Evaluation of a Computer-Based System using Cell Phones for HIV positive people in Peru

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A dissertation

submitted in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy

University of Washington

2012

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Program Authorized to Offer Degree:

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Abstract

Evaluation of a Computer-Based System using Cell Phones
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HIV is one of the biggest infectious killers worldwide. To prevent disease progression and avoid development of resistant strains to HIV, people living with HIV must adhere to complicated antiretroviral therapy (ART). Yet, in Peru, where ART has recently been introduced, adherence to HIV treatment has not yet been addressed properly, and no systematic approaches to evaluate or promote adherence to ART exist. For people living with HIV, innovative approaches using information technologies, such as mobile phones, are needed to increase adherence to ART. In my thesis, I proposed the following specific aims: (1) To conduct formative research to assess culturally-specific behavioral messages to be included in the computer-based system; (2) To develop and test an interactive computer-based system using cell phones both to enhance adherence to ART and to deliver HIV transmission risk reduction messages; and (3) To evaluate the impact of the system on ART adherence. To achieve these aims, I conducted a randomized controlled trial of a 12-month intervention, comparing (1) standard-of-care with (2) standard-of-care plus my mobile phone-based system among patients receiving ART at Via Libre, a non-governmental organization established to help people with HIV, and Hospital Nacional Cayetano

Heredia, a governmental hospital; both in Lima, Peru. This novel trial adds important evidence to the field of mHealth—the provision of health-related services via mobile communications. The trial is potentially scalable as a prevention strategy by the Ministry of Health, and the results could be applied in other settings, not only for ART, but also to encourage patients to follow long-term treatment plans for other chronic diseases. Furthermore, because the intervention is automated using available information and communication technology, it can be scaled up widely without requiring proportionate and expensive staff resources.

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ACKNOWLEDGEMENTS

Many people have been very supportive during my Ph.D. studies and I am deeply grateful to everyone who contributed to accomplish my goals of finishing the program successfully.

Professor Wanda Pratt has been a fantastic advisor and I am very thankful for her mentoring, continuous support, and patience during this project and throughout my Ph.D. studies.

Professor Ann Kurth has been not only a great advisor but a visionary colleague. Her previous informatics-related work inspired me to follow a research career on mobile health.

Professor George Demiris and James Ralston have been extremely supportive through the process and have made this dissertation much stronger through their feedback, mentoring, and intellectual stimulation. They are not only amazing professionals but also wonderful people, and I have been very fortunate to get the chance to work with them and learn from them.

In addition, I want to thank Professor Seth Wolpin who served as a member in my committee during my general exam and provided valuable feedback to my research.

Professors Sherrilynne Fuller and Ann Marie Kimball are two great professionals who have supported me since my Master studies, and I admire their creativity and energy to help strengthen health information systems in developing countries. Special thanks to Professor King K. Holmes for his helpful discussions and support to my research career.

I want to thank Alex Quistberg, Kristen Heitzinger, Greta Castillo and Deanna Kepka for collaborating during the implementation and evaluation of the project. Special thanks to Peter Busse - who is not just a great colleague and professional but a great friend – for his help, intellectual camaraderie, and for creating a great research atmosphere. Many thanks to Alicia Silva and Sandy Turner for assisting me when I needed the most.

I am thankful to my friends at the University of Washington for the academic and personal support during my PhD studies, especially to my Biomedical Informatics fellows Daniel Capurro and Rupa Patel. Without those special friendships and support throughout my time in Seattle these years would have been much harder.

I would also like to thank the Peruvian team: Patricia Garcia, Cesar Carcamo, Jose Perez-Lu, Ernesto Gozzer and Ana Rosa Contreras from Universidad Peruana Cayetano Heredia; Eduardo Gotuzzo, and Katiuska Castillo from Hospital Nacional Cayetano Heredia; Robinson Cabello and Gerald Diaz from Via Libre. All of them have been key collaborators and have helped me during the implementation and evaluation of the project.

I would also like to acknowledge and express appreciation to the U.S. National Institutes of Health that supported much of this work.

Lastly, none of this could have been possible without the support of my family: my lovely wife, Elizabeth Espinoza, for her constant encouragement, support, inspiration and fantastic sense of humor; my parents, sister and brother – Walter, Norma, Gisella and Ivan; my in-laws, Walter, Elsa, Roxana and Paul. They have been with me at every step of my way, and without their love, care and humor I could have invested much more time to finish this huge endeavor.

DEDICATION

I dedicate this dissertation to my lovely family, for all their unconditional love, sacrifice and endless patience. Without their continuous support and good spirit, I would not have the encouragement to pursue my dreams and goals.

Chapter 1. Introduction

"Drugs don't work in patients who don't take them."
Former US General Surgeon C. Everett Koop, M.D.

I describe the design and evaluation of a mobile phone system to improve adherence to antiretroviral therapy. In this chapter, I frame my dissertation work by discussing the importance of adherence in HIV patient care. After briefly discussing the determinants of adherence, I then introduce a explicit theoretic model which provides a clear framework in the context of antiretroviral adherence. I continue the chapter discussing the role of new technologies on antiretroviral adherence, and present my thesis project about supporting adherence with text messages through mobile phones. Finally, I give the outline of the rest of the dissertation.

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The importance of adherence

Adherence is a highly complex behavior and it is usually defined as the act of taking medications as prescribed (Andrews, 2000). Medication nonadherence might take many different forms—e.g., a person missing doses, taking doses at the wrong time, taking an incorrect dose, not filling a prescription or filling a prescription late, not adhering to gastric requirements (with or without food), and taking excess doses.

For HIV, adherence to drugs (called antiretroviral drugs or antiretrovirals) is important to assure a favorable outcome and several components must be in place. First, antiretroviral therapy must be accessible, properly prescribed, and acceptable to the patient. Second, adherence to antiretroviral therapy must be near perfect.

Adherence to antiretrovirals is important at the patient level and supporting adherence can be demanding for the clinician and has implications at the population level (Andrews, 2000). For the patient, a condition that requires taking medication for a long period of time with complex regimens with both short-term and long-term side effects and toxicities is a tough task. Individual regimens can be very complicated, requiring interruption in daily activities,

substantial expense, and confidentiality and privacy in medication administration. The adherent patient often must adapt his/her life to the medication requirements of the regimen. Some people do it very well, but for others, the task is very challenging and even discouraging. Over the course of years and decades of antiretroviral therapy, thousands of pills and dosing intervals will be necessary (Friedland, 1999). For the clinician, adherence issues require special attention at each clinical encounter which can be very demanding. Clinicians in resource-constraint settings are often busy with high work load. The time to see an HIV patient if often very short, and the clinical interaction focuses around medication, side effects monitoring, and adherence discussions (Horvath, 2012). On a population-based level, the success of therapy relates with the increasing number and quality of life of people living with HIV/AIDS. In addition, antiretroviral therapy can lead to marked reductions in mortality at the population level. Adherence to treatment is crucial to prevent drug resistance with resultant treatment failure and need to switch to a second-line regimen. Finally, another benefit of adherence is that patients with a suppressed HIV viral load are significantly less likely to transmit the infection to sexual partners (Horvarth, 2012).

Determinants of adherence

Antiretroviral adherence cannot be predicted only by sociodemographic factors, such as age, gender, class, and marital status. In addition, educational levels and race are not consistent predictors, although some studies have correlated with adherence (Andrews, 2000).

One way for classifying the determinants of adherence is to organize them into characteristics of the patient, the patient-provider relationship, the illness and the treatment regimen.

However, theoretical models can provide additional insights in order to characterize and predict behavior. There is a lack of studies investigating treatment competency factors and also utilizing a health behavior theory in relation to antiretroviral adherence in developing countries (Munro, 2007).

One promising health behavior theory that has been tailored specifically to designing interventions to promote adherence to antiretroviral therapy in developed countries is the

Information, Motivation and Behavioral Skills model (IMB) by Fisher (2006). However, recent studies have applied the model successfully in developing countries, and the IMB has been considered to be relevant in other cultural settings with more collectivistic worldviews (Peltzer et al., 2010; Rongkavilit et al., 2010). In the next paragraph I will describe with more detail the model.

The IMB model was originally developed to understand and promote HIV risk-reduction behavior but it was easily adapted for HIV medication adherence (Fisher et al., 2006). IMB categorizes specific adherence-related variables as information, motivation, or behavioral skills. Fisher states that although information and motivation are important and necessary triggers for antiretroviral adherence, those must be accompanied by behavioral skills to manage complex medication regimens successfully.

I will briefly describe each of those variables. Please refer to Appendix 1 the IMB model of antiretroviral adherence.

Information

Adherence-related information is an essential prerequisite for adequate antiretroviral adherence and includes accurate information concerning one's specific regimen, the factors that constitute correct antiretroviral utilization and adequate adherence, the specific side effects that may occur with one's regimen, and potential drug interactions.

One important problem in evaluating the relationship of knowledge to behavior is that "knowledge" is an ambiguous and inconsistently used term. Information is often "given" in terms and language that patients many times o not understand and without measuring their comprehension. Therefore, inaccurate information plays an important role in negatively affecting adherence.

Motivation

In general, motivation is defined to include all variables that encourage or discourage adherence. Adherence-related motivation includes personal and social motivation to follow one's antiretroviral regimen. Personal motivation includes one's attitudes and beliefs about the potential outcomes of optimal and suboptimal adherence, whereas social motivation includes

one's perceptions of support for adherence behaviors from significant others, as well as one's motivation to comply with significant others' wishes.

It is important to highlight that motivation does not imply accurate information (e.g. a person might be highly motivated to follow what he or she understands to be his or her prescribed regimen regardless of whether that understanding is accurate), nor does accurate information imply high motivation (e.g. a person might be entirely accurate in understanding the requirements of his or her regimen and still feel unmotivated to fulfill those requirements).

Behavioral Skills

To be successful, sufficient information and excellent motivation must be accompanied by medication behavioral skills for antiretroviral adherence. An important and necessary element to achieve adherence is the acquisition of skills required to manage complex regimens.

According to the model, adherence behavioral skills include both the objective ability and perceived efficacy for performing critical adherence-related skills, such as acquiring and self-administering antiretroviral medications, organization of pill taking around daily activities, identification of cues for dosing, identification and coping with side effects, seeking out new antiretroviral-related information when needed, acquiring or mobilizing social and instrumental support for adherence, and developing self-reinforcement strategies for establishing and maintaining adherence.

As shown in Appendix 1, behavioral skills are directly linked to adherence behavior, but adherence-related information and motivation are related to adherence behavior primarily through behavioral skills. A well-informed, highly motivated person who does not have the skills to acquire and take medication as prescribed or confidence in his or her ability to perform such act is likely to have difficulty with adherence.

Motivation and ability to adhere to antiretroviral therapy also can be influenced by several factors (Fisher et al., 2006), such as mental health issues (e.g. depression) and substance use problems (e.g. alcoholism or injection drug use). All these factors can moderate (e.g. strengthen or weaken) the relations between adherence-related information, motivation, behavioral skills, and adherence per se. Although behaviors associated with chaotic lifestyles compromise patients' ability to adhere, it is the severity of these conditions, rather than just their presence or absence that determines the outcome.

Therefore, the IMB model provides a comprehensive, multivariate, theory-grounded approach to conceptualize antiretroviral adherence behavior.

New technologies and antiretroviral adherence

Over the years, several types of interventions have been developed to help patients become more adherent to antiretroviral therapy. Research has shown that many such interventions have positive clinical outcomes. However, most studies of adherence interventions are from developed countries (Simoni et al., 2003). The evidence from these investigations might, however, have limited relevance to Latin America because the effectiveness of interventions is likely to depend on the context in which they are implemented. Tests interventions in developing countries are urgently needed.

In recent years there has been a growing realization that technology can play a valuable role in supporting patients' adherence to antiretroviral therapy. Mobile phones and other new telecommunications technologies are being used to address a broad range of healthcare issues, from improving attendance in primary care (Leong et al,, 2006), to treating sexually transmitted infections (Meonon-Johansoon et al,, 2006), to supporting community-based peer health workers caring for people living with HIV/AIDS (Chang et al,, 2011). I review the healthcare interventions based on mobile technology to support people living with HIV/AIDS in Chapter 3. With adherence to antiretroviral therapy playing such an important role not only in improving individual patient health but also in reducing viral load (Anglemyer et al, 2011), interventions such as mobile phone text-messaging have the potential to make a significant impact on the HIV epidemic. With the rapid expansion of mobile phone networks globally, particularly in regions such as Latin America, it will become more feasible to implement these interventions at large scale.

Supporting adherence with text messages through mobile phones

In my thesis work, I extend the prior work on mobile health technologies by investigating how mobile technology can support antiretroviral adherence of people living with HIV/AIDS. In

particular, I focus on a careful characterization of the message based on an intervention that frames the IMB model (**Figure 1.1**). Specifically, I argue that adherence of people living with HIV/AIDS goes beyond sending a simple reminder. In addition, I argue that people living with HIV/AIDS want a confidential, easy-to-use, socially interactive website with animated characters to assist both their health care providers and themselves in monitoring their HIV medication adherence.

What makes these activities challenging for patients is the context in which they take place: while patients are away from home, while they are experiencing side effects that diminish their attention and memory, or when they simply forget to take their medicines. To assist HIV-positive patients with these important information activities, I have designed a computer-based system, called **Cell POS,** which uses mobile cell phones. Based on the IMB model, **Cell POS** specifically addresses the information, motivation and behavioral skills components.

In my dissertation, I describe and conceptualize the facilitators and barriers of medication adherence, and then describe the iterative user-centered design, a pilot one-month evaluation, and a one-year randomized controlled trial of **Cell POS**.

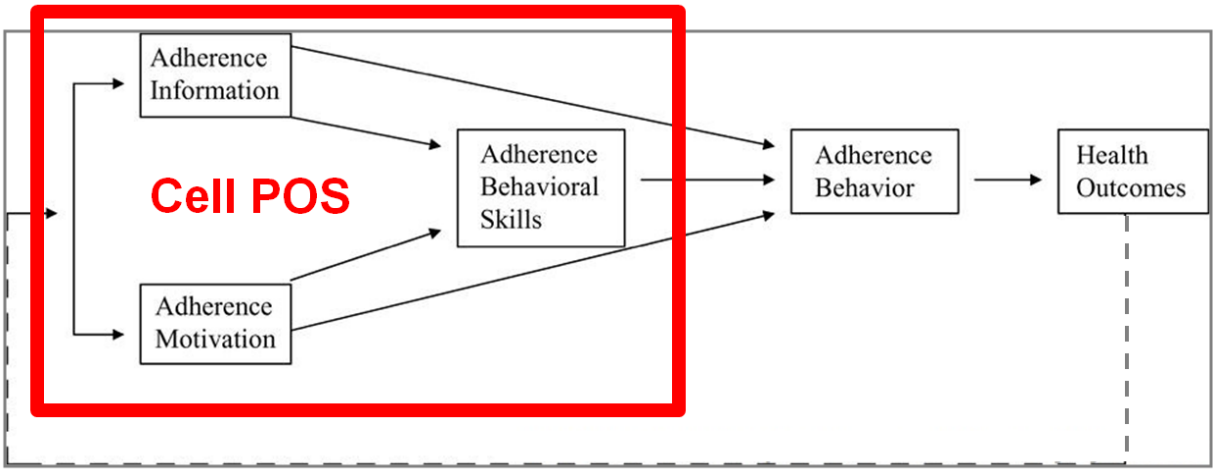

Figure 1.1. Cell POS components based on The Information-Motivation-Behavioral skills model of antiretroviral therapy adherence (adapted from Starace et al., 2006)

For the last five years, our own research group has been working on antiretroviral adherence. **Cell POS** offers a number of unique features. First, it is based on a well-known behavioral theory framework, the IMB model. Second, **Cell POS** was developed based on findings from extensive fieldwork with people living with HIV/AIDS undergoing treatment and was co-

designed with patients. In addition, healthcare staff and the research team participated in the design process. Third, **Cell POS** carefully addresses important issues such as confidentiality and privacy. Fourth, **Cell POS** is a low-cost strategy with high public health impact that was evaluated through a one-year randomized controlled trial with HIV-positive patients who used Cell POS in their daily life to manage their antiretroviral adherence. Fifth, **Cell POS** could be implemented not only in Peru, but also in other developing and developed countries.

Dissertation outline

The rest of this dissertation is structured as follows:

- *Chapter 2* provides a description and conceptualization of facilitators and barriers of antiretroviral adherence. In particular, the chapter presents a qualitative analysis of in-depth interviews from 31 adult HIV-positive patients to describe the social, cultural, knowledge-based, and logistical factors that influence antiretroviral therapy adherence in Peru. I describe the facilitators and barriers that people living with HIV/AIDS experience to deal with antiretroviral adherence—an issue which has remained poorly understood and largely unrecognized in the research of HIV in Peru. In addition, we found that the barrier mostly reported by people living with HIV/AIDS is "simply forgetting", which could be addressed by implementing simple technology strategies, such as text messaging using cell phones.

- *Chapter 3* reviews the current literature on mobile phone interventions to support people living with HIV/AIDS. The chapter describes the opportunities and how mobile phones have been used to support medication adherence. The literature review suggests that mobile phones are playing an important role in supporting health interventions both in developed and developing countries. The key is how to best integrate those devices into our daily lives so mobile phones can produce the desired improvement in the quality of people's lives.

- *Chapter 4* presents the iterative, user-centered design of Cell POS, a computer-based system that uses mobile cell phones and the Internet to enhance adherence to

antiretrovirals. We designed this system to address the specific needs and preferences of patients for HIV care as well as to provide information related to HIV care. I describe the development process of the initial prototype of Cell POS, including a careful characterization of the antiretroviral reminder messages and the description of the supporting Web-based interface. I describe four focus groups that I conducted with HIV positive patients to get a deeper understanding of the functional requirements for Cell POS. Based on the results of the focus groups, I suggest that HIV/AIDS patients want a confidential, easy-to-use, socially interactive website with animated characters to assist both their health care providers and patients in monitoring their HIV medication adherence.

- *Chapter 5* describes the main components of Cell POS, the final architecture and a pilot evaluation to get a better sense of how the system works. Nine people living with HIV/AIDS used the Cell POS system for one month, as a pilot evaluation. I end this chapter with a discussion on perceptions of study participants.

- *Chapter 6* presents the result from a randomized controlled trial to assess whether and how Cell POS works in the long run. I describe the intervention in which 174 people living with HIV/AIDS were enrolled to the study and randomized to use the Cell POS system for one year. I end this chapter with a discussion of the study and of the implications that the study findings have for further development mobile applications for health.

- Finally, *Chapter 7* discusses the contributions of this dissertation to public health and biomedical informatics, as well as the directions for future work.

For quick reference, the key characteristics of each of the studies described in this dissertation are presented in **Table 1.1**. For each study, the table lists where the study is discussed, the study's goals, methods that were used, and the participants that took part in the study.

Table 1.1. Overview of the studies described in the dissertation

Location	Study Goals	Methods	Participants
Chapter 2	(1)Describe the social, cultural, knowledge-based, and logistical factors that influence antiretroviral therapy adherence in Peru. (2) Describe the barriers and facilitators for antiretroviral adherence in Peru.	In-depth interviews at two community-based clinics (Impacta, and Via Libre) in Lima, Peru.	31 adult HIV-positive individuals receiving antiretroviral therapy (90% male, 81% mestizo, 61% education level above high school).
Chapter 4	(1)Assess perceptions regarding cell phones as means for health promotion for people living with HIV/AIDS in Peru.	In-depth interviews at two community-based clinics (Impacta, and Via Libre) in Lima, Peru.	31 adult HIV-positive individuals receiving antiretroviral therapy (90% male, 81% mestizo, 61% education level above high school).
Chapter 5	(1) Characterize effective Antiretroviral therapy reminder strategies for people living with HIV/AIDS in Peru. (2) Describe design preferences and characteristics of a website monitoring the HIV medication adherence of people living with HIV/AIDS	Four focus groups in a community-based clinic (Via Libre) in Lima, Peru.	26 adult HIV-positive individuals receiving antiretroviral therapy (77% male, 88% completed high school).
Chapter 6	(1)Evaluate the perceived ease of use, usefulness and perceptions of Cell POS to support antiretroviral adherence in Peru.	Semi-structured interviews after four weeks of technology use (Cell POS) at Via Libre clinic in Lima, Peru.	Nine adult HIV-positive individuals receiving antiretroviral therapy (67% male, 89% mestizo, 67% completed high school).
Chapter 7	(1) Assess whether mobile phone text messages improve drug adherence to antiretroviral therapy. (2) Understand how Cell POS supports adherence to antiretroviral therapy.	Randomized controlled trial of Cell POS involving HIV-positive individuals in two health care centers (a national hospital and a community-based clinic) in Lima, Peru.	174 adult HIV-positive individuals receiving antiretroviral therapy.

Chapter 2. The challenge of medication adherence for people living with HIV: Barriers and facilitators in Peru

Introduction

People living with HIV/AIDS (PLWHA) now have the chance to live longer and with better quality of live due to the greater availability of antiretroviral treatment (ART). In Peru, antiretroviral therapy has been available through the national ART program since 2004 and is a key component of improving health outcomes for HIV-positive individuals (Echevarria et al., 2006). However, a person living with HIV has to deal with several challenges. One of those challenges is adherence to medication regimen, generally defined as the extent to which patients take medications as prescribed by their health care providers (Osterberg & Blaschke, 2004).

It is clear that the full benefit of medications will be achieved only if patients follow prescribed treatment regimens closely. In particular, HIV patients undergoing treatment have to achieve more than 95 percent adherence to antiretroviral therapy in order to suppress viral replication and avoid the emergence of resistance (Este & Cihlar, 2010). However, achieving such high rates of adherence is very challenging to HIV patients, because many times their regimens include multiple medications that have complex dosing schedules and may cause food interactions and side effects that might result in poor tolerability. In addition, lifestyle factors, stigma and issues in the patient–provider relationship may make adherence difficult (Murphy et al., 2000).

In this chapter, I describe several factors that influence adherence on HIV patients undergoing antiretroviral therapy in Peru. Those factors were poorly understood previously in Peru. I analyze data from interviews with 31 people living with HIV, and describe the social, cultural, knowledge-based, and logistical factors that patients experiment during their treatment. Finally, heightened knowledge of these specific barriers and facilitators for antiretroviral adherence in Peru will highlight a technological approach in the development of useful and needed interventions to promote improved antiretroviral therapy adherence in Peru.

Related work

Many studies have shown that a large percentage of patients, in general, find it difficult to achieve high levels of adherence to a treatment. In a 2004 meta-analysis of 569 studies, patients display a non-adherence rate of approximately 25% on average (Di Matteo, 2004).

Non-adherence is particularly difficult for HIV-positive individuals because ART regimens are complicated, have side effects, and carry associated stigma. Past studies have shown that 12-50% of HIV-positive patients fail to achieve optimal adherence (Heckman et al., 2004; Gifford et al., 2004).

In a 2006 meta-analysis of adherence to ART that included 37 qualitative studies and 47 quantitative studies in developed and developing nations, Mills et al. found that many barriers to adherence were reported similarly in a number of settings and countries. Of the 37 qualitative studies that were conducted, only two qualitative studies were carried out in developing countries (Mills et al., 2006). In Peru, adherence to HIV risk reduction and treatment is becoming increasingly problematic according to anecdotal reports from local AIDS clinicians.

To provide optimal HIV care, strategically developed interventions that are tailored and multi-focused and multi-function strategies are needed to improve ART adherence that include components to increase information (e.g., HIV treatment knowledge and consequences of non-adherence), motivation (e.g., treatment benefits and concerns), and behavioral skills (e.g., methods of enhancing adherence) (Saberi & Johnson, 2011).

However, the development of effective and tailored interventions to improve ART adherence requires an in-depth understanding of the mutable factors that influence it. Few qualitative studies have been carried out in resource constrained international settings (Mills et al., 2006) and there have not been any in-depth qualitative studies conducted in Lima, Peru related to the barriers and facilitators for ART adherence. This chapter examines these issues in one particular health context: ART adherence in Peru.

Methods

Findings presented in this chapter are based on data drawn from a study of an HIV-intervention based on mobile devices conducted by my research group: Deanna Kepka, Robinson Cabello, Patricia Segura and Ann E Kurth. During five weeks, we conducted in-depth interviews with 31 PLWHA undergoing ART therapy. In this section, I describe how this fieldwork was conducted,

who the participants were, and how I analyzed the data related to barriers and facilitations reported in this chapter.

Study procedures

Formative research techniques were carried out to assess adherence barriers and facilitators towards ART in Lima, Peru. This research was done using in-depth interviews with adult HIV-positive people receiving ART and clinical services at two community-based clinics (Impacta and Via Libre).

Both these clinics primarily serve male clients (100% at Impacta, approximately 80% at Via Libre) and demonstrate similar demographic profiles for their patient populations. These two clinics were selected because they are two of the most important clinics for HIV positive individuals in Lima and they have participated in other research studies. Convenience sampling was employed at the two clinics to recruit individuals for study participation (Miles & Huberman, 1994). In addition, flyers were posted at the clinics to recruit participants into the study over the course of six months. To qualify for the study, participants had to be at least 18 years old, HIV positive, and receiving ART.

Topic guide

A topic guide was used, which consisted of open-ended questions related to broad subject areas regarding: lifestyle, living with HIV, and barriers and facilitators of patient adherence to treatment. Past studies informed the development of the topic guide for the semi-structured in-depth interviews (Kurth & Moore, 2005). The topic guide was then reviewed for content validity by HIV consultants in Lima. An outline of questions related to lifestyle, living with HIV, ART medications are listed in Appendix 1.

Data collection and analysis

A trained and experienced psychologist conducted the in-depth interviews in each of the clinics (Impacta and Via Libre). After giving consent, all interviews were conducted in Spanish with each respondent in a private room for approximately one hour. The psychologist recorded all the interviews. All participants signed an informed consent form prior to entry into the study. After

the interview, the psychologist compensated with 30 soles (about 10 dollars) to all participants for travel expenses.

Audio files were transcribed and transcripts were reviewed by myself for initial text element and key word coding. Transcripts were then reviewed separately by me and Deanna Kepka for text element and key word coding, and initial generation of themes.

We used inductive coding which begins with close readings of text and consideration of the multiple meanings that are inherent in the text. We then identified text segments that contain meaning units, and created a label for a new category into which the text segment is assigned. Additional text segments were added to the category where they were relevant (Thomas, 2003). The coding of the text into categories of experiences and beliefs resulted in the emergence of thematic concepts. A theme was then defined as a "common thread that runs through the data" (Richards & Morse, 2007). Summaries of coding practices and thematic concepts were compared and discussed over 10 meetings until a consensus was reached on which themes were most salient to participants' responses. We then reviewed the transcripts to confirm our findings until we reached saturation and identified quotes that best illustrate common theme (Strauss & Corbin, 1998). Quotes were edited for ease of reading but were not substantially altered. Data were entered into Atlas.ti version 5.5 (2008) qualitative data management software (Scientific Software Development, Berlin, Germany) for theme identification using a content analysis approach.

Ethical approval

The study had ethical approval from the University of Washington Human Subjects Division (HSD# 06-1430-G-01) and the institutional review boards of Via Libre and Impacta.

Results

In this section, I describe study participants and then describe the facilitators and barriers.

Study participants

During March-August 2006, 31 people living with HIV were interviewed, 16 at Via Libre Clinic and 15 at Impacta Clinic. Of these participants, 28/31 (90%) were male, 25/31 (81%) were self-identified as mestizo (multi-ethnic and/or multi-racial), and 19/31 (61%) had an education level above high school. All participants were currently on ART.

ART adherence facilitators

In general, participants who were able to describe the effects of the medication appeared to be more comfortable with adhering to the regimen. This "information" element has been theorized to be an important component in ART adherence (Fisher et al, 2006) and is an area that health professionals are well qualified to address. For many people, overcoming the side effects of ART was the first stage that must be addressed to achieve high levels of adherence. The second stage for many individuals was successfully incorporating ART into one's every day routine. Participants reported a number of specific factors that influenced improved levels of adherence to ART.

Patient characteristics

First, many factors were identified that relate to individual level patient characteristics that represented facilitators to improved ART adherence. These factors include seeing positive results (reported by 65% of participants, 20/31), learning to manage (reported by 55% of participants, 17/31), and self-efficacy for high levels of adherence to the ART regimen (reported by 32% of participants, 10/31). Seeing positive results and learning to manage were two of the most frequently discussed adherence facilitators by the participants in this study at the patient characteristics level. Participants who knew that ART was positively impacting their health and those who learned to manage the impact of ART regimens on their everyday lives reported these characteristics as important ART adherence facilitators.

An example of learning to manage is expressed by this participant:

"I made antiretrovirals part of my life. It's true that the pills make me sick, but after some time the [bad sensation/pain] that I felt is something that is not impossible to manage." Male, white, 43 years

Examples of seeing positive results were expressed by these participants:

"The antiretrovirals have helped me to increase my CD4 from 170 to 230 and not only that but also improve my spirit." Male, mestizo, 28 years

"Taking the antiretrovirals helps a lot. I can see for myself: Before I started the treatment, I weighed 52 kilos and now I am at 74 kilos. I believe that the treatment helps because in some way I am seeing the results." Male, white, 48 years

An example of self-efficacy to adhere to ART is expressed by this participant:

"What makes me take my antiretroviral medicines is my spirit. My spirit tells me always that I have to take my pills to feel good with myself." Male, mestizo, 25 years

Positive beliefs about the medication

Second, many factors were identified that relate to beliefs about the medication that related to improved levels of adherence. These include beliefs in efficacy of drugs (reported by 42% participants, 13/31), faith in treatment (reported by 42% participants, 13/31), and understanding the need for compliance (reported by 97% participants, 30/31). Specifically, understanding the need for compliance was one of the most frequently discussed facilitators to adherence in this study as expressed on one participant:

"If I want to continue living, I have to adhere to the treatment because it is the only way to be healthy. This is like a diabetic patient. If he/she does not take their medicine, he/she will die. It's not because of the sugar but because all that occurs when the sugar increases." Male, white, 48 years

Participants who were aware of the need for compliance to their medication regimens were more likely to cite this factor as key to increasing self-motivation for adherence.

Other participants expressed belief in the efficacy of the drugs and a strong faith in treatment that facilitated motivation for adherence. One participant states:

"*Taking my antiretrovirals will make me feel good, I know that I will not be cured, but will help me to live longer*." Female, mestizo, 38 years.

Another participant expresses:

"*Antiretroviral medicines give me the opportunity to continue living, to continue being with my friends and family*." Male, white, 43 years.

Good daily schedules

Third, many factors were identified that relate to daily schedules were associated with strategies for improved levels of adherence. These factors include having a fixed routine (reported by 71% participants, 22/31), and the use of reminder tools (reported by 58% participants, 18/31). Having a fixed routine was the top adherence facilitator that was discussed by participants as related to daily schedules. As expressed by one participant:

"I have my brain alarm, when it's time to take my antiretroviral pills it starts to buzz... it's eight...time to take your pill." Male, mestizo, 35 years

Many participants reported concrete strategies to successfully integrate their pill taking regimens into their lives as key facilitators to adherence such as the use of reminder tools:

"I have programmed the alarm of my cell phone, with a very nice ring tone. When it rings I know automatically that I have to go where my pills are and take them." Male, mestizo, 36 years

Strong interpersonal relationships

Lastly, a number of factors were identified that relate to interpersonal relationships that helped improve levels of adherence. These include family and friends reminding the participants to adhere to their ART regimen (reported by 29% participants, 9/31), and living for someone (reported by 16% participants, 5/31). As expressed by two participants:

"My mom or my sister remind me to take my medicines. For example, my sister tells me "have you taken your "contrita" (a popular name for the medicine)? So I respond 'yes, I took my 'contrita'." Male, mestizo, 34 years

"I live for my daughter, for her, I try to get through." Female, mestizo, 38 years

Many participants reported that the support of others, including their health care provider (e.g. doctor, nurse, counsellor), in their lives was an important and effective adherence facilitator. As represented by the following experience noted by a participant:

"My new doctor is more worried about me...we are working together. We have changed my medication and I feel completely relieved." Male, mestizo, 36 years

Other facilitators

Many other ART adherence facilitators that were briefly discussed by participants include the following. Many participants reported positive and open relationships with their medical providers as an important adherence facilitator (reported by 39% participants, 12/31). Feeling comfortable asking questions, talking about challenges, and feeling a part of decision making with one's medical provider played a key role in facilitating adherence. Next, having a simple regimen was reported by a few participants as assisting in ART adherence. Lastly, medication taking priority over substance use, accepting HIV status, and being open with disclosure of HIV status were noted by a few participants as important adherence facilitators.

ART Adherence Barriers

A wide variety of barriers to ART adherence were discussed by the participants. These were classified into three broad categories: patient characteristics, beliefs about medications, and daily schedules. Patient characteristics

First, patient characteristics include the following factors: simply forgot (reported by 36% participants, 11/31); fear of disclosure/stigma (reported by 23% participants, 7/31); and financial constraints (reported by 13% participants, 4/31). Simply forgetting one's medication was one of

the most frequently cited adherence barriers by the participants within the category of patient characteristics. As represented by this participant's experience:

"I think that forgetting to take your medicines is that you simply miss the time, because you know that you have to follow a scheme, to follow a treatment, but there were moments that I had to take the pill and I missed it." Female, white, 32 years

The participants also discussed difficulties with adhering to medication regimens without disclosing their HIV status to others at work and/or at home. A number of participants touched on this barrier:

"Initially, I took my treatment in a particular way. It was my cross, nobody knew about it, nobody, during five years, nobody, nobody knew about it, only my physician and me." Male, white, 48 years

"I have to hide from my family so they do not know that I'm taking my ART medication. They do not know anything about my disease." Male, mestizo, 36 years

"One time I had a pill box, a hexagon, but it was...very big, and they asked me: hey, 'what are those pills?' 'ah, they are vitamins'." Male, mestizo, 27 years

In addition, financial constraints and fear of disclosure/stigma were also frequently discussed. Specifically, participants noted financial challenges related to acquiring their medications on time. One participant remarks:

"The problem with taking my pills was always economic. At the beginning it was very expensive, then prices went down. Because of this, it is very difficult to maintain an exact frequency for taking my pills and I had holes in the treatment." Male, mestizo, 39 years

Beliefs about the medication

Second, beliefs about the medication were discussed as barriers to ART adherence by the participants. This category included the following factors: side effects—real or anticipated—(reported by 74% participants, 23/31); harmful (reported by 19% participants, 6/31); and not convinced of efficacy (reported by 16% participants, 5/31). Overall, side effects were the most

frequently discussed barrier to adherence by participants. Side effects included both negative symptoms that the participant attributed to the ART regimen and side effects that were anticipated to occur due to the ART regimen. As highlighted by one participant:
"When I started with the treatment I was nauseous all the time. I had headaches. I had a fever. I had cellulitis again. I experienced a lot of illnesses that I had never had before....I was very very bad off." Male, white, 43 years.

Varied and complicated daily schedules

Lastly, daily schedules were reported as additional challenges to ART adherence. This category includes the following factors: dietary requirements difficult to balance (reported by 26% participants, 8/31); being away from home (reported by 23% participants, 7/31); and too busy (reported by 16% participants, 5/31). Specifically, being away from one's household during the course of one's day for work or social engagements was reported as greatly interfering with adherence to the ART regimen. As discussed by three participants:

"I have forgotten to take my pills when I go out in a hurry out of my house or when I had to stay at work. When the time to take my pill passed (8 pm), and I thought: 'oops...my pill...I didn't take it'." Male, mestizo, 35 years

"For me, weekends are terrible because I have to go out to a party or a meeting and I do not take the pill at night. It is a problem for me." Male, mestizo, 28 years

"I have to take my pills with food. This is the problem and what makes me upset is that there are some days that I cannot eat and I cannot take my pills." Male, mestizo, 35 years

A few other participants found the dietary requirements difficult to balance:

"I have to pay attention to my diet and there are some times that I cannot control it. This makes it a little bit difficult to take my pill." Male, mestizo, 36 years

In addition, a number of participants felt that they were too busy to remember their pills. As expressed by one individual: "There are some times that I have so many things in my head that I forget to take my pills." Male, white, 35 years

Other barriers

Other barriers to ART adherence that were briefly discussed by the participants included the following. Some participants lacked trust in their medical provider and felt that this was a barrier to adherence. Some were feeling healthy so they did not see the need to adhere to their ART regimens. Others felt hopeless and not motivated to adhere to their ART regimens. A few others reported that because ART caused unwanted changes to their body, they were reluctant to adhere to the regimen. Lastly, the size of the pill hindered adherence and that substance use takes priority over ART adherence was reported by a few participants.

Discussion

This chapter highlights that having a fixed routine, understanding the need for compliance, seeing positive results, knowledge of treatment, faith in treatment, and use of reminders tools were the most frequently cited facilitators. In addition, side effects, simply forgetting, inconvenient schedule, financial constraints, being away from home, and fear of disclosure/stigma were the most frequent cited barriers in this study conducted in Peru.

The results reported in this chapter are similar to those of other qualitative studies in developing countries. For example, in a study conducted in Brazil, Brigido et al. (2001) reported that forgetfulness and intolerance were the most frequent reasons for non-adherence. Other reasons cited were stopping ART to consume alcohol, misunderstanding of the prescription requirements, difficulty in following recommendations at the workplace, and lack of money for transportation to obtain medication. In Botswana, Weiser et al. (2003) found that the principal barriers to HIV adherence were financial constraints, stigma, travel/migration, and side effects.

In our study, we did not find that migration was a barrier. In Uganda, Byakika-Tusiime (2005) et al. reported that shortage of drugs due to lack of money was the most common reason for non-

adherence. Other reasons included forgetfulness, drug inaccessibility, adverse effects of the drugs, travelling away from home, unclear instructions by the health provider, and being too busy. In another study conducted in Brazil, Pinheiro et al. (2002) found that self-efficacy expectation (personal confidence in the ability to adhere to antiretroviral medication), the perception of negative effects, and physical concerns were associated with adherence.

Similarly, in a qualitative study conducted with Spanish-speaking patients in Los Angeles, Murphy et al. (2003) reported that the most frequent barriers for non-adherence were feeling depressed or feeling overwhelmed, simply forgot, and timing difficulties. Our study, however, did not find feeling depressed/stressed as a common barrier. In the same study, the most frequently identified adherence strategies were making an effort to learn more about the antiretroviral medications, accepting the need to take antiretroviral medications, and refilling prescriptions early or on time.

Lastly, a number of studies have found that patients with a trusting and open relationship with their health care providers are better able to adhere to their ART. Furthermore, patients who lack open communication with their health care providers due to cultural differences, cultural insensitivity, and/or language barriers may find it difficult to adhere to ART (Dahab et al., 2008).

Effective interventions to improve adherence to ART are able to build on adherence facilitators and address adherence barriers. For example, one study at 6 HIV specialty clinics in California that included 437 HIV positive participants, it was demonstrated that participants who participated in a clinic-wide intervention included a brief counseling session with their medical provider that established open communication, built trust, and addressed obstacles to complying with pill taking regimens were more likely to remain adherent to ART (Milam et al., 2005).

In a review of behavioral interventions that promote ART adherence, Simoni et al. (2008) found that there are a number of specific strategies that might be effective at promoting adherence provided that they are culturally sensitive and address structural and individual level barriers. These strategies include solidifying the patient-provider relationship by establishing trust,

promoting social support, employing simple practical strategies, managing side effects, and addressing misinformation related to adherence practices.

In Lima, HIV positive individuals could be in particular need of ART adherence interventions that address strategies to improve adherence through the patient-provider relationship and improve strategies to incorporate ART pill taking regimens into a busy urban lifestyle where individuals may feel stigmatized by their HIV positive status.

Could mobile devices play a role in HIV medication adherence?

The barrier most reported by PLWHA is "simply forgetting" that could be reduced substantially by implementing simple technology strategies, such as text messaging using cell phones. Cell phones have been successfully used to support patient medication adherence in developed countries and in resource-constrained settings such as Uganda, and South Africa. Cell phones might be an ideal tool to improve ART adherences for HIV patients in Lima because they can be private, interactive, efficient, affordable, convenient, and useful as a reminder tool.

Limitations

This chapter reports valuable finding about adherence facilitators and barriers from a group of HIV patients in Peru, but I also need to recognize its limitations. Our study was limited by its use of a convenience sample of people living with HIV/AIDS in an urban population of Lima. The participants in this study cannot be considered representative of people living with HIV/AIDS throughout Peru. However, one of the strengths of this study is that we are confident that we reached saturation because a number of the themes were similar among participants.

Additional qualitative and quantitative studies are needed in Peru that further explore the barriers and facilitators of ART adherence for women and other demographic groups in Lima and for Peruvians living in other rural and urban regions of Peru. Specifically, more research is need on strategies to improve adherence for sex workers who experience high rates of HIV infection. In addition, more research is needed to understand what mechanisms support the transition from managing the ART regimen and side effects to successfully internalizing self-care to achieve high levels of ART adherence. Multi-component, tailored intervention programs that specifically

address the barriers of ART adherence and build on the facilitators of ART adherence in Peru should be developed and pilot tested at clinics and health care facilities that provide ART.

Lastly, in Peru, more widespread public health education campaigns are needed to decrease HIV/AIDS stigma and to increase community acceptance of individuals living with HIV/AIDS. Additional public health programs are needed to increase levels of direct interpersonal social support networks for individuals living with HIV who are on ART.

Conclusion

In this chapter, I described an aspect that was previously poorly understood: exploring the facilitators and barriers of HIV medication adherence in Peru. This works makes two chief contributions. First, I provide a description and conceptualization of important facilitators and barriers reported by PLWHA in Peru ,which have remained poorly understood and largely unrecognized in the research of HIV in Peru. Second, the barrier most reported by PLWHA is "simply forgetting" that could be reduced substantially by implementing simple technology strategies, such as text messaging using cell phones. Such technology, I believe, could have a profound impact on the lives of PLWHA. The rest of the work reported in this dissertation takes a first step towards the goal of designing and evaluating such technology.

Chapter 3. The opportunity of Mobile Health in Resource-constraint Settings

Introduction

The material in this chapter is divided into four parts. First, I briefly discuss the reasons for using cell phones as a delivery infrastructure. I then describe the rationale for using cell phones in Peru. The third part is intended to review the mobile health technologies that have been used for health interventions. Following this discussion, I describe how cell phones have been used to support people living with HIV/AIDS as a main or combined intervention. Finally, the gaps in current research are described and I outline several opportunities for interventions and future work.

Finally, it is important to note that this chapter is not intended to conduct a systematic review nor a meta-analysis of the mapping of mobile health interventions. Therefore, I do not offer a comprehensive review of the design space or effectiveness of mobile phone interventions. For a review of mobile health design recommendations, the reader might refer to: Klasnja & Pratt (2012); and for reviews on effectiveness of mobile health interventions, the reader might refer to: Kaplan (2006), Cole-Lewis (2010) or Riley (2011).

Cell phones as a ubiquitous and available delivery infrastructure

In the last twenty years, cell phones have connected people and have created massive change in our society. Nowadays cell phones have become ubiquitous and have been more creatively enhanced, so in a small device you can include a planner, a Global Positioning System (GPS), etc.

Mobile telephone subscriptions have been growing rapidly since the 1980s in both developing and developed countries (Kaplan, 2006). In 2002, mobile subscribers overtook fixed line subscribers worldwide and this occurred across geographic regions, socio-demographic criteria

(gender, income, age), and economic criteria such as gross domestic product per capita (ITU, 2003). In much of sub-Saharan Africa, there are more mobile phones than fixed-line phones and the use of mobile phones in many Asian countries is on the rise (Vodafone, 2005). There is evidence that the existence of the "digital divide" along the socio-economic gradient is less pronounced in mobile phones than in other communication technologies such as the Internet (Forestier et al., 2002). Furthermore, mobile (i.e., wireless) costs less to rollout over large areas than does a fixed phone line, and mobile networks can be built faster than fixed lines (Vodafone, 2005). The social value of a mobile phone is high even in resource-poor areas. Functionally, mobile phones are easier to use for people with lower level of skills than those needed for computers or the Internet, both of which usually require land lines (Kaplan, 2006).

Pricing policies encourage certain mobile uses, in particular use of the Short Message System (SMS). For example, SMS texting is rapidly growing and is boosted in some countries, such as the Philippines, because a text message is less expensive than a phone call (Paule, 2004). SMS provides low bandwidth digital messaging between users and has surprised some observers by its success. SMS cost less than voice messaging and it can reach people whose phones are switched off. SMS messaging is silent which means that messages can be sent and received in places where it may not be practical to have a conversation (Faulkner, 2005).

Therefore, mobile technology is rapidly growing worldwide becoming ubiquitous and available delivery infrastructure, and Peru is not the exception.

Rationale for using cell phones in Peru

In Peru, the market for cell phones has been increasing since 1993. By December 2011, 77% of households had at least one member who owns a cell phone, which represented a 47% increase compared to 2006 (INEI, 2012), Pre-paid cell phones are the most popular service chosen by users in Peru. In the mid-1990s "cholulares," a nickname for "cholos con celulares" or people who rent cell phones on the streets, was popular in many cities in Peru. But now, more and more people are acquiring cell phones for their own because they have become more affordable (Curioso, 2006).

Previous studies conducted by my research group have reported that it is feasible to collect data with mobile devices including cell phones in urban and rural areas of Peru (Curioso et al., 2005; Bernabe-Ortiz et al, 2008).

I will describe in the next section how cell phones have been used for healthcare purposes.

Cell phone applications for health

Cell phones represent a great opportunity for health. The applications of cell phones and other mobile devices (including sensors) for health purposes, have developed a new field called mobile health or mHealth (Riley, 2011).

Academics, clinicians, and policy makers are increasingly interested about the value of using cell phones to improve health outcomes and quality of life (Kaplan, 2006). Over the last decade the number of publications and applications of mobile health interventions has been growing considerable (Riley et al., 2011).

Kaplan conducted a systematic literature review of health care interventions using cell phones and found that most of articles came from developed countries (Kaplan, 2006). In addition, he found very few literature published on using mobile telephones as a health care intervention for tuberculosis, malaria, and chronic conditions in developing countries. Some well-designed studies using phones have demonstrated efficacy, especially for medication adherence in developed countries.

In developing countries, mobile devices to support healthcare have shown promising results. A 2010 review by Blaya et al, showed that mobile devices can be very effective in improving data collection time and quality. In addition, they found benefit in the reminder systems for HIV and tuberculosis implemented in South Africa and Malaysia, because intermittent treatment puts patients at grave risk of deterioration and death, as well as causing increased drug resistance and further transmission of disease to the wider community (Blaya et al., 2010). However, the authors stated that few scientifically rigorous data have been published on the effectiveness and cost-effectiveness of e-health systems (including mobile health) on developing countries.

In summary, current literature on treatment compliance is focused primarily on the management of chronic diseases (i.e. diabetes, nutrition, smoking cessation, breast cancer) in high-income countries. Thus, more rigorous research on the efficacy of mobile phones from developing countries is warranted because there is still little known about the efficacy of mobile phones as healthcare interventions due to the different outcome measurements and the small number of controlled studies in developing countries. In addition, clinical outcomes are rarely measured in

developing countries. Developing countries could also arguably benefit from cell phones as an inexpensive method of health promotion that builds upon existing infrastructure (Cole-Lewis et al, 2010).

In addition to the widespread adoption and ubiquitous characteristics of cell phones, the fact that people try to keep their cell phone attached to them, make cell phones a good platform for delivering targeted or tailored health interventions.

Cell phones as a healthcare intervention to support people living with HIV

Cell phones have tremendous potential to support HIV and sexually transmitted infections (STI) care (Curioso et al, 2007). In particular, the use of SMS provides many options for public health interventions. In this part of the chapter, I review the published literature regarding the use of cell phones to support HIV and STIs with a particular focus in developing countries. For example, text messaging can be used for: (1) Sending information to patients; (2) Gathering information from health personnel and patients; (3) Getting answers to questions; (4) Connecting people to people; and (5) Performing transactions (Curioso et al, 2011).

Sending information to patients

SMS can be used to send information to patients and general public and it is considered the simplest way to use SMS (Fogg & Allen, 2009). Patients could receive messages from an institution such as a health care organization, clinic, hospital, university, etc. Patients do not need to respond necessarily to the messages. They can just read the text they receive. Three specific applications are described below.

First, SMS can be used for educating patients about sexual health. For example, the San Francisco Department of Public Health currently uses SMS to promote sexual health by sending messages about HIV and STI to adolescents (Dobkin et al, 2007). Mobile devices displaying soap opera videos could be used also to reduce young urban women's HIV sex risk (Jones, 2008).

Second, SMS can be used to notify patients and their relatives. In this case, an institution sends messages whenever is needed, not on schedule. These messages may contain urgent information, such as a critical laboratory result. However, the notifications do not need to be urgent. For

example, cell phones can be used for partner notification. In Australia, a website allows patients diagnosed with an STI to send an SMS or e-mail to partners who may have been exposed (Lim, 2008). Regarding provision of test results, SMS sent to patients with Chlamydia trachomatis infection in a health clinic resulted in a decreased time to treatment of the infection (Menon-Johansson et al., 2006).

Third, mobile phones can be used to send reminders. In this case, the person receives a text message on his/her mobile phone without any need to reply. The reminder could be about remembering to take antiretroviral therapy (ART) each morning (with the aim of increasing antiretroviral adherence). For example, Puccio and colleagues developed a pilot program in California including eight HIV-infected adolescents and young adults (half of them were Latinos) who were either beginning an ART regimen for the first time or transitioning to a new ART regimen (Puccio et al., 2006). Patients received phone calls reminders to improve adherence for 12 weeks. The authors found that cell phone reminders to assist adolescents adherence with HIV medications were practical and acceptable to pilot study participants.

In a 2008 systematic review conducted by Wise and Operario, four out of eight studies showed that patient adherence to ART was significantly improved with the use of electronic reminders as a stand-alone adherence strategy, but data on the improvement of virological or immunological outcomes were not clear (Wise & Operario, 2008).

By April 2012, three randomized controlled trials (RCT) conducted in developing countries have been published on mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. Two RCT were from Kenya and (Pop-Eleches et al, 2011; Lester et al, 2010) one from Brazil (da Costa et al, 2012).

The first RCT was reported by Pop-Eleches et al. with 431 Kenyan adults patients randomly assigned to a control group or one of the four intervention groups. Participants in the intervention groups received SMS reminders that were either short or long and sent at a daily or weekly frequency. The authors found that long weekly text-messaging was not significantly associated with a lower risk of non-adherence compared to standard care (RR 0.79, 95% CI 0.60 to 1.04). Patients receiving weekly text-messages of any length were at lower risk of non-adherence at 48 weeks than were patients receiving daily messages of any length (RR 0.79, 95% CI 0.64 to 0.99). There were no significant differences between weekly text-messaging of any length and between

short or long messaging at either interval. Compared to standard care, any daily text-messaging, whether short or long, did not reduce the risk for non-adherence (Pop-Eleches et al, 2011).

The second RCT was reported by Lester et al. in which 538 Kenyan patients were randomized to an SMS intervention or to standard care (Lester et al, 2010). Text messaging was associated with a lower risk of non-adherence at 12 months (RR 0.77, 95% CI 0.63 to 0.93) and with the non-occurrence of virologic failure at 12 months (RR 0.83, 95% CI 0.69 to 0.99).

Besides the fact that both studies were conducted in Kenya and patients in the intervention arm received messages delivered via SMS, the studies differed in important ways in the manner in which the messages were deployed (Thirumurthy & Lester, 2012). The study by Lester et al. featured weekly two-way interactive communication: once a week patients received a text message enquiring about their health and could reply and seek advice from health-care providers. In the end, patients in the intervention group had adhered to treatment better than those in the control group, who did not receive any messages. The study by Pop-Eleches et al. featured one-way communication; a text message reminding the patient to take the medication was received weekly in one group and daily in the other. Antiretroviral adherence was significantly higher among patients who received a weekly message than among those who received a daily message. This finding suggests that adherence was influenced by supportive factors in the messages that were more intrinsic to the communication than simple daily reminders (Thirumurthy & Lester, 2012).

The third RCT was reported by da Costa et al. with 21 HIV-infected Brazilian women. Eight participants in the intervention group received SMS messages 30 minutes before their last scheduled time for a dose of medicine during the day (da Costa et al, 2012). The authors found that 11 participants (84.62%) remained compliant in the control group (adherence exceeding 95%), whereas all 8 participants in the intervention group (100%) remained complaint. Participants in the intervention group believed that the SMS messages aided them in treatment adherence and 10 (90.9%) responded that they would like to continue receiving SMS messages. Therefore, high-quality evidence from the two Kenyan RCT suggest that mobile phone text-messaging is efficacious in enhancing adherence to ART, comparing to standard care. In addition, high quality evidence from the Lester trial suggests that weekly mobile phone text-

messaging is efficacious in improving HIV viral load suppression. However, none of those three trials included a theory of behavior change. Theory provides a framework guiding the selection of intervention components from a huge array of what might work, it guides the choice of study design and samples, and it helps select appropriate outcomes for measuring the effects of the intervention (Pingree et al, 2010). As electronic health development and testing proceeds, having an explicit theoretic model also provides a clear framework for correction and adaptation of one's intervention (Pingree et al, 2010).

Reminders to take antiretrovirals have been found to be effective, but also appointment reminders have been found to be effective, reducing nonattendance to health clinics. Dyer and colleagues (2003) found that missed appointments decreased by 8% when SMS reminders were implemented in a London sexual health clinic (Dyer, 2003). A study conducted in Australia with outpatient clinics found that patients reminded of their appointment by SMS were significantly less likely to miss an appointment than a control group (Downer et al, 2005). In a study conducted at John Hunter Clinic for Sexual Health in London, Price et al. showed that the use of text appointment reminders to increase utilization of clinic resources was efficient, cost-effective, and acceptable to patients (Price et al., 2009).

Future research on electronic reminders may include the development of software packages designed to support, educate, and remind patients about their treatment regimens. New advances in technological development could transform text reminders into multimedia messages that include realistic images of the medication to be taken (or other preferred images), support messages, and interactive elements.

Gathering information from health personnel and patients

Two technologies are readily available for automated data collection on standard mobile phones: interactive voice response (IVR) and short text messages (Haberer et al, 2010). IVR uses recorded voice messages to collect information through voice or keypad inputs and has been used in the research context for the collection of health-related behaviors, such as alcohol use and condom use, in developed countries (Schroder & Johnson, 2009; Schroder et al, 2007; Perrine et al, 1995; Barta et al, 2007).

Cell PREVEN is an example of a pilot data collection project within a large randomized trial of 20 cities called PREVEN, which sought to lower STI rates in Peru (Curioso et al, 2005). Cell

phones were exclusively used to report adverse events to metronidazole treatment among sexual workers. Health workers reported in real time to the system via IVR. If an adverse event was reported, the central system sent e-mail and SMS alerts to the researchers. Skinner et al. from the Cell Life project found that cell phones made the recording of data very efficient, saving time, reducing the risk of losing patient notes and reducing potential breaks in confidentiality (Skinner, et al., 2007).

Other mobile devices such as PDAs are frequently used for data collection. For example, Colecta Palm was a pilot project that involved the use of PDAs to enhance adherence to antiretroviral treatment and to support safer sex and HIV transmission risk reduction for people living with HIV/AIDS (Curioso et al., 2008). The pilot showed that PDAs could be a culturally appropriate way to approach and support PLWHA in Lima. In addition, low-cost PDAs have been used to collect sensitive sexual behavior data in Peru from young men and women, within the PREVEN study mentioned above, with very high acceptability (Bernabe-Ortiz et al., 2008). Additional promising open-source platforms could be used to develop data collection tools for mobile devices.

Finally, people can send SMS to keep a personal journal related to their health behavior. For example, a person can keep track of his/her diet by texting the number of calories consumed or the steps walked each day if the person is monitoring his/her exercise patterns. Diary entries, or active requests, via SMS have worked well in motivated and self-efficacious patients because mobile phones are a part of people's everyday lives (Anhoj & Moldrup, 2004). A mobile phone-based service would allow a health provider instantly to view which clients are creating daily entries (Mapham, 2008). This would act as a screening device, by revealing which patients are motivated and allowing for more time and effort to be spent on the less motivated patients. One of the disadvantages of this feature is that it is mainly designed for individual use, not for large-scale data analysis by health organizations.

Getting answers to questions

People can ask questions related to health using texting. When they get a response, they receive an answer from a database. One of the advantages of this feature is convenience. Sometimes the phrasing of the messages needs to be changed so that users are more likely to continue using the system. Services need to be in touch with the community they serve in order to create services

that are spread via social networks and recommendations from friends. SexInfoSF, based in San Francisco, uses social marketing to advertise an SMS-based risk assessment for STI (Levine et al., 2007). For example, if your condom broke and you don't know what to do, you can text "sexinfo 1" to 61827 in San Francisco, then the service SexInfoSF.org23 gives you the following information: "U may b at risk 4 STDs + pregnancy S.E.Clinic, Keith at ArmstrongSt, 415-671-7000 M-F9-5, W8-12, City Clinic 356 7th St 415-487-5500 MWF 8-4 TuTh -4."

Another advantage is privacy (or perception of privacy), because the person can request the information without being noticed. One of the main disadvantages is the 160-character limitation of SMS. This issue could be frustrating because people may not receive enough information or even the correct information. Another potential limitation is that the patient might need to know in advance the phrasing of the question they hope to receive an answer to (or be able to select it from a list of options).

Getting Answers from a Real Person

People can send a sexual health question using SMS and receive an answer back from a real person (e.g., a doctor or a nurse), not a computer. In this case, a doctor or a nurse may give more appropriate answers than a computer. One of the advantages is that organizations such as hospitals or clinics can set up specific days for this kind of services. One of the considerations is to adequately train health personnel on how to use SMS. Health personnel might even use regular computers connected to the Internet to send and receive the incoming questions. As one of the counselors in the Cell-Life project (Skinner et al., 2007) mentioned: "The cell phones have made a big difference, as it's easy to reach a client and they can phone me anytime if they have problems." One of the main disadvantages is the cost involved in the operation of the system by health personnel. In addition, privacy and confidentiality issues need to be carefully addressed.

Connecting people to people

Social networks are very popular nowadays. For an effective provision of care for chronic conditions, including HIV, it is necessary to engage the patient and the community which supports him or her (McCann, 1990). Two specific uses follow below.

Physicians and patients can interact via texting. In fact, text messaging is an easy and, many times, a convenient way of allowing patients to keep in touch. Doctors can improve

communication with patients using SMS (Pal, 2003). For example, patients could report adverse events to their doctors using text messages. In addition, peer educators can stay connected with HIV patients and friends can support friends.

Text messaging supports one-to-one conversations as well as many-to-many discussion (Fogg & Allen, 2009). One of the best examples is Twitter, which was launched in 2007. Group support has long been an important strategy in changing health behavior, and now increasingly SMS facilitates group interactions. In fact, support groups, discussion threads, and collective action are now all possible using regular phones and text messaging.

Project Zumbido in Mexico aims to record the usage patterns and evaluate whether a system using mobile phones with unlimited text messaging helps to increase the level of social support experienced by HIV positive patients of an antiretroviral clinic (MobileActive.org, 2012).

Performing transactions

Getting things done is an emerging use of texting. Short text messages have been used for appointment reminders that aim to reduce missed appointments (Car et al., 2008). Text messages, among other communication channels, have the advantage of instant transmission, low cost, smaller chance of being misplaced (compared with postal reminders) and also intrude less on daily life (compared with phone calls). There are peer-reviewed studies of the impact of text message reminders on missed appointments. Kunutsor et al. reminded patients living with HIV/AIDS in Uganda about their missed clinic appointments via voice calls or text messages. Privacy and confidentiality were some reasons why patients preferred to be contacted by SMS text messaging (Kunutsor et al., 2010).

Privacy, security, and confidentiality issues and mobile health

Three key issues related to the use of cell phones for health care are health data privacy, security, and confidentiality. Indeed, these issues are applicable to every stage of the use of cell phones for health care, including capturing personal health-related data from a cell phone, uploading it to a server, transmitting it to a web-based or other form of electronic personal record or medical record, using the data for interpretation and professional judgments in the care of that individual, and responding back to the person via, for example, an SMS message. Another concern is that while a cell phone might be used predominately by a specific person, it may occasionally be

shared or left unlocked in a purse, on the table at home, or on the desk at work (Patrick et al., 2008).

Conclusion

Mobile phones are playing an important role in supporting health interventions both in developed and developing countries. A wide range of cell-phone based technologies are being used for the prevention and control of HIV and STI. In this chapter, I described several uses of cell phones for health interventions, focusing on text messaging to support HIV and STI prevention and care. Data from three randomized controlled trials suggest that mobile phone text-messaging is efficacious in enhancing adherence to ART, comparing to standard care. However, large randomized controlled trials of this intervention are urgently needed. Research in the field of mobile health is currently largely lacking in Latin America.

In addition, none of those three trials included a theory of behavior change (see Chapter 1). Theory provides a framework guiding the selection of intervention components from a huge array of what might work, it guides the choice of study design and samples, and it helps select appropriate outcomes for measuring the effects of the intervention (Pingree et al., 2010). As electronic health development and testing proceeds, having an explicit theoretic model also provides a clear framework for correction and adaptation of one's intervention (Pingree et al., 2010).

Cell phones have become ubiquitous even in resource-constrained settings; thus, more research in their use for the prevention, control and treatment of HIV and STI in those settings needs to be conducted. Integrating those devices into our daily lives, mobile phones can produce a huge effect in the quality of lives of people.

Chapter 4. Designing Cell POS

Introduction

As I highlighted in Chapter 2, people living with HIV face many challenges with medication adherence. One of the barriers mostly cited by patients, as described in this dissertation, is "simply forgetting." This barrier could be addressed by implementing a simple and non-expensive technology strategy, such as text messaging using cell phones. As described in Chapter 3, cell phones have been successfully used to support patient medication adherence in developed countries and in resource-constrained settings such as Kenya.

In Peru, cell phones could be used to improve antiretroviral adherence in HIV patients because those devices could be private, interactive, efficient, affordable, convenient, and useful reminder tools. Although cell phones are common in Peru, it is important to explore whether this technology will be acceptable and useful by the end users. In addition, it is critical to explore perceptions among people living with HIV towards information and communication technologies. If we don't explore carefully the perceptions, we might be implementing a technology that might not be cultural appropriate or perceived as useful by end users.

This chapter has two objectives: the first part reports on information and communication technology perceptions as a means for health promotion to support treatment adherence among people living with HIV in Peru; and the second part describe the process for designing that was used to develop **Cell POS**, that is intended to fill the gap of medication adherence.

I developed **Cell POS** using an iterative user-centered design process. An initial prototype was designed based on a literature review and qualitative work. To refine the functional requirements for the system, I then conducted four focus groups with people living with HIV/AIDS. Based on the results from the focus groups, **Cell POS** was redesigned and implemented as a SMS-based cell phone application with a web-based component.

Perceptions regarding cell phones as a means for health promotion for people living with HIV/AIDS in Peru

To assess perceptions regarding cell phones as means for health promotion for people living with HIV/AIDS in Peru, we conducted formative research using in-depth interviews with adult HIV-positive people receiving ART and clinical services at two community-based clinics (Impacta, and Via Libre) in Lima, Peru (Curioso & Kurth, 2007). Both of these clinics primarily serve male clients (100% at Impacta, approximately 80% at Via Libre).

A qualitative interview topic guide was developed based on a published article by Flicker et al., and an instrument previously used among HIV-positive individuals (Flicker et al., 2004; Kurth et al., 2005). HIV consultants in Lima reviewed the guide to determine its face validity and cultural relevance. Topics covered in the guide pertaining specifically to cell phones are described as follow:

Cell phones topic guide

How do adult HIV-positive people use cell phones?

• Do you ever use cell phones? What for? Frequency?

• Do you ever text messaging (Send/receive)?

• Do you ever use the alarm function of your cell phone? Are you currently? For what?

• If we were going to develop an application for people living with HIV in Peru using cell phones – what sort of things do you would like to see? e.g., automatic reminders, prevention messages. Any preference of using your own cell phone? or a new one?

Inclusion criteria were HIV-positive persons, older than 18 years and receiving ART. Sampling was performed by convenience in two clinics. Participants were demographically similar to those receiving care in both clinics.

Respondents spent approximately one hour for the in-depth interview conducted by an experienced and trained psychologist in each of the clinics (Impacta and Via Libre). After giving consent, all interviews were conducted in Spanish in a private room, and were tape-recorded. Audio files were transcribed and transcripts were reviewed by myself for initial text element and key word coding; these codes and categorizations were then reviewed by a second investigator of my research group (Ann Kurth) for final consensus. Data were entered into Atlas.ti qualitative

software for theme identification using a content analysis approach (Pope et al., 2000). This analysis was intended to understand the information needs, motivations, and behaviors of people living with HIV on ART in Lima (Fisher et al., 2006).

This project and the topic guide used in this study had ethical approval from the University of Washington Human Subjects Division and the institutional review boards of Via Libre and Impacta. All participants signed an informed consent prior to enter to the study. Participants were compensated with 30 soles (about 10 dollars) for travel expenses.

Results

During March–August 2006, 31 people living with HIV were interviewed, 16 at Via Libre Clinic and 15 at Impacta Clinic. Of those people interviewed and currently taking ARV, 24 (77%) were using cell phones at the time of the interview. Some of these, 7/31 (23%), already were using the alarms on their cell phones to remind themselves to take their HIV medication. Two participants (6%) reported using their cell phones to send and receive text messages for connecting with others for social and for sexual purposes. **Table 4.1** provides main themes and representative verbatim quotes from individuals regarding the perceived advantages and disadvantages of cell phones.

Table 4.1. Representative quotes from people living with HIV regarding cell phones

Quotes of people having positive experiences	
As reminder device for medication & safer sex	"Using my cell phone is like having another arm. I always use the alarm function of mine [cell phone] to wake up in the mornings and I use it as a reminder [to take my pills]." Male, 39 years old
	"I use the alarm function to take my medicines. I use my cell phone to send and receive SMS. I think cell phones are good because you have an agenda, an alarm, etc." Male, 29 years old
	"I think it's important [to use cell phones to receive prevention messages] because you can be updated and be prevented." Male, 48 years old
	"It has to get to you. Definitively. Even by chance, you always open your SMS messages, even by chance. And you might find something. You have to be obstinate; you have to be very incisive when you leave your clear message. For example: How is going everything? Did you take care of yourself" Did you use

	your condoms today? It looks like offensive or pushing, but it is a way to attack directly the problem and that people can listen to you. I'd prefer an SMS, and it should be incisive, rather than a pre-recorded voice message." Male, 34 years old
Confidentiality	"For me using cell phones is confidential. I don't give my cell phone to anybody." Male, 39 years old
Quotes of people having negative experiences	
As reminder device for medication & safer sex	"I don't use the alarm function of the cell. I [always] remember to take my medicines. I'd not like to use a cell phone with a recorded voice as reminder. I will not like it. To hear 'you have to take it', no no no; I will feel like a baby." Female, 38 years old
	"I used to use the alarm function of the cell phone at the beginning. Using cell phones as reminders is a good idea. Using cell phones to receive HIV prevention and information messages is a good idea too but up until certain limit because it might be uncomfortable...you know... you are not just living for getting information on HIV... you are doing other things." Male, 35 years
	"It could be useful but mainly for [ART-] naïve patients. For me, it will not work. Now, I automatically know the time of my medication; but it could be certainly useful for naïve patients." Male, 38 years old
Technological features of cell phone (confidentiality concerns)	"The problem with cell phones might be with the confidentiality." Male, 34 years old
	"I HATE cell phones. Lots of people offered me, even for free. I think cell phones ruin your privacy. I NEVER had a cell phone. I think I am the only one that doesn't have a cell phone in my group of friends." Male MSM, 36 years

Most of those interviewed, 23/31 (74%), reported their willingness to use cell phones to receive reminder messages for their HIV medication, either by a pre-recorded voice 17/23 (74% of those willing) or by use of short-text messaging, 17/23 (74% of those willing). Not everyone felt the sustained need for using alarm reminders, after learning how to integrate medication-taking into their lives, but saw that this might be useful for ART-naïve patients particularly.

The majority, 25/31 (81%), expressed their interest in receiving messages about their sexual health over the phone, including information about sexually transmitted infections (STIs). Of

those, 22/25 (88%) would prefer sexual health messages via text-messaging and 17/25 (68%) via calls with a pre-recorded voice. Furthermore, many said they would like to receive general HIV information via cell phones, including advances in HIV treatment and recent research ("Everything on STDs and HIV/AIDS"). Participants underscored the need for up-to-date information.

In general, people perceived that cell phones were confidential, though some voiced concerns about privacy. Most people said they would prefer to use their own cell phones rather than a new one that might be provided by a research study or a health agency.

Discussion

Many individuals living with HIV in Peru already use or are open to using cell phones that might support intervention delivery for HIV treatment adherence. Clear advantages were seen to using these devices, among them greater confidentiality as compared to face-to-face interactions (which was mentioned as a plus by 7 out of 30 participants, as opposed to 3/30 who raised concerns about privacy related to use of these tools).

Our study population perceived that HIV information is important to their health (Curioso & Kurth, 2007). Similar results were found in HIV-positive African American and Puerto Rican men who felt that HIV information is vital to their health yet is not readily available in minority communities (Siegel & Raveis, 1997). In Peru, Internet access is widely available through public centers such as Internet cafes (cabinas publicas) – small-scale storefront operations that offer low-cost and reliable connections (Curioso et al., 2007).

There is great potential to improve health through the use of information and communication technologies in developing countries. The study described in this chapter is the first one to our knowledge that examined perceptions regarding cell phones as a means for health promotion for people living with HIV in Peru. However, the study was limited by its use of a convenience sample of people living with HIV/AIDS in an urban population of Lima. The participants in this study cannot be considered representative of people living with HIV/AIDS in Peru. We also assessed cell-phone use by self-report.

Conclusion

This qualitative study suggested that cell phones in particular are useful and culturally-relevant as a way to support medication adherence among persons living with HIV in Lima. Most participants showed enthusiasm for the potential impact of cell phone interventions using voice-recorded reminders and SMS texting as a way to deliver behavioral messages, and most participants expressed interest in participating in such an intervention. Other advantages of cell-phone delivered behavioral support include the fact that in many resource-constrained settings, cell phone communication infrastructure already is in place at a population-level scale, and thus would not need to be built separately to support persons with HIV (or potentially, other chronic diseases). Based on these encouraging data, our research team devoted to develop the framework for a cell-phone based delivered HIV intervention in Lima. The qualitative data we reported here is useful to decide which user-centered information is pertinent and culturally-relevant for people living with HIV/AIDS in resource-constrained settings.

Chapter 5. Cell POS. A computer-based system using cell phones and the Internet

Introduction

Cell-POS is a computer-based system that uses mobile cell phones and the Internet to deliver HIV-related educational messages, medication and clinic appointment reminders via SMS text messages. The objective of Cell POS is to enhance adherence to ARV, and it is intended to address specific needs and preferences of patients for HIV care and information related to ARV. The research team devoted to Cell POS is a multidisciplinary team of professionals at the Universidad Peruana Cayetano Heredia in Lima, the University of Washington in Seattle, with participation of Via Libre, the Hospital Nacional Cayetano Heredia: and with the partnership of Voxiva Inc, a telecommunications company.

This section describes the development process of the initial prototype of Cell POS. An important element is the process of designing the message to be included in the SMS, which is described here.

How should we remind patients to take medicines using short text messages?

A 2008 systematic review on the use of electronic reminder devices to improve adherence to ARV concluded that there is insufficient evidence supporting the effectiveness of electronic reminders (including via cell phones and pagers) as strategies for improving patient adherence to ARV (Wise & Operario, 2008). A potential limitation of the existing published data is that they overlook the key role of the reminder message. The data are limited by a lack of understanding how patients process such messages in a healthcare setting and how that processing influences their decision-making (Walki & Zhang, 2008).

Several researchers have proposed various characteristics of effective reminders. Don Norman (1988) suggests that all reminders have two essential aspects: the signal or notification modality (that there is something to remember) and the message (what to remember). In addition, an

effective reminder should also have the capability to assess the right context to judge the best moment for reminding (Dey & Abowd, 2000).

These characteristics of messages have the potential to be effectively implemented and leveraged using mobile devices such as cell phones. Context-aware mobile devices are an emerging research area that can address reminders not only from the technological point of view, but also research related to human-computer interaction and privacy issues. Currently there is not a comprehensive list of recommendations for reminder messages targeted to improve adherence for people living with HIV/AIDS.

The objective of this section is to characterize effective ART reminder strategies for PLWHA in Lima, Peru using SMS based on patient perspectives. As I highlighted in Chapter 3, SMS is a potentially powerful tool that meets many of the criteria to be effective reminders, including providing a signal and a message. The study setting provides an excellent opportunity to utilize SMS because of the high penetration of cell phones in Peru. A better understanding of message processing and an exploration of the factors that affect acceptance of such request may help improve adherence of interventions aimed at those patients.

Methods

Participants were recruited at a community-based clinic (Via Libre) in Lima, Peru that serves mostly HIV-positive individuals. Four focus groups were conducted at the clinic. Three of the focus groups were conducted exclusively with males and one group exclusively with females. The rationale for the distribution of focus groups was discussed with the research team and staff at the clinic. We tried to represent a range of subgroups: two groups with only men that have sex with men, one group with heterosexual men, and one exclusive with women. Our decision was guided by previous HIV-related studies with similar methodology (Atuyambe, 2008). Findings presented in this section are based on data drawn from a study of an HIV-intervention based on cell phones conducted by a multidisciplinary research group, and includes: Robinson Cabello, Alex Quistberg, Ernesto Gozzer, Patricia J. Garcia, King K. Holmes, Ann E Kurth, and Wanda Pratt.

Individuals were recruited using flyers and purposive sampling and were required to be HIV-positive adults receiving ARV who owned a cell phone. Eighty-three patients were invited to participate in the study and 56 consented to determining their eligibility. Seven of those

consented were not receiving ARV and four did not own a cell phone and thus were ineligible. Those eligible were invited to attend one of the four focus groups and were offered 30 Peruvian nuevos soles (about $10 US dollars) and a light meal for participating. Of the 45 individuals scheduled for a focus group, 26 (58%) actually attended.

The focus group guide was adapted from previous formative work to specifically assess culturally-appropriate reminder messages (Curioso & Kurth, 2007). HIV consultants in Lima reviewed the topic guide to determine the content validity. The groups were conducted in Spanish at the community clinic by a professionally trained moderator with experience in formative research and co-moderated by myself. The groups lasted about one to one and a half hours, were digitally recorded, and a research assistant took notes.

The group sessions were transcribed by the research staff and reviewed by myself. Data were entered into Atlas.ti version 5.2 qualitative data management software (Scientific Software Development, Berlin, Germany). A Spanish-speaking researcher (Alex Quistberg) and myself coded transcripts independently using a content analysis approach. After coding each group the researchers discussed codes and came to an agreement on the final coding. A list of codes was created based on the first two groups and then applied to the other two groups. Based on the number of shared themes between groups, we estimate that we reached a saturation of themes of at least 80%. The inter-rater reliability between the coders had a Kappa of 0.8289 (standard error= 0.0903, $P<0.0005$). Summaries were compared and discussed until a consensus was reached on which themes were most salient to participants. We then reviewed the transcripts to confirm our findings and identified quotes that best illustrated common themes. Quotes were translated and edited for ease of reading, but were not substantially altered. The institutional review boards of the University of Washington, Universidad Peruana Cayetano Heredia, and Via Libre approved the study. All participants signed an informed consent previous to the participation to the study.

Results

Demographics

During March–April 2008, 26 PLWHA (20 male, 6 female; mean age=37 years, SD:8.5) participated in focus groups at the Via Libre Clinic. All participants (12 heterosexual, 14 gay) were on ARV at the time of recruitment and participation. Most of them (88%) had completed

high school. The majority of participants were frequent users of the Internet and cell phones (including SMS).

Signal-Related Features

The participants preferred text messages over recorded voice messages or phone calls as reminder alerts because they are easier, more confidential, and more readily-available ("I think that a text message would be better because you are sometimes in the car and the recorded message does not play well or you cannot hear it very well…a text message could be read quickly and it reminds you"). One participant pointed out also that "I do not know how to retrieve the voice messages…so, it's easier to read a text message."

Message-Related Features

Perceptions towards reminder messages

Overall participants were in favor of receiving medication reminders on their cell phones ("I believe that [the reminder alert system] is important because sometimes…when you are feeling better, or at work, or due to any other reason…you forget to take your medicines … so, having somebody to remind you is very important").

Characteristics of reminder messages

The most preferred characteristic for the reminders was that they be motivational (e.g., "Remember, it is time for your life"). One participant felt these types of messages were important because "we experience sadness, happiness, and if I receive this message (reminder)…somebody cares about me! This encourages me to move ahead." Another participant also pointed out that receiving motivational reminder could help to assuage feelings of loneliness ("I practically do not have anybody…I sometimes feel a bit depressed"). At least one participant, though, felt that motivational type reminders could be overly dramatic ("My life has so many, so many sides that I would not like the reminder alerts to be so dramatic..."). Other characteristics that the participants thought were important include conciseness ("The reminder could be short, direct"), simple ("I believe that the message should be something

simple"), and shareable ("We sometimes receive messages that we share with friends, relatives, coworkers or with anyone").

Some participants felt that it would also be important to have reminders that had a spiritual tone ("Though I am not a believer, receiving a message like 'Thank God for the time of your life' meets our needs very well. First, it reminds you, and, second, it is completely confidential").

Context-Related Features

Frequency of change

Most of the participants thought it would be a good idea to change the messages with some frequency in to prevent monotony and boredom with them ("You should change the message…because it might become monotonous otherwise…it's the same as how I tire of taking my pills every day"). Some suggested that the messages should change weekly and others preferred daily. Changing the messages frequently was also suggested because "people may be under different kinds of mood, so the messages should be different."

Anthropomorphic features

The participants often anthropomorphized the system with human characteristics such as thinking of it as a "friend," a "guide" or even an "angel." Along with these characteristics was the idea of establishing a long-term relationship with the system. One of the participants mentioned: "I like the idea (of a reminder alert system) … enough that receiving a message via cell phone is not emotionless, it is something that reminds you of something very important. I think it is excellent."

Confidentiality and privacy issues

Keeping the medication reminders confidential was the most important concern that many, though not all, participants expressed. They did not want "sensitive" words (e.g. 'HIV', antiretroviral, etc.) related to HIV included in the system. A suggested alternative to "sensitive" words was using code words or phrases so that only the participants will know what the reminder refers to ("The [message] should be a little more discreet…for example, 'It is time for your candy,' something simple but you know what it is"). A couple of participants also suggested erasing the reminder after receiving it.

Discussion

Our participatory design approach gave us many insights about key, culturally specific issues in the development of reminder messages for ART adherence using SMS among PLWHA in Lima, Peru.

First, we found it very interesting that our participants preferred receiving a readable message rather than a phone call or a pre-recorded voice message. This preference relates to the literature on calm technologies. Weiser and Brown in the book "The Coming age of Calm Technology" proposed that when computing becomes integrated into our lives there are design issues that should be taken into account (Weiser & Brown, 1998). They coined the term "calm technology" meaning that the technology should help us in our daily life, but not demand our attention – it should be invisible in a way. In their theory of calm technology, Weiser and Brown differentiate between the centre and the periphery (of our attention). The calm technology should move easily forth and back between the two because the periphery should be informing without overburdening and we should be able to take control of a matter, when it is necessary. This implies that we might gain a larger degree of control of our periphery, which in turn will calm us. Therefore, calm technology is about your technology serving you in the periphery, so it doesn't require your full attention unless necessary, and then calmly fading into the periphery again.

In this context, text messages are less obtrusive and interrupting than receiving a phone call. They have the advantage of being easily used in a variety of daily activities. Mobile devices that allow patients to receive and send messages also have several attributes that make them very attractive to healthcare providers and researchers, including always being on and with the patients, inexpensive, the potential for surveillance, and geographical positioning. Overall, mobile technologies have the potential to affect behavior change by enabling access to information and communication in novel ways.

The fact that the participants preferred informative and motivational reminder messages reveals that they are interested in not only receiving a reminder, but also something that lifts their self-esteem and gives them encouragement. Previous studies have shown that automated, telephone-based interventions emphasizing social cognitive concepts (e.g. motivation, self-efficacy) have demonstrated shorthand longer-term efficacy.

The participants mentioned some important context-related issues. We found confidentiality issues were very important to most participants. Confidentiality has been found as a very important issue in similar HIV-related mobile phone interventions (Lester et al., 2006). Some of the participants were very concerned about the wording of the messages. The fears they shared with us about confidentiality are likely related to social issues such as empowerment, stigma towards those with HIV/AIDS, and discrimination; the same issues we have found in a previous study (Curioso et al., 2008). An intervention in London to remind teenagers to take their contraceptive pill provided text messages in code to retain confidentiality (Hale, 2004).

Another interesting finding of this study was the use of anthropomorphic characteristics to describe the cell phone system that sends the messages. The anthropomorphization of inanimate objects is a common habit in our everyday lives and has been fairly well studied in human-computer interactions.

We found that the subjects would like to experience the cell phone reminder system as a friend. The portability of "always ready" devices in combination with the messaging interventions can create a synergistic feedback loop between patient and device as evidenced by Milch's finding that "several of the patients allowed that the pager became a trusted friend." The successful mobile interaction through messages should promote an intensive, positive relationship between the user and the mobile application, like a longstanding and comfortable friendship. This is an important feature that should be investigated in future research studies.

An important limitation of our study is its applicability to the general population because our study population was limited to a convenience sample of PLWHA in urban population of Lima. The participants in this study cannot be considered representative of PLWHA throughout Peru or elsewhere. This limitation is somewhat balanced in that we are confident that we reached saturation as many of the responses were similar among participants. Also, the age characteristics of our population are very similar to the national profile of adult PLWHA on ARV in Peru. Another bias to consider is the potential for giving socially desirable responses in focus group settings, though we found that while the participants were ready to agree on many topics, they also strongly disagreed on a number of topics. We believe that many of the ideas and themes we heard during these groups are applicable in other settings, and would encourage other researchers to explore this subject and to tailor our findings to the needs and preferences of the populations they study.

Based on previous research and our findings, our recommendations for designing and using SMS reminders for ART adherence are:

- Use only reminders that have been carefully crafted to ensure credibility, to maintain calmness, and to appropriately ensure privacy and confidentiality.
- Messages should be worded such that the intended content of the message is conveyed clearly to the user because text-only messages lack the intonation and expression of cues that would normally assist in interpreting such information.
- Formulate messages that minimize ambiguity.
- Recommend that users delete the reminder after reading it.
- Messages should be tested with a small group of the target population to ensure acceptability before widespread implementation and use.

In addition to these suggestions, we would also encourage healthcare providers and researchers to consider Fogg's Principles of Mobile Persuasion for the use of mobile technologies for encouraging behavior change. These include sending messages at the right moment, delivering relevant and current information.

Our focus groups allowed us to develop messages that can potentially meet the needs of our target population. In addition, our focus groups gave us important evidence not only for an intervention study, but also for other researchers that want to implement such a system in the developing world or in other settings.

In addition, I explored design preferences and characteristics of a website for monitoring HIV medication adherence. In the next section, I will describe the results of the qualitative evaluation conducted with people living with HIV/AIDS.

Design preferences and characteristics of a website for monitoring HIV medication adherence in Peru

The development of several websites facilitating care and support for PLWHA has been documented in the literature. However, very few studies involved PLWHA in either the creation or evaluation of website design. In a study conducted by Gomez et al., website users, patients,

and clinical experts emphasized the importance of numerous website features including anonymity and security in accessing and using the website, having a very easy-to-use interface, and allowing communication between PLWHA and care providers. No other research has examined the preferences of PLWHA in regards to the design of websites to support their care and such research has not previously been conducted in Peru.

The objective of this section is to document design preferences and characteristics of a website monitoring the HIV medication adherence of people living with HIV/AIDS. The website mainly serves as a support of the cell phone-based adherence intervention using SMS (Cell POS) and will include features such as a survey about prevention and medication adherence and information about HIV/AIDS.

Methods used in this section are the same as the one used in the previous section.

Web-based Prototypes

Computer prototypes were used to evaluate various aspects of the website (Cell-POS) in all focus groups. The initial prototype was created in HTML (Figure 5.1). The groups lasted about one to one and a half hours, were digitally recorded, and a research assistant took notes during each session.

Design results

Display and Appearance

Participants expressed either a preference for a simple combination of certain colors or commented that color was not of major importance for the website:

"[The page] should have a combination of colors…but red kind of gives the page the color of blood. It could be green, or maybe a light green…use a mix because creating a webpage has rules too, doesn't it?...Sometimes they put too many colors everywhere and they might confuse the user."

"In my opinion, the color or the length of the text doesn't really matter. The most important thing is the content."

User Interface

The focus group participants expressed a preference for having all of the questions of a survey appear on a single web-page instead of pressing a "Continue" button to go from one question to the next:

"All of the questions should be in one block."

"Yes, it's good like that, because pressing Continue, Continue…that has happened to me many times…and sometimes, from my perspective, it's tiring to be pressing Continue and in the next page Continue, Continue."

One participant suggested that the ability to save an incomplete survey to complete later would also make the webpage easier to use:

"It would be good if the system let you save the survey [as you complete it]. For example, if somebody interrupts me and I cannot complete the survey, I can save it and continue later. "

If the survey were long, participants suggested including a progress bar. Another participant offered that "the website should be interactive as any webpage."

Animated characters

Participants supported the idea of displaying an animated pet or character on the website to motivate them. However, there was disagreement as to what form the pet or character should take; a dog, a chicken, a pill, and even a tooth were all proposed. Other ideas representative of these discussions were as follows:

"It should be a little animated character. An animated character would be nice - more than a pet, a funny character be-cause we already know the little dog, the cat, and Merlin from Windows©. We already know the robot, the ball, and all of that well enough. Create a little character, an animated character."

"[It should be a pet] because people are too cold."

Personalization

Participants also welcomed the idea that their name would appear upon entry into the website.

"If we have our own login and password, then it's OK if the system welcomes us by displaying our name."

Incentives for Participants

Participants were asked to provide ideas for incentives to keep them motivated to continue participation in the study (which required completing periodic surveys) over the span of several months. Participants did not bring up the issue of financial incentives of any kind during the discussions; instead, participants suggested creating several web features including a blog or a chat group:

"If the issue is to hook us [into the study], it would be great to create something like a 'chat group' to be able to keep us in-formed and for us to be able to communicate with others [in the study]."

"I think the way of connecting us (and keeping us hooked into the program) is through a blog, via the Internet, or through a forum. Being all connected…we know the news out there, we communicate to feel included. "

The limitations of website features as a motivating factor were also discussed, as some participants expressed a desire to receive follow-up calls from study staff, participate in face-to-face group meetings with other PLWHA, and receive group E-mails by subscribing to a list-serv.

Confidentiality and privacy issues

Focus group participants expressed a desire to maintain privacy by removing the reference to HIV/AIDS ("PLWHA") on the initial page of the website:

"For example, for people who work and can access webpages, there are systems that can access your screen and see what you are doing. Therefore, preferably, the initial page of the website shouldn't be so obvious [referencing HIV/AIDS]. Now, I prefer not to access the website at work because they will see [the reference to HIV/AIDS] and in a cabina it's the same. Before entering your username and password, there shouldn't be anything [referencing HIV/AIDS]."

Discussion

This section documents design preferences and characteristics of a website for PLWHA in Peru. Our approach gave us many insights about key culturally-specific issues in the development of a website to support ART adherence among PLWHA in Lima.

Privacy, security and confidentiality issues are of the utmost importance in any strategy to use the Internet in healthcare (Curioso, 2006). Consistent with other HIV research, we cannot assume privacy for PLWHA online (Bull et al., 2007). We found confidentiality issues were very

important to most participants. Some of the participants were concerned about referencing HIV/AIDS on the initial page of the website due to issues of confidentiality.

Participants also noted that the reference to HIV/AIDS in some cases limited their access to the page either at work or in a *cabina* because of fears that either their boss or another *cabina* user would see that they had accessed an HIV/AIDS-related website. Similar issues were noted in a qualitative study by Bull et al., in which participants expressed concern about mentioning sexually transmitted infections (STI) in the title of a STI prevention website (Bull et al., 2007). The fears they shared with us about confidentiality are likely related to social issues such as disempowerment, stigma towards those with HIV/AIDS, and discrimination − issues we have found in a previous study by our research group (Curioso et al., 2008). PLWHA must have confidence in the technology used in order to be confident in its security and confidentiality and not worry about being stigmatized for using it.

An interesting finding of this study was the desire to include an interactive animated agent into the system by including a motivational character as a website feature. Animated characters can enhance the user experience in several important ways, and this topic has been fairly well studied in human-computer interactions (Dehn & van Mulken, 2000; Cole et al., 2003).

In addition, social interaction using chats or blogs was mentioned by participants to keep them motivated in the study. Shelley et al. showed that PLWHA exhibit a tendency to build social relationships with others who share similar attributes such as gender, age, race, attitudes or behavior (Shelley et al., 1995). In many cases PLWHA selectively disclose their status, especially while going through an extremely difficult life-experience, and they can use the Internet to disclose their status and to build social ties with others experiencing the same condition (Mimiaga et al., 2008). This is an important issue that should be investigated in future research studies. For the purpose of this project, we did not include a social interaction component because this might affect the outcome of our adherence intervention, as this issue has been investigated in other studies (Simoni et al., 2009).

In these focus groups, no comment was made about Internet connection speed being a factor in the use of the web-based system. In general, participants could access the Internet somewhere (if not at home, then at an Internet cafe) in urban areas, and even in urban slums. This ease of Internet access was also found in previous research conducted by our group in Peru (Curioso et al., 2007). Nonetheless, Pequegnat found Internet connectivity, software requirements, and user

systems (i.e., PCs, MACs) to be possible issues affecting the ease of use of HIV web-based programs (Pequegnat et al., 2007). For longer surveys, participants suggested including a progress bar. This suggestion was also found in a review conducted by Pequegnat for HIV/STD surveys (Pequegnat et al., 2007). In addition, Bull suggested including some sort of meter on each survey page to indicate users' progress toward survey completion (Bull et al., 2007).

An important limitation of our study is its transferability to the general population because the study population was limited to a convenience sample of PLWHA in urban population of Lima. The participants in this study cannot be considered representative of PLWHA throughout Peru or elsewhere. This limitation is somewhat balanced in that we are confident that we reached saturation as many of the responses were similar among participants (Morse, 1994). Also, the age characteristics of our population are very similar to the national profile of adult PLWHA on ART in Peru (Mesones et al., 2006). Another bias to consider is the potential for giving socially desirable responses in focus group settings, though it is unclear whether web design preferences would be subject to the same social desirability bias that may affect other qualitative studies among PLWHA. We believe that many of the ideas and themes we heard during these groups are applicable in other settings, and would encourage other researchers to explore this subject and to tailor our findings to the needs and preferences of the populations they study. Other approaches such as participatory design could be used to provide greater opportunities for users to influence the website features, and could give users a greater sense of ownership which can lead more successful implementation (Waller et al., 2006). Pequegnat suggests other design considerations in Internet-based HIV surveys (Pequegnat et al., 2007). For example, to avoid high attrition, boring webpages should be avoided, and much attention should be given to integrating graphics and animation into surveys.

Based on previous research and our findings, our recommendations for the design of Internet-based systems for PLWHA, and those implemented in the Cell-POS project, are as follows:

1. Interactive animated agent. We included an animated character which appears after the participant logs into the system.

2. Privacy and confidentiality. Each user is provided with a confidential username and password to access the Cell-Pos system. There is no clear reference in the main page that the project is targeted to HIV/AIDS participants. Patient confidentiality must be protected so that PLWHA can feel secure in the online environment.

3. Easy-to-use website. All the questions for the survey are displayed in one page.

4. To protect confidentiality the website should be designed with mechanisms that ensure each page automatically expires when the user moves to another page. In addition, the participant should be given instructions on how to erase the history of the visit when logging out (Pequegnat et al., 2007). For this project, we implemented a 20-minute expiration time if the user does not use the system.

5. Security. Every communication between the web server and the web site user should occur over a connection with secure socket layer enabled. SSL is a standard cryptographic protocol for secure web communication. Using SSL, data entered by a participant is encrypted on the user's computer and then transferred to the web server (Baer et al., 2002).

Summary

This chapter presented the design process of Cell POS, a mobile phone-based system for supporting medication adherence of people living with HIV/AIDS, both in terms of the message design process and the supporting Web-based interface. The results reported in this section have created a basis to develop a dynamic, personalized and confidential messaging system that can meet the adherence needs of PLWHA in Lima, Peru. Though previous research is inconclusive regarding the use of electronic reminder devices for ARV adherence, these results indicate that the characteristics of the reminder (notification modality, the message, and the context) could play an important role in interventions to improve patient adherence to ARV. In addition, the study presented in this chapter suggests that HIV/AIDS patients want a confidential, easy-to-use, socially interactive website with animated characters to assist both their health care providers and themselves in monitoring their HIV medication adherence. I explore how Cell POS can contribute to patients living with HIV/AIDS' ability to take medicines in the next chapter.

Chapter 6. A pilot evaluation of Cell POS

Introduction

In Chapter 5, I described Cell-POS, a computer-based system that uses mobile cell phones and the Internet, to deliver HIV-related educational messages, medication and clinic appointment reminders via SMS text messages. Our objectives for Cell POS are to enhance adherence to ARV, and to address specific needs and preferences of patients for HIV care with information related to ARV.

I argued that adherence to treatment recommendations of people living with HIV/AIDS goes beyond sending a simple reminder. I concluded in Chapter 5 that the characteristics of the reminder (notification modality, the message, and the context) could play an important role in interventions to improve patient adherence to ARV. In addition, I found that people living with HIV/AIDS want a confidential, easy-to-use, socially interactive website with animated characters to assist both their health care providers and themselves in monitoring their HIV medication adherence

In this chapter, I describe the main components of the system, the final architecture and a pilot evaluation to get a better sense of how Cell POS works. Nine people living with HIV/AIDS used the Cell POS system for one month, as a pilot evaluation. I end this chapter with a discussion on perceptions of study participants and of the implications that the study findings have for further development mobile applications for health.

Main components of the Cell POS system

Cell POS was structured on five main components (**Figure 6.1**):

1. A secure database, Web server and a website. To access the Cell-POS website, users are given a username and password. The authentication and security infrastructure recognizes each user's role (as administrator, clinician, or patient).
2. A secure Web-based interface for clinicians who can start entering the patient into the system from any Internet-connected computer.
3. A secure Web-based interface for patients to customize their reminders and change the frequency of their messages. There is also a demographics, self-report adherence and risk

behavior web-based survey. In addition, there are links to a variety of information resources in Spanish about HIV—regarding care, treatment and prevention.

4. A secure Web-based interface for the administrator.
5. SMS-based communications from the server via cell phones for reminders and messages.

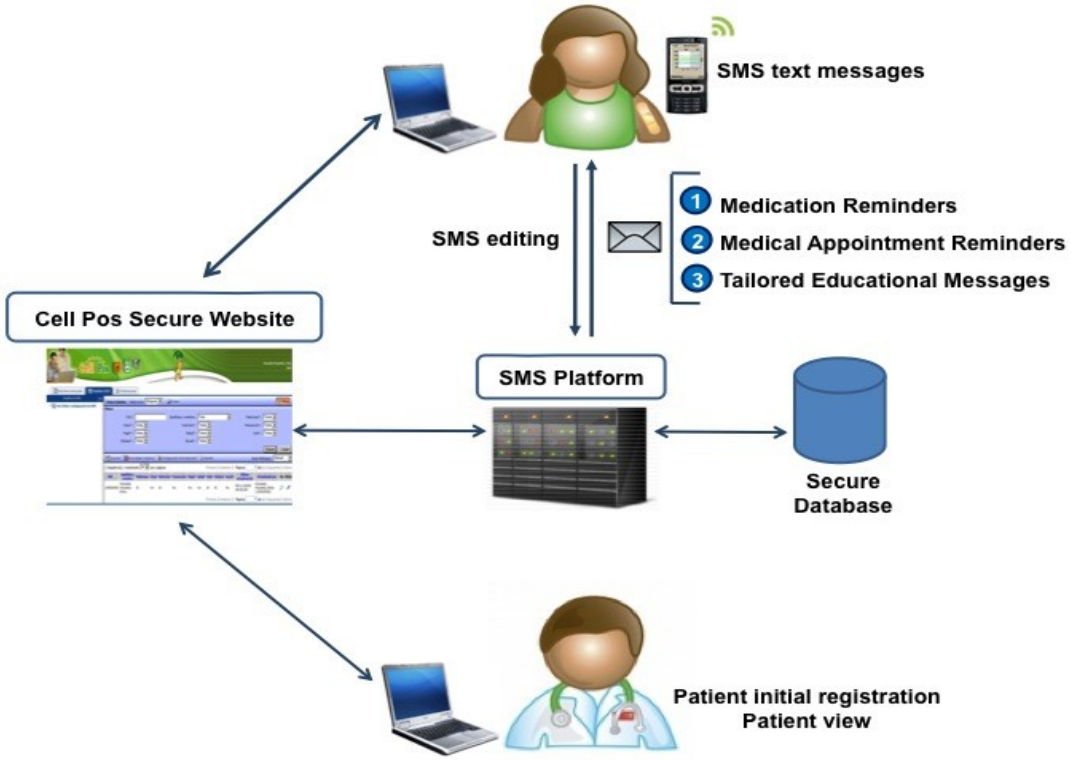

Figure 6.1. Architecture of the Cell-POS system

Main features of the Cell POS web site

Participants are first registered on the system by a clinician, through the Cell-POS website. Once the patient has been registered, the SMS text messages, which are the medication reminders, medical appointment reminders, and educational messages (Health, Nutrition, Life, Social, Women and Prevention) are configured. Through the website, participants also have the ability to add, edit and delete messages, as well as decide their frequency. Users receive their message 30 minutes prior to the scheduled time.

The reporting tool interface on the Cell-POS website is used to record clinical data, such as adherence, which are filled in by the patient on a monthly basis.

Design and content of the SMS text messages

Motivational Messages

This study is based on the Information-Motivation-Behavioral Skills (IMB) model, which is used to understand the predictors of ART adherence (Fisher et al., 2006). In this context, the model states that individuals will be more likely to adhere to ART treatment in the long term and see the health benefits of the treatment if they are well informed, motivated to act and possess the behavioral skills required to act effectively.

Based on focus groups reported in Chapter 4, motivational short text messages were designed with the intention to improve ART adherence and support HIV care. We found that people in Peru want motivational SMS that appropriately notify them, deliver a carefully crafted message, and are sensitive to the context in which they are received.

We designed four types of motivational messages:

- Motivational Attitudinal Message (Example: "It's the time of your life")
- Tailored Motivational Attitudinal Message (Example: "[insert participant's name] It's the moment, say yes to your life")
- Motivational Descriptive Normative Message (Example: "Remember, everybody like you is putting their energies into this now")
- Motivational Injunctive Normative Message (Example: "Remember, people that are important to you are supporting you now")

The messages were designed to match the attitudinal and normative components of the motivational predictor of adherence. The design of the attitudinal messages was informed by the Integrative Model (Fishbein, 2000), which indicates that salient behavioral beliefs determine the attitudes towards a behavior. The design of the normative messages was informed by the Focus Theory of Normative Conduct (Cialdini, 1990), which states that descriptive norms—i.e. what people do—and injunctive norms—i.e. what is ought to be done—are separate normative influences that determine behavior. Finally I evaluated tailoring as a way to improve the effectiveness of the attitudinal message.

Methods for the Pilot evaluation

During March-April 2010, we recruited nine HIV-positive participants undergoing antiretroviral treatment in the one-month pilot study at the Via Libre clinic. The goal of this study was to

evaluate the perceived ease of use, usefulness and perceptions of Cell POS to support antiretroviral adherence in Peru. The study participants, procedures, and data analysis are described below.

Participants

Nine HIV-positive patients participated in the study. Ages ranged from 26 to 50 years, 6 were male and 3 were female. The participants were predominantly people with a mixed heritage, most of them with university education and employed. Demographics characteristics are described in Table 6.1.

Table 6.1. Demographics of Participants from the pilot

	Median	**Range**
Age	35	26-50
	N	**%**
Gender		
Female	3	33.3
Male	6	66.7
Ethnicity		
Mestizo	8	88.9
Black	1	11.1
Education		
High school only	3	33.3
Above high school	6	66.7
Occupation		
Employed	6	66.7
Unemployed	3	33.3

Study design and procedures

For the pilot study, I included people with a confirmed diagnosis of HIV infection who were older than 18 years, were taking antiretrovirals, owned a mobile phone for their personal use (not shared), and knew how to read SMS text messages on their mobile phone. Individuals were recruited through flyers and convenience sampling. Each participant underwent the following procedures over a 4-week period:

Initial in-person session

During the first in-person session, participants were instructed on how to use the system and the research assistant configured the SMS text messages the participant wanted to receive using the Web-based application.

The participant selected to receive SMS from the following types of messages:

- SMS_medicines: medication reminder
- SMS_appointm: appointment reminder
- SMS_nutrition: messages about nutrition
- SMS_prevention: messages about HIV secondary prevention
- SMS_women: messages about HIV care for women
- SMS_health: messages about general health
- SMS_life: motivational lifestyle messages and tips to deal better with the disease
- SMS_humor: jokes
- SMS_social: messages about social aspects and information about legal issues.

SMS configuration

Figure 6.2 displays a screenshot of the section. Participants could add, edit and delete messages, and decide its frequency. As per suggestion from focus groups and from previous studies (da Costa et al., 2012), users received their message 30 minutes prior to the scheduled time.

Figure 6.2. Screenshot of configuration of SMS messages

All participants were given a printed user manual with directions on how to use the system to have a reference resource if they forgot how to do something. The participants were also encouraged to contact the researchers at any time during the study if they had technical problems or other questions.

Security and Privacy

Technical security measures include requiring HTTPS encrypted connections and automatic log-out from the website after five minutes of inactivity. We recommend the participants always log-out and close the browser after they have finished using the Cell-POS website. Additionally security recommendations provided to users were to delete the cookies and browsing history from the browser (i.e. Internet Explorer) and to re-start the PC they are using before leaving. For cell phone security measures we advised that once the message has been received, delete it—this way if someone else gets a hold of their cell phone, they can't read the message.

Measures / Data collection

Using the Web-based interface for patients, I collected demographic characteristics, such as age, gender, ethnicity, education level and occupation. Additionally, to assess acceptability, perceived ease of use, and usefulness towards Cell-POS, I developed a questionnaire using a Likert scale (rating of 1 to 5 where 1 was "definitely disagree" and 5 was "definitely agree") based on an adapted version of Davis' Technology Acceptance Model (Davis, 1989), and previous acceptability surveys developed by the authors (Curioso et al., 2008). Participants completed the survey 30 days after using system. We also conducted individual semi-structured interviews using questions adapted from previous studies (Curioso et al., 2008). Questions focused on participants' perceptions regarding the system.

Semi-structured questions included: "What do you think of the text messages?" "Does the SMS make sense?"; "What do you think of the website Cell-POS? (If not used, describe why?)"; "What were the (3) best parts and / or what do you like best about the system?"; "What would make the system more useful?", "Would you like to continue using the Cell-POS system? (e.g. Would you like to continue receiving SMS text messages?)."

Data analysis

Descriptive statistics were used to summarize demographic and baseline characteristics. Data was analyzed using the statistical package SPSS (version 18.0; SPSS Inc, Chicago). Summary statistics included frequencies, percentages, median, range, means and standard deviations. Qualitative data from the semi-structured interviews were analyzed separately using a content-analysis approach.

Ethical Considerations

All instruments and protocols had ethical approval from the UW Human Subjects Committee, Universidad Peruana Cayetano Heredia Ethics Committee and the institutional review boards of Via Libre. A signed and dated written informed consent was obtained prior to participation to the pilot study.

Results

In this section, I first provide a brief overview of how the participants perceived the system and then describe the study's more general findings.

Overall, Cell POS was very positively received and participants thought that the use of the system helped them manage their antiretroviral adherence better.

Perceived ease of use

The participants reported high perceived ease of use, with three items related to the Cell POS system having a mean greater than four. One question related with the website usage scored a mean less than four.

Perceived usefulness to Cell POS

Participant's scores on perceived usefulness were high above 4.0. The training devoted to use the system was the feature with the highest score, suggesting that the effort involved with each user was important and highly valued. For detailed scores, refer to **Table 6.2**.

Table 6.2. Perceived ease of use and perceived usefulness

Perceived ease of use	**Mean (Std)**
It's easy for me to read the messages sent by the Cell-POS system	4.7 (0.5)
Messages sent by the Cell-POS system are clear and understandable	4.6 (0.5)
It is easy for me to edit (change) my message settings in Cell-POS	3.8 (0.8)
It is easy for me to incorporate the Cell-POS system to my daily activities	4.4 (0.5)
Perceived Usefulness	**Mean (Std)**
How useful are the Cell-POS reminders as an aid for taking your meds?	4.7 (0.5)
How useful are the Cell-POS reminders to help remember your appointments?	4.7 (0.5)
How useful are the educational messages from the Cell-POS system?	4.6 (0.5)
How do you think was the training that was given to use the Cell-POS system?	4.8 (0.4)

Cell-POS enhanced my knowledge related to HIV treatment	4.4 (0.9)
Cell-POS improved my ability to take my medications correctly and on time	4.4 (0.7)
In general, I think it is important that all HIV patients receive reminders from the Cell-POS system	4.7 (0.5)

Scale of 1 to 5 where 1 was “definitely disagree” and 5 was “definitively agree”

Message preference for medication reminders

Participant’s scores on message preferences for medication reminders ranged with the messages. The tailored message that included the name of the participant followed by the motivational phrase “It’s time, say yes to life” was the most preferred message. For complete scores of message preference, refer to Table 6.3.

Table 6.3. Message preference for medication reminders

How did you like the messages for taking medication	Mean (Std)
It's time for your life	3.9 (0.8)
Remember, everyone like you, right now, is putting an effort	4.4 (0.5)
[Participant’s name], it's time, say yes to life	4.8 (0.4)
Remember, people that are important to you are supporting you now.	4.1 (0.6)

SMS text messages received by participants

In one month, participants scheduled their own reminder messages with an average of 5-7 per week, 1-3 times/day, with a total of 43-101 SMS messages received by each participant in a month.

Semi-structured interview results

Text Messages (SMS) and Cell Phones

All participants perceived that the SMS made sense and qualified the messages as good with the following qualities: easy to read, concise and understandable. Six of the nine participants considered the language of the SMS easy to understand, and mentioned that the use of abbreviations helped so that others did not understand what the SMS was about.

All participants considered the SMS text messages relevant to them, motivational, and good reminders. They believed that other people with HIV could comply with them. One person commented that the messages are "recommendations to live better".

Overall experience

The overall experience with Cell-POS was considered positive. Participants perceived that the system met their expectations. Three of the nine participants even shared the educational SMS (nutrition, health and humor) with family and /or a partner. In addition, the webpage was well received by participants; one participant stated that it “looks good, practical and looks easy to use”.

Top cited reasons to use the system were: Cell-POS was easy to read, concise and understandable; that they were able to choose, plan and change the messages on a webpage that seems to be simple and contains links with information; the messages were useful, clear which can be read quickly and help to remember to take pills; the messages were informative; and the messages are motivational and make you feel different because they do not remind you that you are sick instead they are inspiring another life style.

Participants provided a number of suggestions to make the system more useful as including more messages of encouragement such as “be happy” or a smiley face. Two participants also suggested that the webpage should include testimony of persons with HIV and their life changes, as well as topics of "healthy" children with parents with HIV.

They all agreed to continue using the Cell-POS system once the study was done, with everyone wanting to continue receiving the reminders for taking medicine and medical appointments. One participant reported that the fact she was receiving SMS messages made her partner suspicious so she had to decrease the frequency of SMS messages. However, she felt those messages helped her improve her mood and the management of her disease. When her partner issues are resolved she hopes to increase the number of SMS messages.

Discussion

This pilot study examined acceptability, perceived ease of use, and perceived usefulness towards Cell-POS. The primary finding was that participants were satisfied and accepted the Cell-POS platform quickly and without difficulty. Both qualitative and quantitative methods were used to identify these findings. The analysis of the study data provided further evidence for the developing of mobile health interventions to improve HIV adherence, and it pointed out the

importance of properly crafted the SMS text message. In addition, the study results helped elucidate the role that Cell POS played in supporting patients' adherence.

The results demonstrated that the participants perceived that the messages were clear, effective, understandable and easy to incorporate the Cell-POS system to their daily activities. Usefulness of Cell-POS messages were rated high for medication reminders, appointment reminders, and educational messages. Most participants perceived that Cell-POS enhanced their knowledge related to HIV treatment and improved their ability to take their medications correctly and on time. In addition, the high scores for the medication reminders perceived that the participants found all four messages (Motivational Attitudinal, Tailored Motivational Attitudinal, Motivational Descriptive Normative and Motivational Injunctive Normative Messages) useful.

Our results are similar to the ones reported in the literature regarding the value of SMS to improve adherence. For example, studies from developed countries have been published that examine feasibility and user acceptance amongst applications that focus on drug adherence. In Ireland, Sahm et al. evaluated acceptability of SMS reminder to improve medication adherence in 59 patients with depression, 60% of the sample patients reported that text message reminders were acceptable to them (Sahm, 2009). In addition, in Canada, SMS reminders were found to be acceptable in studies such as vitamin C supplement adherence (Cocosila et al., 2009) or a daily sunscreen application in Boston (Amstrong et al., 2009). This evidence is complementary to the literature that highlights that SMS reminders improved appointment attendance as documented in China (Chen et al., 2009), Brazil (da Costa et al., 2010) and the UK (Geraghty, 2008; Milne, 2006).

One of the features of the system that was supported and appreciated by participants was the abbreviation of some words which made them only understandable for the intended recipient and not for other people. Privacy, confidentiality and security are important in any eHealth project, and particularly in HIV mHealth interventions. The messages in this project are meant to be confidential and intended only for those who are to receive it. People with HIV are at risk of being subjected to stigma and discrimination making privacy and confidentiality very important factors.

In addition, system security is also a critical factor. In our project, technical security measures for both text messaging and the webpage are considered, and the message is passed on to the participants. We provided suggestions such as always logging out and closing the browser once they are finished using the website and to delete text messages once they have been read. In addition, including HTTPS-encrypted connections and automatic log-out from the website after five minutes of inactivity contributed as important security features. Finally, we also recommended that participants always log-out and close the browser after they have finished using the Cell-POS website. In addition, we provided users with security, such as deleting their cookies and browsing history from the browser (i.e. Internet Explorer) and to re-starting the PC they were using before leaving.

On a personal level, participants reacted positively about the SMS messages stating that those are "recommendations to live better". The inclusion of a motivational content as previously suggested in focus group and supported by the Information-Motivation-Behavioral Skills (IBM)model was found as relevant and was received positively. Studies show that interventions that use the IMB model result in better HIV adherence outcomes (Pearson, 2007).

Three of the participants shared the educational SMS (nutrition, health and humor) with family and /or a partner. The fact that participants felt comfortable sharing their text messages could reflect a sense of a social network that could be strengthened with modern information and communication technologies, in particular with cell phones as it has happened in this project. Therefore, further studies are needed to explore the role of SMS text messages and technologies such as Multimedia Messaging Service (MMS) or Enhanced Messaging Service (EMS) to further enrich these types of social interactions. Social networks using the Internet have become popular for patients with a variety of conditions (Browstein, 2009; Frost, 2008), including HIV. People with HIV go online to find support groups where they share their experiences, as was reported by researchers from multiple settings globally (Rier, 2007; Bar-Lev, 2008; Mo, 2008).

The fact that one participant expressed concern about receiving messages causing jealousy problems with her partner shows the importance of socio-cultural issues. In this case "machismo," a culturally accepted behavior and attitude" which is very common in Latin American countries, could play an important role affecting the study. A similar situation has been found in other countries where "machismo" was found as a barrier factor for the adoption

of usage of technology amongst women (Youngs, 2007). This issue should be considered when implementing mHealth and eHealth interventions in other Latin American countries and other settings in which machismo could be prevalent.

This pilot study presented some limitations and the above results should be taken with caution, however. For one, the study took place at one specific location, an NGO in Lima Peru, thus it cannot be considered representative of people with HIV across the entire country. Moreover, most of the participants had high education levels. An additional limitation in this study is that although cyber cafés are popular in Peru, the Internet is not easily accessible for everyone. The low scores related to web usage ascertain this to be relevant. In our study, the participants have to use the Internet if they wish to edit their SMS messages as well as to view related information about HIV/AIDS, which could be a barrier for some users that do not have access to the Internet, particularly because of privacy and security concerns. In addition, the number of participants in the study was too small to show statistical significance. However, all of them completed the one-month follow-up evaluation. Finally, the short study duration could affect the results of the participants' responses to the study (excitement with getting a text message for a short period of time) rather than any genuine effect of the program itself. The current study was not long enough to truly assess how well Cell POS fit into the participants' daily lives, but the possibility, suggested by these results, that a mobile application could contribute to improve adherence and facilitate tighter integration to other everyday activities is encouraged and should be investigated further.

Finally, while the prevalence of smartphones is on the rise in Peru and globally, they are still complex devices that could be difficult to learn how to use, especially for older individuals and those who has complications or co morbidities—like people living with HIV/AIDS. Those pieces of technology need to be investigated further regarding different applications to support adherence.

In spite of these difficulties, the value of Cell POS was clear to all participants. Further development of this kind of SMS-related services seems like a promising direction for supporting adherence people living with HIV/AIDS.

Conclusion

In this chapter, I reviewed the results of a four week study of Cell POS. Participants in this pilot study were satisfied and accepted Cell-POS very well. Cell-POS was user-friendly and perceived as useful. Although studies to date highlight the potential of mHealth interventions, most of these studies have evolved in developed countries. Our preliminary findings already demonstrate that innovative mHealth strategies can have a positive impact on its users in developing countries such as Peru. This pilot study not only gave us some insight about the promises that this study has to offer in a developing country, but it also gave us helpful directions for a randomized controlled trial to measure not only acceptability, perceived ease of use, and usefulness of Cell POS, but also health outcomes such as viral load and CD4 levels with a one-year follow-up duration. This randomized controlled trial will be described in Chapter 7. Our preliminary findings already demonstrate that innovative mHealth strategies can have a positive impact on its users.

Chapter 7. Supporting Adherence with Cell POS

Introduction

In this chapter, I describe the one-year randomized trial evaluation study of the Cell-POS system (introduced in Chapter 6) including 174 people living with HIV/AIDS to get a better sense of how Cell POS works in the long run. I end this chapter with a discussion of the study and of the implications that the study findings have for further development mobile applications for health.

Methods

Patients

Patients undergoing antiretroviral therapy were recruited from two different HIV health care settings in Lima: Via Libre and Hospital Nacional Cayetano Heredia. Via Libre is an NGO clinic. This clinic was selected because it is one of the most important clinics for HIV positive individuals in Lima, and Via Libre has participated as a collaborative institution in other research studies with Cayetano Heredia University. Hospital Nacional Cayetano Heredia is a large general and specialty university teaching hospital situated in a low-income district in Lima. It is funded by the Ministry of Health and serves both the general and HIV-positive populations of lower to middle socioeconomic status who live in nearby districts and in the Lima metropolitan area. We chose these two locations because they should represent the regional diversity of health settings regarding HIV care.

Patients were eligible for study participation if they were: HIV-positive healthy male or female over 18 years old, on antiretroviral therapy, with a mobile phone for their personal use (not shared), who knew how to retrieve text messages on their mobile phone, and who signed and dated a written informed consent prior to admission to the study. In addition, patients met the following inclusion criteria: willingness and ability to receive medication reminders and educational messages to their cell phones via text messages during one year. People were recruited using flyers.

The study protocol was approved by the ethics review boards of: the University of Washington (Seattle, USA), the NGO Via Libre, the Hospital Nacional Cayetano Heredia , and the Universidad Peruana Cayetano Heredia in Peru.

This trial is registered with ClinicalTrials.gov, NCT01118767, available at: http://clinicaltrials.gov/ct2/show/NCT01118767.

Randomization and masking

Cell POS was an individually randomized controlled trial. Patients were randomly assigned (1:1) by simple randomization to the SMS intervention or to standard care (control group). A project epidemiologist generated the randomization blocks of size four with an algorithm in Visual FoxPro v 7.0 (Microsoft Corp, Redmond, WA). Written allocation of the assignment was sealed in individual opaque envelopes marked with study identification numbers, which were distributed to both study sites. Randomization and analysis were done by investigators masked to treatment allocation; however, study participants and clinic staff could not be masked because the intervention required overt participation.

Procedures

Antiretroviral drugs were provided by the government of Peru, and consisted primarily of three drug combinations containing zidovudine or stavudine, plus lamivudine, plus efavirenz or nevirapine as first-line drugs.

Typically, the two sites provided two counseling sessions on nursing, psychology and social services before antiretroviral initiation. Disclosure of HIV status, pairing up with a treatment adherence partner, and participation in support groups was encouraged but not insisted upon. Additional brief counseling was provided at each site during dispensation of the drugs in the health care site.

As stated in Chapter 6, we thought that regular, structured mobile phone communication through text messages between healthcare workers and patients could improve patient outcomes by both reminding patients to take their antiretroviral drugs and by providing information, motivation and behavioral skills, under the IMB framework (Fisher et al., 2006).

The intervention was planned in consultation with investigators, clinic staff, and patients (see Chapter 5 and 6).

All participants underwent scheduled counseling sessions according to the national guidelines promoted by the Ministry of Health. All intervention participants received brief training for use of the SMS intervention from the study coordinator. They were informed that the SMS support service did not replace existing adherence counseling or emergency services. The study coordinator configured the SMS text messages the participants wanted to receive using the Web Based application described in Chapter 5. In addition, all participants were given a printed user manual with directions on how to use the system in order to have a reference resource if they forgot how to do something. Security and privacy considerations were described in Chapter 5. Participants were instructed that the study coordinator was available to respond during health care hours only. All mobile communications between the healthcare workers and patients were recorded in the study log.

Primary outcome

The primary outcome was patient adherence to antiretroviral medication at twelve months. This outcome was assessed using a self-reported medication adherence standard questionnaire: The Simplified Medication Adherence Questionnaire (SMAQ). Self-reported adherence is the most practical method of assessing adherence because it closely represents the regional standard care Lester et al., 2010). The SMAQ is a recommended self-report scale to measure adherence as primary outcome. This questionnaire was drawn both from the literature and from clinical experience. In addition, it incorporates use of normalizing language (Simony et al., 2006). This scale was validated originally in Spanish by Knobel et al. (2002) and was previously used very well in Peru (Alvis et al., 2009). It is based on the Morisky score (Morisky et al., 1986) and Samet et al. (1992). The sensitivity is 72%, specificity is 91%, positive predictive value is 91%, and negative predictive value is 80%, and the Cronbach's alpha level is 0.75. The scale is simple to use and culturally appropriate to use in this population. The questionnaire contains 6 questions and classifies patients as nonadherent if they answer yes to any of the qualitative questions: more than 2 forgotten doses in the last week, or more than 2 days without taking medication in the last three months. In addition, the SMAQ was used as a method of self-reported adherence in other studies including randomized controlled trials (Ruiz et al., 2010).

The SMAQ questions are:

(1) `Do you ever forget to take your medicine?'; Yes/No

(2) `Are you careless at times about taking your medicine?'; Yes/No

(3) `If at times you feel worse, do you stop taking your medicine?'. Yes/No

(4) Thinking about the last week. How often have you not taken your medicine?; Never / 1-2 / 3-5 / 6-10 / >10

(5) Did you not take any of your medicine over the last weekend?; Yes/No

(6) Over the past 3 months, how many days have you not taken any medicine at all?. 2 days or less / >2

Secondary outcomes

For a secondary outcome measure, we used self-reported adherence based on a visual analogue scale (VAS) that simply asks the patient to indicate by marking on a linear scale their adherence to each medication in the last 4 weeks (Walsh et al., 2002) We used the VAS because it is more quickly assessed, it is able to obtain data about a longer time frame, and it places a lower response burden on the patient (Giordano et al., 2004). The VAS has been used in cross-sectional studies and its results have correlated with HIV viral load (Walsh).

In addition, we used The LifeWindows Information-Motivation-Behavioral Skills ART adherence questionnaire (LW-IMB-AAQ, 2006). Each LW-IMB-AAQ item represents a barrier primarily falling within the I (Information), M (Motivation), or B (Behavioral Skills) constructs. Adherence information is assessed with five items. Example for an information item: “I know what to do if I miss a dose of any of my HIV medications (for example, whether or not to take the pill(s) late).” Responses to items include “yes,” “no,” or “don’t know” ("don’t know” responses were keyed as incorrect responses). Adherence motivation is assessed with ten items. A “motivation” sample item: “I am worried that other people might realize that I am HIV+ if they see me taking my HIV medications.” Response options were 1 = strongly disagree to 5 = strongly agree. Behavioral skills are assessed with 14 items. An example of a behavioral skills item: “How hard or easy is it for you to stay informed about HIV treatment?” Response options were 1 = cannot do at all to 5 = certain you can do.

Finally, we used an adapted version of Davis' Technology Acceptance Model (TAM) to evaluate users' acceptance of Cell POS at the end of the study (Davis, 1989). In addition, we asked participants their perceptions of the system using a semi-structured interview form. The TAM

model proposed that two factors, perceived ease of use and perceived usefulness of system, could reliably and validly predict user's acceptance of new information technology. All question stems will be presented with 5 point numerical Likert scale responses ranging from 1-5 with the 1 and the 5 anchored by 'Definitely Disagree' and 'Definitely Agree'.

Examples of the perceived easy-of- use questions included:
1. Messages sent by the Cell-POS system are clear and understandable
2. It is easy for me to incorporate the Cell-POS system to my daily activities

Examples of the perceived usefulness questions included:
3. How useful are the Cell-POS reminders as an aid for taking your meds?
4. How useful are the Cell-POS reminders to help remember your appointments?
5. How useful are the educational messages from the Cell-POS system?
6. Cell-POS enhances my knowledge related to HIV treatment
7. Cell-POS improves my ability to take my medications correctly and on time
8. In general, I think it is important to receive reminders from the Cell-POS system

Statistical analysis

We calculated that a sample size of at least 154 participants would be required to detect a 20% improvement in adherence, with 85% power and 0.025 level of significance. Demographic and covariate information were recorded at baseline (month 0) and at scheduled visits at 6 and 12 months. Self-reported adherence to antiretrovirals was assessed by two standardized questionnaires at each follow-up visit. Study staff maintained a study register to record all SMS sent to participants as well as other mobile phone communications with patients.
The intervention arm was compared against the control arm for the primary analysis. We used the chi-squared test for binary outcomes, and Students t test for continuous outcomes. The analysis of primary outcomes was by intention to treat. For subgroup analysis, we used regression methods with appropriate interaction terms (respective subgroup x treatment group). Multivariable analysis was based on the Generalized Linear Model for binary outcomes and multiple linear regression for continuous outcomes.

We calculated Relative Risk (RR) and RR Reductions (RRR) with corresponding 95% confidence intervals to compare dichotomous variables, and difference in means was used for additional analysis of continuous variables.

As a measure of absolute effect size, we also calculated the number needed to treat (NNT) and its associated 95% CI for the unadjusted primary outcome. We also did a per-protocol (complete-case) analysis of the primary outcome, in which only participants who had complete primary outcome data (self-reported adherence at 6 and 12 months) were included.

Secondary outcomes were compared with the chi-squared test. We used the Fisher's exact test for outcomes that were reported in five patients or less to estimate p values. In the subgroup analysis in the intention-to-treat population, we compared the intervention groups within each subgroup of patients with the chi-squared test.

The criterion for significance was set at alpha=0.05. For all models, the results are expressed as an estimate of effect size, with 95% CIs and p values. All statistical analysis were done with Stata 11.2 (Stata, Inc., College Station, Texas).

Role of the funding source

The sponsor of the study (US National Instituted of Health) had no role in the design of the original study protocol, data collection, data analysis, and data interpretation.

Results

Between May, 2010, and December, 2010, we enrolled 210 participants (Figure 7.1: trial profile). Consecutive enrolment was attempted in two sites. After screening, 36 patients were excluded: 32 because they did not fit the inclusion criteria for the study (12 did not have cell phones, 10 were not receiving therapy yet, 8 shared cell phones, and 2 did not use his/her cell phone very well)m and 4 declined participation. Accordingly, 174 patients were randomly assigned: 78 to the SMS intervention and 78 to standard care. No participants withdrew from the study after random allocation. Table 7.1 reports the demographics characteristics of patients. No difference between groups was determined at the baseline.

Table 7.1. Demographics of Participants from the RCT

	Median	**Range**
Age	35	19-66
	N	**%**
Gender		
Female	42	28.8
Male	104	71.2
Ethnicity		
Mestizo	120	82.2
Black	2	1.4
White	24	16.4
Education		
Bellow high school	19	14.0
High school only	86	63.2
Above high school	31	22.8

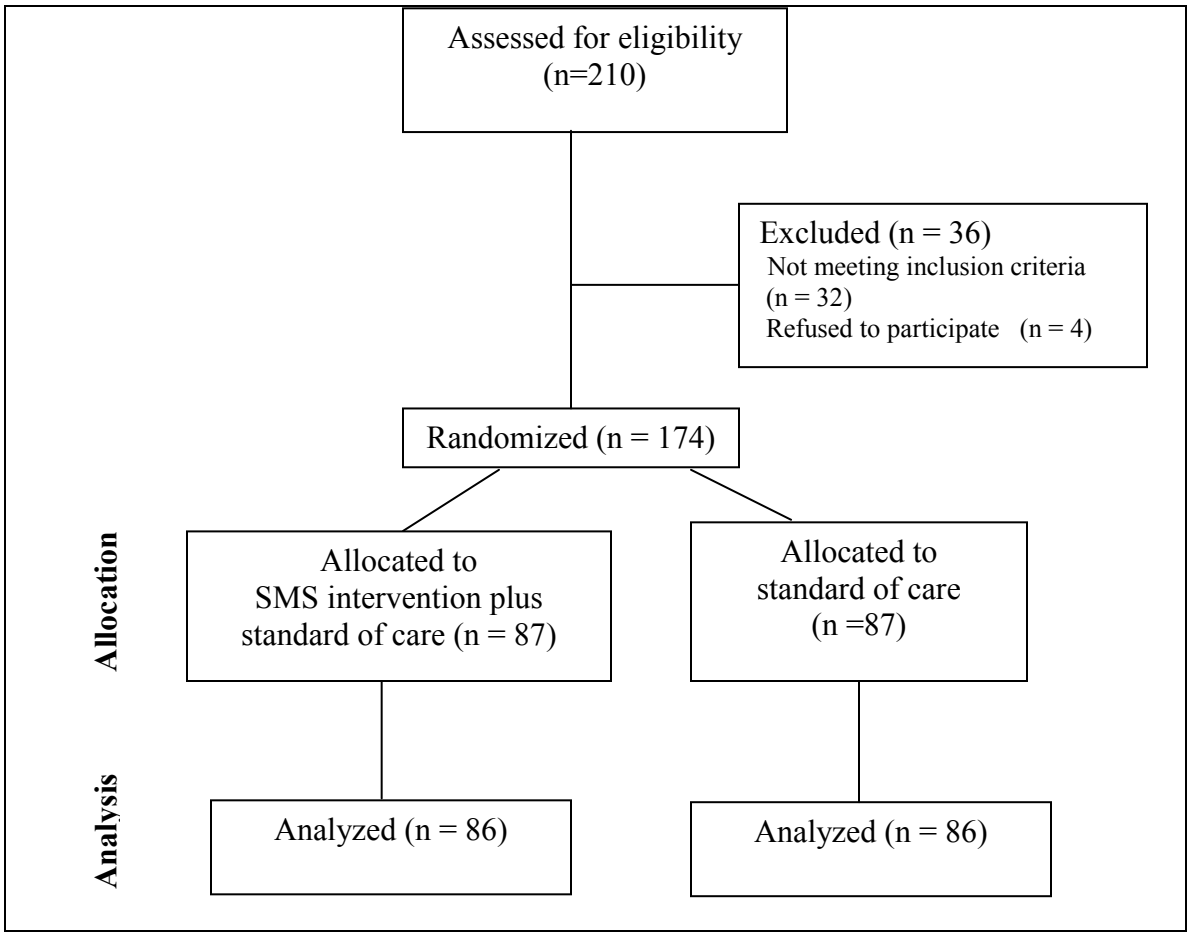

Figure 7.1. Trial profile

Patients in the SMS intervention group had higher scores of self-reported adherence than in the control group (Table 7.2). Similar results were found in the complete-case analysis. After adjusting for baseline covariates, self-reported adherence remained significantly better in the SMS group than the control group.

After adjusting for the number of visits, self-reported adherence remained significantly better in the SMS group than the control group (risk ratio [RR] 2.77, 95% CI 1.58-4.84; $p < 0.01$). The NNT for adherence was 3.65 (95% CI 2.52 - 7.27).

Table 7.2. Primary and secondary outcomes

	Intervention group (frequency [%]/ mean[SD]) n=87	Control group (frequency[%]/ mean [SD]) n=87	RR (95% CI)	P value
Primary outcome				
Intention to treat analysis				
Self-reported adherence (SMAQ)	36 (42.9)	13 (15.5)	2.77 (1.58 – 4.84)	<0.01
Complete-case analysis				
Self-reported adherence (SMAQ)	36 (41.4)	13 (14.9)	2.77 (1.58 – 4.84)	<0.01
Secondary outcomes				
Self-reported adherence (VAS)	98.1 (3.9)	92.6 (12.4)	5.48 (2.68 – 8.27)	<0.01
IMB Score	109.1 (12.2)	104.4 (15.1)	4.76 (0.56-8.96)	0.03
Information Score	30.9 (3.7)	29.3 (4.5)	1.64 (0.39-2.90)	0.01
Motivation Score	30.2 (6.4)	31.2 (7.9)	-1.0 (-3.20-1.20)	0.37
Behavioral Score	47.9 (5.9)	44.0 (7.5)	3.9 (1.85-5.98)	< 0.01

SMAQ: Simplified Medication Adherence Questionnaire; VAS: Visual Analogue Scale

The intervention group is 2.77 times more likely to be adherent than the control group using the SMAQ, and, the intervention group is 5.48 times more likely to be adherent than the control group using the VAS.

The mean score of the IMB in the intervention group was 4.76 more than the control. Analyzing all three sub-components, the mean of the information score in the intervention group was 1.64 more than the control. The mean of the behavioral score in the intervention group was 3.92 more than the control. Both were statistically significant. The motivation score was not significant.

Table 7.3. Type of SMS that participants received and association with medication adherence

	% who recieved types of SMS (n=86)	Bivariate		Multivariate*	
		RR (IC95%)	p	RR (IC95%)	P
SMS_medicines	100				
SMS_appointm	29	1.60 (0.99 - 2.58)	0.05		
SMS_nutrition	47	0.74 (0.45 - 1.21)	0.23		
SMS_prevention	2	2.41 (1.86 - 3.12)	< 0.01	4.85 (1.93 - 12.20)	< 0.01
SMS_women	5	0.93 (0.31 - 2.82)	0.90		
SMS_health	22	0.56 (0.27 - 1.17)	0.13	0.35 (0.15 - 0.78)	0.01
SMS_life	23	1.59 (0.99 - 2.57)	0.06	1.87 (1.20 - 2.90)	< 0.01
SMS_humor	16	1.42 (0.84 - 2.40)	0.19		
SMS_social	6	1.63 (0.87 - 3.05)	0.13		

* Adjusted by the prevention, health and life SMS

SMS_medicines: medication reminder; SMS_appointm: appointment reminder; SMS_nutrition: messages about nutrition; SMS_prevention: messages about HIV secondary prevention; SMS_women: messages about HIV care for women; SMS_health: messages about general health; SMS_life: motivational lifestyle messages and tips to deal better with the disease; SMS_humor: jokes; SMS_social: messages about social aspects and information about legal issues.

Regarding the type of messages, we found that the patients that received the SMS_prevention messages were 4.85 times more likely to be adherent to treatment, and those that received the SMS_life messages were 1.87 times more likely to be adherent to treatment (Table 7.3).

No adverse event directly attributable to the mobile phone SMS communication, such as breaches of confidentiality (eg. if non-participants found out the participant's HIV status in an unintentional way) or injury (eg. caused by driving or riding a bike whilst reading a text message), was reported in the weekly study logs or during follow-up visits with health-care workers.

Regarding frequency, we found no difference in adherence between receiving 1 SMS pill reminder per week versus receiving more than 1 SMS pill reminder per week. RR= 0.87 (IC95%: 0.46 - 1.63; p = 0.664).

In addition, we found an association between the types of SMS received and medication adherence. If the participant received 5 or more types of SMS there is 2.3 times more likely to be adherent (**Table 7.4**).

Table 7.4. Association between the types of SMS received and medication adherence

		Bivariate	
	N (%)	**RR (95% CI)**	**p**
1-2 types	36 (41.9)	1	
3-4 types	45 (52.3)	0.85 (0.49 – 1.47)	0.056
5 types or more	5 (5.8)	2.33 (1.59 – 3.43)	< 0.01

Types were: SMS_medicines, SMS_appointm, SMS_nutrition, SMS_prevention, SMS_women, SMS_health, SMS_life, SMS_humor and SMS_social

In the following section, I provide a brief overview of how the participants perceived the system and then describe the study's more general findings (**Table 7.4**).

Perceived ease of use

The participants reported high perceived ease of use, with two items related to the Cell POS system rated very high. At the end of the study, participants perceived that it was easier to incorporate the Cell-POS system to their daily activities compared to the 3-month evaluation.

Perceived usefulness to Cell POS

Participant's scores on perceived usefulness increased progressively over time. At the end of the study, participants perceived that the Cell-POS reminders for remembering their appointments and the educational messages were more useful compared to the 3-month evaluation.

In addition, patients perceived that Cell-POS enhanced their knowledge related to HIV treatment, improved their ability to take their medications correctly and on time, and participants perceived that it is important to receive reminders from the Cell-POS system. Participant's perceptions were consistent over time.

Table 7.4. Perceived ease of use and perceived usefulness

	3 months Median (range) / % (agree-completely agree)	6 months Median (range) / % (agree-completely agree)	12 months Median (range) / % (agree-completely agree)
Perceived ease of use			
It's easy for me to read the messages sent by the Cell-POS system	5 (5-5) 100%	5 (5-5) 100%	5 (5-5) 100%
It is easy for me to incorporate the Cell-POS system to my daily activities	5 (3-5) 94.2%	5 (4-5) 100%	5 (3-5) 98.8%
Perceived Usefulness			
How useful are the Cell-POS reminders as an aid for taking your meds?	5 (4-5) 100%	5 (5-5) 100%	5 (5-5) 100%
How useful are the Cell-POS reminders to help remember your appointments?	4 (2-5) 65.2%	4 (3-5) 61.6%	4 (3-5) 67.4%
How useful are the educational messages from the Cell-POS system?	5 (3-5) 82.6%	5 (3-5) 80.2%	5 (3-5) 91.9%
Cell-POS enhanced my knowledge related to HIV treatment	5 (4-5) 100%	5 (4-5) 100%	5 (4-5) 100%
Cell-POS improved my ability to take my medications correctly and on time	5 (4-5) 100%	5(4-5) 100%	5 (4-5) 100%
In general, I think it is important to receive reminders from the Cell-POS system	5 (4-5) 100%	5 (4-5) 100%	5 (4-5) 100%

Scale of 1 to 5 where 1 was “definitely disagree” and 5 was “definitively agree”

Discussion

The study reported in this chapter shows that patients who received the SMS support during one year were more likely to report adherence to antiretroviral therapy than patients who received the standard care alone.

We found a difference between the self-reported adherence scales. This difference could be because of a recall or social desirability bias in VAS self-reporting adherence.

Our results are similar to recent studies that show mobile health to be a potential effective tool that improves patient outcomes. In Kenya, Lester et al.’s multisite randomized trial showed that the patients from the intervention group that received SMS support has significantly improved antiretroviral adherence and rates of viral suppression than the control group, specially a 12% increase (Lester et al., 2010).

In general, the SMS intervention was well received by patients, and the reminders were considered important by participants. Similar results were reported in and SMS intervention in

Kenya, where participants reported that they felt “like someone cares” and most patients recommended for the SMS program to continue. (Lester et al., 2010). Similarly, Martini da Costa in a randomized controlled trial of SMS to improve HIV adherence in Brazil found that patients in the intervention group felt that the medical center or someone else “cared about them” (da Costa et al., 2012)

The randomized controlled trial reported in this chapter is, to our knowledge, the first effectiveness study assessing the ability of a mobile health technology intervention to influence HIV outcomes in Peru. However, pilot studies of mobile health technologies are emerging (Curioso et al., 2010).

In developed countries, mobile health technology interventions are gaining a clear evidence base for management and prevention of a broad range of disorders and conditions.

Mobile health also offers new possibilities for improving health services. For example, mobile phones could also be used to support and track patients who transfer between antiretroviral provision sites.

Overall, the study reported in this chapter has implications for policy makers and global funders of antiretroviral programs. The SMS intervention is inexpensive (each SMS costs about US$ 0.1, equivalent to $40 per 100 patients per month – sending 1 SMS per week-) and the mobile phone protocol uses existing infrastructure. This intervention is also probably less expensive than in-person community adherence interventions, on the bases of travel costs alone. Thus, the intervention could be both cost effective and cost saving. The intervention could theoretically translate into huge health and economic benefits if the program will successfully scale up. Innovations in management of automated text messaging and public-private partnerships with mobile health technology developers could improve program efficiency and scalability.

The applicability of the study reported in this chapter to other countries and other diseases and conditions remains to be assessed. Factors that influence adherence are often common within Latin America, Africa and other global settings. There are still many gaps in cell phone penetration. However, we strongly believe that mobile health will play an important role in patient care, particularly regarding timely support of a patient by a health professional.

Chapter 8. Contributions and Future Work

Introduction

In this chapter, I present significant contributions mainly to two disciplines: public health and biomedical informatics. Here, I review the main contributions of my dissertation and then briefly discuss the future work that can build on its results.

Dissertation's contributions

Contributions to public health

Mobile phones and other portable health information technologies offer unprecedented opportunities to improve public health and reach traditionally underserved subgroups (e.g., rural communities, low-income groups, and ethnic minority populations).

The work presented in this dissertation extends our understanding of antiretroviral adherence of patients living with HIV/AIDS by describing an aspect of patient information that has received little attention: the facilitators and barriers of adherence, such as the factors that influence patients to take their medications throughout the day to manage their care. I also describe the circumstances that make such activities challenging, and report several strategies—some using information and communication technologies—that patients use to deal with these challenges.

The description of adherence facilitators and barriers extends prior literature on antiretroviral adherence in Peru, which was previously not properly characterized. For example, I identified facilitators such as the use of reminding tools (e.g. cell phones) and reported that the main barrier was "simply forgetting."

In addition, I provide in Chapter 5 a conceptual framing for supporting antiretroviral adherence through text messages using the Information, Motivation and Behavioral Skills model. This simple and well-tested model identifies adherence-related information, motivation and behavioral skills as critical determinants of antiretroviral adherence amongst people living with HIV (Amirco et al., 2005).

This framing is valuable not only because it provides a recognized model that identifies adherence-related information, motivation and behavioral skills but also because it can guide the design of systems aimed at supporting patient's adherence.

In particular, if antiretroviral adherence is made challenging because it occurs under conditions of lack of motivation and information, it can be supported by information and communication technologies that address those sources, such as with cell phones.

Cell POS, the application developed during the course of this dissertation, provides patients with information, motivation and behavioral skills through short text messages delivered to cell phones in situations where patients typically don't have what they need to manage care-related antiretroviral adherence effectively. Future work should investigate how other factors related to adherence could be mitigated and what role technology can play in those efforts. In addition, Cell POS could guide the design of cell phone based-systems to improve behavior change of other public health conditions (e.g. hypertension, diabetes, cancer, etc).

Contributions to biomedical informatics

In relation to biomedical informatics, the dissertation makes two chief contributions. First, my description of the message design process for reminders in the context of antiretroviral adherence is a useful strategy that could be used in other mobile health interventions. Though previous research is inconclusive regarding the use of electronic reminder devices for antiretroviral adherence, I state that the characteristics of the reminder (notification modality, the message, and the context) play an important role to improve patient adherence to antiretrovirals. By bringing our attention to these reminder characteristics, this dissertation helps us to better understand patient information needs and to develop interventions that support those needs more adequately. The dissertation also sheds light on the usability issues related to mobile technologies aimed at people living with HIV/AIDS, including the frequency for medication reminders. This latter insight is particularly important for health applications where the regularity with which the system is used—e.g., how regularly the user receives the antiretroviral reminders—is a key determinant of the system's usefulness. In general, participants were satisfied and the overall

experience with Cell POS was very positive and rewarding and participants perceived that the system met their expectations.

In addition, my results presented in this dissertation suggest that HIV/AIDS patients want a confidential, easy-to-use, socially interactive website with animated characters to assist both their health care providers and themselves in monitoring their HIV medication adherence. The new social media of Web 2.0 is just beginning to be explored by researchers. Social media sites such as Facebook and Twitter offer potentially unprecedented access to millions of people – to collect data, to interact with people about health promotion messages, or simply to share and disseminate health information (Bull et al., 2011). Further studies should investigate interventions involving social media tools such as Facebook or Twitter to improve antiretroviral adherence.

Second, the development and evaluation of Cell POS extends our understanding of the types of tools that patients need to effectively engage in their care. Most of the literature published on health informatics in developing countries has been on electronic health records, research/data collection systems, and pharmacy information systems (Blaya et al., 2010). The results of this dissertation suggest that while those information systems are clearly important, they are not enough. Patient-centered health information systems, including mobile health applications, have brought positive results among persons of low socioeconomic status and ethnic minority. Information and communication technologies—such as cell phones, smart phones and text messagin—that are already a part of people's daily lives have great potential for improving people's health by assisting them with behavior modification and disease self-management.

A system such as Cell POS is just one example of the kind of technical systems that can help patients manage their antiretroviral adherence care more effectively. We hope to be able to make the Cell POS system available to patients at the national level in the near future. The space for innovative technologies that can help patients to actively engage in their care and improve adherence is wide open, however.

Future work

Several limitations can be mentioned in this dissertation and some issues can be explored in future work. First, an important limitation of all adherence studies described in this dissertation was that they were done only with people living with HIV/AIDS. However, there are patients

with many types of conditions with adherence problems such as asthma, cancer, depression, diabetes, epilepsy, hypertension, and tuberculosis. It would be important to learn to what extent the findings described in my dissertation generalize to other types of conditions not only in Peru, but also globally.

Second, although the evaluation study discussed in Chapters 6 and 7 yielded valuable insights into how participants used Cell POS, the study reported in Chapter 7 involved one year of technology use. Adherence to antiretrovirals is not static but dynamic. Different types of antiretroviral treatment have their own unique information management requirements. In addition, patients themselves change over the course of the treatment, both with the respect to their levels of stress and anxiety, and their familiarity with the medical system, their disease, and what is required of them to effectively navigate the care process. Even a one year trial could not assess how Cell POS would be used over a course of treatment or in what circumstances patients would find it most valuable. Similarly, if the system was used over a longer period of time, new problems and the need for additional functionality would surely surface.

A longer study in which Cell POS is given to participants at the beginning of their treatment and which follows them over several years of treatment would provide a more complete understanding of whether Cell POS supports patients' medication adherence. Such a study could also help us understand more deeply how the web and mobile components of the system integrate in patients' daily lives and how patients adapt these systems to use them for purposes other than those we originally envisioned. I hope I get involved in such a study in the future.

In addition, an important study to be conducted in the future is to evaluate how text-messaging interventions compare with other interventions designed to encourage better adherence, such as directly observed therapy, feeding programs or home visits by community health workers (Thirumurthy & Lester, 2012).

A cost-effectiveness analysis could be important to quantify. Cost-effectiveness studies should take into account not just the interventions' low marginal costs, but other costs as well, including the cost of any necessary equipment and time devoted by staff to training and implementation (Thirumurthy & Lester, 2012).

Patients' willingness to pay for inexpensive periodic text messaging is also worth exploring in future studies (Thirumurthy & Lester, 2012).

Finally, I will mention a number of ways in which Cell POS could be improved and further developed.

The website component could integrate social networks interaction such as Facebook or a web-based forum. However, we need to consider very carefully the confidentiality and security issues. In addition, the focus groups showed that patients want to share their messages, a feature that could be interesting to investigate in current platforms such as Twitter. For example, Talk HIV (@talkHIV) is a part of CDC's Act Against AIDS campaign that focuses on encouraging young African Americans to talk about HIV and what can be done to prevent it. Users share and "re-tweet" messages shared on Twitter. Other related accounts with HIV information are: CDC HIV/AIDS (@CDC_HIVAIDS), HIV Working Group (@fighthivindc) and the HIV-Network (@HIVNetwork). Another feature to consider in further studies is the possibility to interact with a health professional such a physician, nurse or nutritionist specialized on HIV/AIDS treatment and management via Web or via cell phones. Those features would make Cell POS more useful and easier to use and would result in better adherence support and care management that would ultimate in improving the quality of life of people living with HIV.

In summary, this work shed many lights into an important public health problem such as medical adherence of people living with HIV and the impact of mobile health. We believe that the timely support of short text messages is universal and appropriate mobile telecommunications can produce a significant impact in the lives of people living with HIV.

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Appendix 1. Outline of questions for the topic guide related to lifestyle, living with HIV, ART medications

Lifestyle

Describe a normal day in your life.

• With whom are you living right now?

• Who are the important people in your life?

• What are your major concerns right now?

Living with HIV

• When did you first find out you were HIV positive? What was that like for you? Has HIV changed your life?

• Have you told anyone in your life about your HIV status? Why or why not? If yes, what was their reaction?

• What sources of support for living with HIV have you been able to find?

ART

• What have you heard about medicines that are used to treat HIV/AIDS (antiretrovirals)? How is it that they work in the body?

• What have you heard about 'HIV viral load'? What have you heard about 'CD4' (good immune cells)?

• How well do you think these medicines help people with HIV/AIDS?

• Do you believe these medicines harm people with HIV/AIDS? Why?

• How long have you been on these medicines? How has that been for you? Have you had any problems on these medicines?

• How important do you think it is to take all of your doses of this medication? What happens if people miss doses?

• Has your day-to-day life had to change to take these medicines? How?

There are certain ways people are told to take these medicines. For example, take a certain number of pills at a certain time of day.

• How has it been for you to take these medicines this way?

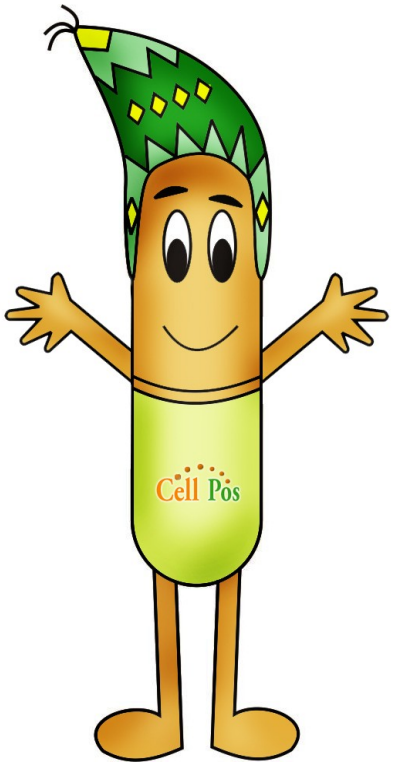
• What makes it hard to take these medicines? (cost, transportation, childcare, stigma?)

• What helps you take these medicines? (pill boxes, daily routine, reminders, regular meal times, privacy, support of friends or family, not drinking as much alcohol?)

• How serious is it to have HIV now that medicines to treat people with HIV/AIDS are here?

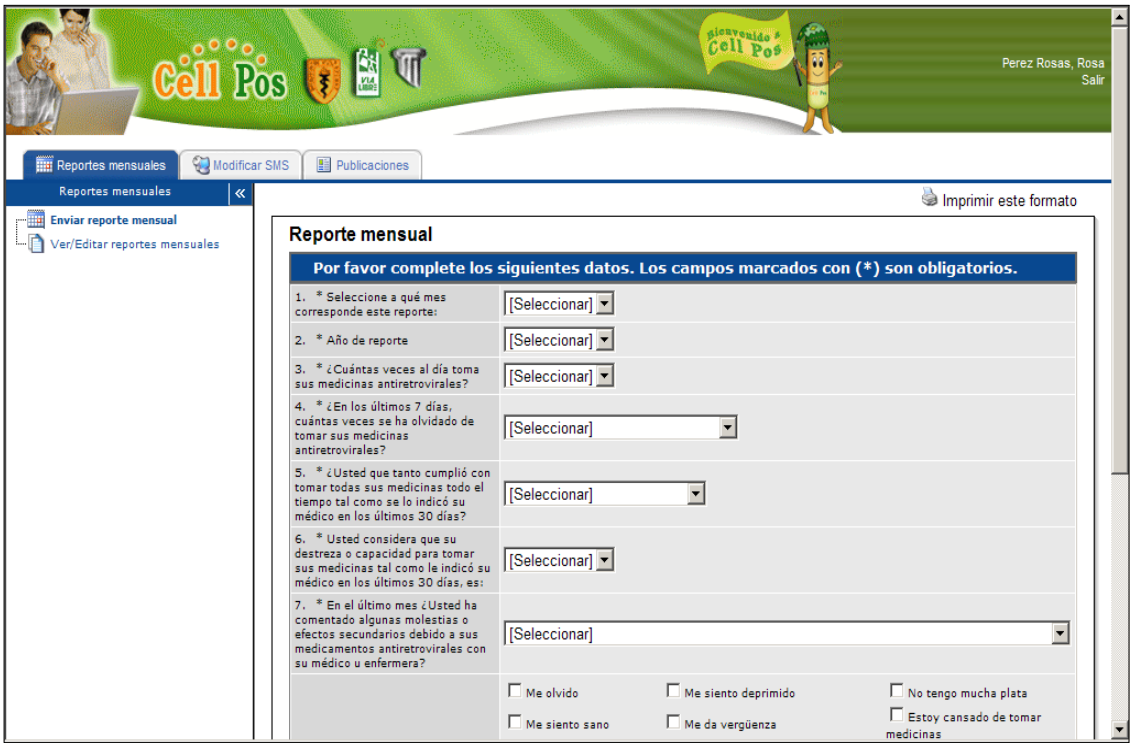
Appendix 2. Initial prototype showing the main page and the main menu

Appendix 3. Animated character used in the Cell-POS system



Appendix 4. Final prototype showing the main page

Appendix 5. Final prototype showing the survey



Vita

Walter H. Curioso, M.D., M.P.H. is a Research Professor at the Universidad Peruana Cayetano Heredia (UPCH) in Lima, Peru. Dr. Curioso received his M.D. from UPCH, and his M.P.H. from the University of Washington. By the time of his Ph.D. dissertation defense, he was working at the Peruvian Minister of Health as General Director of the General Office of Statistics and Informatics. His latest projects involve using mobiles devices to support adherence among HIV and diabetic patients, using cell phones to support prenatal care among pregnant women, and using cell phones and the Internet to develop a real-time surveillance system for adverse events. Dr. Curioso had developed a graduate program on health informatics at UPCH. He has written more than 100 publications on health informatics and information technology, evidence-based medicine, public health in developing countries, and clinical medicine. After his Ph.D. dissertation defense, Dr. Curioso will continue joining the Department as Affiliate Assistant Professor in the Division of Biomedical and Health Informatics in the School of Medicine at the University of Washington.