have not [1,22,23].
Clinical setting and health system factors may influence use of services and adherence [19].

Adherence to ART in Cameroon

Cameroon has one of the highest rates of HIV in west and central Africa, with 5.3% of the adult population living with HIV. Of these, only 30% are receiving ART [24]. Adherence to ART in Cameroon has changed over the years for a multitude of reasons. Health system changes like the decentralization of HIV treatment centres and the subsidy of costs of medication and testing over the years have contributed to the variations in the reported adherence rates. A substantial reduction in costs occurred in 2004 [25] and ART has been provided for free since 2007 [26]. As a result, the designs and the contexts of the studies reporting rates of adherence to ART in Cameroon also vary. The set of similar and varying contextual factors in Cameroon make it a worthwhile case study to examine adherence to ART and learn lessons that could be applied across the country. Adherence rates in Cameroon have been measured using patient reports, pharmacy refill data, attendance at scheduled visits and blood testing [25-35]. These different methods have spawned adherence rates varying from 10.1% to 97.5%, between 2000 and 2010. Faced

with these enormous discrepancies, we sought to use data from a recent trial [36] to describe adherence to ART and the associated determining factors. Adherence rates are not only a predictor of treatment success, but also an indication of how many resources should be invested in adherence enhancement research and practice. This cannot be done without stable estimates for adherence or a comprehensive list of locally relevant determinants.

Additionally, in a changing world where new methods and technologies arise to improve adherence rates, and levels of stigma are declining, there may be a shift in patients' attitudes and practices related to adherence.

The objectives of this paper are:

- to review the literature on adherence in Cameroon with specific emphasis on ART adherence rates and its correlates or determinants, and
- to report the factors associated with adherence to ART at baseline in the Cameroon Mobile Phone SMS trial (CAMPS;36).

Methodology

Literature review of ART adherence rates in Cameroon

We searched electronic databases (PubMed, Google Scholar, Web of Science, CINAHL, EMBASE and PSYCINFO) for publications on adherence to ART in Cameroon (from January 1999 to May 2012) using appropriate combinations of keywords such as *Cameroon*, *Cameroun* (*French*), *adherence*, *compliance*, *antiretroviral therapy*, *antiretroviral treatment* and *HIV*. ART was introduced in Cameroon in 1999 [37]. No language restrictions were set. Citations were screened and full text obtained if they reported any measure of adherence to ART in Cameroonian subjects. Completeness and adequacy of reporting in the selected studies were assessed in duplicate by noting their compliance to the 22-item Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [38]. Data were also extracted in duplicate: citation details; year study was conducted, city in which study was conducted, adherence rate, method of measure of adherence, study design, sample size and the cost of ART at the time. Discrepancies were resolved by discussion. We examined the evolution of adherence rates taking into account the above characteristics. We also identified the reported factors associated with adherence and classified them as patient variables, medication variables, patient-provider relationship and health system characteristics. These categories have previously been identified in literature [16,19]. No statistical pooling was performed. The factors associated with adherence were extracted only if they resulted from multivariable analyses. The reported odds ratios and p-values were used to confirm the associations reported.

Adherence to ART in CAMPS

We conducted a cross-sectional analytical study based on the baseline data for the Cameroon Mobile Phone SMS (CAMPS) trial [36]. Data were collected from a subset of patients (eligible for the trial) aged 21 or older, who owned mobile phones and who agreed to take part in the trial. The independent variables included socio-demographics like age (in years), gender (male or female), level of education (none and primary or secondary and university), disclosure of status to family members (family aware or not aware of HIV status); clinical features like presence or absence of an opportunistic infection, Centers for Disease Control and Prevention (CDC; [39]) classification (categorised as AIDS defining condition or not), regimen (first line or second line), duration on treatment (in months); the number of drug side-effects experienced and the number of recall methods used. All the independent variables were those reported in literature and collected for the CAMPS trial [36]. The dependent variables were adherence measured using a visual analogue scale (0–100), self report on the number of missed doses and whether the doses were taken on time in the week preceding the interview. We also designed a composite measure of adherence based on all three measures, which we dichotomized as adherent (VAS=100; number of missed doses=0; all doses taken on time=yes) and non-adherent (VAS<100; missed doses >0; all doses taken on time=no).

We performed multivariable logistic regression with adherence (dependent variable) dichotomized at the VAS cut-offs of 90 and 95% (Model I and II). These cut-off points represent the levels of adherence at which sustained viral suppression can occur [5], and those often used in literature [40,41]. We also analyzed the data using the self reports of adherence as the dependent variable, in which case one or more missed doses was considered as non-adherence and no missed dose was considered as good adherence (Model III). We repeated these analyses using the composite measure of adherence (Model IV). The interaction between independent variables was investigated based on associations reported in the general literature and specifically for Cameroon. Variables were introduced into the model in blocks defined by the following categories: socio-demographic, disease-related and medication-related. Model fit was assessed using the Hosmer and Lemeshow goodness of fit statistic [42].

Data were analysed using Predictive Analytic Software (PASW) Version 17.0 (SPSS, Inc., 2009, Chicago, IL, USA). Statistical significance was set at alpha= 0.05. Adjusted odds ratios (AOR), 95% confidence intervals (CI) and p-values are presented. The forest plot was drawn using Stata Statistical Software (STATA) Release 12 (StataCorp LP, 2011, College Station, TX, USA).

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Results

Literature review

We identified 9 studies conducted between 2000 and 2010 which reported adherence rates in Cameroon. The mean number of reported items on the STROBE checklist was 19.7 (standard deviation [SD] 1.38). Data from the CAMPS trial was included in the analysis [36]. Five of them were conducted in Yaoundé, the capital city of Cameroon. The characteristics of these studies are reported in Table 1. We observed an increasing trend in adherence rates over time, which corresponds to the reductions in cost of ART (Figure 1). Two studies were outliers to this quasi-linear relationship. The first was Kouanfack *et al.* [27], which reported high adherence rates (88.7% and 97.5%, using biological markers and self report respectively). This study was a drug trial and participants received medication free of charge at a time when medication costed 51.2 USD/month. The second, Mosoko *et al.* [25], reported very low adherence rates (10.1% using hospital records of the number of scheduled clinic visits attended). These data may be affected by inaccuracies in hospital records (incompleteness was handled using imputation techniques); participants who lived far away were sometimes given medication for more than one month; patients who lived in the nearby city of Douala had other ART opportunities and this measure (scheduled visits) considers all deaths and lost to follow-up as non-adherent. Ideally, the cases of death should be excluded from the denominator. The other study using attendance of scheduled visits [29] also reported low adherence rates (<50%).

Determinants of, and factors associated with ART adherence

In addition to the nine papers that reported adherence rates, we identified two papers which reported on the determinants of adherence to ART. These studies were conducted in cross-national cohorts of patients from Cameroon, the Democratic Republic of Congo and Burundi (Table 2). These papers were provided additional information on factors associated with adherence [34,35]. They were not used in the trend analysis.

These factors were found to reduce adherence to ART: binge drinking, drug use, tobacco use, lack of family support, experience of stigma, switching regimen, advanced stage of disease, cost of care, distance from clinic, large hospital size and no task shifting from physician to other staff [25,28,30-35].

These factors increased adherence to ART: Female gender, age greater than 49 years, higher levels of education, positive perceptions of treatment, high motivation, using reminder methods, satisfaction with information provided by physician, higher CD4 count at initiation of ART, and being transferred-in from another clinic [30,31,33-35].

High monthly income [31,32] and increased duration on medication [30,33,35] were both reported to either increase or reduce adherence.

Table 1 Characteristics of studies reporting adherence to ART in Cameroon

Reference	Year	City	Study design (sample size)	Adherence rate	Method	Cost of ART/month for that year in USD*
Laurent et al.	2000-2003	Douala	Cross-sectional retrospective (788)	<50% [μ]	Scheduled visits attended	128
Kouanfack et al.	2002-2003	Yaoundé	Prospective cohort (60)	88.7%, (97.5%)	Biological markers, (Self Report)	51.2 (free for participants)
Mosoko et al.	2002-2005	Limbe	Cross-sectional retrospective [α] (2920)	10.1%	Scheduled visits attended	51.2
Boyer et al. [28]	2006	Yaoundé	Cross-sectional (532)	56.6%	Self Report [β]	12.8
Rougemont et al.	2006	Yaoundé	Prospective cohort (312)	64% (78%)	Pharmacy data (Self report)	12.8
Boyer et al. [32]	2006-2007	Multiple locations	Cross-sectional (3151)	53.9%	Self report [β]	12.8
Roux et al.	2006-2008	Yaoundé	Prospective cohort (401)	61-73%	Self report [β]	12.8
Mahy et al.	2007-2008	Tokombere	Cross-sectional (56)	95% (80%)	self report [β] (Pharmacy data)	0
Mbopi-Keou et al.	2010	Dschang	Cross-sectional (356)	80.2% (48.7)	Self report [β] (Pharmacy data)	0
CAMPS	2010	Yaoundé	Cross-sectional (200)	90.5%	Self report [β]	0

*Costs vary per regimen, the highest costs are reported.
[α] Cross- sectional analysis of previously collected data without planning for needs of an investigation.
[β] All methods in which all information used to measure adherence was obtained by interviewing the participant with either one question or a series of questions.
[μ] 50% was imputed to represent the trend graphically.

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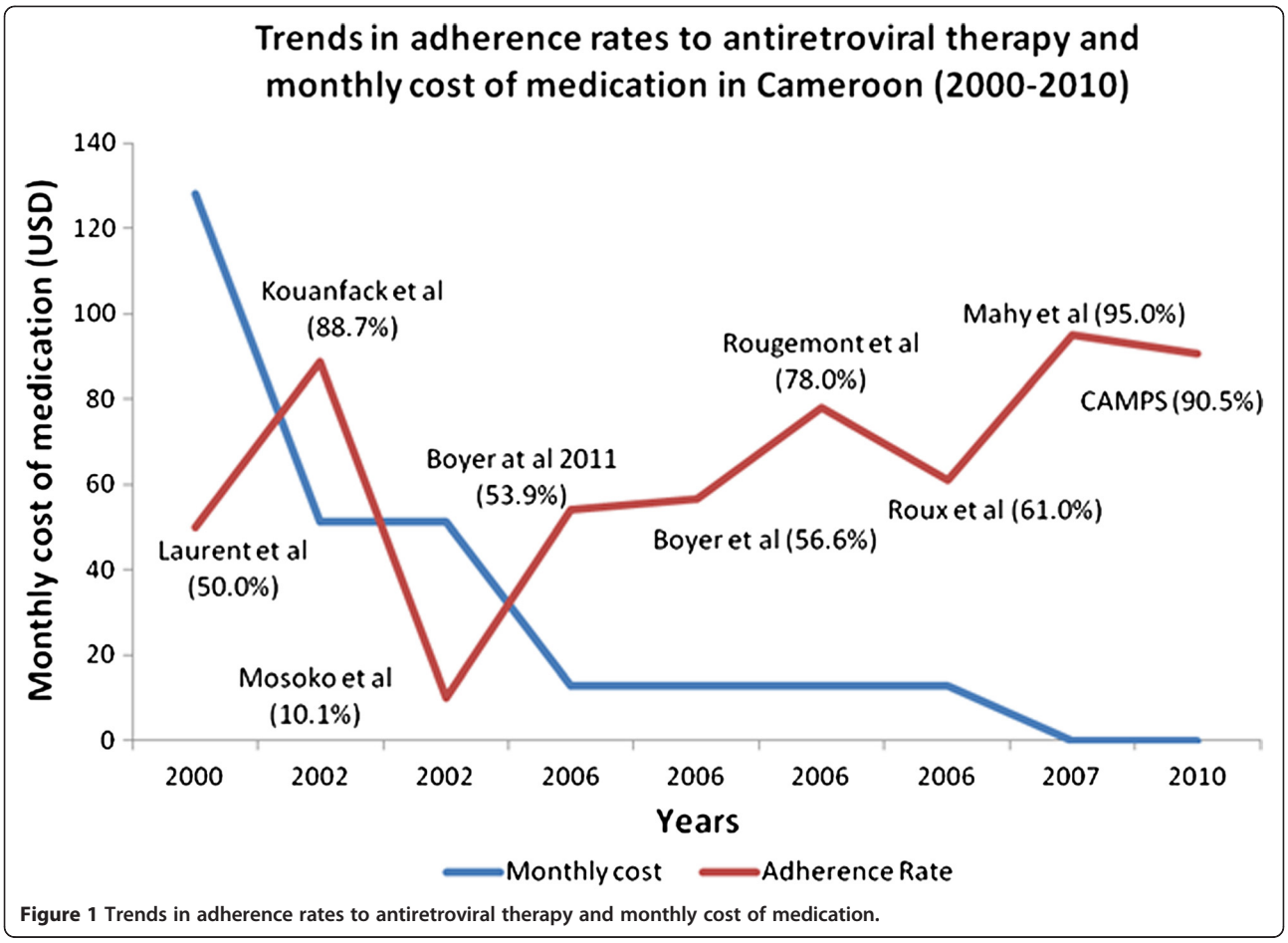

Figure 1 Trends in adherence rates to antiretroviral therapy and monthly cost of medication.

Factors associated with adherence to ART at baseline in the CAMPS Trial

In this sample of 200 adults, one fifth was older than 50 years, three-quarters were female, 98% had at least primary education, and 90% reported that their families were aware of their HIV status. The rest of their characteristics are reported in Table 3. All the factors associated with adherence that were collected in this data set were used in the regression analysis. The baseline data for participants in the CAMPS trial are reported in Table 3.

In the first model, we dichotomized adherence using the VAS at 95%. Using multiple recall methods was significantly associated with adherence >95% (AOR 6.7, 95% CI 2.69, 16.56; p<0.001). In our second model, adherence was dichotomized at 90%. Female gender was associated with adherence >90% (AOR 0.28, 95% CI 0.09, 0.90; p=0.032), while secondary education (AOR, 4.4 95% CI 1.64, 11.92; p= 0.003) and multiple recall methods (AOR, 7.89 95% CI 3.22, 19.33; p<0.001) were associated with adherence >90%. In the third model we used the number of missed doses as our measure of adherence. Experiencing more side effects (AOR 2.25, 95% CI 1.13, 4.50; p= 0.021) and using multiple recall methods increased the odds for not missing doses (AOR 7.28, 95% CI 3.06, 17.32; p<0.001). In our last model we used a composite measure of adherence that incorporated the VAS, number of missed doses and timing of doses. Only the use of multiple recall methods was associated with adherence (AOR 4.11, 95% CI 1.89, 8.91; p<0.001). The Hosmer and Lemeshow goodness-of-fit statistic for all the four models had p-values greater than 0.05 implying a good fit [42]. These models are displayed in Figure 2.

Discussion

By reviewing the literature on adherence rates in Cameroon, and analysing a new data set we have produced an explanatory account of the trends in adherence observed and the reported determinants. We also identified another plausible means of enhancing adherence to ART: using multiple reminder methods.

Despite the different study designs, locations and sample sizes there is a clear improvement in adherence rates over time irrespective of how it is measured. This finding confirms and supports health policies that reduce

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Table 2 Factors associated with adherence to ART in literature reports from Cameroon

Factors	Reference (findings)
Patient variables	
Female gender	Rougemont et al. (↑)
Age>49 years	Newman et al.* (↑); Freeman et al.**(↑)
High monthly income	Rougemont et al. (↓); Boyer et al. ([28] ; ↑)
Education	Freeman et al. (↑)*
Binge drinking	Boyer et al. ([32] ; ↓); Roux et al. (↓); Newman et al.(↓)*
Drug use	Freeman et al.(↓)*
Tobacco use	Freeman et al.(↓)*
Lack of family support for adherence	Boyer et al. ([32]; ↓);
Experiencing discrimination and stigma	Boyer et al. ([32]; ↓);
Positive perception of treatment	Roux et al. (↑)
Being transferred-in to HIV clinic	Mbopi-Keou (↑)
Medication variables	
Switching regimen	Boyer et al. ([32]; ↓);
High motivation	Roux et al.(↑)
Using a reminder method	Roux et al.(↑)
Patient Provider Relationship	
Satisfaction with information provided by physician	Roux et al.(↑)
Disease characteristics	
Advanced stage of disease	Rougemont et al. (↓); Roux et al.(↑)
Increased duration on medication	Roux et al.(↓); Freeman et al.(↑)*Mbopi-Keou (↑)
Higher $CD4^{¥}$ count at initiation of ART ^{β}	Mbopi-Keou (↑)
Health System/clinic Characteristics	
Cost of care/Having to pay for care	Mosoko et al.(↓), Boyer et al. ([32] ; ↓) ; Boyer et al. ([28] ; ↓) Laurent et al. (↓)
Increased distance from clinic	Mosoko et al. (↓)
Large hospital size	Boyer et al. ([32]; ↓);
No task shifting from physician to other staff	Boyer et al. ([32]; ↓);

↓Reduces adherence; ↑increases adherence; * Cohort included participants from Cameroon, Burundi and the Democratic Republic of Congo; ** Cohort included females from Cameroon, Burundi and the Democratic Republic of Congo; ¥ CD4-positive-T-lymphocyte; β Antiretroviral therapy.

the cost of care to improve access and use. This is also in line with studies reporting that the main hindrances to adherence in Africa are related to health system weaknesses such as inadequate supply, human resource shortages and poor infrastructure [29,32].

The determinants of adherence to ART identified in the Cameroonian literature are a subset of factors identified elsewhere [19]. However, there are discrepancies as to the role of monthly income and duration on ART on adherence. Boyer *et al.* [32] reported better adherence with a higher monthly income, while Rougemont *et al.* [31] reported the contrary. Both studies were initiated in the same period (2006) and therefore the cost of medication is unlikely to be the reason for this discrepancy. On the other hand Boyer *et al.* conducted a multisite (27 sites) study with a larger sample size (n=3151) compared to Rougemont *et al.* (n=312) in a single site. The results from Boyer *et al.* may be more plausible in the Cameroonian context where, apart from free ART, other related services are still funded by out-of-pocket payments and having to pay for care has been identified as a cause of non-adherence [25,28,29,32]. The larger sample is also more likely to have more accurate and generalizable data, especially since one of the sites included in Boyer *et al.* is the same site where the Rougemont study was conducted.

Roux *et al.* [30] noted a drop in adherence rates with increased duration on ART while Freeman *et al.* and Mbopi-Keou *et al.* [33,35] noted the contrary. However, these two samples differ greatly. Roux *et al.* describe a multisite study in the Centre region of Cameroon, in 401 PLHIV over two years. Freeman *et al.* describe a cross-national cohort of 8419 women from Cameroon, Burundi and the Democratic Republic of Congo followed up for two years. Female gender has been reported as a factor for better adherence [31] and this discrepancy may explain the interaction between gender and duration on

Table 3 Baseline characteristics of participants in the CAMPS trial

Variable	Statistic
Age (years) : mean (SD) [α]	40.1 (10.10)
21-49	157 (79.3)
50+	41 (20.7)
Gender: n (%)	
Female	147 (73.5)
Level of education: n (%)	
None or primary	78 (39.0)
Secondary or university	122 (61.0)
Family aware of HIV status: n (%)	180 (90.0)
Presence of an opportunistic infection: n(%)	62 (31.0)
BMI : mean (SD) [β]	25.2 (4.00)
Underweight	4 (2.2)
Normal	90 (48.6)
Overweight	91 (49.2)
CDC* classification - AIDS defining illness§:n (%)	146 (73.0)
Regimen: n (%)[δ]	
First line	179 (90.9)
Second line	18 (9.1)
Duration on ART (months): median (Q1, Q3) [α]	28.5 (9.0, 48.0)
CD4 (cells per mm^3): median (Q1, Q3)	336.0 (200.5,487.7)
Adherence	
Visual Analogue Scale: mean (SD) [ε]	90.5 (12.76)
Number of missed doses: mean (SD) [μ]	1.0 (0.00)
No missed doses: n (%)	127 (65.1)
Treatment taken on time: n (%)	108 (54.0)
Reasons for missing doses: n (%)	
Forgot	54 (27.0)
Out of home	23 (11.5)
Out of tablets	7 (3.5)
Too busy	8 (4.0)
Side effects	2 (1.0)
Other reason	5 (2.5)
Medication side effects experienced: n (%)	
None	127 (63.5)
One	43 (21.5)
Two	30 (15.0)
Reminder methods: n (%)[¥]	
None	49 (25.7)
One	125 (65.4)
Multiple	17 (8.5)

SD: standard deviation; BMI: body mass index; *Centres for Disease Control, § =CDC classifications: A3, B3, C1, C1, C3 [39]; α= 2missing; δ=3 missing; β=15 missing; ε= 10 missing ¥= 9missing; μ= 5 missing.
The reminder methods reported were: personal verbal reminders by individuals, phone alarms, meal times, timing with TV shows and watches.

medication. Mbopi-Keou *et al*. suggest that this trend might be the effect of continuous psycho-social support [33].

One study reported higher levels of adherence for patients who initiated ART with high levels of CD4-positive-T-lymphocytes [33]. This finding is in favor of earlier initiation of ART. Why patients who were transferred to the clinic would have better adherence rates is unclear. However, if they left their previous clinics due to service provision issues or unsatisfactory interactions with clinic staff, the latter clinic may provide a more favorable environment for adherence.

Using multivariable analysis we identified gender, education, side effects experienced, and number of reminder methods as factors that affect adherence rates.

The male gender has often been reported as the most likely to be non-adherent, maybe because males are more likely to engage in other behaviours that influence adherence such as binge drinking, tobacco use and drug use [19]. This effect was not found in all models and is not consistent across studies [19].

Level of education seems to play a role in adherence behaviour. A significant difference in adherence exists between people with secondary and those with no education. Further increments in educational level show no effect. This may imply that as concerns adherence to ART there are no benefits to be gained from very high levels of education. The benefits of education on adherence to ART can be obtained from secondary education. This effect was not consistent across all models.

Our findings regarding side effects are contrary to what is reported in literature. People who experienced more side-effects were more likely to be adherent. No other Cameroonian studies have identified side effects as a determinant for adherence to ART. In the CAMPS trial only 1% of those who missed doses reported side effects to be the reason for not taking medication (Table 3).

Only the number of reminder methods was associated with adherence in all the models. Another Cameroonian study reported the use of reminder methods to be associated with better adherence [30]. This is the first study to show that multiple reminders may have a cumulative effect. A randomized clinical trial in Kenya found alarms to have no effect on virological outcomes [43]. Simple electronic alarms are not as complex as the reminder methods described in this population (personal verbal reminders by individuals, phone alarms, meal times, timing with TV shows and watches). Other studies have reported the use of mobile phone beeps and prayer times by Muslims to remind them of when to take their medication [44]. The use of multiple and varied reminder methods may address other causes of non-adherence like forgetfulness and lack of social support.

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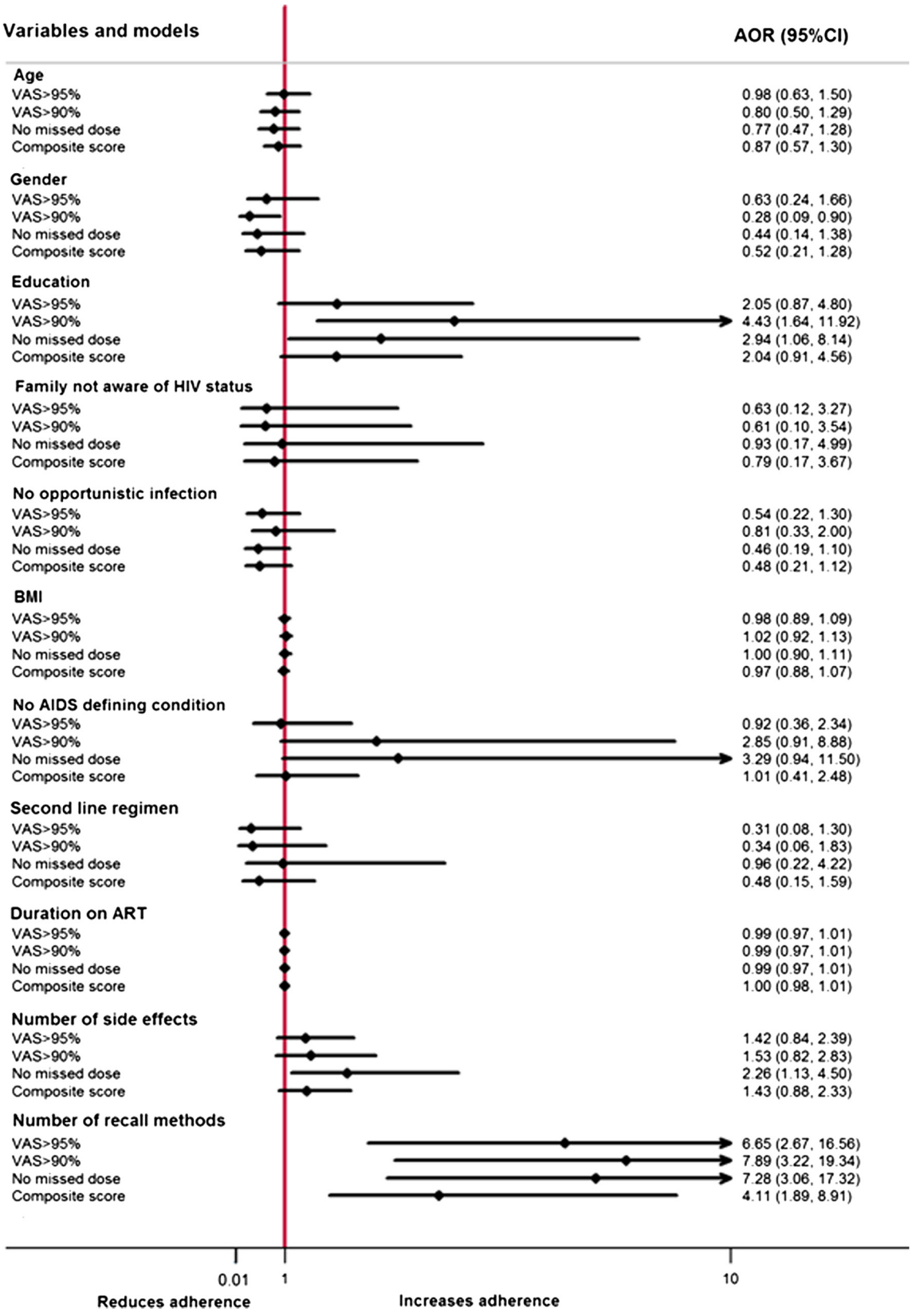

Figure 2 Multivariable analysis using different measures of adherence.

The difference in the four models suggests that the factors associated with adherence depend somewhat on how adherence is defined and the thresholds for acceptable adherence. Different levels of adherence are associated with different factors. It is unclear how this issue can be resolved without a uniform and validated tool for measuring adherence rates in clinical practice or research, as all methods have their advantages and flaws [16,45]. Self reported adherence is by far the most popular method used, but how it is used varies greatly [16,46]. On the one hand, a simple visual analogue scale can be used to situate a patient's adherence; and on the other a series of questions related to number of pills, timing, missed doses and identification of pills, all fall under the canopy of self report.

In low resource settings, self report, attendance-based and dispensing-based adherence measuring methods can predict important clinical outcomes [46] and should be collected routinely. Some measure of drug availability or the occurrence of drug stock-outs should be documented to explain trends in adherence behaviours.

Both sections of this paper may have limitations. Even though we observed an increasing trend in adherence as the cost of ART reduces, other temporal factors may contribute to this trend, notably health system improvements over the years and reductions in stigma and discrimination. These factors are reported as potential threats to optimal adherence and are very likely to change over time. The availability and use of reminder methods like mobile phones may also enhance adherence over time [25,32]. Participants in this study (CAMPS) may not adequately represent all the people living with HIV, but a subgroup who are already on ART, and who own mobile phones. Even though mobile phone ownership is widespread in Cameroon, those who own them may differ significantly from those who don't.

Conclusions

A prerequisite to optimal adherence is the availability of free or cheap medication. Irrespective of how it is measured, adherence rates tend to improve as the cost of medication is reduced. Improved financing mechanisms for ART are an important way of ensuring adequate adherence and improving outcomes for people living with HIV. Multiple and varied reminder methods are more likely to improve adherence than any single method alone. Further research is required to elucidate what combinations of reminder methods can produce the most desirable effects.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LM and LT conceived of the study; LM and SN performed the searches and extracted the data; LM, LT, SN, POZ, DY, LD and MS provided intellectual content and revised several versions of the manuscript. All authors read and approved the final manuscript.

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The Cameroon Mobile Phone SMS (CAMPS) Trial: A Randomized Trial of Text Messaging versus Usual Care for Adherence to Antiretroviral Therapy

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Abstract

Background: Mobile phone technology is a novel way of delivering health care and improving health outcomes. This trial investigates the use of motivational mobile phone text messages (SMS) to improve adherence to antiretroviral therapy (ART) over six months.

Methodology/Principal Findings: CAMPS was a single-site randomized two-arm parallel design trial in Yaoundé, Cameroon. We enrolled and randomized HIV-positive adults on ART, aged 21 years and above to receive a weekly standardized motivational text message versus usual care alone. The primary outcome was adherence measured using a visual analogue scale (VAS), number of doses missed (in the week preceding the interview) and pharmacy refill data. Outcomes were measured at 3 and 6 months. Service providers and outcome assessors were blinded to allocation. Analysis was by intention-to-treat. Between November and December 2010, 200 participants were randomized, with 101 in the intervention group and 99 in the control group. At 6 months, overall retention was 81.5%. We found no significant effect on adherence by VAS>95% (risk ratio [RR] 1.06, 95% confidence interval [CI] 0.89, 1.29; p = 0.542; reported missed doses (RR 1.01, 95% CI 0.87, 1.16; p>0.999) or number of pharmacy refills (mean difference [MD] 0.1, 95% CI: 0.23, 0.43; p = 0.617. One participant in the intervention arm reported a possible disclosure of status.

Conclusions/Significance: Standardized motivational mobile phone text messages did not significantly improve adherence to ART in this study. Other types of messaging or longer term studies are recommended.

Registration:

1. Pan-African Clinical Trials Registry; PACTR201011000261458
2. Clinicaltrials.gov; NCT01247181

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Introduction

There is increasing recognition for the potential of new technologies to improve health care, and the World Health Organization (WHO) prioritizes the use of new technologies to assist health delivery in resource-limited settings [1]. One technology that is widely used in resource-limited settings is the mobile telephone, as they are more reliable and less cumbersome than landlines [2].

Even though private ownership and use of mobile phones is not as widespread as in other more developed countries [3], Africa has shown great uptake of mobile phone technology [4]. For example, between 2000 and 2005 mobile phone subscriptions in Cameroon increased by 270% per annum [5]. In 2008, 37% of the adult population owned a mobile phone [6]. Given the aforementioned trend in mobile phone subscriptions it is reasonable to infer that a large majority of the adult population now own and use mobile phones. However, ownership is higher in urban areas [5].

The potential for text messages to improve health outcomes in resource limited settings is still being explored. In South Africa, SMS text messages have been used to improve HIV health care service delivery by improving communication between patients and health personnel, and also as an appointment reminder [7]. Two clinical trials in Kenya have evaluated the benefits of using mobile phone text message reminders to improve adherence to antiretroviral therapy (ART). The WelTel trial reported improvements in adherence and viral load [8], a second reported an improvement in adherence and a reduction in treatment interruptions [9]. A recent Cochrane systematic review summarized the evidence described in these two Kenyan trials [10]. The WHO recommends more research on adherence to long-term therapies because poor adherence leads to poor health and increased health costs [11]. However, the evidence on mobile phone text messaging to improve adherence to ART in developing countries is limited to one country (Kenya).

Given the importance of understanding the effectiveness of interventions to improve retention and adherence among people living with HIV in Africa, we conducted a randomized clinical trial to evaluate the utility of weekly motivational SMS texts on improving adherence and other important outcomes among a representative sample of HIV-positive adults in Cameroon.

Objectives

The primary objective of our trial was to test the effectiveness of sending weekly motivational text messages via mobile phone versus no text messaging to improve adherence, measured using a VAS, the number of missed doses and pharmacy refills among HIV positive patients over a 6-month period at the Accredited Treatment Centre (ACT) of the Yaoundé Central Hospital (YCH). This is a busy urban treatment centre in Yaoundé, the capital city of Cameroon.

Our secondary objectives were to evaluate the effects on weight, body mass index (BMI), opportunistic infections (OI), CD4-positive-T-lymphocyte count, viral load, quality of life (QOL) measured using the SF-12 QOL assessment form [12], all-cause mortality, retention in care, adverse events and patient satisfaction. Subgroups of interest included age group, gender, level of education and treatment regimen.

Methods

We report here a brief overview of the methods. Details can be obtained from the published protocol [13]. Using a parallel group design, eligible and consenting patients were randomized to intervention and control arms with a 1:1 allocation ratio. Our findings are reported using the (CONsolidated Standards of Reporting Trials) CONSORT guidelines [14].The protocol for this trial and supporting CONSORT checklist are available as supporting information; see Checklist S1 and Protocol S1.

Participants

Participants were recruited from the Yaoundé Central Hospital (YCH) Accredited Treatment Centre (ATC). The adult prevalence of HIV in Cameroon was 5.3% in 2009 [15]. The YCH is a referral hospital with a capacity of 381 beds, and staffed by 95 doctors and 270 nurses [16]. The ATC registers approximately 40 new cases per week and caters to approximately 6500 regular clients. It is the largest HIV/AIDS management clinic in Cameroon and enabled rapid recruitment.

We included subjects who were aged above 21 years; owned a mobile phone; who could read text messages; and who had been on ART for at least one month. Only those who provided informed consent, orally and in writing were allowed to participate.

We excluded individuals who had been on ART for less than one month at the time of enrollment, and were aged less than 21 years. Participants who had used ART for at least one month were chosen so that we could obtain a baseline adherence rate which we used to evaluate the success of randomization along with the other baseline covariates.

Participants were enrolled from the waiting rooms of the YCH ATC from the 22 November to the 22 December, 2010. The purpose of the trial was explained to consenting participants and baseline data were collected. Immediately after enrolment, trial codes and phone numbers were sequentially linked to predetermined allocation codes.

Ethics

Ethical clearance was obtained from the Cameroon National Ethics Committee (authorization number 172/CNE/SE/2010). All participants included in the study provided both verbal and written consent.

Interventions

We sent a short text message to each participant in the intervention (SMS) group, once a week, in either French or English, based on the participant's language preference. Messages were developed based on data collected from focus group discussions [17] and the health belief model of behavior change [18]. The content of the message was motivational, with a reminder component. The message also contained a phone number that they could call back if they needed help. The content was varied and contemporary (e.g. messages would contain season's greetings) so as to retain participants' attention throughout the study period and to explore the various aspects of behavior change. An example of a message would be, "You are important to your family. Please remember to take your medication. You can call us at this number: +237 xxxx xxxx." The messages made no mention of HIV. We used a series of 11 messages that were changed every week. The program secretary used a list of phone numbers disclosed after randomization. One message was sent every week on Wednesdays at 9:00 am and the "delivery report" function of the mobile phone was used to determine if the message was actually received and opened. Text messaging was an add-on to usual care that includes regular ART counseling and home visits determined on a case-by-case basis.

In the control (no SMS) group, participants received only usual care. They did not receive any text messages, but they were interviewed at baseline, 3 months and 6 months. Data on satisfaction was collected only for the intervention arm, as it would have been inappropriate to ask people who did not receive text messages if they were satisfied with the intervention.

Outcomes

Our primary outcome was adherence, measured using three methods: a Visual Analogue Scale (VAS); Self Report (SR); and Pharmacy Refill Data (PRD). Our Secondary outcomes were clinical: weight, body mass index (BMI), opportunistic infections (OI); QOL: Measured using the SF-12 QOL assessment form [12]; all cause mortality and retention in the trial.

Sample size

Our study was designed to detect a 20% increase in adherence in the intervention arm. Sample size was calculated using WINPEPI (PEPI- for-windows) version 9.5 software [19]. Details

of the assumptions used to arrive at a sample of 198, taking into account an attrition rate of 20% are reported in the protocol [13]. In brief, the study had 80% power to detect a statistically significant relative risk (alpha set at $\alpha = 0.05$) using a two-tailed chi-squared test and assuming 60% and 80% adherence rates in the control and intervention groups respectively. Based on other studies using SMS to improve adherence [20] and reported adherence rates in Cameroon [21], it was estimated that at least a 20% increase in adherence was necessary to achieve adherence rates above 95%.

Randomization, allocation concealment and implementation

Using a parallel group design, eligible and consenting patients were randomized to intervention and control arms with a 1:1 allocation ratio. A computer generated randomization list was established using random block sizes of 2, 4 and 6, by the Father Sean O'Sullivan Research Centre Biostatistics Unit at St Joseph's Healthcare/McMaster University (http://www.thecem.net/sjhsrn.php) in Canada. The allocation codes were then sequentially affixed to the phone numbers of consecutively recruited participants by trained research staff at the YCH ATC. This sequence was sent to the research centre by email, and concealed in a password-protected computer until interventions were assigned.

Blinding

Trained interviewers – blinded to group allocation – collected data using a pre-tested data collection form containing socio-demographic data, clinical information and adherence rates at baseline, 3 and 6 months. From the point of enrollment, patients were identified only by their phone numbers and their sequential trial numbers. The interviewers transmitted the phone numbers of the enrollees to the research staff. The research staff responsible for allocation had access to the allocation codes and the phone numbers of participants. The program secretary responsible for sending the text messages received the allocations (SMS or No SMS) and corresponding phone numbers weekly. The data analyst was also blinded to group allocation. Only the participants were aware of their allocation.

Statistical methods

We adopted the intention-to-treat principle to analyze all outcomes, meaning that data from participants was analyzed according to the group to which they were randomized irrespective of whether they actually received the intervention. We also used multiple imputation techniques to handle missing data [22]. Variables for which there was too much missing data to perform imputation were excluded from the analysis but are reported (CD4-T-lymphocyte cell count and viral load). All outcome variables had some degree of missing data ranging from 0 to 35%. Multiple imputation was used to create a new data set which was the average of five data sets of imputed values. This final data set was used for all analyses. We used the t-test to compare groups on continuous outcomes and the chi-squared test for binary outcomes. All statistical tests were performed using two-sided tests at the 0.05 level of significance. The Bonferroni method was used to adjust the level of significance for testing of secondary outcomes. For group comparisons, the results are expressed as mean difference (MD) and risk ratio (RR) for binary outcomes, corresponding two-sided 95% confidence intervals (95% CIs) and associated p-values. Adjusted analyses using baseline covariates (age, gender, educational level, duration on ART, HIV staging, BMI and the presence of an OI) were performed using standard binary logistic regression techniques to investigate the residual impact of these characteristics on the primary outcome. We included the interaction term for the intervention variable and the following covariates: age group, gender, level of education and regimen. These covariates are reported to affect adherence rates to ART [11]. Goodness-of-fit was assessed by examining the residuals for model assumptions and the Hosmer and Lemeshow test of goodness-of-fit. The p-values for the interaction terms are reported. All analyses were performed using SPSS (Statistical Package for the Social Sciences) version 16.0 for Windows and WINPEPI [19].

Results

Recruitment, baseline data and participant flow

Between November and December 2010, 228 patients were approached for enrollment. Twenty declined to participate and 8 did not meet the eligibility criteria. Two hundred participants were randomized to either the SMS intervention arm (n = 101) or the control arm (n = 99). One participant in the intervention arm withdrew due to loss of privacy. Initial retention in the trial for both arms at 6 months was 42% (participants who came for scheduled clinic visits), but increased to 82% (after a phone call inviting them to come for a final interview). Participants were followed up from December 2010 to May 2011, when the intervention was stopped. During this period, we received 99 phone calls and 55 text messages (154 responses) from 48 participants in the intervention arm. The content of these responses is the subject of another manuscript. Figure 1 displays the flow of participants in the study. Data for all 200 participants were analyzed. After randomization, both groups were similar in baseline characteristics (table 1).

Outcomes and estimation

At 6 months, we found no effect on the number of participants achieving >95% adherence by VAS (RR 1.06, 95% CI 0.89, 1.29; p = 0.542) or reporting missed doses (RR 1.01, 95% CI 0.87, 1.16; p>0.999). The mean number of pharmacy refills was also not different between groups (mean difference [MD] 0.1 95% CI −0.23, 0.43; p = 0.617). However, on sensitivity analysis, more participants in the SMS group achieved adherence of >90% at 6 months (RR 1.14 95% CI 1.01, 1.29; p = 0.027). The details for the other secondary outcomes at 6 months are reported in table 2.

At 3 months, fewer participants in the SMS group had an adherence rate of >95% (RR 0.77, 95% CI 0.63, 0.94; p = 0.029) or >90% (RR 0.61 95% CI 0.32, 1.14; p = 0.094); equal numbers reported missed doses (RR = 0.97, 95% CI 0.85, 1.10; p = 0.622), and the mean number of pharmacy refills was not significantly different (MD 0.10, 95% CI −0.03, 0.23; p = 0.139). The other secondary outcomes at 3 months are reported in table 3.

Ancillary analyses

Regression. We performed regression analyses to determine the impact of baseline covariates on the primary outcomes. Higher levels of education (OR = 5.32, 95% CI 2.51, 11.30; p<0.001) and being on a second line regimen (OR = 11.06, 95% CI 3.75, 32.65, p<0.001) were statistically significant predictors of adherence >95%. The Hosmer and Lemeshow goodness-of-fit test was as follows: chi-squared 56.7, degrees of freedom = 8, p<0.001.

We also added an interaction term between covariates and the intervention variable. The interaction terms were not statistically significant for age group (p = 0.633) and gender (p = 0.268), but

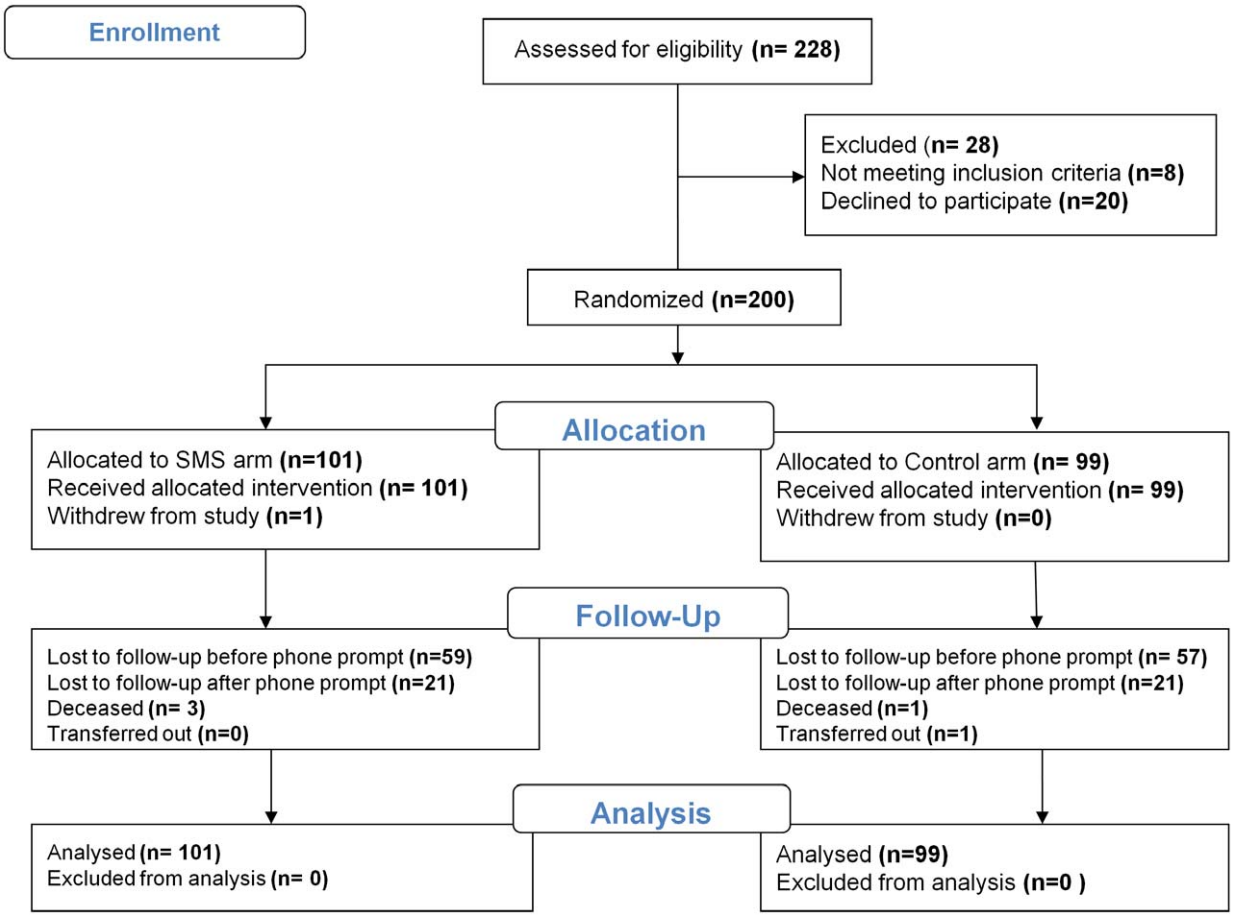

Figure 1. CONSORT flow diagram for CAMPS trial.
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statistically significant for level of education ($p<0.001$) and regimen ($p<0.001$).

Adverse events. One female in the intervention arm requested to withdraw from the study because she felt it had compromised her undisclosed status. No other undesirable effects were reported.

Satisfaction. Satisfaction with the text message was measured using four questions (Table 4): rating of the SMS; if it helped improve adherence; if they wanted it to continue and if they would recommend it to a friend. Moderate levels of satisfaction (65% reported that the messages were good, very good or excellent) were reported by the participants who received the text messages.

Discussion

Our study did not find a significant effect of motivational SMS texts on improving adherence to ART over a 3 to 6 month period. This trial was unique in that it was the first to report the effect of an SMS intervention on ART adherence among treatment experienced patients in Africa. Two recent trials in Kenya demonstrated improved ART adherence among patients initiating ART, but used different intervention protocols [8,9].

Our study had some important limitations. Firstly, our primary measures of adherence (by interviews) might have resulted in overestimates of the true adherence rate [23,24] and the adherence reported for the last week may not adequately reflect adherence behaviors over longer periods because patients may become more adherent in the few days preceding their appointment [25]. However, pharmacy refill data showed similar findings to self-reports. The trial design did not interfere with patient care by providing medication or lab tests so there are large amounts of missing data for CD4-positive-T-lymphocyte count and viral load. Drug stock-outs were also frequent in the last two months of the trial. This may explain why some participants missed their scheduled appointments. Importantly, participants in the control arm were not prohibited from using other reminder methods, so additional benefits may have been difficult to detect. Previous studies conducted in the same parent population suggest that up to 25% have systematic reminder methods [17]. Finally, our sample size was powered to detect a 20% difference in adherence between both arms. The difference we found was much less.

Our findings should be interpreted in light of the published trials in Kenya [8,9], which show some improved adherence rates after twelve months, also reported in a Cochrane review synthesizing data from both trials [10]. The interventions evaluated were somewhat different. While our trial used motivational messages, with the intention to produce a change in adherence behavior, and no compulsory feedback, the Weltel trial used a simple SMS inquiry on the participants' health and was therefore interactive [8]. The second trial used short and long one-way messages: the longer message with encouraging content, but no option for feedback [9]. Even though we used optional feedback, we did not detect any improvements in adherence. Only 48 participants in the intervention arm used the feedback option. We also used

Table 1. Demographics and baseline.

Variable	SMS group (n = 101)	Control group (n = 99)
Age (years): mean (SD)	41.3 (10.1)[&]	39.0 (10.0)[&]
Gender: n (%)		
Female	69 (68.3)	78 (78.8)
Level of education: n (%)		
None	1 (1.0)	3 (3.0)
Primary	42 (41.6)	32 (32.3)
Secondary	46 (45.5)	51 (51.5)
Tertiary	12 (11.9)	13 (13.1)
Family aware of HIV status: n (%)	88 (87.1)	92 (92.9)
Presence of an opportunistic infection: n(%)	36 (35.6)	26 (26.3)
BMI : mean (SD)	25.3 (4.1)[ε]	25.2 (4.0)[β]
CDC* classification - AIDS defining illness§:n(%)	76 (75.2)[α]	70(70.7)[δ]
Regimen: n (%)		
First line	91 (90.1)	88 (88.9)
Second line	7 (6.9)	11 (11.1)
Duration on ARV (months): median (Q1, Q3)	31.0 (15.0, 50.5)	22.0 (7.0,46.0)[μ]
CD4 (cells per mm^3): median (Q1, Q3)	347.0 (211.0, 527.5)	327.0 (194.0,475.0)
Adherence (Visual Analogue Scale): mean (SD)	88.8 (13.42)[ε]	92.4 (11.84)[δ]

& = 1 missing;
β = 8 missing;
ε = 6 missing;
α = 3 missing;
δ = 4 missing;
μ = 2 missing;
SD: standard deviation; CDC: Centres for Disease Control, § CDC classifications: A3, B3, C1, C1, C3 [1]; CD4: CD4-positive-T-lymphocyte; Q1: first quartile; Q3: third quartile.
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Table 2. Outcomes at 6 months.

Outcome	Type	SMS group (n = 101)	Control group (n = 99)	Effect Estimate[μ]
Primary	**Binary**	**n (%)**	**n (%)**	**RR (95%CI);p**
	VAS>95%	72 (71.3)	66 (66.7)	1.06 (0.89,1.29; 0.542
	Self report (no missed doses)	80 (79.2)	78 (79.0)	1.01 (0.87,1.16;) >0.999
	Continuous	**Mean (SD)**	**Mean (SD)**	**MD (95% CI);p**
	Pharmacy Refill Data	3.8 (1.48)	3.7 (1.34)	0.1 (−0.23,0.43); 0.617
Secondary*[¥]	**Binary**	**n (%)**	**n (%)**	**RR (95%CI);p**
	VAS>90%	91 (90.1)	78 (78.8)	1.14 (1.01,1.29);0.027
	Presence of a new OI	20 (19.8)	17 (17.2)	1.15 (0.64,2.07); 0.632
	Mortality	3 (2.9)	1(1.0)	2.94 (0.31–27.79); 0.322
	Retention	80 (79.2)	83 (83.8)	0.95 (0.83,1.08); 0.399
	Continuous	**Mean (SD)**	**Mean (SD)**	**MD (95% CI);p**
	Weight (kg)	71.8 (11.97)	70.2 (11.87)	1.60(−1.72,4.92); 0.344
	BMI	26.54 (4.254)	25.73(3.823)	0.81(−0.32,1.94); 0.159
	Quality of life (SF-12 scale score)	3.79 (0.585)	3.75 (0.583)	0.04(−0.12,0.20); 0.629

(SMS: short message service; RR: risk ratio; CI: confidence interval; SD: standard deviation; MD: mean difference; VAS: visual analogue scale; BMI: body mass index; OI: opportunistic infection; CD4: CD4-positive-T-lymphocyte; SF: short form).
*Bonferroni adjustment for secondary outcomes: 0.05/8 = 0.006.
[¥]Insufficient data for CD4 count (n = 34 for intervention and 26 for control; MD-24.4; 95% CI: −101.3, 52.6; p = 0.599) and viral load (n = 0).
[μ]P-values obtained using the chi-squared test and the t-test for binary and continuous outcomes respectively.
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Table 3. Outcomes at 3 months.

Outcome	Type	SMS group (n = 101)	Control group (n = 99)	Effect Estimate[μ]
Primary	**Binary**	**n (%)**	**n (%)**	**RR (95%CI);p**
	VAS>95%	52(51.5)	66(66.7)	0.77(0.63,0.94);0.029
	Self report (no missed doses)	82 (81.2)	83(83.8)	0.97(0.85,1.10);0.622
	Continuous	**Mean (SD)**	**Mean (SD)**	**MD (95% CI);p**
	Pharmacy Refill Data	2.3(0.50)	2.2 (0.45)	0.10 (−0.03,0.23);0.139
Secondary*[¥]	**Binary**	**n (%)**	**n (%)**	**RR (95%CI);p**
	VAS>90%	60(59.4)	70(70.7)	0.61(0.32,1.14);0.094
	Presence of a new OI	39(38.6)	32(32.3)	1.19 (0.82,1.74);0.353
	Mortality	0	0	Not estimable
	Retention	85(84.2)	84(84.8)	0.99(0.88,1.12); 0.893
	Continuous	**Mean (SD)**	**Mean (SD)**	**MD (95% CI);p**
	Weight (kg)	70.9(12.18)	71.2(12.96)	−0.30 (−3.81,3.21);0.866
	BMI	26.24(4.087)	26.07(4.175)	0.17 (−0.98,1.32);0.771
	CD4 (cells per mm^3):	406 (230)	375 (225)	31 (−32.5,94.5); 0.337
	Quality of life (SF-12 scale score)	3.67 (0.623)	3.69 (0.615)	−0.20(−0.19,0.15);0.820

(SMS: short message service; RR: risk ratio; CI: confidence interval; SD: standard deviation; MD: mean difference; VAS: visual analogue scale; BMI: body mass index; OI: opportunistic infection; CD4: CD4-positive-T-lymphocyte; SF: short form).
*Bonferroni adjustment for secondary outcomes: 0.05/8 = 0.006.
[¥]Insufficient data for viral load (n = 0).
[μ]P-values obtained using the chi-squared test and the t-test for binary and continuous outcomes respectively.
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weekly messages like the Kenyan trials, but did not observe any significant benefits. Both Kenyan trials ran for up to one year, while our trial ended at 6 months. The duration of our trial might not have been sufficient to observe a significant effect.

Another important difference is the fact that both Kenyan trials enrolled participants who had recently initiated ART [8,9]. The median duration on ART at baseline in this study was 31 and 22 months for the intervention and control groups respectively. This may also explain the negative results, since duration on ART has been shown to have negative effects on adherence to ART in Cameroon [26]. We speculate that the SMS may be more effective in treatment-naïve populations. While the risk of disclosure of status has been mentioned in some studies [27], this is the first study documenting a case of withdrawal for privacy reasons. In Cameroon, there is still a lot of stigma associated with HIV, and it is a known cause of poor adherence [28]. Although we did not include the term "HIV" in the content of the text messages, we did include "medications" and gave a clinic number which could arouse suspicion by non-participants reading the message. Interestingly, we had a very high proportion of clients in this study who reported having disclosed their status to their families. This may have reflected a selection bias for enrolment, and larger benefits may have been observed in individuals who do not realize the support of disclosing. Confidentiality and disclosure are important considerations for the scale-up of text message interventions [29].

Table 4. Satisfaction with the text message among the participants who received text messages (n = 101).

Question	Count (%)*
How would you rate the text message?	
Excellent	12 (11.8)
Very good	30 (29.7)
Good	21(20.8)
Average	17 (16.8)
Bad	5 (4.9)
Very bad	16 (15.8)
Did it help you remember to take your medication?	
Yes	92 (91.1)
No	9 (8.9
Do you want to continue receiving text messages?	
Yes	66 (65.3)
No	35 (34.7)
Would you recommend it to a friend?	
Yes	82 (81.2)
No	19 (18.8)

*Percentages may not add up to 100 due to rounding off.
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High levels of satisfaction have been documented in other text message trials, particularly in those which offer two way communication [8,30]. While the majority of participants in our trial were satisfied with the text messages, a considerable number did not want the intervention to continue. A study conducted prior to this trial reported that patients would like to receive messages with a wide variety of characteristics in terms of timing, content and source [17]. Some participants might not have wanted to continue if the messages weren't tailored to their needs. Yet, more than 80% would recommend it to their friends. Further research is needed on how best to tailor text messages. It is unclear whether the content of the message played a role in the outcomes, as other trials with no motivational component have reported improvements in adherence [8,9].

The ancillary analyses reported above need to be considered as secondary and therefore interpreted with caution in the light of our main findings.

In conclusion, motivational text messages did not significantly improve adherence to ART among treatment experienced patients in Cameroon after 6 months. Although interactive SMS associated with access to health advice has demonstrated to be effective in at least one large clinical trial [8], and is reflected in current guidelines [31] more work needs to be done to determine how motivational content can be delivered by SMS alone. Text messages may come with a small risk of disclosure of status. Further trials are critical to determine what interventions should be taken to scale.

Supporting Information

Protocol S1 Research Protocol.
(PDF)

Checklist S1 CONSORT checklist.
(DOC)

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Author Contributions

Conceived and designed the experiments: LM LT RTL POZ EJM. Performed the experiments: LM LT CK POZ. Analyzed the data: LM LT LD MS. Contributed reagents/materials/analysis tools: LM LT. Wrote the paper: LM LT POZ MS RTL EJM LD MS.

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SHORT REPORT Open Access

Opening communication channels with people living with HIV using mobile phone text messaging: insights from the CAMPS trial

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Abstract

Background: Using two-way mobile phone text messages to improve adherence to antiretroviral medication enhances communication between patients and health workers. We describe the implications of participants' responses to text messages in the Cameroon Mobile Phone SMS (CAMPS) trial.

Findings: This is a cross-sectional analysis of data from the intervention arm of the CAMPS trial. CAMPS was a randomized controlled trial of motivational text messaging versus usual care to improve adherence to antiretroviral medication among people living with HIV in Yaounde, Cameroon (n = 200) over a 6 month period. Participants in the intervention arm (n = 101) were given a contact phone number, but were not required to respond to their reminder messages. If they did, their responses were noted and reported as counts and percentages. We received 99 phone calls and 55 text messages (154 responses) from 48 participants during the study period. The median number of responses was 1 (first quartile [Q1]: 1; third quartile [Q3]: 3). Half (n = 79, 51.1%) of them were expressions of gratitude. The rest included requests for logistical (n = 21, 13.6%), medical (n = 20, 12.9%) and financial (n = 11, 7.1%) support.

Conclusion: Initiating two-way mobile communication opens more channels for people living with HIV to express unmet needs. Researchers, policy makers and clinicians should be ready to respond to the needs expressed by patients who respond to text messages.

Trial registration: Pan-African Clinical Trials Registry: PACTR201011000261458; Clinicaltrials.gov: NCT01247181

Keywords: Text messaging, SMS, HIV, Adherence, Antiretroviral therapy, Communication, Cameroon, CAMPS trial

Findings

Health communication using mobile phones

Despite numerous advancements in Human Immunodeficiency Virus (HIV) care and treatment, poor adherence is still a potential threat to universal access to antiretroviral therapy (ART) [1]. Due to the multifactorial nature of the determinants of patient adherence [2] and diversified research efforts to respond to each of these factors, mobile phones have emerged as a potentially useful tool to improve adherence rates [3]. Due to their ubiquity in countries most affected by HIV [4], the use of mobile phones to improve HIV related health outcomes is receiving more attention as emerging evidence suggests reminder messages can increase adherence to ART and retention in care, decrease viral load and treatment interruptions, and improve communication with healthcare personnel [5-7]. Such mobile health (mHealth) interventions can also be used to address other health behaviors and to provide useful and timely information to health workers [8]. Other studies report the potential of using the SMS for other types of health related communication and the promotion of additional health services, yet there is limited information as to how this can be achieved [5,6].

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The relative novelty of text messaging as part of mHealth results in a lack of generalizable policy frameworks and guidelines for care. Health text messaging guidelines developed by the United States Department for Human and Health Services do not cover how to manage direct feedback and recommend using text messaging as part of a larger communication strategy [9]. For such frameworks and guidelines to be implemented, the issues most relevant to patients or the success of mHealth must be taken into account.

Although automated mobile phone text messages are less labor intensive than manually composed messages, they may not permit feedback to be addressed in real time and thus neglect urgent concerns from the responders. Likewise, standardized messages may contain insufficient or unclear information and prompt the need to address other related issues. Furthermore, urgent responses may be missed if they are sent after working hours when mHealth phones are not monitored. Given the above, the expectations for the parties on the sending end and the responsibilities of those on the receiving end need to be investigated. As such, we pose the following question: *what do people living with HIV hope to benefit from text communication with health workers and how can health workers prepare to respond to the needs identified through text messaging?*

The responses and feedback of clients who receive text messages can provide important clues as to the most effective way of designing and organizing text messaging interventions. The aim of this paper is to describe the responses from the participants in the Cameroon Mobile Phone SMS (CAMPS) trial, [10,11] and the implications for health service providers.

Methods

We conducted a cross-sectional analysis of the responses from participants in the intervention arm of the CAMPS trial. The CAMPS trial was a two-arm single blinded randomized controlled trial of weekly motivational mobile phone text messages versus usual care for improving adherence to ART, at the Yaoundé Central Hospital in Cameroon. Ethical clearance was obtained from the Cameroon National Ethics Committee (authorization number 172/CNE/SE/2010). All participants included in the study provided verbal and written consent. The methods are described in detail elsewhere [10,11]. In brief, 200 eligible participants were randomized to receive text messages (n = 101) or usual care (n = 99). Usual care involved adherence counseling as determined by care givers. Eligibility was determined based on age (21 or older), ownership of a mobile phone, use of ART for at least one month, and willingness to participate in the trial. The trial ran from November 2010 to July 2012 (Figure 1). The motivational text messages were sent once a week and included a phone number that participants could call if they required assistance. Participants did not receive communication credit so all the responses occurred at their expense. We noted the content of the responses (phone calls and text messages) and grouped them into categories: expressions of gratitude, inquiries about the trial, logistical support (related to provision of services), medical, counseling, requests for financial assistance, and others. Participants who left "missed calls" were called back; this was noted as a phone call. The phone number provided to the participants in the text message was different from the one from which the messages were sent. Participants who accidentally responded to the sending number were redirected to the "help" number. The help number phone connected to an experienced HIV clinician (available twenty-four hours a day every day) who was part of the research team, but not clinic staff, and therefore did not have access to patient records. Based on the participants' inquiry they were channeled to the appropriate department of the HIV clinic. The participant characteristics were determined by matching the responses to the phone numbers collected at baseline.

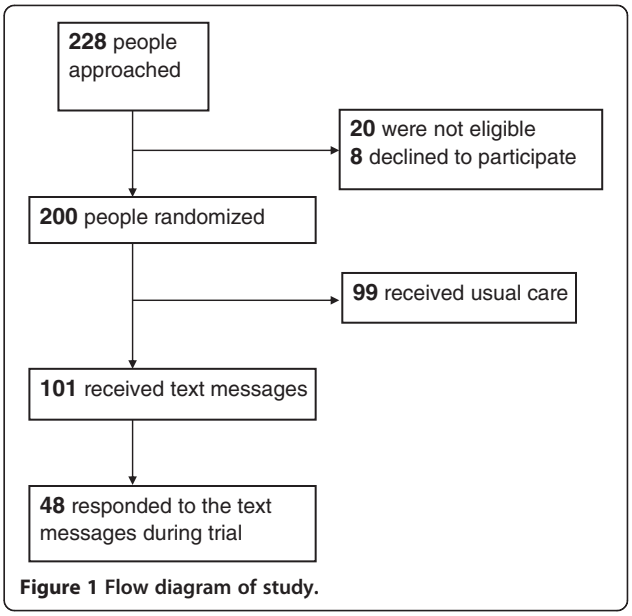

Figure 1 Flow diagram of study.

Results

All messages received could be linked to participants in the intervention arm of the trial (mean age 42.6 years [Standard Deviation - SD 9.80]; 35 [72.9%] were female). All had received some formal education. Most patients had disclosed their HIV status to family members (n = 43, 89.6%) and were on a first line ART regimen (n = 41, 91.1%). The median duration on ART was 33 months (first quartile [Q1]: 17.25; third quartile [Q3]: 56.25). Detailed socio-demographic and clinical characteristics are reported in Table 1 (see Table 1).

Table 1 Socio-demographic characteristics of participants who responded to messages in the CAMPS trial (n = 48)

Variable	Statistic
Age (years): mean (SD)	42.6 (9.80)
Gender: count (%)	
Female	35 (72.9)
Level of education: count (%)	
Primary	20 (41.7)
Secondary	22 (45.8)
University	6 (12.5)
Family aware of HIV status: count (%)	43 (89.6)[μ]
CDC[¥] classification - AIDS[£] defining illness: count (%)	32 (69.6)[β]
Regimen: count (%)	[α]
First line	41 (91.1)
Second line	4 (8.9)
Duration on ART (months): median (Q1, Q3)	33.0 (17.25, 56.25)
Adherence/Visual Analogue Scale: mean (SD)	88.15 (14.351)
Quality of life [α]: mean (SD)	3.2 (0.40)

[μ]1 missing; [β]2 missing; [α]3 missing; Quality of life was measured using Short Form −12 (http://www.sf-36.org/tools/sf12.shtml); SD: standard deviation, [¥]CDC: Centers for disease control and prevention; Q1: first quartile; Q3: third quartile; [£]AIDS: Acquired Immune Deficiency Syndrome.

Of the 101 participants who received text messages, 48 (47.5%) responded at least once either by phone call or by text message. We received 99 phone calls and 55 text messages (154 responses) over a period of six months. These responses tended to cluster around the day the messages were sent. The median number of responses was 1 (Q1: 1; Q3: 3). Responses came in as early as 7.30 am and as late as 10.30 pm. Characteristics of responses are reported in detail in Table 2 (see Table 2).

Half of them (n = 79, 51.1%) were expressions of gratitude. Some participants (n = 9, 5.8%) wished to verify the authenticity of the text messages and who was responsible for sending them. Respondents who required medical help (n = 20, 12.9%) complained about side-effects and other ailments; how to handle unwanted pregnancies, how to take medication, and what to do after missing a dose (see Table 2).

Messages for logistical support (n = 21, 13.6%) included requests for assistance in collecting results from laboratory, re-scheduling appointments, complaints of stock-outs at the hospital pharmacy, and requests to ameliorate clinic wait times.

Counseling was requested regarding HIV testing within a committed relationship (n = 2, 1.2%). Financial help (n = 1, 7.1%) was sought for a variety of reasons, including setting up small businesses and other personal requests.

The last group (classified as other) included messages from participants reporting that their phones were missing (and providing a new contact number), reporting the death of the owner of the phone, and requesting to withdraw from the study (n = 12, 7.8%).

Table 2 Characteristics of responses to messages in the CAMPS trial

Content of message	Mode of contact		Count (%)*
	Phone call	Text message	
Expression of gratitude	35	44	79 (51.1)
Logistical	19	2	21 (13.6)
Medical	19	1	20 (12.9)
Other	9	3	12 (7.8)
Financial assistance	7	4	11 (7.1)
Inquiries about study	8	1	9 (5.8)
Counseling	2	0	2 (1.2)
Total	**99**	**55**	**154**

*Percentages may not add up to 100 due to rounding off.

Discussion

This observational study within a randomized clinical trial highlights the needs of people with HIV and weaknesses within the health system identified through the lens of new and rapidly spreading mobile phone technology.

First, it must be noted that the use of a text message reminder system was overall appreciated and half of the responders communicated only to express their gratitude. These results coincide with other studies which have documented high levels of satisfaction with two-way text messaging [6,12].

Secondly, these messages highlighted unmet needs regarding disease counseling. Patients contacted the research team seeking additional information regarding medication procedures, consequences of and compensation for a missed dose, and expected side effects.

Third, these findings provide a comment on the human resource shortages and organizational difficulties which plague many health systems in resource limited countries - often demonstrated by long waiting times, stock-outs, and delays in obtaining lab reports [13,14]. The most dangerous of these is the frequent stock-outs of ART. They are a major cause of poor adherence and directly counteract adherence enhancing interventions [13]. They also reduce patients' confidence in an already fragile health system.

A major barrier to the success of mHealth programs is the unavoidable interaction with other weak components of the health system [14,15]. For example, it is difficult to enhance adherence through text messaging when the medication is unavailable or insufficient human resources prevents timely quality care. The potential for text messaging to enhance care may be limited by these health system challenges and therefore scaling up the program

would require additional resources to handle the new demands.

Other potential costs of routine use of text messaging for health care needs must also be considered. Such costs would include the cost of technology and additional staffing. Although additional, the relatively low cost of text messaging and staff willingness to participate in text messaging programs in Cameroon are encouraging factors that may boost the uptake of a cost-effective adherence program [16].

Fourthly, these communications have demonstrated the feasibility of using mobile phone technology as a means to open additional communication channels with patients beyond clinical hours and to provide professional assistance in real time. It is important to note the level of commitment and expertise utilized in the CAMPS trial. The recipient of each response should be well versed in, or able to channel patients to the necessary assistance. In future renditions of this strategy, it would be desirable to have a toll free number, with an experienced HIV clinician, a social worker, or someone capable of locating lab results, to schedule appointments and facilitate the provision of care. Access to patient records may also be desirable in order to provide personalized care. At this point, policy frameworks and guidelines must be developed to assist health workers providing effective, ethical, and efficient remote support [15]. Such guidelines should explicitly state that text messaging does not replace emergency care and should not delay appropriate health care.

This study has some limitations. Of note is the fact that these responses were initiated at the expense of the participants. Even though this may serve as a measure of their need for mobile services, many participants who did not respond to the text messages may not have done so because they lacked communication credit. Therefore, these findings reflect the views of only a portion of the wealthier, more health-conscious participants who received text messages in the CAMPS trial [11].

Conclusion

Text messaging for adherence to ART is a relatively new intervention. While it is unlikely that large scale messaging can be individually tailored, it is important to identify the needs of those receiving these messages. Researchers, policy makers and clinicians must recognize that two-way text messaging provides space for dialogue for patient needs which can then be addressed. These needs may be logistical, medical or informational.

Abbreviations

ART: Anti-Retroviral Therapy; CAMPS: Cameroon Mobile Phone SMS trial; CDC: Centres for Disease Control and Prevention; HIV: Human immune deficiency virus; mHealth: Mobile Health; Q1: First quartile; SD: Standard deviation; SMS: Short Message Service.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LM and LT designed the study. LM and POZ collected the data. All authors analyzed and interpreted the data; and reviewed all versions of the manuscript. All authors read and approved the final manuscript.

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Mobile phone text messages for improving adherence to antiretroviral therapy (ART): an individual patient data meta-analysis of randomised trials

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ABSTRACT

Objectives: Our objectives were to analyse the effects of text messaging versus usual care in improving adherence to antiretroviral therapy (ART) in people living with HIV using individual patient data meta-analysis. Adjusted, sensitivity and subgroup analyses were conducted.

Setting: 3 randomised controlled trials conducted between 2010 and 2012 in rural and urban centres in Cameroon and Kenya (two studies) were used.

Participants: A total of 1166 participants were included in this analysis (Cameroon=200; Kenya=428 and 538).

Primary and secondary outcomes: The primary outcome was adherence to ART >95%. The secondary outcomes were mortality, losses to follow-up, transfers and withdrawals.

Results: Text messaging improved adherence to ART (OR 1.38; 95% CIs 1.08 to 1.78; p=0.012), even after adjustment for baseline covariates (OR 1.46; 95% CI 1.13 to 1.88; p=0.004). Primary education (compared with no formal education) was associated with a greater intervention effect on adherence (OR 1.65; 95% CI 1.10 to 2.48; p=0.016) and also showed a significant subgroup effect (p=0.039). In sensitivity analysis, our findings were robust to a modified threshold of adherence, multiple imputation for missing data and aggregate level data pooling, but not to fixed-effects meta-analyses using generalised estimation equations. There was a significant subgroup effect for long weekly (p=0.037), short weekly text messages (p=0.014) and interactive messaging (p=0.010). Text messaging did not significantly affect any of the secondary outcomes.

Conclusions: Text messaging has a significant effect on adherence to ART, and this effect is influenced by level of education, gender, timing (weekly vs daily) and interactivity. We recommend the use of interactive weekly text messaging to improve adherence to ART, which is most effective in those with at least a primary level of education.

Strengths and limitations of this study

- We employed robust analytical strategies that incorporate the within-study and between-study differences.
- The interventions use text-messaging communication in different ways (content, frequency and interactivity).
- The studies included were conducted in sub-Saharan Africa where HIV infection is most prevalent.

INTRODUCTION

Adherence to prescribed medication is a key principle of medical care.[1] This is especially true with HIV infection, where poor adherence to antiretroviral therapy (ART) can lead to drug resistance, AIDS and subsequent morbidity and mortality.[2 3] Other consequences of suboptimal adherence include increased transmissibility of the virus and greater health system costs associated with more frequent and longer hospital stays.[3 4] With more that 30 million people living with HIV worldwide, of which close to half are already on ART,[5] there is a need to ensure that ART is taken consistently.

The widespread use of mobile phones, including in resource-limited settings, has led to numerous studies investigating how they can be used to improve healthcare delivery. Many mobile health interventions have been based on text messaging, an inexpensive way to enhance communication between patients and healthcare personnel.[6 7] Evidence from two Kenyan trials suggests that mobile phone text messaging can improve adherence to ART, reduce viral load and reduce treatment interruptions[8 9]; however, a third trial in Cameroon did not show significant improvement on adherence.[10] These trials suggest that a number of factors, such as age, gender, level of education, duration on treatment and specific characteristics of the text messages such as interactivity, timing and

content can influence an intervention's efficacy. Differences in effectiveness between and within studies can best be investigated using individual patient data (IPD) meta-analysis. This meta-analysis synthesises the three trials using mobile phone interventions for ART adherence and examines their effectiveness in important subgroups.[11]

Objectives

The objectives of this IPD meta-analysis are to

1. Summarise the evidence from three trials on the use of mobile phone text messaging compared with usual care to improve adherence to ART in people;
2. Analyse the effect of the intervention in subgroups defined by age, gender, level of education, duration on ART and type of message;
3. Examine the use of multiple statistical methods and their effects on outcomes.

METHODS

The methods have been documented in a published protocol.[12] In brief, we conducted an IPD meta-analysis of three randomised controlled trials (RCTs) investigating the use of text messaging to improve adherence to ART. The first of these was the WelTel Kenya1 RCT that was a multisite two-arm trial of weekly interactive text messaging versus usual care conducted in Kenya.[8] The second trial was a single site five-arm trial conducted in Kenya that compared short daily, short weekly, long daily and long weekly one-way text messages to usual care in a five-arm trial in Kenya.[9] The two Kenyan trials ran for 12 months. The third trial was the Cameroon Mobile Phone SMS (CAMPS) trial, which was a single site two-arm trial of weekly motivational text messaging versus usual care to improve adherence to ART over 6 months.[10] The first two trials showed significant improvement in adherence to ART while the latter did not. These were the only trials identified by the Adherence Trialists Collaboration and a PubMed search for RCTs of text messaging for ART adherence.

Data management

Only anonymised data were collected and used for this study. Data from all three trials were recoded and merged in a safe and secure computer system with backup. After merging, data were compared with the published manuscripts to ensure accuracy. Only variables available in all three data sets were used. Similar variables were pooled together. Categorical variables were modified to create new uniform categories across all studies. For example, categories such as 'lower primary', 'upper primary' and 'completed primary' were merged into 'primary education'. A new data set was created with the following baseline covariates: age (years), gender (male/female), level of education (none, primary, secondary or higher) and duration on ART (months). These covariates were used for the subgroup analysis. The intervention was defined as text messaging versus no text messaging. For the subgroup analysis, text messaging was further divided into short daily,[9] long daily,[9] short weekly[8 9] and long weekly messages[9 10], motivational[9 10] versus non-motivational[8] and interactive,[8 10] versus non-interactive.[9] Motivational messages were considered as those with words of encouragement. The primary outcome was adherence greater than 95% as measured by the authors. In other words, irrespective of how adherence was measured participants whose level of adherence was rated above 95% were considered to have achieved the primary outcome. Two of these trials used self-reported adherence,[8 10] while the third used medication event monitoring system (MEMS) caps.[9] The secondary outcomes were mortality, and the number of participants lost to follow-up, transferred out or withdrawn.

Statistical methods

Baseline data for all included participants were summarised as mean (SD) or median (first and third quartiles, Q1, Q3) for continuous variables and number (%) for categorical variables. The primary outcome was adherence to ART (defined as adherence above 95%). We used IPD random-effects meta-analysis to determine the effects of text messaging on the primary outcome. In this model, each study was considered as a random effect. ORs and 95% CIs are reported. The level of statistical significance was set at α=0.05. This primary analytical method was repeated for the secondary outcomes.

In an adjusted analysis, we investigated the effects of baseline covariates (age, gender, level of education and duration on ART) on the primary outcome. They were inserted in the model as fixed effects.

We also conducted four sensitivity analyses: (1) we changed the method of analysis (using generalised estimation equations (GEE)) for exploratory purposes; (2) we changed the threshold for adherence (>90%), as the recent literature suggests that viral load suppression can be achieved at lower levels of adherence[13 14]; (3) we used multiple imputation techniques to deal with missing data; and (4) we calculated pooled estimates of effect (aggregate data meta-analysis). We present heterogeneity statistics and forest plots for the aggregate data meta-analysis.

In addition, we looked at the effects of text messaging in different subgroups defined by age, gender, level of education, duration on ART, type of message (short daily, long daily, short weekly and long weekly), content of message (motivational vs non-motivational) and interactivity (two-way vs one-way). The p values of the interaction terms are reported. Data were analysed using Statistical Analysis Software (SAS) V.9.2 (SAS Institute, Cary, North Carolina, USA, 2009).

RESULTS

Baseline characteristics

The three trials included 1166 participants. Approximately two-thirds (67.0%) were female, and almost half (47.5%) had above a primary level of education. The median age

Table 1 Baseline characteristics of participants in the three text-messaging adherence trials

	Control arm (n=663) n (%)	SMS arm (n=503) n (%)	Total (n=1166) n (%)
Categorical variables			
Number of participants			
Lester *et al*[8]	265 (22.7)	273 (23.4)	538 (46.1)
Pop-Eleches *et al*[9]	139 (11.9)	289 (24.8)	428 (36.7)
Mbuagbaw *et al*[10]	99 (8.5)	101 (8.7)	200 (17.2)
Gender*			
Male	159 (32.7)	207 (33.2)	366 (33.0)
Female	327 (67.3)	416 (66.8)	743 (67.0)
Level of education*			
None	70 (14.4)	121 (19.4)	191 (17.2)
Primary	164 (33.7)	227 (36.4)	391 (35.3)
Secondary or higher	252 (51.9)	275 (44.1)	572 (47.5%)
Continuous variables	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Duration on ART (months)†	5.99 (16.00)	5.73 (15.342)	5.84 (15.626)
Age (years)‡	37.19 (9.192)	37.33 (9.476)	37.27 (9.348)

*57 missing.
†11 missing.
‡63 missing.
ART, antiretroviral therapy.

was 36 years (range=66), and the mean duration on ART was 5.8 months (SD=15.63). The details of the baseline characteristics are reported in table 1.

Primary analysis

In this random effects meta-analysis SMS text messaging significantly improved adherence to ART above 95% (OR 1.38, 95% CI 1.08 to 1.78, p=0.012; see figure 1).

Adjusted analysis

In the adjusted analysis, female versus male gender (OR 1.38, 95% CI 1.05 to 1.82; p=0.022) and primary education compared with no formal education (OR 1.65, 95% CI 1.10 to 2.48; p=0.016) were significant predictors of adherence >95%. Age and duration on ART were not significantly associated with better adherence (see figure 1).

Sensitivity analysis

Text messaging did not significantly improve adherence to ART in the sensitivity analysis using GEE (OR 1.11, 95% CI 0.88 to 1.41; p=0.373). The intraclass correlation coefficient for the primary outcome was 0.18, suggesting considerable differences between the studies. When we considered a threshold of 90% for adherence (OR 1.51, 95% CI 1.07 to 2.13; p=0.018), used multiple imputation techniques (we created five data sets of plausible values that were merged into one for analysis) to replace missing data (OR 1.34, 95% CI 1.05 to 1.72; p=0.021) or conducted a random-effects aggregate data meta-analysis (OR 1.35, 95% CI 1.05 to 1.73, p=0.020, τ^2=0; I^2=0%) text messaging had a positive effect on adherence to ART. These results are displayed in figure 1.

Subgroup analyses

In the subgroup analyses primary education (p=0.039), long weekly (p=0.037), short weekly text messages (p=0.014) and interactive messages (p=0.010) had significant positive interactions with text messaging. Age, gender, duration on ART and motivational content showed no subgroup effects. These results are summarised in figure 1.

Secondary outcomes

Text messaging did not significantly reduce mortality or losses to follow-up. Transfers and withdrawals were also not significantly affected by text messaging (see table 2).

DISCUSSION

This IPD meta-analysis of three trials found that text messaging had a positive effect on adherence to ART. This effect is stronger in women and in those with a primary education. Weekly and interactive messages are also more effective. Our findings confirm the efficacy of text messaging in improving adherence to ART but demonstrate that this effect may be nuanced and work for some patients more so than others. While there is widespread support for text messaging, our analysis suggests guidelines should be specific about what design text messaging interventions should be implemented.[15 16]

Three issues stand out in this analysis. First, primary education stood out in the adjusted and subgroup analysis as an important factor influencing the effect of text messaging on ART. Understandably, education is related to literacy and consequently the ability to read text messages. It would seem, however, that beyond primary education, there are no further benefits to be gained, as can be seen in the subgroup analysis, where there was no

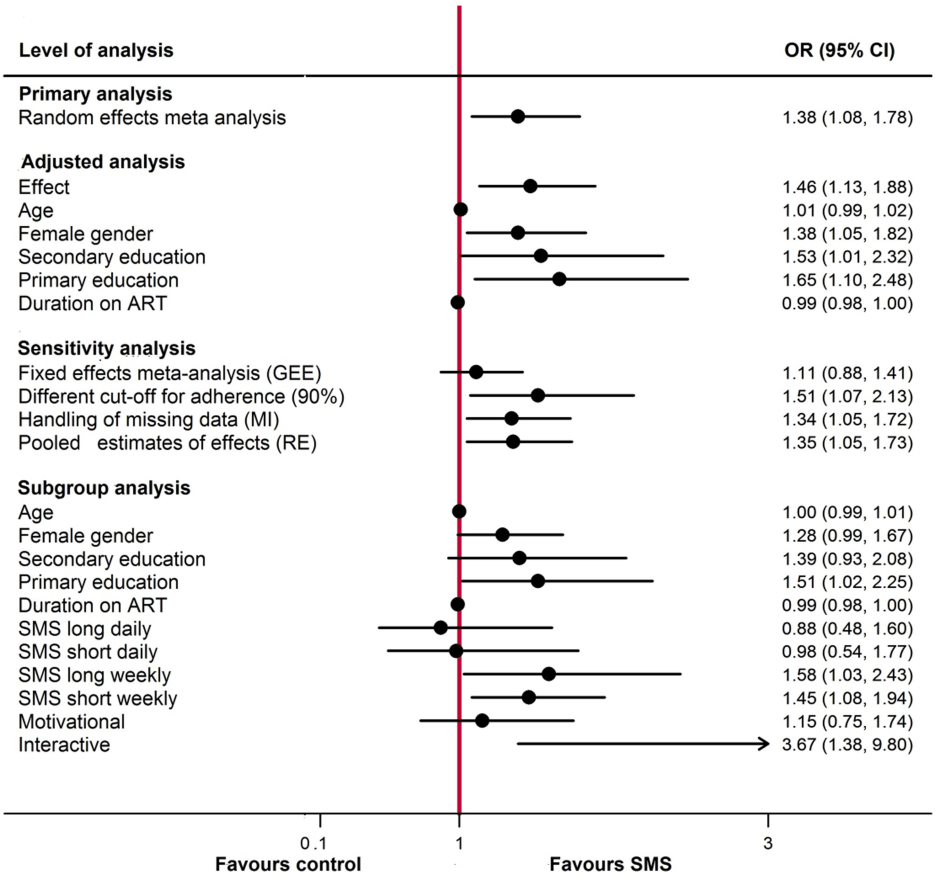

Figure 1 Forest plot for primary, adjusted, sensitivity and subgroup analysis of text messaging to improve adherence to ART. ART levels of education are compared with no formal education; types of text messages are compared with control; 3.3% missing data for primary outcome. ART, antiretroviral therapy; GEE, generalised estimation equations; MI, multiple imputation; RE, random-effects.

interaction with secondary education. The potential marginalisation of people with limited literacy with regard to text messaging has been described in other studies.[11 17 18] Second, the subgroups that received weekly messages were more likely to achieve adherence above 95%. This may be because daily messages are intrusive, cause user fatigue and therefore rendered ineffective. However, these analyses should be treated with caution, as the data for daily messages came from only one of the trials.[9] Further research is necessary to understand the role of timing on the efficacy of text messaging.

Third, text messaging did not have a significant effect when we used GEE. A GEE approach estimates population averaged effects, and the estimate of SE is very variable when there are few clusters.[19] In this IPD analysis with only three clusters, GEE may not be the appropriate parameter estimator.

Table 2 Summary of results for secondary outcomes

Secondary outcomes	OR (95% CI)	p Value
Mortality	0.87 (0.52 to 1.43)	0.591
Lost to follow-up	0.87 (0.63 to 1.19)	0.387
Transfers	1.40 (0.56 to 1.48)	0.463
Withdrawals	2.55 (0.67 to 9.71)	0.170

In addition, motivational content seemed to provide no additional value, and may not be necessary in many cases. On the other hand, interactivity boosted the intervention effect and should be encouraged. Still, we advise caution with this interpretation as the effect of interactivity may be a between-study difference. Data for interactivity came from all the participants in the two trials.[8 10]

This study is not without limitations, notably the fact that the three studies included in this review were conducted in Africa and therefore these findings may not be applicable to other settings. However, this is also strength as adherence enhancing interventions are particularly relevant to Africa, the heart of the HIV pandemic. Combining widely variable text messaging interventions in this meta-analysis may also limit the interpretation of our findings. The generalisability of our findings may also be affected by the differences in the way adherence was measured in the included studies and the average duration on ART (about 6 months); however, our primary choice of analytical method was meant to account for these differences between studies. Even though we did not conduct a systematic search for other RCTs of text messaging to improve adherence to ART, we reached out to the Adherence Trialists Collaboration to identify other trials and none were identified. Other such RCTs, if any, can be included in subsequent iterations of these analyses. Only one of the studies used viral load as a measure of adherence. It is

possible our results would be different had we had access to viral load data.

The strengths of this analysis include the use of IPD, an analysis of whether text messages are more effective in patients with certain characteristics, the use of robust statistical techniques to account for within-study and between-study differences, and our focus on Africa where our research is most needed.

CONCLUSION

Test messaging has a significant effect on adherence to ART. We recommend the use of interactive weekly text messaging to boost adherence to ART, especially in clients with at least a primary level of education. Further research endeavours should investigate the cost-effectiveness of text-messaging interventions and approaches to scaling up.

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Competing interests RTL is the founder of WelTel, a non-profit organisation designed to scale-up evidence-based mHealth interventions. MLV is supported by a Canadian Institutes of Health Research Doctoral Award—Doctoral Foreign Study Award (October 2012), offered in partnership with the CIHR Strategy for Patient-Oriented Research and the CIHR HIV/AIDS Research Initiative. RTL is supported in part by an mHealth grant from Grand Challenges Canada.

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CHAPTER 6

A FRAMEWORK FOR COMMUNITY OWNERSHIP OF A TEXT MESSAGING PROGRAMME TO IMPROVE ADHERENCE TO ANTIRETROVIRAL THERAPY AND CLIENT-PROVIDER COMMUNICATION: A MIXED METHODS STUDY

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Abstract:

Background:

Mobile phone text messaging has been shown to improve adherence to antiretroviral therapy and to improve communication between patients and health care workers. We sought to investigate community acceptability and readiness for ownership of a text message programme among clients living with human immunodeficiency virus (HIV) at the Yaoundé Central Hospital Accredited Treatment Centre (YCHATC), Yaoundé, Cameroon and to develop a framework for implementation.

Methods:

We used the mixed-methods sequential exploratory design. In the qualitative phase we used 10 focus group discussions (57 participants) to elicit themes related to acceptability and readiness. In the quantitative phase we explored the generalizability of these themes in a survey of 420 clients. Qualitative and quantitative data were merged to generate meta-inferences.

Results:

Both qualitative and quantitative data showed high levels of acceptability and readiness despite low rates of participation in community projects. In the qualitative strand more people were willing to pay for a text messaging service, preferred participation of health personnel and preferred that the project be based in the hospital. Some of the limitations identified were lack of management skills in the community, financial, technical and literacy challenges. Participants who were willing to pay were more likely to find the project acceptable and expressed positive feelings about community readiness.

Conclusion:

Community ownership of a text messaging programme is acceptable to people living with HIV at the YCHATC. Our framework for implementation includes training community members in project management, securing sustainable funding, demonstrating clear benefits to users, allowing a trial period and high levels of confidentiality. The project can be evaluated using participation rate, clinical outcomes, satisfaction with the service, cost and feedback from users.

Key words:

Text messaging, community ownership, HIV, mixed methods, Cameroon

Background:

Worldwide, more than 35 million people are living with human immunodeficiency virus (HIV) (UNAIDS, 2013). Despite the increasing numbers of people on life-saving antiretroviral therapy (ART), millions of people continue to suffer the morbidity and mortality associated with HIV (UNAIDS, 2013). In low-and middle-income countries only 34 % of eligible individuals are actually receiving ART. Among those who are receiving ART, suboptimal levels of adherence to medication often occur and are a major challenge to HIV care (Boyer et al., 2012). Considerably high levels of adherence are required to suppress viral replication and boost CD4-positive-T-lymphocyte count (Gill, Hamer, Simon, Thea, & Sabin, 2005; Haubrich et al., 1999; Mannheimer, Friedland, Matts, Child, & Chesney, 2002; Paterson et al., 2000). The consequences of poor adherence to ART include not only accrued morbidity and mortality, but also higher transmission rates, the development of resistant viral strains (Gill et al., 2005; Haubrich et al., 1999; Mannheimer et al., 2002; Paterson et al., 2000), and overall increments in health care costs. Adherence to medication, generally speaking, and specifically for ART is linked to multiple factors which may be related to the patient, provider, health system or the medication itself (WHO, 2003). The WHO encourages multi-faceted adherence improvement initiatives that are tailored to patients' needs (UNAIDS, 2013; WHO, 2003). In recent years, text messaging has emerged as an effective supporting tool for adherence to ART (Horvath, Azman, Kennedy, & Rutherford, 2012; Lester et al., 2010; Pop-Eleches, 2011; UNAIDS, 2013). Currently, there is ongoing research on how best to scale-up text messaging interventions and how to tailor them to suit patient characteristics (Mbuagbaw, van der Kop, et al., 2013).

About 70% of people living with HIV reside in sub-Africa (UNAIDS, 2012). Among the West and Central African countries, Cameroon has one of the highest prevalence of HIV, with 4.6% of

the adult population infected (UNAIDS, 2012). The situation is worsened by sub-optimal adherence to antiretroviral medication and a fragile health system plagued by human resource shortages and medication stock-outs (GIP ESTHER, UNICEF, & WHO, 2008). An impressive mobile phone penetration rate of 52% (2013) and affordable cellular communication offer an opportunity to resolve some of these difficulties through mobile-health (m-Health) interventions.

Community involvement is a frequent characteristic of successful health care programmes (Mbuagbaw & Shurik, 2011), and can play an important role in improving adherence (UNAIDS, 2013). This is most likely because of the potential for better outreach and the possibility of mobilising community resources such as finances, human capital and material. We argue that communities have the right to take part in decisions affecting their lives and are in the best position to defend their own interests, therefore it is only wise that they be involved in developing community-run programmes (Mbuagbaw & Shurik, 2011).

This research is built on previous research findings, indication the effectiveness of text messaging in improving adherence to ART, especially two-way weekly text messages (Horvath et al., 2012; Mbuagbaw, van der Kop, et al., 2013), and the potential of text messaging to begin resolving other unmet communication needs (Mbuagbaw, Thabane, & Ongolo-Zogo, 2013; van der Kop, 2012). There is also evidence for health worker support of text messaging programmes (Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012). Putting the available evidence together suggests a favorable environment for scaling up text messaging interventions but leaves important knowledge gaps regarding how best to take text messaging programmes to scale and how to use text messaging to enhance communication and care in general. Owing to the fact that text messaging, though technology-based, is a relatively simple intervention, and community

involvement comes with numerous advantages, we sought to investigate community willingness and readiness to own and run a text messaging programme using mixed-methods.

For the purposes of this study, "community" will refer the group of individuals living with HIV and receiving care from the Yaoundé Central Hospital Accredited treatment Centre (YCHATC) and ownership as "as a process in which the community members design, manage and reap benefits from a programme" (Mbuagbaw, Ongolo-Zogo, & Thabane, 2013).

The purpose of this research is to identify key factors linked with community willingness and readiness to own a text messaging programme, and to use this information to develop a framework for transfer of text messaging-based initiatives to community groups.

Research paradigm:

We adopted a pragmatist paradigm to shape and design our research. In order to develop a framework for community ownership that is applicable in the real world, we used both deductive and inductive reasoning to determine what factors would enter the framework. Pragmatism has been argued to be a preferred paradigm for mixed-methods research as it allows the use of "what works" best in data collection and analysis, incorporates multiple perspectives and links subjective and objective knowledge (Creswell & Plano Clark, 2011; Tashakkori & Teddlie, 2010; Yvonne Feilzer, 2010). In this paradigm we acknowledge that our research is occurring within specific social, economic and political contexts (Creswell, 2009).

Theoretical framework:

Admittedly, text messaging for health care is not so new, as the medical literature is growing with examples of text messaging interventions will favorable outcomes in HIV care (da Costa et

al., 2012; Dowshen, Kuhns, Johnson, Holoyda, & Garofalo, 2012; Lester et al., 2010; Maduka & Tobin-West, 2013; Mbuagbaw, Thabane, et al., 2013; Pop-Eleches, 2011). However, community ownership of such, to the best of our knowledge, has not been described or investigated. The theory of "diffusion of innovations" suggests that innovation factors (relative advantages to be gained, compatibility with existing practices, simplicity of use, trialability and observable results) receiver factors (attitude to change, perceived need) and social system factors (social norms and tolerance for deviancy) will affect the adoption of community ownership of a text messaging. Adoption would occur in five steps: knowledge, persuasion, decision, implementation and confirmation. We sought to identify the roles of these factors and integrate them in the framework development process (Rogers, 2003).

Why mixed methods:

Mixed methods are now being recognised as a strong research option for complex research questions that cannot be answered by either qualitative or quantitative methodologies applied singly (O'Cathain, Nicholl, & Murphy, 2009). Mixed methods can reap the advantages of breadth and generalizability obtained from quantitative methodologies, and also the depth in understanding phenomena from qualitative methodologies. Overall, mixed methods offer a more complete picture for a research question (Johnson, Onwuegbuzie, & Turner, 2007). In this work, we sought to complement the qualitative with the quantitative, to initiate new ways of thinking and to expand existing knowledge (Greene, Caracelli, & Graham, 1989). We provided further justification for our use of mixed methods in the protocol (Mbuagbaw, Ongolo-Zogo, et al., 2013).

Research questions:

This work was guided by qualitative, quantitative and mixed research questions (Mbuagbaw, Ongolo-Zogo, et al., 2013).

Qualitative research questions

- Will people living with HIV in Yaoundé, Cameroon accept community ownership of a text messaging programme and are they ready to take ownership?

Quantitative research questions

- How many of the people living with HIV in Yaoundé, Cameroon are willing to accept and ready to own a text messaging programme and what factors are associated with acceptability and readiness

Mixed methods research questions

- How generalizable are the themes related to acceptability and readiness to a larger sample of people living with HIV in Yaoundé, Cameroon?
- What are the similarities and differences between the qualitative and quantitative strands?

Methods:

Our methods have been described in detail in a published protocol (Mbuagbaw, Ongolo-Zogo, et al., 2013). The essential portions are reported here.

Ethics:

Ethics approval was obtained from the Institutional Review Board (IRB) of the Yaoundé Central Hospital (N°288L/MINSANTE/SG/DHCY/Stages on the 16 May 2013).

Design and rationale for design:

We employed the exploratory sequential design for this study. Simply put, it entails an initial qualitative strand that leads to thematic variables which are converted into questions for the second quantitative phase, after which the findings from both stands are merged and correlated to generate meta-inferences. This design enhances our ability to generalise qualitative findings, develop an instrument or questions to measure community acceptability/readiness and to facilitate collaboration between researchers with qualitative and quantitative backgrounds (Creswell & Plano Clark, 2011). It is also the most appropriate design for instances where there is no existing guiding framework (Creswell & Plano Clark, 2011).

Even though the exploratory sequential design is not the typical mixed methods design used in the pragmatic paradigm (Creswell, 2009), it was the most appropriate for our purposes.

Setting:

This study was conducted in the Yaoundé Central Hospital Accredited HIV Treatment Centre (YCHATC), located in the capital city of the central African nation of Cameroon. It caters for about 6500 clients and receives close to 40 new clients every week. Eight physicians provide daily care for clients. The services provided include screening for HIV, clinical care, psycho-social support, routine lab testing and hosting community associations of people living with HIV. In preceding years, this centre has been the focus of text messaging research. (Mbuagbaw, Bonono-Momnougui, & Thabane, 2012; Mbuagbaw, Thabane, et al., 2013; Mbuagbaw, Thabane, Ongolo-Zogo, & Karanja, 2012; Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012) The adult prevalence of HIV in Cameroon is 4.5% (UNAIDS, 2013).

Sampling:

We employed a two-stage sampling procedure, using purposive and probabilistic sampling techniques to ensure that data was collected in depth and breadth (Teddlie & Yu, 2007).

For the quantitative strand we sought individuals who were living with HIV, receiving care from the YCHATC or who fulfilled any of the following criteria: 1) they belonged to an association of people living with HIV (as leaders or members), 2) they were community health workers, 3) they were willing to participate in a community owned text messaging programme. Participants with significantly different characteristics were interviewed separately to create homogenous groups. Focus groups of 6 to10 participants were constituted until saturation of ideas.

For the quantitative strand, we applied the sample size formula proposed by Cochran for surveys (Cochran, 1977). For a total population of people living with HIV at the YCHATC of 6500, assuming an α level of 0.05, a 5% margin of error (for categorical data) and a standard deviation of 0.5 (for our binary primary outcome- willingness to participate in a community-led text messaging programme), after considering a 10% "refusal to participate" rate [obtained from a previous text messaging study in the same setting (Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012)] we arrived at a sample size of 402 participants (Mbuagbaw, Ongolo-Zogo, et al., 2013).

Data collection:

In the qualitative strand, two teams of data collectors were formed, each made up of one moderator and one note taker, neither of whom were staff of the hospital. They were all dressed

in plain clothes. During the daily information-education-communication (IEC) sessions held for clients of the YCHATC, clients were invited to take part in focus group discussions. The consenting participants were invited into a separate room. Basic socio-demographic data were collected (age and gender), and participants were invited to pick a name they would wish to be addressed by during the discussions. The moderator introduced the session and initiated the discussions based on a focus group discussion guide (Mbuagbaw, Ongolo-Zogo, et al., 2013). All the discussions were recorded. The note taker also noted relevant parts of the discussion and important non-verbal cues that could not be captured by the audio recorder. The FGDs lasted about 60 minutes each. Participants were compensated for the time spent during the FGDs (1000 Frs CFA ~2 USD).

In the quantitative strand, clients in the waiting rooms of the YCHATC were approached and invited to take part in a survey. Our questionnaire (developed from the qualitative strand) was revised with the interviewers and pilot tested on ten participants for clarity. Four hundred and twenty nine clients were approached, of which nine declined to participate in the study. After oral consent was obtained, a questionnaire was administered. The questionnaire contained basic socio-demographic and clinical data, and questions derived from the themes which arose in the qualitative strand. The interviews lasted about 15 minutes each.

Data analysis:

We conducted a thematic analysis for the qualitative data. The notes taken were used to supplement the audio-recordings, which were transcribed into text. Codes were generated by identifying repetitions in the text (Bernard & Ryan, 2010). Similar codes were grouped and

themes generated from these groupings. Two coders worked on the data to verify agreement on the themes generated. In the case of disagreement, the final themes were determined by consensus. The themes were then converted into thematic variables and employed in the survey as questions. Quotes of illustrative significance are reported.

Quantitative data were analysed using Statistical Package for Social Sciences (SPSS) V.20.0 (SPSS, Inc, 2009, Chicago, Illinois, USA). Baseline characteristics and responses to questions are reported as counts (%) or mean (standard deviation [SD]). Community willingness to participate in a community-led text messaging programme was dichotomized and used as the dependent variable in logistic regression models. Independent variables such as age (years), gender (male or female), level of education (none, primary, secondary, university), profession (working, unemployed, retired, student), marital status (married or living together, single, divorced, widow or widower), residence, lodging situation (common or individual), time since diagnosis (months), duration on ART (months), self-reported adherence to medication (seven-point Likert scale), and self-reported adherence to appointments (seven-point Likert scale). The purpose of this adjusted analysis was to determine if there are any underlying factors which influence willingness to participate and which must be addressed in the development of a framework. The level of statistical significance was set at $\alpha=0.05$. Adjusted odds ratios (OR) are reported with 95% confidence intervals (CI). Model fit was estimated using Hosmer and Lemeshow's goodness of fit statistic.

Data integration:

Patient characteristics and responses were compared numerically and graphically. In order to represent the merged data graphically we estimated confidence intervals around the proportions

for key patient characteristics in both strands, themes (in the qualitative strand) and corresponding thematic variables (in the quantitative strand). We considered data convergence to exist if the confidence intervals overlapped in a forest plot. The confidence intervals were estimated for graphical purposes using the recommended formula based on standard errors.(Rumsey, 2003) This provides a graphical appraisal of comparability between samples with different denominators.

Validation checks:

The purpose and objective of this study were pre-specified in a published protocol (Mbuagbaw, Ongolo-Zogo, et al., 2013). In the qualitative strand, we used member-checking, audio recorders and duplicate coding to ensure the accuracy of our data. We limited facilitator bias by using a discussion guide. In the quantitative strand we estimated an appropriate sample size, revised and pilot-tested our questionnaire, and performed adjusted analyses to account for potential confounders.

Team composition:

Our research team at the Centre for Development of Best Practices in Health (CDBPH; http://www.cdbph.org) was constituted of a mix of researchers with expertise in both qualitative and quantitative research methods. We included public health physicians, anthropologists, sociologists, HIV clinical expert, experts in health policy and statisticians.

Results:

Qualitative results:

Participants

Seven focus groups discussions were conducted. Six of these were made of heterogeneous individuals with regards to age, gender, level of education and profession. The last focus group discussion included four leaders of HIV associations with a minimum of 11 years of experience with community activities. In total, 67 participants were included of which only 8 were male. The mean age (SD) was 38.8 (11.1). Close to half (54.3%) had a primary education, the rest had either secondary or university education. The strongest themes that emerged from these discussions were: weak participation in community activities, willingness to participate in a text messaging initiative and mixed feelings about community management.

Participation in community activities

Almost three-quarters of the participants did not participate in any community activities or belong to any specific community association. Some of them were not even aware that there were existing community associations. A few others described failed attempts at creating their own associations of people living with HIV. Generally speaking, participants felt they did not have sufficient information with regards to the functioning of community associations within and out of hospitals.

"I don't know where to find them (community associations)."
"We are not informed about associations."

Acceptability

We set out to access community "acceptability of ownership" of a text messaging programme. Our findings led us to rethink the question and present it in a way that was more understandable to participants. For this reason the discussion was presented as "willingness to participate" in a text messaging programme at any level. Opinions were favorable with regards to participating in a text messaging programme in six out of seven groups. They recognised the potential of such a programme in improving their adherence, quality of life and cohesion among people living with HIV.

"People will join because they need more information on the illness, so they'll come."
"I will join if it will help my brothers and to sensitize others."
"They will come if it's free"

One group unanimously decried the purpose of a text messaging programme. They urged for more self-management, as the text message would not affect the main components of care which they stated as having to come to the hospital and experience problems such as long wait times.

"I am not in support"
"Really, I am indifferent."
"I think that with this project, patients will no longer make any efforts"

The participants who thought favorably of text messaging proposed that it could be used as a reminder for medication and appointments, to explain lab tests, as a source of solace, to provide general information (nutritional and educative) and as a social tool. They also expressed the need for an interactive service in which users can contact health workers for specific requests.

"I want to be reminded of the time to take my medication."
"…to deal with individual problems."
"I need psychosocial support."
"I should be told when medication is available at the pharmacy"
"We want to be able to call in case of specific problems."

However, they identified a number of challenges with the management of a text messaging programme such as limited financing, power outages (that would prevent them from charging their phones), the risk of accidental disclosure of status, limited organisational skills in associations of people living with HIV, lack of expertise in technological issues, phone network issues, tension between patients, illiteracy, no clearly outlined benefits to participation in the programme.

"*We don't have the financial means."*
"I think these text messages would not be useful to people who did not go to school."
"…mismanagement by the leaders of the association."
"We don't have network (mobile phone signal) where I live."

Community readiness

Discussions about community readiness for ownership highlighted concerns about the resources required to sustain the programme. The participants expressed mixed feelings with regards to sources of financing and provided as list of potential funders: the state, para-public companies, private companies, non-governmental organisations and patients themselves.

"The persons who had the idea should finance the project."
"It's the state……"
"It depends on my income."
"I can contribute."

They felt that despite community involvement driven mostly by information needs, management by health personnel and social workers would be a valuable asset.

"They (health personnel) are better informed than we are so…"
"They (health personnel) have a big role to play."

They also identified a number of factors that would impede the implementation of such a programme such as cost, the involvement of people who are not infected with HIV, the lack of integration with regular hospital services and the potential for disclosure of status.

"People who are not sick may cause us trouble."
"It will be very difficult for this community."
"… Limited financing of the SMS"
"…shame of being recognised by others."

They were, however, optimistic about voluntarism and were willing to be involved.

"I think there are always volunteers who are devoted to the care of patients."
"We will try and see."

Quantitative results

Participants

Four hundred and twenty participants (420) respond to the survey. Contrary to the qualitative sample, more men participated in the surveys (71.2%). Half of the participants had a secondary education (54.5) and two-thirds were employed (67.7%). The mean duration on antiretroviral therapy was 43.2 months (standard deviation [SD] = 37.06). The rest of their socio-demographic and clinical characteristics are displayed in table 1.

Table 1: Socio-demographic characteristics of 420 participants in the quantitative phase of the study

Data on the practical functioning of a text-messaging programme were also collected. Responses to these questions are summarised in table 2.

Table 2: Practical functioning of a text messaging programme

Factors associated with current participation in community activities

Only 6.7% (n=28) of the participants were currently involved in any community support programme. Only primary education (OR 30.15; 95% CI 1.88-483.15; p=0.016) was associated with current participation in a community support programme. The Hosmer and Lemeshow goodness-of-fit test was as follows: chi-squared 3.26, df=9, p=0.833.

Factors associated with willingness to participate (acceptability) in a text messaging programme

Eighty percent (n=336) of the participants expressed willingness to join a text messaging programme. Higher self-reported adherence to ART was associated with higher willingness to participate (OR 1.57; 95% CI 1.16-2.14; p=0.004) and higher duration on ART was weakly associated with less willingness to participate (OR 0.95; 95% CI 0.92-1.00; p=0.049). In

addition, people who were not willing to pay for the text messaging were less willing to participate (OR 0.03 95% CI 0.00-0.28; p=0.003). The Hosmer and Lemeshow goodness-of-fit test was as follows: chi-squared 7.188, df=8, p=0.519.

Factors associated with positive feelings (readiness) about community management

Three quarters, 73.6% (n=309) though the community could run the programme in a sustainable way and two-thirds, 61.7% (n=259) were willing to participate in the development of the programme. Again participants who were less willing to pay where less likely to believe the community could run the project (OR 0.35; 95% CI 0.18-0.68; p=0.002). The Hosmer and Lemeshow goodness-of-fit test was as follows: chi-squared 13.14, df=8, p=0.107.

Challenges to programme

Participants were able to identify a number of challenges that the community would face in setting up a text messaging programme. They reported lack of motivation among stakeholders (24.5%); limited funding (60.5%); participants phones out of order (25.2%); irregular phone network (38.6%); power outages (25.5%); fragile community organisations (6.9%); poor management from the people living with HIV (36.9%); poor management form health personnel (32.9%); and limited experience in the implementation of the programme (13.3%);

Proposed measures

They proposed that people living with HIV should be involved in the management of the programme (27.6%); the programme should be based in the YCHATC (15.0%); ensure

participation of health workers (54.0%); any communication should be coded (60.7%); and that messages should be personalised (25.2%).

Potential limitations

Illiteracy among people living with HIV was the most frequently cited limitation (58.8%). Other problems cited were: financing (7.8%), non-ownership of phones (1.4%), language of the message (0.2%), inability to manipulate text messaging function (0.2%); lack of information on the programme (0.7%); lack of satisfaction with programme (0.2%); slow responses to participants' queries (0.2%); medication stock-outs (0.2) and the stigma associated with HIV (0.2%).

Data integration:

A data matrix is presented in table 3. The characteristics of the participants in both strands differed, with more urban dwellers in the quantitative strand, more females in the qualitative strand and more participants with a secondary or higher level of education in the quantitative strand. There was convergence in willingness to adhere to a text messaging project (acceptability) and the belief that the community could run a text messaging programme in a sustainable way (readiness). Similar numbers confirmed current participation in community support programmes. Data regarding willingness to pay, participation of health workers and where the programme should be based did not converge. See figure 1.

Table 3: Mixed-methods data matrix

Figure 1: Graphical display of merged data

Discussion:

In this paper, we have explored the willingness of people living with HIV at the YCHATC to participate in a community led SMS support programme, and their readiness. Overall, people living with HIV would adhere to such an initiative and believe they are capable of managing the programme, with some reserve. Choices regarding how the initiative should be financed, and where the programme should be based and how much health worker participation is desirable were areas of relative incertitude.

In our protocol we sought to investigate acceptability and readiness, however, in the course of our research the questions changed somewhat. Acceptability was better conceptualised as willingness to participate. Also, in our discussions about "readiness", participants perceived readiness not only as having the skills and resources to manage a programme, but rather expressed positive or negative feelings with respect to community management. Given, the small numbers of participants who were already involved in a community programme (less than 8% in both strands), it is possible that many participants had no prior anchor which they could use to gauge readiness, and sought to conceptualise it in their own way.

We noted large differences in the composition of the participants in the qualitative and quantitative strands, notably with regards to gender and level of education. The qualitative strand (85.9% were females) seemed to reflect the gender distributions of people living with HIV who receive care at the YCH-ATC and who participate in text messaging studies (close to two-thirds

were females) (Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012). The inverse was seen in the quantitative phase (only 28.1%). However, these differences did not seem to affect acceptability and readiness as gender was not found to be an explanatory variable in the regression analyses. Also there were more participants with primary education in the qualitative strand (54.3%) compared to the quantitative strand (27.9%). Primary education was associated with current participation in community projects, even though very few participants in either strand participated in any community projects.

We also developed an innovative way of integrating qualitative and quantitative data, using forest plots. By estimating the confidence intervals around the point estimate, we are able to visually explore the extent of data convergence or divergence when the point estimates and sample sizes differ in the qualitative and quantitative strands. The confidence intervals give us a sense of the precision in our estimates coming from two samples with different sizes. However, these confidence intervals are estimated only for graphical purposes and should not be used for statistical inference. We used them to objectively infer convergence when there is overlap in the confidence intervals.

Addressing the research questions:

Acceptability of ownership of a text messaging programme is strong among YCHATC, but readiness as perceived by both researchers and participants requires that a number of issues be addressed. The main impediments to readiness were a lack of management skills and finances. Implementation of community ownership would therefore require training and maintaining a

strong managerial body, and ensuring sustainable sources of funding, some of which were cited in the interviews.

The main limitation, with regards to implementation was the inability of some participants to read text messages. This implies that messages will have to be conceived in the plainest possible language. Another option worth considering is having participants use confidants to read the messages. Up to 43.4% reported having people who could receive and communicate text messages to them. The qualitative and quantitative strands were similar with regards to willingness to participate and readiness, but differed on where the programme should be based and whether health workers should be involved. For issues on which community opinions are divergent, feasibility and cost should be considered.

Factors associated with acceptability and readiness

Participants with higher self-reported adherence to ART were more likely to find a text messaging project acceptable. This may reflect their understanding of the importance of high levels of adherence. On the other hand participants with a higher duration on ART were not willing to participate. Patient who have received ART for long periods may have developed other adherence enhancing strategies and would not be willing to include yet another (Mbuagbaw, Thabane, Ongolo-Zogo, Yondo, et al., 2012). They may also have developed hard-to-change medication taking habits. However, adherence to long term medication is known to wane over time and such patients require additional support (Mannheimer et al., 2002; Mbuagbaw, Thabane, Ongolo-Zogo, Yondo, et al., 2012). For such patients it is necessary to build on the other benefits to be reaped from such a project. Participants who were willing to pay for a text messaging project were more likely to be willing to participate and to be ready to own

one. Reducing the cost of the project, or increasing the value for money by augmenting the services provided may help in reaching participants who are less willing to pay.

Explaining the lack of convergence:

Less participants were willing to pay for a text messaging project in the quantitative strand (34.4%) compared to the qualitative strand (83.3%). This difference may reflect the flexibility in data collection used in the qualitative strand, with more opportunity for participants to discuss and consider different payment options, as opposed to the rigid closed-ended yes-no type questions in the quantitative strand. This also highlights the complementarity of both methodologies in eliciting a variety of responses for the same question. In the qualitative strand, more people wanted (86.5%) participation of health personnel than in the quantitative strand (54.4%). This divergence would suggest that there are unknown reasons why health worker participation may be perceived differently depending on how data were collected and should be investigated further. Some amount of health personnel participation is necessary to link participants to care, however their role as managers in a community led project is questionable. Previous research suggests high acceptability among health workers to take part in a text messaging programme despite the extra work involved (Mbuagbaw, Thabane, Ongolo-Zogo, & Karanja, 2012). The way forward would be to involve health workers only when necessary, by providing a permanent go-to person in the health facility. They was much more divergence with regards to where the project should be based, with 67.1% in the qualitative versus 15.0% in the quantitative strand proposing that it should be hospital-based. This may be a reflection of the expected participation of health workers, as health workers may be expected to participate more if the programme is hospital-based. It may also indicate the amount of independence that

community members expect from the programme. A hospital based intervention holds numerous advantages in this context. Firstly, the hospital is the only common ground for all the people living with HIV since they reside in various locations around the city of Yaoundé and it will be challenging to choose a convenient community location. Secondly, in the hospital it is easier the link the enhanced communication services of the text messaging programme with medical care and laboratory tests. Thirdly, the programme will benefit from the hospital infrastructure (locale, security, and internet). For smaller rural hard-to-reach communities, an outreach station may be beneficial. Such options warrant further consideration.

Influence of context and researchers

Our findings should be interpreted as being relevant to the context of the health facility which in the previous years has been used for text messaging research among people living with HIV (Mbuagbaw, Bonono-Momnougui, et al., 2012; Mbuagbaw, Thabane, et al., 2013; Mbuagbaw, Thabane, Ongolo-Zogo, & Karanja, 2012; Mbuagbaw, Thabane, Ongolo-Zogo, Lester, et al., 2012). We cannot assume that participants were entirely naïve to the notions of text messaging and their responses in both the qualitative and quantitative strands may have been influenced by these. These findings are also tied to socio-economic, cultural and political factors which are specific to Cameroon.

Diffusion of innovation

Within the theoretical framework of the diffusion of innovations theory, we have identified a number of innovation factors that will guide our framework development. Table four is a summary of these factors as they relate to community ownership of a text messaging programme.

Table 4: Diffusion of innovation as applied to community ownership of a text messaging project

Framework development:

Based on our findings, we propose the following guidelines/framework for initiating community ownership of a text messaging programme: incorporate health worker participation; the location may be community or hospital based (hospital based-preferable); add other benefits to text messaging: provide other types of information, assistance with appointments, lab tests, collecting medication etc.; establish participation costs with potential participants; provide a free test period; personalize as much as feasible; build on community confidence – work with people they know and trust; ensure high levels of confidentiality; publicize, take time to inform clients of new service; train community participants on relevant issues: confidentiality, programme management; outline clear benefits for users. This guidelines should be applied in a cyclical manner, dropping off the less useful aspects and building on the strengths of the successful ones. Figure 2 is an illustration of this framework.

Figure 2: Framework for community ownership of text messaging programme

Strengths and limitations:

The strengths of this study include the use of both qualitative and quantitative methodologies to elicit community acceptability and readiness of a text messaging programme, and employing cross-paradigm checks to ensure both internal and external validity.

Some limitations do exist, such as the lack of convergence in some variables and the fact that we have no direct measure of socio-economic status. A measure of socio-economic status would have been useful to bring more meaning to the data on acceptable cost.

Conclusions:

Our findings suggest that it is possible to initiate a community-owned text messaging project for people living with HIV in Yaoundé, Cameroon. Community ownership is acceptable and potential users are willing to participate. Such a project can be developed by considering user-perspectives and needs, promoting capacity building in community project management, strengthening user confidence and developing a sound sustainable funding mechanism. This could be an important option for scaling-up text-messaging interventions that empowers the community and doesn't weight on the limited human resources for health.

List of abbreviations:

ART	Antiretroviral therapy
CDBPH	Centre for the Development of Best Practices in Health
CI	Confidence Interval
HIV	Human Immunodeficiency Virus
IEC	Information Education Communication
IRB	Institutional Review Board
OR	Odds Ratio

SD Standard Deviation

YCHATC Yaoundé Central Hospital Accredited Treatment Centre

Competing interests:

The authors declare that they have no competing interests.

Author's Contributions:

LM, LT, MS and POZ conceived of the study and developed the design, implementation and drafting of the manuscript. RCBM led the qualitative components of the study including design, analysis and drafting. CK participated in the design and write-up. All authors read and approved the final manuscript.

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Tables:

Table 1: Socio-demographic characteristics of 420 participants in the quantitative phase of the study

Variable	**Statistic**
Age (years): mean (SD)	39.7 (10.28)
Gender[&]: n (%)	
Male	299 (71.2)
Female	118 (28.1)
Level of education: n (%)	
None	8 (1.9)
Primary	117 (27.9)
Secondary	229 (54.5)
University	66 (15.7)
Occupation: n (%) *	
Working	284 (67.6)
Unemployed	101 (24.0)
Retired	16 (3.8)
Student	15 (3.6)
Marital status: n (%)	
Married or living together	185 (44.0)
Single	169 (40.2)
Divorced	16 (3.8)
Widow or widower	50 (11.9)
Residence: n (%)	
Urban	344 (81.9)
Rural	76 (18.1)
Lodging: n (%) [#]	
Common	357 (85.0)
Individual	56 (13.3)
Time since diagnosis (months): mean (SD)	57.2 (43.94)
Duration on ARV (months): mean (SD)	43.2 (37.06)
Adherence to medication (7point scale) : mean (SD)[#]	5.6 (2.55)
Adherence to appointments(7point scale): mean (SD) [$]	6.0 (2.20)

[&] 3 missing; *4 missing; [$] 6 missing; # 7 missing

Table 2: Practical functioning of a text messaging programme

Question	**N (%)**
For what reasons would you like to receive a text message?	**333**
Medication reminders	121 (36.4)
Appointment reminder	84 (25.2)
Assistance with drug refill	68 (20.4)
Assistance with lab test	28 (8.4)
Others (psychosocial support, nutritional counselling)	32 (9.6)
Is there someone else who can receive the message and transmit it to you?	**351**
Yes	154 (43.8)
How often would you be willing to pay to receive text messages?	**143**
Monthly	83 (58.0)
Quarterly	42 (29.4)
Yearly	18 (12.6)
How should fees be charged?	**138**
Flat rate	96 (69.6)
Number of text messages expected	42 (30.4)
How much are you willing to pay per month (Frs CFA*)?	**136**
0-200	70 (51.4)
200-500	30 (22.1)
500+	36 (26.5)
Why would you not participate	**345**
Risk of disclosure of status	161 (46.7)
Inability to pay	122 (35.4)
Lack of confidence in organisers	55 (15.9)
Intervention is not useful	7 (2.0)
What can be done to make people living with HIV adhere to the programme?	**414**
Sensitization	209 (50.5)
Offer specific advantages	121 (29.2)
Offer additional services	84 (20.3)
What kind of community organisation is best suited to run a text messaging programme?	**314**
Non-governmental organisations	150 (47.8)
Associations of people living with HIV	85 (27.1)
Health Committee	77 (24.5)
Government	2 (0.6)
Would you advise a people living with HIV to join a text messaging programme	**413**
Yes	**382 (92.5)**

*1 USD= ~500Frs CFA (minimum wage~59 USD)

Table 3: Mixed-methods data matrix

Strand							
Qualitative		**Quantitative**					
Themes identified	**Number of times mentioned n/N (%)**	**Thematic variable**	**Representativeness n/N (%)**	**Influence on acceptability**		**Influence on Readiness**	
				OR (95% CI); p	**aOR (95% CI); p**	**OR (95% CI); p**	**aOR (95% CI); p**
Acceptability	61/67 (91.0)	**Would adhere to an SMS support initiative**	344/420 (81.9)	--	--	--	--
Readiness	63/80 (78.7)	**Believes community can run programme in a sustainable way**	295/420 (73.6)	--	--	--	--
Acceptable cost	175/210 (83.3)	**Willing to pay to receive SMS**	118/417 (34.4)	0.09 (0.01-0.68); 0.020	0.03 (0.00-0.29)	0.45 (0.26-0.80); 0.006	0.35 (0.18-0.66); 0.002
Affinity to community projects	6/96 (6.6)	**Currently participates in a community support initiative**	57.2 (43.94)	0 (0.0-0.0); 0.998	0 (0.0-0.0); 0.998	0.99 (0.41-2.40); 0.982	1.09 (0.41-2.97); 0.855
Independent management	58/67(86.5)	**Prefers participation of health personnel**	227/417 (54.4)	0.92 (0.56-1.56);0.751	0.84 (0.49-1.43); 0.841	1.12 (0.72-1.75); 0.613	1.26 (0.77-2.02); 0.344
Independent management	45/67 (67.1)	**Prefers project be based in hospital**	63/419 (15.0)	0.79 (0.38-1.65); 0.543	0.83 (0.37-1.84); 0.648	1.17 (0.97-3.08); 0.060	1.62 (0.85-3.10); 0.142
n=numerator; N=denominator (derived from total of ideas raised); OR=odds ratio; aOR=adjusted odd ratio							

Table 4: Diffusion of innovation as applied to community ownership of a text messaging project

Relative advantages to be gained
Improved adherence to medication and appointment, assistance with pharmacy refills, psycho-social support, improved cohesion among people living with HIV
Compatibility with existing practices
Weak participation in community activities, text messaging widely used for other purposes
Simplicity of use, trialability and observable results
Non-ubiquitous phone ownership and literacy, high trialability (opting out always possible), results can be appreciated by users
Receiver factors (attitude to change and perceived need)
High acceptability and perceived need
Social system factors (social norms and tolerance for deviancy)
Highly flexible system, positive health worker support

Figures:

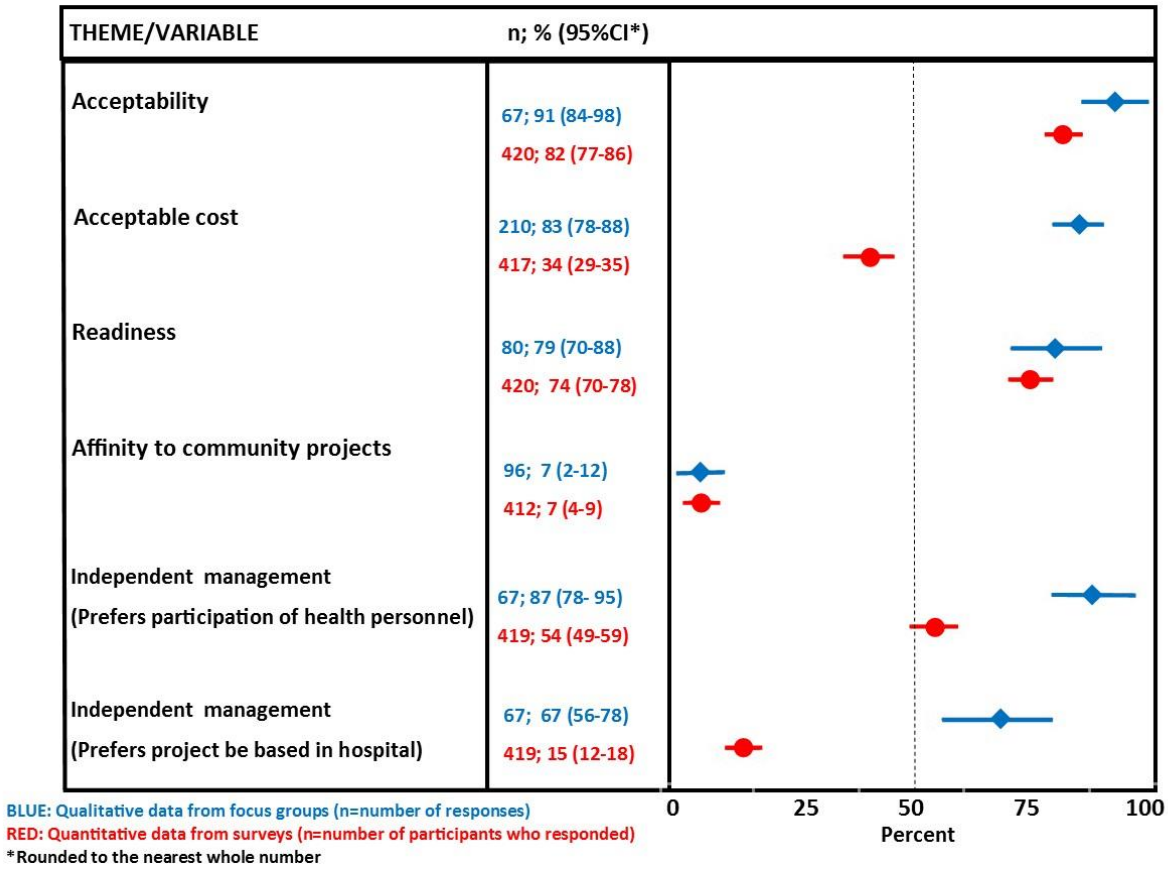

Figure 1: Graphical display of merged data

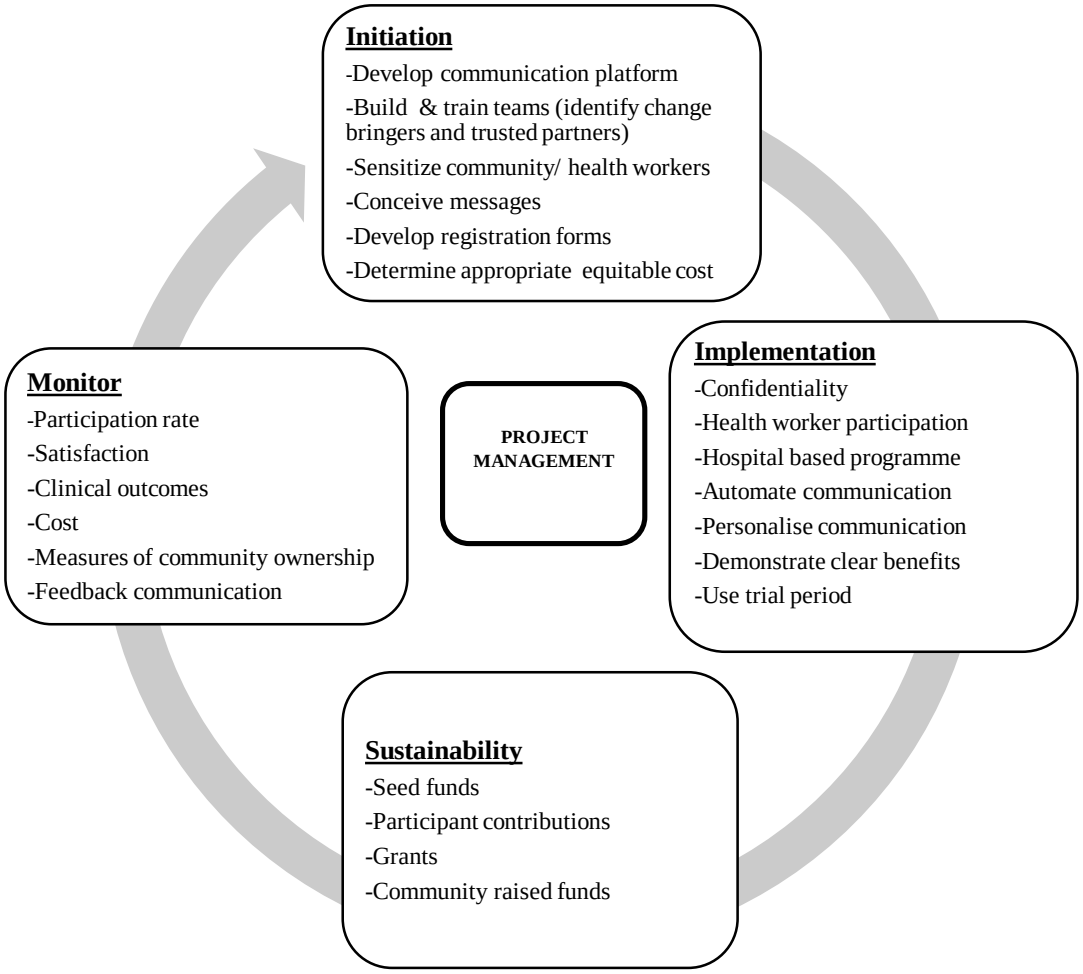

Figure 2: Framework for community ownership of text messaging programme

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CHAPTER 7

MOBILE PHONE TEXT MESSAGING INTERVENTIONS FOR HIV AND OTHER CHRONIC DISEASES: AN OVERVIEW AND FRAMEWORK FOR EVIDENCE TRANSFER

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Abstract:

Background:

Strong international commitment and the widespread use of antiretroviral therapy have led to higher longevity for people living with human immune deficiency virus (HIV). Text messaging interventions have been shown to improve health outcomes in people living with HIV. The objectives of this overview were to: map the state of the evidence of text messaging interventions, identify knowledge gaps, and develop a framework for the transfer of evidence to other chronic diseases.

Methods:

We conducted systematic review of systematic reviews on text messaging interventions to improve health or health related outcomes. We conducted a comprehensive search of PubMed, EMBASE (Exerpta Medica Database), CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, Web of Science (WoS) and the Cochrane Library on the 17th April 2014. Screening, data extraction and assessment of methodological quality were done in duplicate. Our findings were used to develop a conceptual framework for transfer.

Results:

Our search identified 135 potential systematic reviews of which nine were included, reporting on 37 source studies, conducted in 19 different countries. Seven of nine (77.7%) of these reviews were high quality. There was some evidence for text messaging as a tool to improve adherence to antiretroviral therapy. Text messages also improved attendance at appointments and behaviour change outcomes. The findings were inconclusive for self-management of illness, treatment of

tuberculosis and communicating results of medical investigations. The geographical distribution of text messaging research was limited to specific regions of the world. Prominent knowledge gaps included the absence of data on long term outcomes, patient satisfaction, and economic evaluations. The included reviews also identified methodological limitations in many of the primary studies.

Conclusions:

Global evidence supports the use of text messaging as a tool to improve adherence to medication and attendance at scheduled appointments. Given the similarities between HIV and other chronic diseases (long-term medications, life-long care, strong link to behaviour and the need for home-based support) evidence from HIV may be transferred to these diseases using our proposed framework by integration of HIV and chronic disease services or direct transfer.

Introduction:

HIV (human immune deficiency virus) is a major cause of morbidity and mortality all over the world. There are close to 2.6 million new infections each year, representing a 33 percent decline from 3.4 million, over the past ten years (UNAIDS, 2013). There has also been a drop in the number of AIDS (Acquired Immune Deficiency Syndrome) related deaths, due largely to the development and use of life-saving antiretroviral therapy (ART). As a result, there are more people living with HIV—over 35 million—many of whom are eligible for ART. However, treatment coverage is low worldwide, and among the people receiving ART, adherence to medication is low (UNAIDS, 2013).

Mobile telephone technology is emerging as a tool in chronic disease management (Lester & Karanja, 2008). Mobile phone ownership and use is experiencing its greatest growth in Africa, where HIV is rife (Lester, Gelmon, & Plummer, 2006). These two factors have led to the recent rise in research efforts regarding the use of mobile phones to enhance HIV care. On the African continent recent reports suggest that mobile phone text messages can be used to improve outcomes in people living with HIV (Horvath, Azman, Kennedy, & Rutherford, 2012; Lester et al., 2010; Mukund Bahadur & Murray, 2010; Pop-Eleches et al., 2011).

Alongside HIV, tuberculosis and malaria benefit from considerable resources from The Global Fund (http://www.theglobalfund.org/en/about/diseases/). It is indisputable that these disease are responsible for many deaths in sub-Saharan Africa, yet, many other chronic non-communicable diseases (NCDs) still cause significant mortality and morbidity, owing in part to their long lasting nature and debilitating consequences. Close to 45% of the disease burden in adults living in low and middle-income countries can be attributed to NCDs (WHO, 2005). In sub-Saharan

Africa these chronic diseases are on the rise and do not receive sufficient attention (de-Graft Aikins et al., 2010). There is also an unmet need for affordable medication for many NCDs in low and middle income countries (Bollyky, 2013), a problem resolved in HIV care through sustained commitments to disease control (Bollyky, 2013). Addressing research, practice, and policy limitations are important steps towards alleviating the burden of disease due to chronic disease, however, many lessons can be learnt from the better resourced diseases like HIV, in which global investments have stabilized the epidemic by reducing the number of new cases and deaths (UNAIDS, 2010). Furthermore, people living with HIV are at a higher risk for developing many NCDs due to the effect of the virus itself, the effects of antiretroviral therapy (ART) and due to aging (Nigatu, 2012). The meeting point of HIV and NCDs present challenges for health systems in meeting up with the needs of the population, but also provides opportunities for transfer of knowledge. There is also a case to be made for extending HIV research to other chronic diseases as questions of equity arise when one considers the disproportionate distribution of funds in favor of HIV.

One critical similarity between HIV and the NCDs is that they both require long term and life-long medication. For this reason there is an enormous potential for poor adherence to medication and care. Secondly, both affect a considerably large portion of the population and thus merit concern as a public health problem (WHO, 2012). The third factor is that they all have a strong behavioural component regarding their prevention, hence in both cases, behavioural modifications are required to reduce the risk of further complications. People living with HIV are encouraged to adopt healthy sexual practices to prevent the transmission of infection as well as potential acquisition of new strains from others; to take medication to control the disease; and to

undergo frequent testing to monitor disease control. People with diabetes and high blood pressure, for example, are encouraged to modify their diets and incorporate exercise in their lifestyles, in addition to medication and testing. These behaviour modification similarities make it possible to apply information from HIV research to address certain issues in NCDs (Nigatu, 2012).

Both conditions also require considerable amounts of social support to sustain effective home-based-care. Family members may be involved in preparing meals that follow specific dietary restrictions, accompanying patients to the hospital, or administering medication.

With regards to health system weaknesses, HIV and NCDs share a number of barriers and challenges. These include demand-side barriers, inequitable availability of services, human resource shortages, limited adherence support, lack of infrastructure and equipment, unreliable drug and diagnostics supplies, poor referral and linkage systems, the need for community engagement; as well as stigma and discrimination (Rabkin & El-Sadr, 2011).

HIV and NCDs have very different pathogeneses and clinical features (Nigatu, 2012). The levels of stigma and discrimination with regards to HIV are considerably higher than for NCDs, where in some places NCDs are considered to be diseases of the rich in low-resource settings and people are therefore more likely to discuss such conditions more freely that they would with HIV. However for some NCDs such as diabetes, cancer, and mental disorders, there is still a considerable stigma (Rabkin & El-Sadr, 2011). The demographics are also quite different, with HIV affecting younger populations than the NCDs. Furthermore, in sub-Saharan Africa, women are disproportionately affected by HIV (WHO, 2012).

The purpose of the this paper is to map the scope of mobile phone text messaging research to identify opportunities for knowledge transfer, geographical coverage of text messaging research, and avenues for further research and scale-up. We describe the current state of the evidence, identify knowledge gaps, and highlight the points were lessons can be shared or more research is needed. We hope to use the available evidence on the application of text messaging in HIV and other chronic diseases to develop a framework for extension where the most appropriate kinds of interventions can be tested or taken to scale and duplication of efforts avoided.

Why it is important to do this overview:

In recent years, text messaging has emerged as an important communication tool in healthcare, yet there is limited information of what interventions work best and which should be taken to scale. In addition, given the disproportionate funding mechanisms for research, especially in low-resource settings, research efforts are directed toward conditions such as HIV, malaria and tuberculosis, often neglecting other chronic or NCDs. We purport that there is room for research findings to be transferred from the more favored conditions, given their similarities.

Objectives:

- To appraise the scope of text messaging interventions in health care
- To develop a framework for transfer of research findings from HIV to NCDs.

Research questions:

- What is the current state of evidence regarding mobile phone text messaging interventions for management and prevention of HIV and other health conditions?
- What is the geographical coverage of text messaging interventions in the world?

- How can the application of technology be transferred from HIV to NCDs?

Methods

This paper is as systematic review of systematic review.

Criteria for considering systematic reviews for inclusion:

Our inclusion criteria were: full systematic reviews (with predetermined objectives, eligibility criteria, at least two data bases searched, data extraction, and quality assessment of included studies) that included at least one randomized trial, which examined the effectiveness of a text messaging intervention (automated or manual, two-way or one-way, irrespective of content) compared to no intervention or any other intervention, to improve a health or health-related outcome. The participants could be health workers (professional or lay persons) or consumers of health care (prevention or management). We excluded abstracts, non-systematic reviews and other overviews. We also excluded studies that addressed the broader field of mHealth, which would include smart phone applications (of which some may include text messages) and other portable medical devices.

Search methods for identification of systematic reviews:

We conducted an overview of systematic reviews to April 7, 2014 in the following electronic data bases and in all languages: PubMed, EMBASE (Exerpta Medica Database), CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, Web of Science (WoS) and the Cochrane Library. We sought systematic reviews of text messaging interventions in preventive or curative health care. We applied the following search terms in various combinations adapted for each database:

1. *mobile phone OR cell* phone*
2. *text messag* OR SMS* OR text*
3. *systematic review OR meta-analysis*

We also searched the reference lists of identified reviews and institutional websites including the World Health Organisation (WHO), the National Institute for Health and Care Excellence (NICE), and the Joint United Nations Programme on HIV/AIDS (UNAIDS).

Systematic review selection, data collection and analysis:

Duplicate citations were deleted, and the remaining abstracts were screened for relevance to our research questions. The abstracts of the retrieved citations were screened in duplicate by two authors (LM and SM). Full text manuscripts for relevant citations were retrieved and assessed for inclusion. We extracted data from included studies, using a piloted data extraction form, on the following: number and type of included studies, number of participants, target population, location of the studies, key conclusions, knowledge gaps and reporting quality. Data were extracted in duplicate (SM, LL) and verified by an adjudicator (LM). The reviews were checked for overlap, in case one study was included in more than one systematic review. We assessed the methodological quality of the included systematic reviews using the AMSTAR (Assessment the methodological quality of systematic reviews) tool (Shea et al., 2009). AMSTAR can be used to assess how well systematic reviews avoid bias against 11 criteria. Based on the number of items adequately reported a systematic review can be scored as high quality (8 to 11 items), medium quality (4 to 7 items) and low quality (3 or less items) (Shea et al., 2007). The reviews were checked for overlap, since one study may be included in more than one systematic review. Agreement on screening and quality assessment was measured using the Kappa statistic, which

measures agreement beyond chance (Viera & Garrett, 2005). Our findings are reported on the systematic review and sources study level.

Results:

Results of search:

Our search retrieved 135 citations of which 74 abstracts were screened after removal of duplicates. Fifty-six (56) full text of relevant articles were retrieved and screened for eligibility by LL and SM. Agreement on screening of titles and abstracts was fair (Kappa= 0.34; 95% CI 0.12-0.55; p=0.002). Citations for which there was disagreement were moved forward into the next round of screening. Agreement on screening of full text was high (Kappa=0.94; 95% CI 0.81-1.00; p<0.001). We included a total of 9 systematic reviews. The screening process is detailed in a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram (Figure 1).

Description of included systematic reviews:

The nine (9) included systematic reviews were all published in the English language, between 2010 and 2014, and reported on data from a total of 37 individual studies (Cole-Lewis & Kershaw, 2010; de Jongh, Gurol-Urganci, Vodopivec-Jamsek, Car, & Atun, 2012; Finitsis, Pellowski, & Johnson, 2014; Gurol-Urganci, de Jongh, Vodopivec-Jamsek, Atun, & Car, 2013; Gurol-Urganci, de Jongh, Vodopivec-Jamsek, Car, & Atun, 2012; Horvath et al., 2012; Militello, Kelly, & Melnyk, 2012; Nglazi, Bekker, Wood, Hussey, & Wiysonge, 2013; Vodopivec-Jamsek, de Jongh, Gurol-Urganci, Atun, & Car, 2012). Five where Cochrane Collaboration reviews (de Jongh et al., 2012; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012; Horvath et al., 2012;

Vodopivec-Jamsek et al., 2012). Five addressed text messaging interventions in non-specific populations (Cole-Lewis & Kershaw, 2010; de Jongh et al., 2012; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012; Vodopivec-Jamsek et al., 2012), two focused on people living with HIV (Finitsis et al., 2014; Horvath et al., 2012), one was on patients will tuberculosis (Nglazi et al., 2013), and one was on children and adolescents (Militello et al., 2012). Among those with non-specific disease targets (i.e. HIV or tuberculosis), text messaging was investigated in the following diseases and health conditions: hypertension, diabetes, asthma, smoking, vitamin C, weight loss, physical activity, diet, circumcision and antenatal care. They covered a wide range of study designs, such as parallel group RCTs, crossover RCTs, quasi- experimental designs (non-randomized comparisons and before-after studies), and observational studies. In all the reviews the text messaging interventions targeted patients, and were used for the prevention of disease, disease management, or both. None of the interventions targeted health workers. The wide variety of participants, interventions and outcomes precluded meta-analyses in four systematic reviews. Details on the included studies are reported in Table 1.

Characteristics of text messaging interventions:

Of the 37 source studies, 35 (94.6%) used mobile phones to deliver text messages. Two studies used text-enabled pager devices. Nine-teen (51.3%) of them delivered interactive messages (with the possibility of response from receiver or the sender), 24 (64.8%) used personalised messages, and 13 (35.1%) used automated delivery. Personalised messages were adapted to suit patient needs by tailoring of timing (to match timing of dosing, set according to patient preference or before appointments) and content (reminders, medical advice, appointment details or feedback on behaviour change activities). Text messages where used to improve adherence to medication

(13 studies), as reminders for medical appointments (9 studies), for self-management of disease (for example, information on warning signs in pregnancy, and reminders to measure blood glucose to blood pressure; 8 studies), for behaviour change (for example, diet, sedentary time and exercise; 6 studies), and to deliver test results (1 study). Table 2 is a detailed description of the characteristics of the text messaging interventions.

Excluded systematic reviews:

We excluded 45 articles that did not meet our inclusion criteria. A full list of excluded studies and the reasons for exclusion is reported Table 3.

Quality of included systematic reviews:

The median AMSTAR ranking was 9 (first quartile (Q1): 7.5; third quartile (Q3): 10). Two reviews (22.2%) were rated as medium quality (Cole-Lewis & Kershaw, 2010; Militello et al., 2012) and seven (77.7%) were rated as high quality (de Jongh et al., 2012; Finitsis et al., 2014; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012; Horvath et al., 2012; Nglazi et al., 2013; Vodopivec-Jamsek et al., 2012). Agreement on the AMSTAR rankings was moderate (estimated Kappa = 0.53 95% CI 0.31-0.74; $p<0.001$). The items for which there was a lot of disagreement were scoring whether publication bias was assessed and whether conflict of interest was included in the review. Disagreements were resolved by adjudication of a third author (LM) using AMSTAR documentation (Shea et al., 2009). The final AMSTAR rankings reflect the guidance from this document. Most studies did not report on conflicts of interest. A full report of the AMSTAR rankings is reported in Table 4.

Effects of text messaging interventions in HIV:

The findings from two high quality systematic reviews suggest that text messaging can be used in HIV to improve adherence to medication, as well as biological outcomes such as viral load (Finitsis et al., 2014; Horvath et al., 2012).

Effects of text messaging interventions for other conditions:

Only one high quality review investigated the effects of text messaging on a adherence to tuberculosis medication, and the evidence was inconclusive (Nglazi et al., 2013). Two medium quality reviews targeted health promotion in pediatric and adolescent populations, and behaviour change across many conditions. They both supported the use of text messaging to promote health behaviour change (Cole-Lewis & Kershaw, 2010; Militello et al., 2012). One high quality review described limited direct impact on health outcomes when text messaging was used for self-management of illness (de Jongh et al., 2012). Two high quality reviews found that text messages increased attendance at scheduled appointments, and may be used in preventive health care alongside other interventions (Gurol-Urganci et al., 2013; Vodopivec-Jamsek et al., 2012). The findings on the use of text messages to communicate results of medical investigations, from one high quality review, were inconclusive (Gurol-Urganci et al., 2012).

Locations of included studies:

The 37 studies were conducted in 19 countries. Eight (8) studies were conducted in the USA, four (4) in Kenya, three (3) the UK, two (2) each in Malaysia, China, Korea, South Africa, New Zealand and one (1) each in Argentina, Australia, Austria, Brazil, Cameroon, Canada, Croatia,

Finland, France, Spain and Thailand. Figure 2 is a world map highlighting the locations where text messaging intervention research in this study were conducted.

Knowledge gaps identified:

These systematic reviews identified many knowledge gaps in the literature and avenues for further research. Most of them addressed the was the need for higher quality studies (Cole-Lewis & Kershaw, 2010; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012; Militello et al., 2012), as well as the investigation of long-term effects (Cole-Lewis & Kershaw, 2010; de Jongh et al., 2012; Militello et al., 2012). Three studies highlighted the importance of delving further into the characteristics of the text messages in order to optimise outcomes (Cole-Lewis & Kershaw, 2010; Finitsis et al., 2014; Horvath et al., 2012). Other knowledge gaps identified included risks and harms (de Jongh et al., 2012; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012; Vodopivec-Jamsek et al., 2012), user satisfaction and acceptability (de Jongh et al., 2012; Gurol-Urganci et al., 2013; Gurol-Urganci et al., 2012), cost effectiveness (Gurol-Urganci et al., 2013; Vodopivec-Jamsek et al., 2012), and dose response (Militello et al., 2012). A full description of the knowledge gaps identified is reported in Table 1.

Overlap of systematic reviews

The 9 included systematic reviews reported on a total of 49 studies, relating to 37 unique studies. Two studies appeared in three reviews, and 8 studies were included in two reviews. The overlap was highest among the systematic reviews with broad target populations and health problems addressed (Cole-Lewis & Kershaw, 2010; de Jongh et al., 2012; Militello et al., 2012; Vodopivec-Jamsek et al., 2012). Both studies included in Horvath's 2012 systematic review

(Horvath et al., 2012) were included in Finitsis et al's 2014 systematic review (Finitsis et al., 2014). This overlap, and all others were taken into account in the mapping process and source studies were considered only once.

Discussion:

What is the state of the evidence of mobile phone text messaging technology for management and prevention of HIV and other diseases?

A considerable body of evidence is building in favour of text message interventions for improving health outcomes. Text message interventions are tested across a wide variety of conditions for prevention and management. There is room for the exploration of text messaging in younger populations, care givers, and in higher income settings. The only behaviour change intervention targeted in people living with HIV was adherence to medication. The effects on behaviour change and health promotion are inconsistent, and almost null for self- management of illness, communicating results of medical investigations and adherence to TB medication. Though the results seem promising, almost all the included systematic reviews highlighted important methodological limitations in the source studies, and the need to investigate the effects of text messaging on long term outcomes. Text messaging is used for a wide variety of purposes, medical conditions and in different formats. The commonality between all the text messaging interventions is enhanced communication between health care providers and consumers.

What is the geographical coverage of text messaging interventions in the world?

The locations of the source studies were unevenly distributed around the globe. Eight studies on HIV were located in four countries: four in the US, two in Kenya, and one each in Cameroon and

Brazil. There were no text messaging studies for NCDs conducted in Africa and only one on improving attendance at scheduled appointments, in the general population. There were no HIV studies in Europe and Asia.

How can the application of the technology be transferred from HIV to NCDs?

Two approaches can be adopted in extending HIV research to NCDs. The first is integration of services (Nigatu, 2012). If HIV services and NCD services were integrated, a lot could be gained in terms of shared human, financial, material and community resources. Yet, given the often separate funding mechanisms for these vertical programmes and persistent stigma and discrimination against people living with HIV, such integration may be less well received than integration of tuberculosis and HIV services or antenatal care with prevention of mother to child transmission of HIV – both of which are more similar in terms of service provision. However, it is important to consider that modern HIV management will likely result in the development of concurrent chronic diseases in patients. Some programs have successfully integrated HIV care with NCD in Cambodia and Kenya (Janssens et al., 2007). The second approach would be transferring evidence-based practices or leveraging HIV successes for NCD care. Successes in HIV which contributed to controlling the epidemic include: improved planning and managing of resources, better financing mechanisms, human resources strengthening, augmented infrastructure, developing and strengthening supply systems, better data management and clinical services and behaviour change interventions among patients and providers (Rabkin & El-Sadr, 2011). Such transfers may be easier to implement if the evidence developed from HIV research is applicable to NCDs.

In the field of health economics, a number of guidelines have been published to determine if an interventions is suitable to be transferred from one geographic location to another. Some of these can also be used, albeit with some modification, to determine if technologies are transferable across disease conditions. Borrowing from Heyland's Generalizability criteria, items such as: similarities between patients, clinical setting, cost, outcome measures and safety must be considered (Heyland, Kernerman, Gafni, & Cook, 1996).

Despite the difference in demographics between people living with HIV and those with NCDs, we now recognise the accrued risk of NCDs, especially cardiovascular diseases in people with HIV (Hemkens & Bucher, 2014). Owing to the fact the people living with HIV are now living longer lives, they are more likely to merge with the age group of people who experience NCD morbidity and mortality. The demographics are becoming more and more similar. With regards to text messaging only level of education seems to a factor affecting response (Mbuagbaw et al., 2013).

The cost of care for HIV is considerably higher than for NCDs, but many of these costs reduced in places where testing and ART are provided free of charge. However, there is no reason to suspect that a text messaging intervention will cost more for NCDs compared to HIV.

Similar outcomes are of interest in both conditions, notably adherence to medication and lifestyle modifications, both of which can be achieved using mobile phone technology (Ramachandran et al., 2013; Wizner, Gaciong, Narkiewicz, Szykula, & Grodzicki, 2010).

In addition to these generalizability criteria, the flexibility of text messaging interventions as seen in the diversity of intervention types is an advantage for transfer. Personalisation, timing

and content can be modified to adapt a text messaging intervention to another population or health system. Automated messages, may reduce the human resource requirements but limit interactivity. However, many of these interventions were used in an experimental setting on a small number of participants, and it is unclear how they will perform on a large scale.

The more challenging question relates to geographical transfer. Given the marked difference in health systems, disease burden, culture and use of mobile phones, the most appropriate approach to transfer may involve efforts to replicate or improve research findings in other settings.

Conceptual Model:

Building upon the existing body of evidence, we propose a conceptual framework for the transfer and implementation of research findings from HIV to NCDs. This framework highlights the similarities between HIV and NCDs, options for transfer, the target participants, the interventions, the important outcomes for HIV, NCDs or both, and potential obstacles. These obstacles are stigma, which can be addressed through education and integration of services; issues related to confidentiality, which can be addressed using appropriate content in the text messages; and health system limitations such as lack of infrastructure and human capital. The transfer process can be facilitated by integration of services, saved costs, enhanced client-provider communication and the fact that the HIV and NCD demographics are merging. The items for which further research is required are identified in Figure 3, a graphical representation of this framework.

Limitations and strengths:

This study is not without limitations, notably the stringent inclusion criteria for systematic reviews, which may have led to the exclusion of some text messaging studies that were considered in other reviews under the canopy of mHealth. Some text messaging studies that did not make it into reviews, either because they did not meet individual systematic review inclusion criteria or are more recent would have been missed in this overview. In addition, many studies were unable to produce a pooled estimate of effects due to diversity in study design, participants and outcomes. The strengths of this study include a geographic mapping, a summary of knowledge gaps, and a framework for transfer of evidence generated for HIV to other chronic conditions**.**

Conclusions and recommendations:

Implications for practice

Individual medical practices can use text messaging interventions to improve adherence to medication and attendance at clinical appointments, as long as the correct precautions relating to patient confidentiality are incorporated.

Implications for research and policy

A systematic survey of the evidence demonstrates a paucity of research evidence on how text messages can be used to improve care in patients with NCDs in Africa. The findings from HIV research can for the most part be transferred to NCDs and may represent cost savings for donors, governments and taxpayers. Given that the conditions are not identical, we recommend a gradual approach to technology transfer, building on experiences from other geographical regions.

Interestingly, despite high rates of TB/HIV, comorbidity there isn't much evidence supporting the use of text messaging to enhance TB outcomes. This would be a worthwhile and conservative step towards extending evidence from HIV research.

Text messaging research should be conducted with adolescent populations with HIV, and people who care for children or adults with HIV. Other populations of interest for text messaging research include health care professionals, and community health workers. The current evidence is in favor of weekly, two-way messaging, but "dose response" and in-depth understanding of messaging characteristics both warrant further investigation. Given that text messaging is emerging as an add-on to usual care, and may also support other adherence enhancing interventions, comparisons to other interventions may mask its value, yet comparisons of different contents, durations and combinations would be informative. We recommend that further research focus on long term clinical outcomes like viral load and exploration of any harms that may occur. In addition, strategies to ensure confidentiality should be developed.

Tables:

Table 1: Characteristics of included systematic reviews

Study ID (Reference)	Number and type of included studies	n	Target population	Health problem addressed in review (disease)	Prevention or Management	Location of studies	Conclusions	Effect sizes	Knowledge gaps identified
Cole-Lewis 2010(Cole-Lewis & Kershaw, 2010)	12 studies RCTs (9), Crossover RCT (2), Quasi-experimental trial (1)	2408	Not specified	Behaviour change (weight loss, physical activity, diabetes, asthma, adherence to vitamin C)	Both	Canada (1), Finland (1), New Zealand (2), USA (2), France (1), Korea (2), UK (1), Croatia (1), and Austria (1)	There are short term effects on behavioral or clinical outcome related to disease prevention and management. Text messaging is a useful tool for behavior change interventions.	NA	1. Methodological limitations in studies 2. Text message characteristics and combinations should be explored 3. Long term effects should be investigated
De Jongh 2013(de Jongh et al., 2012)	4 studies RCT (4)	182	Not specified	Self-management of illness (diabetes, hypertension, asthma)	Management	Scotland (1), Croatia (1), USA (1), Spain (1)	Text messaging may support the self-management of long term conditions but have few direct impacts on health outcomes	NA	1. Limited evidence of efficacy 2. Long-term effectiveness unknown 3. Risks and limitations and consumer satisfaction are unknown
Finitsis 2014(Finitsis et al., 2014)	8 studies RCT (8)	1785	People living with HIV	Adherence to medication (HIV)	Management	USA (4), Kenya (2), Brazil (1),	Researchers should consider the adoption of	Odds ratio for	1. Comparisons of design and intervention

						Cameroon (1)	a less than daily frequency of messaging that is individually timed and tailored and designed to evoke a reply from the recipient.	adherence =1.39; 95% CI=1.18-1.64 (8 RCTs)	characteristics to obtain optimal effect are needed.
Gurol-Urganci 2012(Gurol-Urganci et al., 2012)	1 study RCT (1)	2785	Not specified	Communicating results of medical investigations for anxiety (Down's syndrome prenatal screen)	Management	Taiwan (1)	Unable to draw reliable conclusions dues to low quality of evidence coming from only one study. Positive and negative results delivered by text message may have different effects on anxiety	Mean anxiety score = -2.48; 95% CI-8.79 to 3.84 (1 RCT)	1. Methodological limitations in studies 2. Some outcomes of interest are: health-seeking behaviour, patients' evaluation of the intervention, costs, economic benefits, and potential adverse effects.
Gurol-Urganci 2013(Gurol-Urganci et al., 2013)	8 studies RCT (8)	6615	Not specified	Attendance at healthcare appointments (not specified)	Both	China (2), UK (2), Malaysia (2), Kenya (1), Australia (1)	Mobile phone text message reminders increase healthcare appointment attendance rates when compared to no reminders and postal	Relative risk for attendance rate at appointment = 1.14; 95 % CI 1.03	1. Methodological limitations in studies 2. Some outcomes of interest include: health effects, adverse effects and harms, user evaluation of the intervention and user perceptions of

							reminders. The current findings are insufficient to inform policy decisions	to 1.26 (7 RCTs)	its safety.
Horvath 2012(Horvath et al., 2012)	2 studies RCT (2)	969	People living with HIV	Adherence to medication (HIV)	Management	Kenya (2)	Weekly text messages are efficacious in improving adherence to ART in resource limited settings and may be efficacious in suppressing viral load.	Risk ratio for non-adherence at 48-52 weeks = 0.78; 95% CI 0.68 to 0.89 (2 RCTs)	1. Larger RCTs in adolescent populations, and in persons who care for children and infants with HIV. 2. Trials in high and middle-income countries are needed. 3. Data on acceptability, and culture-specific issues such as message-content and message-length are needed.
Militello 2012(Militello et al., 2012)	6 studies RCT (4), Crossover RCT (1), Quasi-experimental trial (1)	433	Pediatric and adolescent populations	Health promotion (diabetes, antirejection medication adherence, physical activity, diet and sedentary behaviour)	Both	USA (3), UK (2), New Zealand (1), Austria (1)	Text messaging should be considered as an add-on to clinic care to improve health behaviours	NA	1. Methodological limitations in studies 2. Long term effects and dose response data are of interest
Nglazi 2013 (Nglazi et al., 2013)	4 studies RCT (1), Observational (3) studies	565	Patients with tuberculosis	Adherence to medication (tuberculosis)	Management	Argentina (1), Kenya (1), South Africa (2)	The evidence is inconclusive on text messaging to improve	Risk ratio for adheren	1. Outcome measures for TB cure, successful completion of TB

							adherence to TB treatment, but there is some potential	ce = 1.49; 95 % CI 0.90 to 2.42 (one RCT).	treatment, and development of drug resistance should be standardized.
Vodopivec-Jamsek 2012(Vodopivec-Jamsek et al., 2012)	4 studies RCT (4)	1933	Not specified	Preventive health care (antenatal care, smoking, physical activity, diet and sedentary behaviour, adherence to vitamin C)	Prevention	Canada (1), Thailand (1), New Zealand (1), USA (1)	Text messages have the potential to contribute to health behaviour change in the short term alongside other media of health prevention information. .	NA	1. Long term effects are unknown 2. Data is needed on costs, and possible risks and harms 3. More information is needed for scale-up

NA=Not applicable (no pooled estimates); N= Total number of participants

Table 2: Characteristics of text messaging interventions

Study name	Timing	Interactivity	Content	Duration	Automated	Personalisation	Condition
Benhamou 2007	1/week	Yes	Medical advice based blood glucose	12 months	Not reported	Yes	Adult diabetics
Bridges 2005	Daily	No	Not reported	Not reported	Yes	Not reported	Patients on TB medication
Broomhead 2012	Daily on opening of pill bottle	No	Signal for opened pill bottle	Not reported	NA	NA	Patients on TB medication
Chen 2008	Once; 72 hours before appointment	No	Participants name and appointment details	NA	Yes	Yes	Adults with scheduled appointments
Cheng 2008	Once	No	Results of screening test	NA	Not reported	Yes	Women who underwent screening for Down's syndrome during pregnancy
Cho 2009	Every other week	Yes	Medical advice based blood glucose	3 months	Not reported	Yes	Adult diabetics
Cocosila 2009	1-2/day for 2 weeks;0-2/day intermittently for two weeks	Yes	Reminder to take Vitamin C	1 month	Yes	No	Healthy adults
Da Costa 2012	3/week	No	Not reported	5 months	Not reported	No	Adults with HIV
Fairhurst 2008	Once; about 12 hours before appointment	No	Not reported	NA	No	Not reported	Adults with scheduled appointments
Franklin 2006	1/week and daily	No	Reminder of goals set, tips and information and reminders to reinforce goal	12 months	Yes	Yes	Diabetes
Haapala 2009	Set by participant	Yes	Messages to reduce daily food intake, increase physical activity	12 month	Yes	Yes	Overweight adults

			and encourage weight recording				
Hanauer 2009	Set by participants	Yes	Reminders to check blood glucose, with feedback provided with each submission of blood glucose and every Sunday	3 months	Not reported	Yes	Diabetics aged 12-25
Hardy 2011	Daily, matched to time of medication dosing	Yes	Not reported	1.4 months	Not reported	Yes	Adults with HIV
Iribarren 2012	2/week; and daily for defaulters	Yes	Education messages, reminders/check in	2 months	Yes	Not reported	Adults taking TB medication
Jareethum 2008	2/week	No	Information and warnings relating to abnormal symptoms	From 28 weeks gestation till delivery (about 3 months)	Not reported	Yes	Healthy pregnant women
Koury 2005	Once	No	Not reported	NA	Yes	No	Adults at ear-nose-throat clinic
Leong 2006	Once; 24-48 hours before appointment	No	Participants' name and appointment details	NA	Not reported	Yes	Participants from primary care clinics
Lester 2010	1/week	Yes	Not reported	12 months	Not reported	No	Adults with HIV
Liew 2009	Once; 24-48 hours before appointment	No	Not reported	NA	Not reported	Yes	Patients with chronic diseases
Lin 2012	Twice per day on days 1 and 4 before the appointment	Not reported	Appointment details and importance of timely management	12 months	Not reported	Yes	Parents of children with cataracts scheduled for surgery
Marquez-Contreras 2004	2/week	No	Information on hypertension, compliance promotion, good health and dietary habits	6 months	Yes	No	Ambulatory hypertensive adults

Mbuagbaw 2012	1/week	Yes	Not reported	6 months	Not reported	No	Adults with HIV
Miloh 2009	1/day	Yes	Reminder messages sent to patient or caregiver to administer medication	12 months	Not reported	Yes	Liver transplant patients
Musser 2001	1/day	Yes	Not reported	0.5 months	Not reported	No	Adults with HIV
Newton 2009	1/week	No	Motivational	3 months	Yes	Not reported	Diabetic adolescents
Odeny 2012	Daily	No	Post-operative instructions and request to attend appointment	0.25 months	Not reported	Yes	Males who had undergone circumcision
Ostojic 2005	1/day	Yes	Medical advice on therapy based on PEF results	4 months	Not reported	Yes	Asthmatic adults
Owiti 2012	Once, a day before clinic appointment	No	Not reported	NA	Not reported	Yes	Patients on TB medication
Patrick 2009	2-5/day	Yes	Behavioural and dietary strategies, goal setting and weight monitoring	4 months	Yes	Yes	Overweight adults
Pop-Eleches 2011	1/week and 1/day	No	Not reported	12 months	Not reported	No	Adults with HIV
Rami 2006	4/day	Yes	Support for glycaemic control	3 months	Yes	Yes	Diabetic adolescents
Rodgers 2005	5x/day for 6 weeks then 3x/week for 20 weeks	Yes	Advice, support and distraction delivered in non-formal language	6.5 months	Yes	Yes	Adult smokers
Safren 2003*	Matched to time of medication dosing	No	Not reported	2.8 months	Not reported	Yes	Adults with HIV

Shapiro 2008	2/day 1 for child and 1 parent	Yes	Feedback message tailored to information on physical activity, sweetened beverage consumption and TV time	2 months	Yes	Yes	Children aged 5-13
Simoni 2009*	Matched to time of medication dosing	Yes	Not reported	3 months	Not reported	Yes	Adults with HIV
Taylor 2012	Once; 2 days before or on the day of appointment	Yes	Appointment details	NA	Not reported	Yes	Patients in need of physical therapy
Yoon 2008	Set by participants but at least 1/week	Yes	Treatment adjustment based on blood glucose	12 months	Not reported	Yes	Diabetic adults

*Text message pager devices

Table 3: List of excluded studies

Reason for exclusion	Reference
Abstract only	1. Kobos P. How has mobile phone text messaging been studied in pregnancy-related research? Communicating Nursing Research. 2013;**46**:718-18.
No Quality Assessment	2. Buchholz SW, Wilbur J, Ingram D, et al. Physical activity text messaging interventions in adults: a systematic review. Worldviews on evidence-based nursing. 2013;**10**:163-73. 3. Buhi ER, Trudnak TE, Martinasek MP, et al. Mobile phone-based behavioural interventions for health: A systematic review. Health Education Journal. 2013;**72**:564-83. 4. Deglise C, Suggs LS, Odermatt P. SMS for disease control in developing countries: a systematic review of mobile health applications. Journal of Telemedicine and Telecare. 2012;**18**:273-81. 5. Guy R, Hocking J, Wand H, et al. How effective are short message service reminders at increasing clinic attendance? A meta-analysis and systematic review. Health Services Research. 2012;**47**:614-32. 6. Head KJ, Noar SM, Iannarino NT, et al. Efficacy of text messaging-based interventions for health promotion: A meta-analysis. Social Science & Medicine. 2013;**97**:41-48. 7. Williams AD. Use of a text messaging program to promote adherence to daily physical activity guidelines: A review of the literature. Bariatric Nursing and Surgical Patient Care. 2012;**7**:13-16.
Not a systematic review	8. Jardim C. Mobile phone-based interventions for smoking cessation. Sao Paulo Medical Journal. 2010;**128**:106-07. 9. Lunny C, Taylor D, Memetovic J, et al. Short message service (SMS) interventions for the prevention and treatment of sexually transmitted infections: a systematic review protocol. Systematic reviews. 2014;**3**:7. 10. Mbuagbaw L, Thabane L, Ongolo-Zogo P, et al. Trends and determining factors associated with adherence to antiretroviral therapy (ART) in Cameroon: a systematic review and analysis of the CAMPS trial. AIDS Res Ther. 2012;**9**:37. 11. Mbuagbaw L, van der Kop ML, Lester RT, et al. Mobile phone text messages for improving adherence to antiretroviral therapy (ART): an individual patient data meta-analysis of randomised trials. BMJ Open. 2013;**3**. 12. Mbuagbaw L, van der Kop ML, Lester RT, et al. Mobile

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Not on text messaging exclusively	18. Holtz B, Lauckner C. Diabetes management via mobile phones: a systematic review. Telemed J E Health. 2012;**18**:175-84. 19. Johnston W, Lederhausen A, Duncan J. Mobile technology: A synopsis and comment on "mobile phone-based interventions for smoking cessation". Translational Behavioral Medicine. 2013;**3**:231-32. 20. Krishna S, Boren SA. Diabetes self-management care via cell phone: a systematic review. Journal of diabetes science and technology. 2008;**2**:509-17. 21. Krishna S, Boren SA, Balas EA. Healthcare via Cell Phones: A Systematic Review. Telemedicine Journal and E-Health. 2009;**15**:231-40. 22. Lau PWC, Lau EY, Wong DP, et al. A Systematic Review of Information and Communication Technology-Based Interventions for Promoting Physical Activity Behavior Change in Children and Adolescents. Journal of Medical Internet Research. 2011;**13**. 23. Liang X, Wang Q, Yang X, et al. Effect of mobile phone intervention for diabetes on glycaemic control: a meta-analysis. Diabetic Medicine. 2011;**28**:455-63.

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Table 4: Methodological quality of included studies using the AMSTAR checklist

CRITERIA	**Cole-Lewis 2010(Cole-Lewis & Kershaw, 2010)**	**De Jongh 2012(de Jongh et al., 2012)**	**Finitsis 2014(Finitsis et al., 2014)**	**Gurol-Urganci 2012(Gurol-Urganci et al., 2012)**	**Gurol-Urganci 2013(Gurol-Urganci et al., 2013)**	**Horvath 2012(Horvath et al., 2012)**	**Militello 2012(Militello et al., 2012)**	**Nglazi 2013(Nglazi et al., 2013)**	**Vodopivec-Jamsek 2012(Vodopivec-Jamsek et al., 2012)**
Was an 'a priori' design provided?	0	1	0	1	1	1	1	1	1
Was there duplicate study selection and data extraction?	0	1	1	1	1	1	1	1	1
Was a comprehensive literature search performed?	1	1	1	1	1	1	1	1	1
Was the status of publication (i.e. grey literature) used as an inclusion criterion?	0	1	1	1	1	1	0	1	1
Was a list of studies (included and excluded) provided?	0	1	1	1	1	1	0	1	1
Were the characteristics of the included studies provided?	1	1	1	1	1	1	1	1	1
Was the scientific quality of the included studies assessed and documented?	1	1	1	1	1	1	1	1	1
Was the scientific quality of the included studies used appropriately in formulating conclusions?	1	1	1	1	1	1	1	1	1
Were the methods used to combine the findings of studies appropriate?	1	1	1	1	1	1	1	1	1
Was the likelihood of publication bias assessed?	0	0	0	1	1	1	0	0	0
Was the conflict of interest included?	0	0	0	0	1	0	0	0	0
AMSTAR scores	5	9	8	10	10	10	7	9	9
Ranking	**Medium**	**High**	**High**	**High**	**High**	**High**	**Medium**	**High**	**High**

Figures:

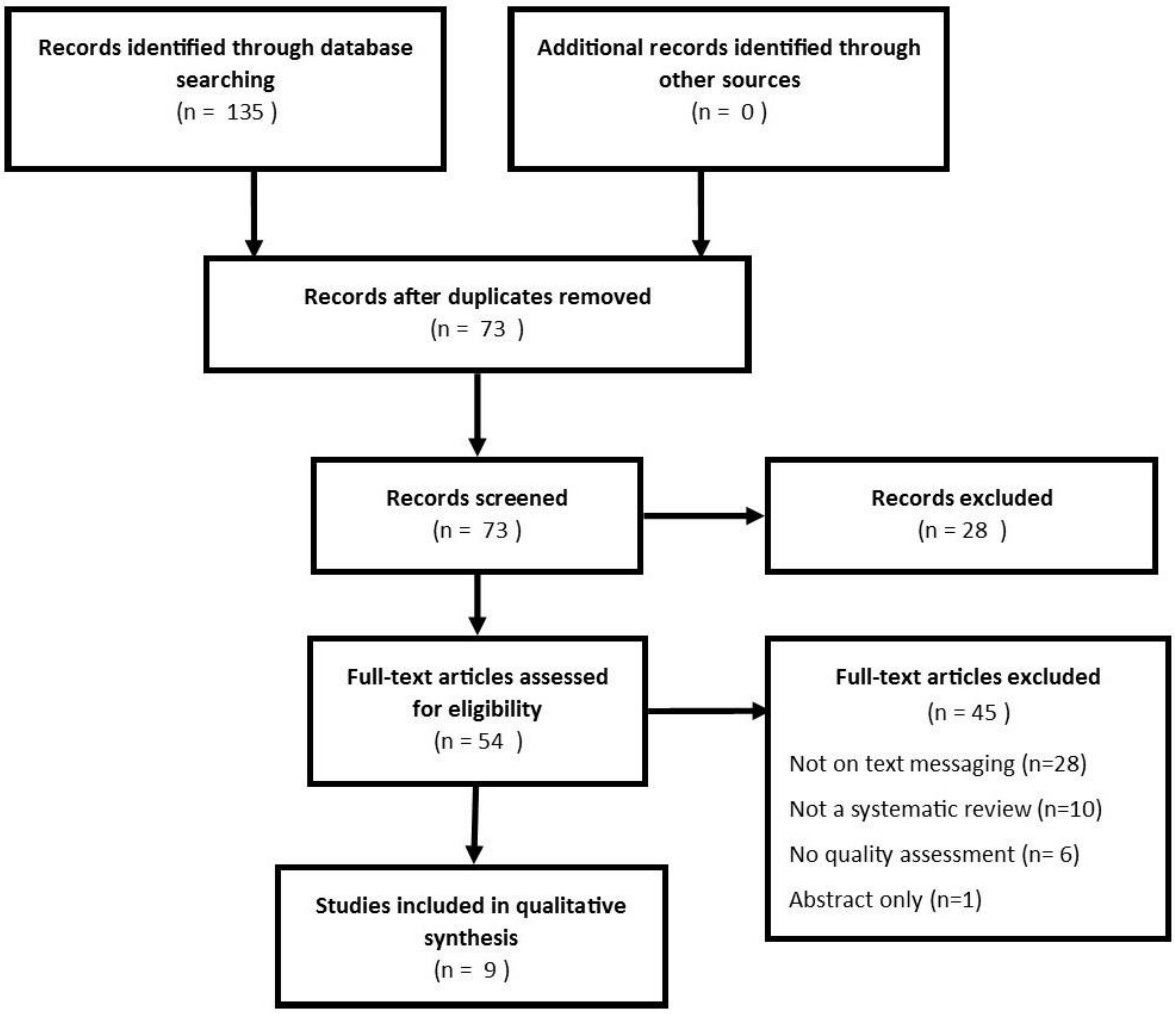

Figure 1: PRISMA flow diagram of study selection

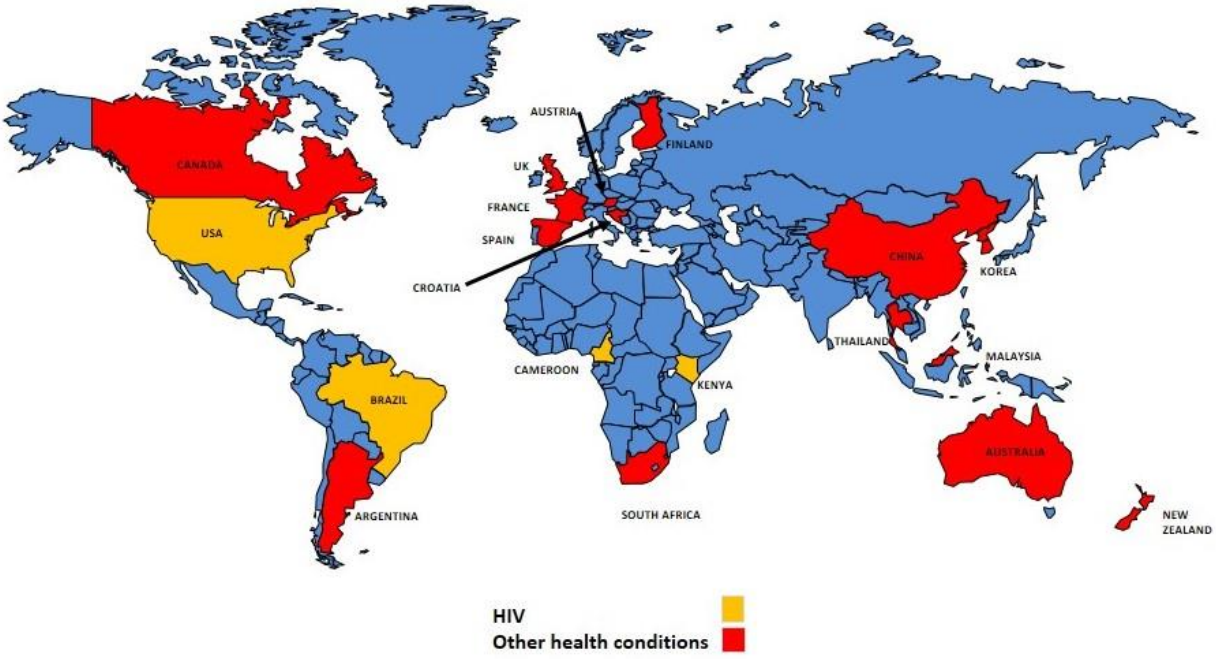

Figure 2: World map illustrating geographical distribution of text messaging interventional research as of May 2014

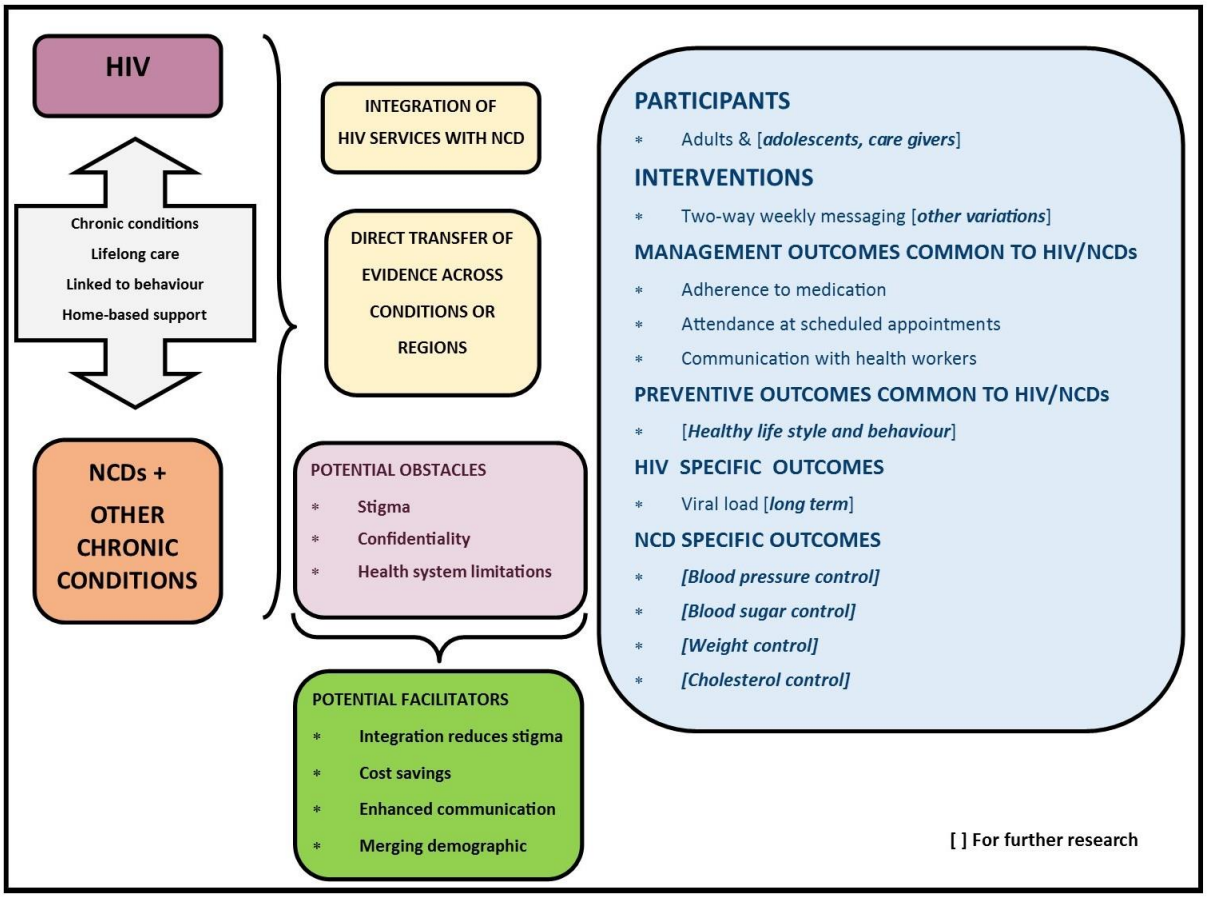

Figure 3: A framework for transfer of text messaging evidence in HIV and chronic diseases

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CHAPTER 8

CONCLUSION

This section summarises the findings from the thesis by addressing the research questions that guided this work. We also highlight implications for research, practice and policy; and comment on the substantive contributions of this thesis.

Part 1: Addressing the research questions

What factors determine adherence to antiretroviral therapy?

Adherence to antiretroviral therapy is multifactorial. Our findings in this thesis, are no different from those reported in literature (Ickovics & Meade, 2002; Mills et al., 2006,; Singh et al., 1996) but we generated evidence in support of the following substantive and methodological issues. First, levels of adherence tend to rise as the cost of medication drops. This ecological (study-level) finding is in line with findings from individual studies which suggest that in parts of the world where the bulk of cost of health care is borne by the patient, the cost of medication plays a significant role in how much medication is consumed (Boyer et al., 2009; Mosoko et al., 2011). Second, the factors associated with adherence differ depending on how adherence is measured. We demonstrated that by changing, our definition of adherence, only those factors with the strongest effects were consistently influential. This finding suggests that measures of adherence for research and clinical practice should be chose with care. Third, multiple reminder methods were a strong predictor of adherence to antiretroviral therapy. Another study has demonstrated that reminder alarms were ineffective in improving adherence to antiretroviral therapy (Chung et

al., 2011). Our findings suggest that using more than one type of reminder may be a relevant strategy in optimising adherence.

Is text messaging effective in improving antiretroviral therapy?

In the CAMPS trial, motivational weekly text messages did not significantly improve adherence to antiretroviral therapy above 95%. However, there was an improvement in adherence above 90%. We demonstrated the efficacy of text messaging in improving adherence to ART in our individual patient data meta-analysis (Mbuagbaw et al., 2013). These findings were confirmed in three other systematic reviews (Finitsis, Pellowski, & Johnson, 2014; Horvath, Azman, Kennedy, & Rutherford, 2012; Mills et al., 2013). We postulate that the CAMPS trial may have been underpowered to detect the small differences in adherence that existed between the intervention and control groups, and that it might have been too short to detect an effect (6 months compared to 12 months in other studies). More so, the CAMPS trial seems to have adopted a more pragmatic approach in many aspects. For example the inclusion criteria were quite flexible, there were no restrictions on other potential co-interventions, the comparison was usual care and follow-up visits occurred only at scheduled clinic appointments. This might explain why the effect of text messaging was not statistically significant in this trial.

What are client perceptions regarding the use of text messages for HIV care?

Client perspectives with regards to text messaging are both positive and hopeful. In our analysis of feedback from the clients in the intervention arm of the CAMPS trial close to half of the feedback were expressions of gratitude. In addition 91% thought it helped them remember to take their medication, 65% wanted to continue receiving messages and 81% would recommend it

to a friend. Clients also appreciated the new communication channel and sought to use if for counselling, to seek information on medications, to get information on how to manage side-effects and to set up clinic or pharmacy appointments. Such positive findings have been reported in other text messaging studies (van der Kop et al., 2012).

In what subgroups are text messages most effective?

The subgroup analyses in the CAMPS trial suggested that text messages may work better in people with higher levels of education. This subgroup effect was confirmed in our individual patient data meta-analyses. Text messages are more effective in improving adherence to antiretroviral therapy in clients with at least a primary education (Mbuagbaw et al., 2013).

What types of text messages are the most effective?

We found that weekly interactive messages were more effective. These findings were confirmed in another systematic review (Finitsis et al., 2014).

Are communities ready to own and run a text messaging programme?

Our mixed methods study demonstrated, using both qualitative and quantitative methods that clients at the Yaoundé Central Hospital are willing to own and run a text messaging programme. This finding is not without note-worthy caveats, such as the lack of experience of clients with community-led programmes, and the lack of convergence of data regarding cost, participation of health workers and the location of the project. Evidently, the lowest possible cost will be the most acceptable to all; and it will be challenging to run such a project without health worker involvement to link communication to actual delivery of care. Likewise it may not be feasible for

the project to be located out of hospital grounds. Yet, community involvement is essential for strong uptake, and we propose a framework to ensure success.

How can a text messaging program be transferred to the community?

Our proposed framework outlines important steps in initiating, implementing, sustaining and monitoring a community led text messaging project. We highlight the importance of working with opinion leaders, demonstrating the benefits of the programme and offering a trial run with the possibility of opting out. A variety of funding sources from local, national and international levels are proposed. We also included critical points for monitoring such as clinical outcomes, satisfaction with the programme and communication feedback.

What is the state of the evidence on text messaging technology?

We identified a variety of uses for text messaging to improve outcomes in health care. Text messaging was used to improve adherence to medication, promote behaviour change and as reminders for clinic appointments. Research in various regions of the world focus on different conditions. The modalities of use of text messaging vary greatly in terms of timing, interactivity, content, duration and personalisation. HIV is the single condition for which there is conclusive evidence on its role in improving outcomes.

How can text messaging technology be transferred from HIV to other conditions?

We highlighted the similarities between HIV and other chronic diseases and the benefits that can be reaped from transferring technology directly or integrating services. Integration of services is more straightforward and would include provision of HIV care alongside other chronic conditions. The health care providers would be expected to have a broader range of

competencies, the facilities should be able to conduct the relevant lab tests, and care should be provided to people with HIV, any other chronic diseases or both. As such, text messaging interventions would target the condition(s) for which the patients seek care. One reminder message could promote adherence for multiple medications.

Transfer of services should include a replication of HIV messaging strategies for other conditions. Regular care providers (non- HIV) would adopt the practices from the HIV clinics and develop a new set of messages and messaging modalities for their clients. We recommend that this process be gradual after setting the appropriate groundwork: client characteristics and preferences, need for adherence enhancement and a core set or outcomes they are hoping to affect with the messaging intervention.

Part 2: Implications for research, practice and policy

Implications for research:

There is a growing body of research on text messaging applications for health care, but there are still important knowledge gaps. We recommend that further research be conducted in carers of children living with HIV, and for people with other conditions especially in Africa where no text messaging studies for chronic diseases were identified. Text messaging interventions seem to be optimal when they are sent weekly, but it is unclear if they would be effective at a less frequent rate. Further exploration of the appropriate content, duration and tailoring is warranted. Further research should focus on clinical outcomes in the short and long term, economic evaluations of text messaging and the possibility of harms.

Implications for practice:

Medical facilities can use text messaging interventions to enhance communication, to improve adherence to medication and as appointment reminders. Such initiatives should take into account available mobile phone service provider packages and determine the most efficient way to deliver messages to clients in an ethical and confidential manner.

Implications for policy:

Policy makers are faced with the task of determining the utility of text messaging in overburdened health systems. As an effective and cheap communication device, with low human resource requirements, capable of linking geographically distant consumers to health care, text messaging seems to be the best option. In the event that text messaging programs are adopted by communities for their own personal benefit, supportive policies can be put in place to ensure that communities get high quality services.

Final comments:

In this thesis, we have confirmed the findings from other studies regarding the efficacy of text messaging in HIV care (Finitsis et al., 2014; Horvath et al., 2012), client appreciation of a novel communication strategy (van der Kop et al., 2012), and superiority of weekly and interactive messages over daily and unidirectional messages (Finitsis et al., 2014). We have created new knowledge regarding the ecological effect of cost on adherence to antiretroviral therapy, the relevance of threshold used to measure adherence on its determining factors, the role of education as an enhancing factor for text messaging, a powerful scale-up strategy through community ownership and a framework for transfer of HIV text messaging knowledge to other conditions. We employed a numbers of study designs, including a randomized controlled trial,

two cross-sectional studies, and an individual patient data meta-analysis, as systematic review, a mixed methods study and a review of systematic reviews. We hope that this thesis serves are a demonstration that complex research questions require complex and complimentary research methodologies.

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