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Results of a randomized controlled trial to assess the effects of a mobile SMS-based intervention on treatment adherence in HIV/AIDS-infected Brazilian women and impressions and satisfaction with respect to incoming messages

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Abstract

Objective—To assess whether a warning system based on mobile SMS messages increases the adherence of HIV-infected Brazilian women to antiretroviral drug-based treatment regimens and their impressions and satisfaction with respect to incoming messages.

Design—A randomized controlled trial was conducted from May 2009 to April 2010 with HIV-infected Brazilian women. All participants ($n = 21$) had a monthly multidisciplinary attendance; each participant was followed over a 4-month period, when adherence measures were obtained. Participants in the intervention group ($n = 8$) received SMS messages 30 min before their last scheduled time for a dose of medicine during the day. The messages were sent every Saturday and

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Author contributions

- Thiago Martini da Costa: proposed the initial idea and design of the project, participated in system development, analyzed the results and wrote the manuscript.
- Barbara Jacqueline Peres Barbosa: actively participated in both conducting the project and the data analysis.
- Durval Costa and Alex Gomes: participated in the trial design, conducting the project and data analysis.
- Daniel Sigulem: proposed the idea of the project, system development and critical review of the manuscript.
- Heimar Fátima Marin: critical review of the project and manuscript.
- Adauto Castelo Filho: participation in the initial idea of the project, clinical study design and critical review of the manuscript.
- Ivan Torres Pisa: proposal of the initial idea and project design, participation in system development, examining the results, guidance, supervision and writing of the manuscript.

Conflicts of interest

The authors state that they did not receive any financial reward to conduct this research. This study was conducted in an academic environment by independent researchers. The Biwereless Comunika SMS Company has not participated in any part of the research, only donated the SMS.

Sunday and on alternate days during the working week. Participants in the control group ($n = 13$) did not receive messages.

Measurements—Self-reported adherence, pill counting, microelectronic monitors (MEMS) and an interview about the impressions and satisfaction with respect to incoming messages.

Results—The HIV Alert System (HIVAS) was developed over 7 months during 2008 and 2009. After the study period, self-reported adherence indicated that 11 participants (84.62%) remained compliant in the control group (adherence exceeding 95%), whereas all 8 participants in the intervention group (100.00%) remained compliant. In contrast, the counting pills method indicated that the number of compliant participants was 5 (38.46%) for the control group and 4 (50.00%) for the intervention group. Microelectronic monitoring indicated that 6 participants in the control group (46.15%) were adherent during the entire 4-month period compared to 6 participants in the intervention group (75.00%). According to the feedback of the 8 participants who completed the research in the intervention group, along with the feedback of 3 patients who received SMS for less than 4 months, that is, did not complete the study, 9 (81.81%) believed that the SMS messages aided them in treatment adherence, and 10 (90.90%) responded that they would like to continue receiving SMS messages.

SMS messaging can help Brazilian women living with HIV/AIDS to adhere to antiretroviral therapy for a period of at least 4 months. In general, the results are encouraging because the SMS messages stimulated more participants in the intervention group to be adherent to their treatment, and the patients were satisfied with the messages received, which were seen as reminders, incentives and signs of affection by the health clinic for a marginalized population.

Keywords

Adherence; Compliance; HIV; AIDS; Reminding; Cell phones; Wireless text messaging; SMS

1. Introduction

Due to its pandemic characteristics and severity, Acquired Immunodeficiency Syndrome (AIDS) represents one of the major public health problems facing the world today [1]. According to the World Health Organization (WHO) [2] in 2008, 33.4 million people around the world are living with Human Immunodeficiency Virus (HIV). In Brazil, more than 592,914 cases of AIDS have been identified since 1980 (the date of the first identification of an AIDS case in Brazil) and June of 2010 [1].

Despite the alarming prevalence of HIV worldwide, modern antiretroviral therapies are fairly effective at suppressing HIV, promoting an increase in life expectancy and quality that was not possible in the past. However, for antiretroviral therapies to be effective, patients must correctly adhere to the prescribed therapies.

According to Rueda et al. [3], people living with HIV/AIDS need to maintain high levels of adherence for the various antiretroviral regimens to be beneficial; however, the average rate of adherence to treatment for chronic conditions such as HIV is only approximately 50% [3].

Four factors have been reported as predictors of adherence problems to antiretroviral medication: regimen characteristics, patient factors, doctor–patient relationships and the care system [4]. Each of these factors plays an important role; however, studies have indicated that one of the most common forms of non-adherence is forgetting to take one's medication [4,5]. The use of temporal reminders or tips can significantly aid in overcoming this problem [5].

Low compliance is a major barrier to successful health care, where this is a problem that requires action [4]. Due to the multifactorial characteristics associated with low compliance, several strategies should be combined to achieve the desired effects. New strategies based on communication and information technology can increase therapy adherence because they can serve as reminders and enhance the transmission of information [6].

The use of short messaging service (SMS) by sending messages to patient cell phones has been shown to improve non-attendance rates [7,8], aid in changing habits and behaviors in diabetes management [9-11], promote preventive activities (such as taking vitamin C) [12] and increase vaccination rates among travelers [6].

The use of SMS messages sent to women was assessed by studies like Fjeldsoe et al. [13] who conducted a randomized controlled trial evidencing statistically significant results due to SMS on improving physical activity in postnatal women. Another study focusing women and using SMS was conducted by Cheng et al. [14] who evidenced that SMS reduces anxiety in pregnant women while waiting for test results of screening for Down syndrome.

According to Holmes [15], the next step of the evolution of Rwanda is the widespread of an innovation, based on UNICEF-developed rapid SMS system communication between local health workers, health centers, and hospitals. The system was initially designed to improve maternal health. Preliminary results show that SMS break down the barrier distance, and the delays in providing treatment when it is necessary to the pregnant or postpartum women and their children.

Despite the encouraging results of the use of SMS messages in these different studies, the preliminary results of a systematic review [16] indicate that there are few randomized controlled trials on the topic. Kaplan [17] noted that there are almost no studies analyzing the use of mobile phones as a tool for health intervention in patients infected with HIV, tuberculosis, malaria and other chronic conditions in developing countries. In addition, the first studies on the effects of SMS on patients living with HIV/AIDS are recent, and the applicability of such studies in other settings remains to be evaluated [18].

The objective of the study is to present the results of a randomized controlled trial that was conducted to assess whether an early warning system based on mobile messages, such as SMS, increases antiretroviral-drug treatment adherence in HIV-infected Brazilian women. Another objective is to evaluate the impressions and satisfaction of participants who received such messages.

2. Methods

The action strategy of this study was to send SMS messages to women infected with HIV through the HIV Alert System (HIVAS) web system as an intervention to enhance treatment adherence.

A randomized controlled trial was conducted over a period of 4 months with women living with HIV/AIDS who were served by the Multidisciplinary Center for Infectious Diseases in Pregnancy (NUPAIG-Núcleo Multidisciplinar de Patologias Infecciosas da Gestação), Federal University of São Paulo (UNIFESP-Universidade Federal de São Paulo). The experiment was approved by the Ethics in Research Committee of UNIFESP (under the number 0096/08), and informed consent was obtained from each study participant. The clinical research was registered at NUPAIG.

2.1. System development – HIVAS

To record study participant information, participant attendance, measures of adherence and send SMS messages, a web system here called HIVAS, was developed based on open-source technologies. The construction of the HIVAS followed the traditional software engineering phases of requirement gathering, fast design, system coding and testing [19].

The system architecture was modular, with 4 modules that were developed using the programming language PHP 5 [20] and the database system manager MySQL 5 [21].

As illustrated in Fig. 1, health providers and researchers access the system via a web interface (step 1) available on one of the UNIFESP servers. Any interaction with the HIVAS passes through the business logic (2), which queries the access control module (3) to verify that the user has authorization for the action (4). Aspects of the business logic include the registration and issue of sociodemographic characteristics of participants, registration and editing of data on participant attendance with their measures of adherence, the allocation of participants into one of two groups (control or intervention), the export of tabular data and the request for scheduling of SMS messages to the participants in the intervention group by others besides the system administrators. The business logic uses the database to hold records, for data editing (5) and for queries (6). The business logic processes the data and provides information on the web site (7), which can be viewed by the healthcare provider or the study investigators (8). It should be noted that each user has an access profile that limits his spectrum of action in HIVAS, thus ensuring the integrity of the research. Finally, the module for sending SMS messages, when triggered by the business logic (step A), is responsible for contacting a broker (B) that sends text messages to participants' mobile phones (C).

2.2. Study participants

The following were inclusion criteria for study participation: female gender, HIV infection diagnosis confirmed by western blot [22], patients taking first or second antiretroviral regimens containing two nucleoside analogs plus a protease inhibitor (with or without ritonavir reinforcement) or a non-nucleoside analog, patients with viral load below 400 copies/ml for at least three months and patients with CD4+ cell counts greater than 200/ mm^3.

The study excluded patients on prophylactic medications or therapies for opportunistic infections, patients who did not possess cell phones, illiterate patients and patients who refused to participate in the study.

2.3. Study design

The participants were recruited at the NUPAIG, where the nursing staff was instructed to forward to the researchers all patients who met the inclusion criteria. The study researchers presented the study, informed potential participant about data confidentiality and made it clear to the patients that they could refuse participation or withdraw consent with no influencing in their treatments. If a patient agreed to participate in the study, she was told that she could be placed in one of two groups (control or intervention), and she was asked not to inform any professional of the multidisciplinary team that would interact with her whether or not she was receiving text messages.

All study participants were provided the same kind of assistance by a multidisciplinary team composed of doctors, nurses, psychologists and, if necessary, nutritionists. None of the professionals who assisted the participants knew to which group a given patient was allocated. Although a multidisciplinary team provided care, only a medical professional

(DAGC) and nurse (BJPB) were part of both the treatment team and the study investigation team.

The study investigators who were part of the multidisciplinary team enrolled participants in the HIVAS. After 20 participants were registered, the system automatically randomly distributed the patients between the control and intervention groups, trying to maintain an equal number in each group. The allocation process went as follows: a random number was generated using the PHP mt rand function [23], whose result was a number between 0 and 2,147,483,647. If the random number generated was even, then the participant assigned to the intervention group, if it was odd, then the participant was assigned to the control group. After these 20 participants were allocated, a new draw was held monthly for participants who subsequently registered.

After the allocation, participants attended the NUPAIG monthly for 5 consecutive months. It took 5 meetings to obtain 4 months of treatment adherence. In these 5 meetings, the participants received conventional multidisciplinary care, during which all medical results of interest, along with data on adherence, were registered in the HIVAS by the doctor or nurse on the multidisciplinary team. In addition to the care provided and the collection of information, participants were provided with pill containers containing medications that were to be taken until the next visit.

According to the implemented process, during the last visit (in the 5th month), if the participant was allocated to the intervention group, then the HIVAS web system asked the investigator to interview the patient about her impressions and satisfaction in receiving text messages. Thus, the multidisciplinary team who treated the patients and collected data on adherence only knew participant group allocations at the end of the study. The blinding of the teams to the control and intervention groups protected data collection from possible bias. Beside this, it should be stressed that although not all patients were recruited at the same time, data from all participants were analyzed at the same time in November 2010.

2.4. Intervention

The intervention group strategy was to send, automatically through the HIVAS, an SMS message 30 min before the required time of the last required medication dose in a day. The messages were sent every Saturday and Sunday and during the working week on alternate days over 4 months. The content of the SMS message was chosen by consensus by the multidisciplinary team involved in patient care and the researchers: “The UNIFESP informs: take good care of your health.” The participants in the intervention group were not asked to respond to the messages. The costs for sending the messages (US$ 0.10 per SMS) were borne by the study through a grant from a telecommunications company.

Similar to other SMS intervention studies [12,18], the participants in the control group received no SMS messages. However, as a prerequisite for entering the study, these participants were required to possess cell phones to ensure full compatibility between groups.

No patient received any financial reward or reimbursement. In Brazil, government policy through the National Health System (SUS – Sistema Único de Saúde) ensures free access to medications necessary for treatment. We would like to make clear the ethical care used in designing the study to ensure the integrity of the study results.

2.5. Measurements

At the first meeting with the participants, we collected socioeconomic data, clinical data (viral loads and CD4+ levels), drugs and alcohol consuming, data on current patient

prescriptions of antiretroviral drugs, and mobile phone profiles of use among participants. Over the next 4 months, clinical information on the following measures of adherence to treatment was also collected: self-reported adherence, pill counting and MEMS microelectronic monitors (Aardex, Zug, Switzerland). During the last meeting, in addition to the adherence assessment, interviews were conducted with participants about their impressions and satisfaction with the SMS reminders. The investigators conducted the interviews on impressions and satisfaction using subjective and objective questions (Likert scale).

The socioeconomic status of the study participants was assessed using a validated questionnaire [24] that categorized the respondents into social classes, from A to E, in Brazilian standard scale. This questionnaire consisted of several items, each weighted for the categorization of the population, including education, education of the head of the household, average household income and ownership of assets such as a refrigerator, stove and television. As an example, social class labels were presented in terms of mean monthly household income (using the conversion of R$ 1.00 to US$ 0.61). Income was categorized into the following classes: A1, US$ 6008.02; A2, US$ 4051.85; B1, US$ 2147.53; B2, US$ 1252.59; C1, US$ 737.65; C2, US$ 448.15; D, US$ 299.38; and E, US$ 170.99.

The self-reported adherence [25] was a subjective measure of adherence, as it consisted of participants' self-reports on the ingestion of prescription drugs. As in similar study [18], patients were interviewed about the missed pills in the last 30 days. The adherence percentage was automatically calculated by the HIVAS as the total number of pills that the participant should have taken minus the number of pills that the participant reported that she had forgotten to take, divided by the total number of pills that the participant should have taken.

Pill counting [4] is an objective measure of adherence in which each participant received a container during the previous meeting for each prescribed antiretroviral medication with a certain number of pills. In the following monthly meeting, the participant was asked to bring the medication containers so the number of remaining pills could be counted. The difference between the number of pills given and the number of pills remaining in each container was an estimate of how many pills were taken between the two visits. The adherence percentage was calculated automatically by the HIVAS as the estimate of the number of pills taken divided by the number of pills that the participant should have taken.

The MEMS monitors [26] were pill containers with a special cover that stored the time and date each time the container was opened or closed. Health providers had a system which, when connected to the container, read the dosage history into a computer program that provided data on adherence. Due to budget constraints, this project could only use the MEMS containers for only 1 of the antiretroviral drugs prescribed for each participant.

As similar studies [4,18,27,28], participants were considered compliant if their intermeeting calculated adherence percentage was greater than 95%.

The interviews concerning patients' impressions and satisfaction in receiving text messages were all conducted in Portuguese language, the patients' native language. The qualitative feedback was translated from Portuguese to English by the American Journal Experts (http://www.journalexperts.com) by means of the service Premium Translation. In this service the paper was sent to a translator specialist in the field, a managing translator, a subject-expert editor, a senior editor, and a managing editor. After this process, the authors of the presenting paper reviewed the translations in a back-translation procedure.

2.6. Statistical methods and sample size

We used the Shapiro–Wilk test [29] to identify normality within numerically independent variables because the sample contained a small number of cases (less than 2000).

The averages of age of participants in intervention and control groups were compared using Mann–Whitney test [30]. For comparisons of two independent proportions we used the *Z*-test for proportions comparison [31]. Chi square test was not appropriate in the tables constructed due to the small sample size (less than 40), and the expected values lower than 5 [32]. The significance level used in this study was 95%.

The cross comparison of qualitative feedback and profile of participants was done using JMP software (http://www.jmp.com). Likelihood ratio and Pearson correlation were calculated to the variables analyzed.

According to Lester et al. [18], the percentage of participants who reported adherence to the antiretroviral therapy was 61.54% and 49.81% for intervention and control groups respectively. Considering this scenario, the sample size necessary for each group to achieve the significance level of 95%, and a power of 80%, considering one-sided and two-sided tests, was 221 and 281 patients respectively. Similar to Cocosila et al. [12] the online script available at http://stat.ubc.ca/~rollin/stats/ssize/index.html (cited 2011 August 18) was used to estimate the sample size of two-independent proportions and to calculate the power of this study.

Because this was an exploratory study, we used data from all participants we could enroll who fit the study inclusion criteria.

3. Results

Results are presented in four subsections: the HIVAS system, participant data, the effects of SMS on adherence and satisfaction and participant impressions of the SMS received.

3.1. HIVAS

The HIVAS, the system that received participant data and enabled SMS messages, was developed over 7 months during 2008 and 2009. In addition to study participant data, the HIVAS recorded data on CD4+ cell counts, viral loads, other prescription drugs and diagnostic hypotheses secondary to HIV. It is worth mentioning HIVAS also supported the data from other study concerning adherence of people living with HIV/AIDS.

3.2. Baseline data

We interviewed 59 patients from May 2009 to April 2010, according to the project chronogram and budget. Of these patients, 2 refused to participate in the study because they could not justify one absence per month at work, and 23 patients did not fit the inclusion criteria for the study (21 did not have cell phones, and 2 did not have detectable viral loads at the beginning of the study). The 29 remaining patients were randomly assigned to the control group (15) or the intervention group (12). Of the control group, 2 dropped out of the study (one did not return to the medical center, and another obtained a job and could not justify a monthly absence). Of the participants in the intervention group, 5 did not receive SMS for the entire 4-month period (3 were assaulted and had their mobile phones stolen, one had her mobile phone broken, and one stopped the follow-up meetings before the end of the 4 months because she moved to another city). The enrollment flow diagram of the study participants is represented in Fig. 2.

Participants were characterized according to age, race, economic class and education to verify compatibility between the two groups. The baseline features of the participants did not show a normal distribution according to the Shapiro–Wilk test [29]. The average age of participants was 34.62 ± 6.92 years. There was no significant difference (p-value = 0.447) between the average ages of participants between groups, which were 33.69 ± 5.34 and 36.13 ± 9.14 years, for the control and intervention groups respectively. There were no statistically significant differences in the other baseline characteristics, except on the marital status where the proportion of married women in the control group is higher ($p = 0.026$) then in the intervention group as illustrated in Table 1.

Seven (53.84%) participants in the control group reported to drink alcohol in the last 30 days, while only 1 (12.50%) participant in the intervention group reported drink alcohol (p-value = 0.058). The participants in the control group who mentioned to drink alcohol in the last 30 days, ranged from 1 to 5 in the number of days in which they drink it, on the other hand, the participants in the intervention group who affirmed drink alcohol stated to drink it in 22 days from the last 30. No participant (0.00%) in the control group reported to have already used drugs; while 4 (50.00%) participants in the intervention group reported have already used some kind of drug (p-value = 0.005). The drugs mentioned by participants in the intervention group were cigarettes 3 (37.50%, p-value = 0.017), marijuana 2 (25.00%, p-value = 0.058), cocaine 2 (25.00%, p-value = 0.058), and ecstasy 1 (12.50%, p-value = 0.192). Two (25.00%, p-value = 0.058) participants in the intervention group mentioned the use of drugs every day in the last 30 days, the other two (25.00%, p-value = 0.058) participants in the intervention group who have already used drugs stated they did not use drugs for longer than 6 months.

The mobile phone profiles of use among participants before the study are presented in Table 2. Only on two categories there were statistically significant differences. More patients in intervention group reported receiving messages from advertising (p-value = 0.027) and news (p-value = 0.017).

3.3. Effects on adherence

The adherence percentage of participants in the intervention and control groups was measured by the following methods: self-reported adherence, pill counting and micro-electronic monitoring. The results are presented in Table 3, both month-by-month and by the totals during the 4-month period in terms of the percentage of participating members who adherent to their treatment (percentage of participants with adherence > 95%).

3.4. Impressions and satisfaction regarding the SMS messages received

At the end of the 4-month period, in the 5th month, the participants who received SMS messages were interviewed to assess their level of satisfaction with the service provided. All interviews were conducted by the same interviewer. The results presented in this section refer to the 8 patients who were analyzed in the intervention group, along with the data of 3 patients who were assigned to the same group but who received the messages for the 1st, 2nd or 3rd months only. We believe that the feedback from these 3 patients who received SMS for less than 4 months is still important and needs to be reported.

The answers to the objective questions, with their respective Likert scale values (from 1 to 5 and from 1 to 3), are reported in terms of the number of response and percentages of respondents in Table 4.

The cross comparison of the questions ‘Helped to take medications’ and ‘Would like to continue receiving SMS’ with some profile of the participants variables are presented in Table 5. In order to do these analyzes Likert 4 and 5 were considered as helped to take

medications, and Likert 1, 2 and 3 were considered as not helped to take medications. The answers 'Yes', and 'Yes with changes' were considered as would like to continuing receiving SMS. Some profiles of participants were also grouped in two different groups, for example, 'Elementary' and 'Middle School' were grouped as 'Not Completed High School', and 'Completed High School' continued with the same label; B1 and B2 classes were a group, and C1, C2, and D classes become another group. No statistic significant correlation was found.

The answers to subjective questions were grouped as appropriate. Some representative responses and comments from participants are listed.

Three participants (27.27%) stated that the time at which the messages were sent did not require modification, 3 participants (27.27%) stated that the timing of the messages should be closer to the time of medication intake, and 5 participants (45%) made no comment regarding the timing of the messages.

Concerning the SMS message content, 10 participants (90.90%) suggested that the text did not need to be changed, and 1 (9.09%) suggested that the wording should be changed daily. Two comments illustrative of the participant responses follow: "It would not change. The message is short and reminds us that we have to take care of ourselves," and "Yes, change the content of messages daily. Example: Alert, do not forget your medicine."

In general, the participants mentioned more than 1 positive aspect of the SMS approach. Among the highlighted strengths were the following: 7 participants (63.63%) mentioned that it helped them to remember the time at which they should take their medication, 5 (45.45%) said the messages provided an incentive to take their medications or to take better care of their health, 3 (27.27%) reported that they felt that the medical center or someone else cared about them, and 1 (9.09%) mentioned that the project allowed for family involvement in her treatment. Some comments representative of the thoughts expressed by the participants are as follows:

> "It helped me remember the intake time when I'm at home or on vacation."
>
> "First, it reminded me to take my medication on time. The message is very good, it tells us to take care of our health, but does not say why. If someone took the phone and looked at the message, they would not find out what it was."
>
> "It is an incentive to take care of ourselves. Someone cares about you at that moment, someone thought of me. There was also an involvement of my family because the children tell me when the message arrives, even when I'm away from home."

Unlike with the cited positive items, none of the 4 participants who listed negative items mentioned more than a single negative issue with the SMS method. There were 3 mentions (27.27%) of the length of time between the arrival of the SMS message and the actual time of medication intake and 1 complaint (9.09%) of receiving several text messages on the same day for a few days. Two statements exemplify the negative points mentioned: "*too far away from the true time of medicine intake*," and "the days in which I received numerous text messages at various times as I was traveling."

A question soliciting suggestions or general feedback was provided at the end of the interview. Five participants (45.45%) offered no other suggestion or comment, 3 (27.27%) suggested that the study messages should continue as they had been, 1 (9.09%) suggested that the message should be sent at most 5 min before the time of medication intake, and 2 (18.18%) used the question space to comment on what happened during the study, for

example, reporting that they had been assaulted. An interesting comment from one of the participants should be emphasized: “Continue the way it is. I liked this study, I want it to continue. I think people should participate in this study, receiving the message, everyone who has HIV disease, because people often think about quitting, I thought about it (*quitting*), but not anymore, the messages help me not to give up.”

4. Discussion

Treatment adherence is a challenge in clinical practice because it requires the optimization of constant monitoring. According to the literature [5], a combination of strategies will provide practical and effective help for most patients, including keeping the diet as simple as possible, negotiating priorities with the patient, providing clear instructions, reminding patients about their appointments, monitoring adherence to treatment, calling patients who have missed appointments to follow them more closely and emphasizing the importance of a high level of treatment adherence during each visit. At the NUPAIG, the service provided to all patients, regardless of the study in question, follows most of these guidelines. In the present study, we tried to add an item to this list of strategies to improve adherence, the use of SMS messages.

SMS messages have shown a potential benefit in helping patients to remain adherent to treatment [6,9,10,12,18]. These messages have distinct advantages in terms of reducing intrusions into the patient’s life and their relative simplicity and low cost compared to voice communications [18,33]. However, there is a paucity of randomized controlled trials on how messages can help with the management of chronic diseases [16].

In a systematic review of the Cochrane literature in 2010 on the types of aid and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS, Rueda et al. [3] included 19 studies, none of which used SMS to help patients with HIV with this kind of treatment. The authors mentioned that they excluded several items from their analysis due to low methodological quality, in which the most common problems were lack of comparison with the control group, the use of only subjective measures of adherence, and failure to report the measure of adherence for both groups for at least 6 weeks. These results corroborate the findings of Thyra et al. [16] about the scarcity of randomized controlled clinical trials relating to text messaging to improve the compliance of patients living with HIV/AIDS and taking highly active antiretroviral therapy.

According to Lester et al. [18], the only previously randomized controlled trial examining text messaging and treatment adherence was their study in Kenya that was published in December 2010. The authors [18] conclude that although their study is the first of its kind and showed positive results, its applicability to other countries needs to be evaluated.

We conducted a randomized, controlled study with both objective and subjective measures of treatment adherence for 16 weeks. Both groups (control and intervention) received the same treatment and care in the NUPAIG clinic, with the only exception being that the intervention group received SMS messages during that period in addition to conventional care. The parallel care allowed us to evaluate the effect of the SMS intervention in isolation and not in conjunction with a package of strategies.

Moreover, Rueda et al. [3] found in his review that the groups that benefit less from adherence-improvement strategies are women, Latinos and patients with a history of alcoholism. In our study, we focused on a specific group of people living with HIV/AIDS who are Latina women; in our case, they were Brazilian women.

The percentage of participants who completed high school (38.10%) is similar to the Brazilian women with HIV/AIDS (33.0%) [34]. Despite this, the percentage of participants in this study who have completed the College (14.29%) is greater than Brazilian percentage (4.2%) [34]. A possible explanation is that the study was conducted in São Paulo metropolitan area, one of the most developed Brazilian area.

The main occupations among the participants are in general simple and do not need higher education, for example, housewife (42.86%), cleaning assistant (9.52%), sales person (9.52%), the only one exception was the teacher occupation (9.52%).

The social class C1 (33.33%) and B2 (33.33%) were the most common among the participants. In São Paulo metropolitan area, the place where this study was conducted, C1 and B2 are respectively the first and third most frequent social class [24].

Most participants (90.48%) have a prepaid phone. Just over half of respondents (66.67%) use the mobile phone for personal and professional purposes; the others use it only for personal purposes. Participants say they have the habit of reading SMS messages (90.48%), but the percentage of patients who stated to have the habit of sending SMS was lower (61.90%). The habit of sending SMS messages with images was declared by fewer participants (19.05%).

Reading SMS was a common habit among the participants before the study. When asked from whom the patients often receive SMS, the main categories listed were: friends (71.43%), relatives (66.67%), advertisements (57.14%) and news (14.29%). None of the patients indicated that she have already received messages from an outpatient clinic.

We used three measures of treatment adherence: 2 objective measures and 1 subjective measure. The subjective measure, the self-reported adherence, granted the researchers an indication of what the patients think about their treatment adherence. In the study by Lester et al. [18], the only direct measure of adherence used was the self-reported adherence during the final 30 days. However, as the authors asserted, overestimation can occur during such interviews, due to factors such as the difficulty in remembering all details of the drugs, patient attempts to please their doctors or avoid confrontation or a combination of several factors [5]. Objective measures also have advantages and disadvantages; however, it is not within the scope of this study to discuss the effectiveness of each method. We used the 3 most common measures of adherence to facilitate comparison of our results with those of other studies and to provide a more reliable evaluation of compliance.

The messages were not sent every day of the week, because researchers assumed that the daily delivery of messages could aggravate the participants or lead them to trivialize the messages. The choice to send messages on Saturdays, Sundays and on alternate days on weekdays was based on the clinical experience of the researchers designing the study as well as in studies such as that of Bachhuber et al. [35], which determined that treatment adherence for people living with HIV/AIDS can be significantly lower on weekends than during the week, although the authors mentioned that more studies need to be performed because there is a lack of strong evidence in support of such claims.

Lester et al. [18] used a different approach, in which a single SMS message was sent on Monday morning, asking, “How are you?” to all participants in the intervention group. If the participant did not answer or responded negatively to the SMS, a phone call was made. The authors [18] sent fewer messages than in our study. However, the participants had to pay the costs of responding to the messages, and phone calls were often necessary.

Although our initial idea was to send different messages, it was decided during the planning of this study send a single, identical message during the study. Because this was an exploratory study with a small sample size, and there was no prior idea of how an SMS message or a change in SMS wording might impact the subsequent analysis, avoiding changes in wording eliminated potential problems that would have made the data analysis more difficult.

We had some difficulty to recruit the desirable sample size, and we could not obtain it. It is worth to mention some of the factors that contributed to the small sample size. The first two were to limit the population to women and to those who possess cell phones. According to DATASUS, in Brazil 39.24% of the new cases of HIV were in women in 2010. We interviewed 59 patients, 21 (35.60%) did not posse cell phone. These two factors by themselves start limiting our sample.

The main barriers to conduct this study, that should be taken into account while conducting similar studies, were the methods applied. It was very time consuming to measure adherence the way we did. In the same consultation, the following additional procedures were performed: patients were interviewed about pills not taken; the number of remaining pills in each container were counted; the pills to each retroviral that the patient would receive until next month were counted and packed in specific containers; data from MEMS were uploaded to the web system; and finally, everything was registered in HIVAS. According to nurses, these additional procedures double the time of the usual consultation. Although it is important to use more than one method to improve the scientific validity of the research, we found that it was not possible to do this in a public Brazilian outpatient clinic with the usual human resources. An extra doctor and nurse had to integrate the outpatient clinic staff in order to make this research possible. Nevertheless even conducting the research through more than a year only 29 patients were allocated, and only 21 finished the study. Indeed we enrolled all patients that could be enrolled with our limitations.

Four participants in the intervention group were dropped from the study in an attempt to maintain study blinding. With better planning, such a loss could have been avoided. At the beginning of the study, the participants were not informed to notify the medical center and the study's investigators if any communication difficulties arose. Theft of mobile phones, broken phones and moving to areas with no signal were all factors that impeded the ability of patients to receive messages throughout the study. With better planning, such difficulties could have been circumvented.

The adherence of participants from both treatment groups was generally good. We believe that similar circumstances might have contributed to such good treatment adherence. For example, both treatment groups were subject to previous NUPAIG measures that were designed to increase adherence, such as a month-long monitoring (usually held quarterly) and sporadic actual measurement of monthly adherence.

There were differences among the three methods used to measure adherence. It is not within the scope of this study to discuss which method was better at measuring adherence; however, it is worth noting that using only a single method to measure adherence might mask actual patient behavior.

Overall, participant adherence in the intervention group was slightly higher than that in the control group, considering both individual months and the full 4-month period. In all 3 methods used to measure adherence, and during every month of the 4-month period, the percentage of participants who maintained a compliance rate of 95% was higher in the intervention group than in the control group. The power of this study, given the sample size obtained and the confidence level of 95% was calculated as 15% for one-sided test and 9%

for two-sided test. Probably due to the small sample size, we found no statistically significant difference between the results of the control and intervention groups, but the fact of all 15 measures show better adherence of the intervention group than control group need to be highlighted.

Lester et al. [18] evaluated adherence by the self-reported adherence in the last 30 days on two occasions, the 6th and 12th months. Considering the full period of 1 year, the authors [18] found that 168 participants in the intervention group (62%) had a compliance rate of 95%, whereas 132 participants in the control group (50%) remained adherent, a difference of 12.00%. In our study, considering the full period of 4 months, and the self-reported adherence method, 8 participants in the intervention group (100.00%) remained adherent in every month compared to 11 (84.62%) in the control group, a difference of 15.38%.

Participant views on the use of SMS messaging were another important result of this study. Overall, participants rated the amount of messages they received on their mobile phones as very good (54.54%) or good (36.36%) The timing of the messages pleased most participants (72.72% – Likert 4 and 5), was received indifferently by a few participants (9.09% – Likert 3) and displeased some other participants (18.18% – 1 and 2 Likert). Participants who did not like the message schedule requested that it be sent closer to the time of medication intake, such as five minutes before their required intake time.

These data show that perhaps only the schedule of messages should be adjusted (closer to the time at which the participant must take his or her medication), whereas the number of messages should be maintained, as 100.00% of patients (Likert 4 and 5) liked the amount of messages received. Thus, the choice not to send messages every day, only on certain days during the working week and on weekends, seems appropriate.

The wording of the messages was well received by the participants. Interviews with the study participants showed that 90.90% (Likert 4 and 5) of study participants suggested that the wording of the message should not change.

All participants (Likert 1 and 2) mentioned that the messages did not disrupt their intake of medication. A few (27.27%) noted some negative complaints concerning the study approach. It is noteworthy that one of the participants who raised a negative complaint traveled to another state, and during the period in which she was traveling, she received up to 20 messages in a single day due to technical problems.

Most participants (81.81% – Likert 4 and 5) reported that the messages aided them in taking their medications, while only 1 (9.09% – Likert 3) could not identify whether the messages helped. None of the participants (0.00% – Likert 1 and 2) reported that the messages did not help.

Several strategies can be combined to assist HIV/AIDS patients in maintaining treatment adherence. Thus, further long-period studies examining the use of SMS in increasing treatment adherence of HIV/AIDS patients should be encouraged. Such research should be conducted both to aid in the search for the best techniques to ensure greater adherence and also for patient satisfaction.

5. Conclusion

The results of this study show that SMS messages can help Brazilian women living with HIV/AIDS to remain adherent to antiretroviral therapy for a period of 4 months. As measured by the 3 methods used to assess adherence, the percentage of participants in the intervention group who remained adherent to treatment was greater than the percentage of

participants in the control group. There were differences between the results measured by the different methods. These differences suggest that for consistent evaluation, more than one method is necessary.

The study had a small sample size due to the difficulty of conducting a fully randomized, controlled trial with consistent measures of adherence for such specific inclusion criteria. However, the overall results were encouraging, as the SMS messages stimulated more participants in the intervention group to be adherent to treatment, at a low cost and with low interference in the patients' lives. The message method was also relatively simple, and the patients were very satisfied with receiving the messages. Text messages were viewed by participants as reminders, incentives, as someone caring for them and as an act of affection by the health clinic toward a marginalized population.

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REFERENCES

[1]. Ministério da Saúde do Brasil [Internet]. [accessed 18.05.11] AIDS No Brasil, Ministério da Saúde, Coordenação Nacional de DST/Aids, Brasil. 2011. Available from: http://www.aids.gov.br/pagina/aids-no-brasil

[2]. UNAIDS World Health Organization (WHO). AIDS Epidemic Update: November 2009, WHO Library Cataloguing-in-Publication Data. Geneva: 2009.

[3]. Rueda S, Park-Wyllie LY, Bayoumi A, Tynan AM, Antoniou T, Rourke S, Glazier R. Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. Cochrane Database Syst. Rev. Jul.2006 3 doi:10.1002/14651858.CD001442.pub3, CD001442.

[4]. World Health Organization (WHO). Adherence to Long-term Therapies: Evidence for Action, WHO Library Cataloguing-in-Publication Data. Geneva: 2003.

[5]. Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: clinical applications. JAMA. Dec 22.2002 288:2880–2883. [PubMed: 12472330]

[6]. Vilella A, Bayas JM, Diaz MT, Guinovart C, Diez C, Simó D. The role of mobile phones in improving vaccination rates in travellers. Prev. Med. Apr.2004 38:503–509. [PubMed: 15020186]

[7]. Costa TM, Salomão PL, Martha AS, Pisa IT, Siguem D. The impact of short message service text messages sent as appointment reminders to patients' cell phones at outpatient clinics in São Paulo, Brazil. Int. J. Med. Inform. Jan 1.2010 79:65–70. doi:10.1016/j.ijmedinf.2009.09.001. [PubMed: 19783204]

[8]. Downer SR, Meara JG, Da Costa AC. Use of SMS text messaging to improve outpatient attendance. Med. J. Aust. Oct 7.2005 183:366–368. [PubMed: 16201955]

[9]. Kim HS, Kim NC, Ahn SH. Impact of a nurse short message service intervention for patients with diabetes. J. Nurs. Care Qual. 2006; 21(3):266–271. [PubMed: 16816608]

[10]. Volcke D, Snoeck P, Festjens T, Kowalski J, Jones R, van Hoorde S. Feasibility and acceptability of short message service (SMS) text messaging to support adherence in patients receiving quetiapine: a pilot study. Abstract for poster sessions. Eur. Psychiatry. 2007; 22:S221, S341.

[11]. Lee TI, Yeh YT, Liu CT, Chen PL. Development and evaluation of a patient-oriented education system for diabetes management. Int. J. Med. Inform. 2007; 76(9):655–663. doi:10.1016/j.ijmedinf.2006.05.030. [PubMed: 16815741]

[12]. Cocosila M, Archer N, Haynes RB, Yuan Y. Can wireless text messaging improve adherence to preventive activities? Results of a randomized controlled trial. Int. J. Med. Inform. 2009; 78(4): 230–238. doi:10.1016/j.ijmedinf.2008.07.011. [PubMed: 18778967]

[13]. Fjeldsoe BS, Miller YD, Marshall AL. MobileMums: a randomized controlled trial of an SMS-based physical activity intervention. Ann. Behav. Med. May 2.2010 39:101–111. [PubMed: 20174902]

[14]. Cheng PJ, Wu TL, Shaw SW, Chueh HY, Lin CT, Hsu JJ, Hsieh TT, Soong YK. Anxiety levels in women undergoing prenatal maternal serum screening for Down syndrome: the effect of a fast reporting system by mobile phone short-message service. Prenat. Diagn. May 5.2008 28:417–421. [PubMed: 18395869]

[15]. Holmes D. Rwanda: an injection of hope. Lancet. Sep; 2010 376(9745):945–946. [PubMed: 20857547]

[16]. Thyra DJ, Ipek GU, Vlastra VJ, Josip C, Rifat A. Mobile phone messaging telemedicine for facilitating self management of long-term illnesses (protocol for a cochrane review). Cochrane Libr. 2010; 1

[17]. Kaplan WA. Can the ubiquitous power of mobile phones be used to improve health outcomes in developing countries? Global Health. May.2006 2:9. [PubMed: 16719925]

[18]. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, Jack W, Habyarimana J, Sadatsafavi M, Najafzadeh M, Marra CA, Estambale B, Ngugi E, Ball TB, Thabane L, Gelmon LJ, Kimani J, Ackers M, Plummer FA. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomized trial. Lancet. 2010; 6736(10):61997–62006. doi:10.1016/S0140.

[19]. Pressman, RS. Software Engineering: A Practitioner's Approach. 6th ed.. McGraw Hill: 2005.

[20]. PHP: Hypertext Preprocessor PHP [Internet]. [accessed 18.05.11] PHP: Hypertext Preprocessor PHP. 2011. Available from: http://www.php.net

[21]. MySQL [Internet]. [accessed 18.05.11] MySQL: The World's Most Popular Open Source Database. 2011. Available from: http://www.mysql.com

[22]. Burnette WN. Western blotting": electrophoretic transfer of proteins from sodium dodecyl sulfate-polyacrylamide gels to unmodified nitrocellulose and radiographic detection with antibody and radioiodinated protein A. Anal. Biochem. Apr 2.1981 112:195–203. [PubMed: 6266278]

[23]. PHP: Hypertext Preprocessor PHP [Internet]. [(accessed 18.05.11)] Function mt rand – Generate a Better Random Value. 2011. Available from: http://php.net/manual/en/function.mt-rand.php

[24]. Associação Brasileira de Empresas de Pesquisa (ABEP) [Internet]. [accessed 9.02.11] Critério de Classificação Econômica Brasil. 2008. Available from: http://www.abep.org/novo/Content.aspx?ContentID=139

[25]. Walsh JC, Mandalia S, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS. 2002; 16:269–277. [PubMed: 11807312]

[26]. AARDEX [Internet]. [accessed 18.05.11] MEMS Products. 2011. Available from: http://www.aardexgroup.com/aardex_index.php?group=aardex&id=85

[27]. Bangsberg DR, Hecht FM, Charlebois ED, Zolopa AR, Holodniy M, Sheiner L, Bamberger JD, Chesney MA, Moss A. Adherence to protease inhibitors, HIV-1 laod, and development of drug resistance in an indigent population. AIDS. 2000; 14(4):357–366. [PubMed: 10770537]

[28]. Vaz, MJR. PhD thesis. Universidade Federal de São Paulo; São Paulo: 2003. Aderência ao tratamento com drogas anti-retrovirais entre mulheres grávidas e não grávidas infectadas pelo vírus da imunodeficiência humana.

[29]. Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). Biometrika. 1965; 52(3):591.

[30]. Anderson, DR.; Sweeney, DJ.; Williams, TA. Estatística aplicada à administração e economia. 2nd ed.. Thomson Learning; São Paulo: 2007.

[31]. Siegel, S. Estatística Não-Paramétricapara as ciências do comportamento. McGraw Hill do Brasil; São Paulo: 1975.

[32]. Arango, HG. Bioestatística teórica e computacional. 3rd ed.. Guanabara Koogan; Rio de Janeiro: 2009.

[33]. Stucken, A. [accessed 18.05.11] What is SMS.BBC. 2010. Available from http://www.bbc.co.uk/webwise/guides/about-sms

[34]. Ministério da Saúde do Brasil [Internet]. Boletim Epidemiológico AIDS/DST 2010 – Versão preliminar. Brasília: Dec. 2010 Avaliable from http://www.aids.gov.br/publicacao/boletim-epidemiologico-2010 [accessed 30.05.11]

[35]. Bachhuber M, Bilker WB, Wang H, Chapman J, Gross R. Is antiretroviral therapy adherence substantially worse on weekends than weekdays? J. Acquir. Immune Defic. Syndr. 2010; 54(1): 109–110. [PubMed: 20418726]

Summary points

What was already known on the topic?

- Interventions targeting marginalized people living with HIV/AIDS, including women, Latinos, and patients with past history of alcoholism, have demonstrated a lack of success in increasing adherence.
- SMS messages have demonstrated potential in aiding patients in adhering to their treatments.
- There is a lack of randomized controlled studies that help to highlight the effects of SMS messaging in patient adherence to highly active antiretroviral therapy for HIV/AIDS.

What this study added to our knowledge?

- Evidence of the effects of SMS on the adherence of Brazilian women living with HIV/AIDS to antiretroviral treatment.
- The feedback of patients who had received SMS messages about the service.

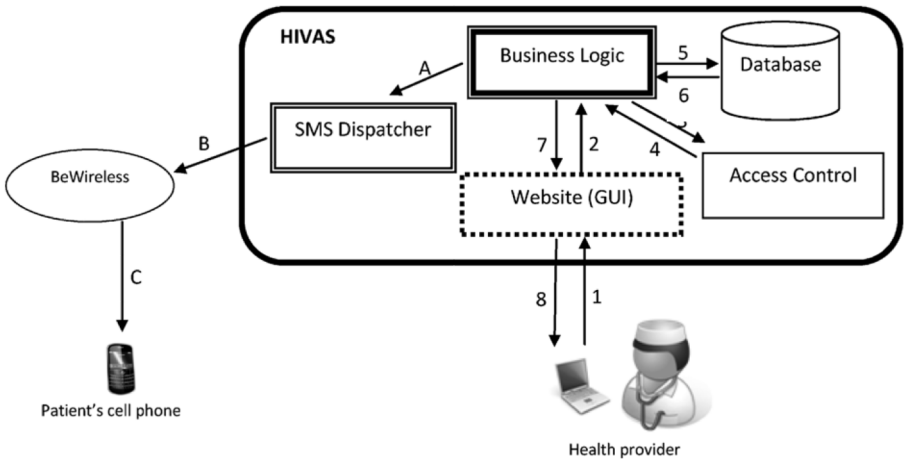

Fig. 1. Architecture of the HIV Alert System – HIVAS

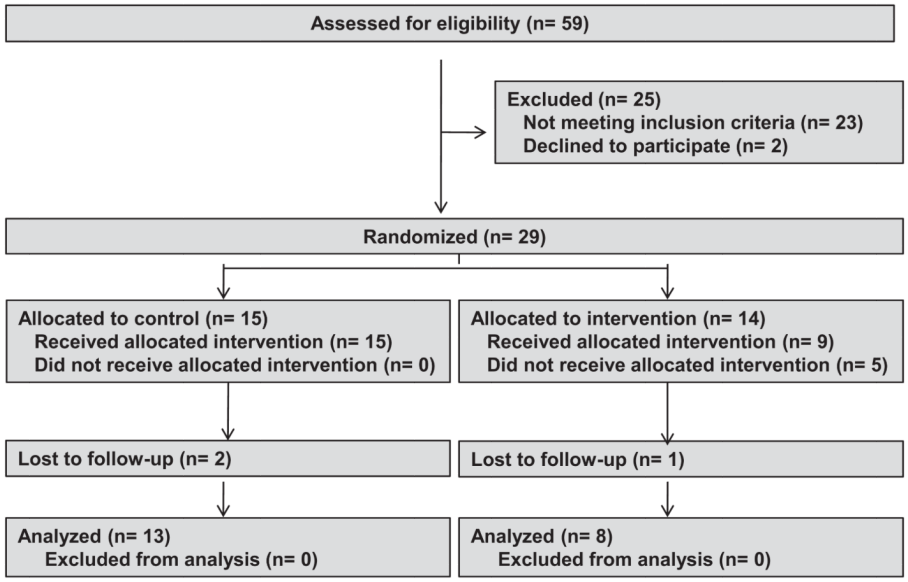

Fig. 2. Enrollment flow chart of the study participants

Table 1

Baseline features of both groups. Socioeconomic status here is represented in parentheses by the mean monthly household income in dollars.

	Control	Intervention	Total	Z-test	*p*-Value
Sex					
F	13 (100.0%)	8 (100.0%)	21 (100.0%)	–	–
Race					
White	3 (23.08%)	1 (12.50%)	4 (19.05%)	0.599	0.549
Indian	1 (7.69%)	0 (0.00%)	1 (4.76%)	0.804	0.422
Black	3 (23.08%)	3 (37.50%)	6 (28.57%)	0.711	0.477
Mulatto	6 (46.15%)	4 (50.00%)	10 (47.6%)	0.171	0.864
Social class					
B1 (US$ 2147.53)	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.365	0.716
B2 (US$ 1252.59)	6 (46.15%)	1 (12.50%)	7 (33.33%)	1.589	0.112
C1 (US$ 736.65)	3 (23.08%)	4 (50.00%)	7 (33.33%)	1.271	0.204
C2 (US$ 448.15)	2 (15.38%)	1 (12.50%)	3 (14.29%)	0.183	0.854
D (US$ 299.38)	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.364	0.716
Schooling					
Completed elementary	1 (7.69%)	3 (37.50%)	4 (19.05%)	1.689	0.091
Completed middle school	5 (38.46%)	1 (12.50%)	6 (28.57%)	1.279	0.201
Completed high school	4 (30.77%)	4 (50.00%)	8 (38.10%)	0.881	0.378
Completed college	3 (23.08%)	0 (0.00%)	3 (14.29%)	1.468	0.142
Marital status					
Single	2 (15.38%)	3 (37.50%)	5 (23.81%)	1.155	0.248
Married	11 (84.62%)	3 (37.50%)	14 (66.67%)	2.224	0.026*
Widow	0 (0.00%)	2 (25.00%)	2 (9.52%)	1.895	0.058
Occupation					
Housewife	6 (46.15%)	3 (37.50%)	9 (42.86%)	0.389	0.697
Cleaning assistant	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.365	0.716
Sales person	2 (15.38%)	0 (0.00%)	2 (9.52%)	1.166	0.244
Teacher	2 (15.38%)	0 (0.00%)	2 (9.52%)	1.166	0.244
Security	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.385	0.716
Assistant general service	0 (0.00%)	1 (12.50%)	1 (4.76%)	1.306	0.192
Administrative assistant	0 (0.00%)	1 (12.50%)	1 (4.76%)	1.306	0.192
Credit analyst	1 (7.69%)	0 (0.00%)	1 (4.76%)	0.804	0.422
Retiree	0 (0.00%)	1 (12.50%)	1 (4.76%)	1.306	0.192
Total	13 (61.90%)	8 (38.09%)	21 (100.00%)	–	–

*p-Value < 0.05.

Table 2
Mobile phone profiles of use among participants.

	Control	Intervention	Total	Z-test	*p*-Value
Payment type					
Prepaid	12 (92.31%)	7 (87.50%)	19 (90.48%)	0.365	0.716
Postpaid	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.365	0.716
Purpose of use					
Only personal	3 (23.08%)	4 (50.00%)	7 (33.33%)	1.271	0.204
Personal and professional	10 (76.92%)	4 (50.00%)	14 (66.67%)	1.271	0.204
Habit of reading SMS					
Yes	12 (92.31%)	7 (87.50%)	19 (90.48%)	0.365	0.715
No	1 (7.69%)	1 (12.50%)	2 (9.52%)	0.365	0.715
Habit of sending SMS					
Yes	7 (53.85%)	6 (75.00%)	13 (61.90%)	0.969	0.332
No	6 (46.15%)	2 (25.00%)	8 (38.10%)	0.969	0.332
Habit of sending SMS with images					
Yes	1 (7.69%)	3 (37.50%)	4 (19.05%)	1.689	0.091
No	12 (92.31%)	5 (62.50%)	17 (80.95%)	1.689	0.091
Usually receive SMS from					
Friends	9 (69.23%)	6 (75.00%)	15 (71.43%)	0.284	0.776
Relatives	8 (61.64%)	6 (75.00%)	14 (66.67%)	0.635	0.525
Advertising	5 (38.46%)	7 (87.50%)	12 (57.14%)	2.205	0.027*
News	0 (0.00%)	3 (37.50%)	3 (14.29%)	2.385	0.017*
Bank institutions	0 (0.00%)	2 (25.00%)	2 (9.52%)	1.895	0.058
Soccer	0 (0.00%)	1 (12.50%)	1 (4.76%)	1.306	0.191
Others (not specified)	2 (15.38%)	0 (0.00%)	2 (9.52%)	1.166	0.244
Total	13 (61.90%)	8 (38.09%)	21 (100.00%)	–	–

*p-Value < 0.05.

Table 3

Percentage of participants who remained adherent (adherence percentage >95%) during the 4-month study

Month	Percentage of participants who adhered to their treatments (adherence percentage >95%)											
	Self-reported adherence				Pill counting				MEMS			
	Control	Intervention	Z-test	*p*-Value	Control	Intervention	Z-test	*p*-Value	Control	Intervention	Z-test	*p*-Value
1st	13 (100.00%)	8 (100.00%)	–	–	9 (69.23%)	6 (75.00%)	0.2842	0.7763	8 (61.54%)	6 (75.00%)	0.6355	0.5251
2nd	13 (100.00%)	8 (100.00%)	–	–	8 (61.54%)	5 (62.50%)	0.0441	0.9649	8 (61.54%)	6 (75.00%)	0.6355	0.5251
3rd	12 (92.31%)	8 (100.00%)	0.8038	0.4215	7 (53.85%)	6 (75.00%)	0.9694	0.3324	8 (61.54%)	7 (87.50%)	1.2789	0.2009
4th	12 (92.31%)	8 (100.00%)	0.8038	0.4215	6 (46.15%)	5 (62.50%)	0.7284	0.4664	7 (53.85%)	6 (75.00%)	0.9694	0.3324
1st to 4th	11 (84.62%)	8 (100.00%)	1.1663	0.2435	5 (38.46%)	4 (50.00%)	0.5189	0.6038	6 (46.15%)	6 (75.00%)	1.2972	0.1946

Table 4

Participant impressions (*n* = 11) upon receiving SMS in absolute numbers followed by percentages in parentheses. The indices of the Likert scale are shown in parentheses next to the classification labels.

Item	Classification				
	Very bad (1)	**Bad (2)**	**Satisfactory (3)**	**Good (4)**	**Very good (5)**
Number of messages received, *n* (%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	4 (36.36%)	6 (54.54%)
Time when the SMS arrived, *n* (%)	0 (0.00%)	2 (18.18%)	1 (9.09%)	6 (54.54%)	2 (18.18%)
Content of the SMS, *n* (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	9 (81.81%)	2 (18.18%)
Item	Classification				
	It did not help (1)	(2)	(3)	(4)	Helped (5)
Helped to take medications, *n* (%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	2 (18.18%)	7 (63.63%)
Item	Classification				
	Did not disrupt (1)	(2)	(3)	(4)	Disrupted (5)
Disrupted medication intake, *n* (%)	9 (81.81%)	2 (18.18%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Item	Classification				
	No (1)	Yes, with changes (2)			Yes (3)
Would like to continue receiving SMS, *n* (%)	1 (9.09%)	4 (36.36%)			6 (54.54%)

Table 5
Cross comparison of qualitative feedback and participants' profile.

Profile	Qualitative feedback
Social class	
B1 and B2	All participants (2; 100.0%) said SMS helped to take medications
	All participants (2; 100.0%) would like to continuing receiving SMS
C1, C2 and D	2 (22.2%) said SMS not helped, 7 (77.8%) said SMS helped to take medications
	1 (11.1%) said she would not, and 8 (88.9%) would like to continuing receiving SMS
Schooling	
Not completed high school	All participants (5; 100.0%) said SMS helped to take medications
	All participants (5; 100.0%) would like to continuing receiving SMS
Completed high school	2 (33.3%) said SMS not helped, 4 (66.7%) said SMS helped to take medications
	1 (16.7%) said she would not, and 5 (83.3%) would like to continuing receiving SMS
Age	The median age of participants who said messages helped to take medicines is greater than the average age
	1 participant, 27 years old, said she would not like to continuing receiving SMS, while median of those who would like is greater than the average age
Habit of sending SMS	
Yes	6 (75.0%) said SMS not helped, 2 (25.0%) said SMS helped to take medications
	8 (100.0%) said she would like to continuing receiving SMS
No	3 (100.0%) said SMS helped to take medications
	1 (33.3%) said she would not, and 2 (66.7%) would like to continuing receiving SMS
Habit of sending SMS with images	
Yes	1 (33.3%) said SMS not helped, 2 (66.7%) said SMS helped to take medications
	3 (100.0%) said she would like to continuing receiving SMS
No	1 (12.5%) said SMS not helped, 7 (87.5%) said SMS helped to take medications
	1 (12.5%) said she would not, and 7 (87.5%) would like to continuing receiving SMS