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Challenges and solutions implementing an SMS text message-based survey CASI and adherence reminders in an international biomedical HIV PrEP study (MTN 017)

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ABSTRACT

Background: We implemented a text message-based Short Message Service computer-assisted self-interviewing (SMS-CASI) system to aid adherence and monitor behavior in MTN-017, a phase 2 safety and acceptability study of rectally-applied reduced-glycerin 1% tenofovir gel compared to oral emtricitabine/tenofovir disoproxil fumarate tablets. We sought to implement SMS-based daily reminders and product use reporting, in four countries and five languages, and centralize data management/automated-backup.

Methods: We assessed features of five SMS programs against study criteria. After identifying the optimal program, we systematically implemented it in South Africa, Thailand, Peru, and the United States. The system consisted of four windows-based computers, a GSM dongle and sim card to send SMS. The SMS-CASI was, designed for 160 character SMS. Reminders and reporting sessions were initiated by date/time triggered messages. System, questions, responses, and instructions were triggered by predetermined key words.

Results: There were 142,177 total messages: sent 86,349 (60.73%), received 55,573 (39.09%), failed 255 (0.18%). 6153 (4.33%) of the message were errors generated from either our SMS-CASI system or by participants. Implementation challenges included: high message costs; poor data access; slow data cleaning and analysis; difficulty reporting information to sites; a need for better participant privacy and data security; and mitigating variability in system performance across sites. We mitigated message costs and poor data access by federating the SMS-CASI system, and used secure email protocols to centralize data backup. We developed programming syntaxes to facilitate daily data cleaning and analysis, and a calendar template for reporting SMS behavior. Lastly, we ambiguated text message language to increase privacy, and standardized hardware and software across sites, minimizing operational variability.

Conclusion: We identified factors that aid international implementation and operation of SMS-CASI for real-time adherence monitoring. The challenges and solutions we present can aid other researchers to develop and manage an international multilingual SMS-based adherence reminder and CASI system.

1. Introduction

Adherence to product use in microbicide and other biomedical intervention HIV prevention trials is critical to measuring the product's safety and efficacy [1–3]. The outcome of clinical trials is closely related to participant adherence to the study's biomedical and behavioral

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protocols [4]; low patient adherence with prescribed treatments is a very common problem that can seriously distort the validity and generalizability of outcomes. Variations in adherence to biomedical protocols can lead to diverse statistical outcomes and conclusions [4,5]. In contrast, when adherence is consistently high, studies can recruit, enroll, and follow fewer people, which decreases costs [2,5,6]. Better adherence also increases statistical certainty of results [7]. However, since product adherence is often participant-dependent, it is difficult to ensure that proper dosing, administration, and product use are taking place. Therefore, real-time monitoring and adherence improvement mechanisms help to guarantee that trials proceed successfully [7].

Short message service (SMS) or text messaging has been used to collect real-time data and to monitor adherence [3,8,9]. Collecting data in real-time mitigates recall-bias and allows researchers to address many data collection, analytic, or behavioral (non-response or non-adherence) issues early [3,8]. Researchers also have a greater number of opportunities to identify and mitigate many adverse experiences during the course of product use [3,10]. For instance, Coomes et al. reviewed the literature on people living with HIV, use of SMS, and medication adherence and found that SMS-based interventions that incorporate the elements of interactivity, timing, and tailoring of messages could be implemented to encourage greater medication adherence [11]. Moreover, SMS has been shown to impact other mutually reinforcing behaviors and factors (e.g., increasing patient involvement and social support, reducing risk behaviors, and promoting general health and well-being) that support better healthcare quality and clinical outcomes [11–13]. Additional studies have evaluated the use of SMS in medical settings and have found a positive effect on adherence [10,11,14].

As mobile phone technology increases in popularity and surpasses 6.8 billion users worldwide, its varied implementation in research has grown [3,15–17]. Many studies on the ubiquity of SMS have shown that SMS allows researchers to provide behavioral reminders and collect adherence data remotely and in real-time, with low levels of intrusiveness, and at a low-cost, respective to other modalities [11,15,16,18].

This paper describes the challenges and solutions to implementing an international SMS-based adherence reminder and computer-assisted self-interview (CASI) system in an HIV prevention trial, MTN-017. We describe a "system specification assessment" of several SMS text messaging applications, detail critical challenges to developing and managing an international SMS-based CASI system and explain how challenges were resolved. In MTN-017, SMS was used for real-time data collection and to send reminder messages to support behavioral adherence to the study's three biomedical regimens (daily oral tablet, daily rectal gel, receptive anal intercourse [RAI] associated rectal gel). Lastly, we will determine the feasibility of developing and managing an international multilingual SMS-based CASI and adherence reminder system.

2. Materials and methods

2.1. Study design

The Microbicide Trials Network (MTN), funded by the United States National Institutes of Health, is a worldwide collaborative clinical trials network focused on developing methods for prevention of the sexual transmission of HIV. MTN-017 was a phase 2 trial designed to evaluate the safety and acceptability of a reduced glycerin formulation of 1% tenofovir gel used daily (i.e., daily rectal regimen) or used before and after sex (i.e., RAI rectal regimen), as well as daily use of the oral tablet of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF, i.e., daily oral regimen) in HIV-negative transgender women and men who have sex with men (MSM). Participants (N = 187) followed each of the three study regimens for eight weeks in a crossover design. Each washout period was one week long (see Fig. 1) [19]. Study protocols and participant samples are detailed in two other publications [20,21].

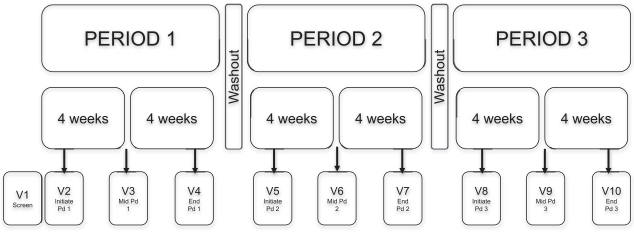

Fig. 1. MTN-017 study design. PERIOD 1–PERIOD 3 [Pd1–Pd3]: Are the different treatment crossover periods for each of the three regimens. V1–V10: Are the visits that participants were required to make during each period of their treatment regimens [19].

To support and monitor adherence, we implemented an SMS system that allowed for daily reminders and data collection on product use. SMS-CASI was conducted daily for each of the eight-week regimen periods. SMS-CASI also continued during both one-week washout periods and up to one week during scheduling and completion of the participant's final interview, for a total of 27 weeks of SMS-CASI reporting. This system was implemented in four countries (i.e., South Africa, Thailand, Peru, United States) and five languages (i.e., Xhosa, Afrikaans, Thai, Spanish, and English).

2.2. SMS protocol and system design

2.2.1. Adherence measurement

SMS was employed in MTN-017 as part of a mixed methods "convergence" approach to promote and monitor adherence. Fig. 2 shows how SMS was one part of our convergence of multiple data sources to get at the truth of the data. Additional methods used to monitor product use included counts of returned study product at each visit and pharmacokinetic drug levels taken from plasma samples at study visits. At mid- and end-period visits, participants met with an adherence counselor to review their adherence data together, and a participant-centered approach was used to discuss any discrepancies in order to converge the data and determine the most likely number of doses taken. A detailed description of the convergence process and adherence measurements are published elsewhere [19].

2.2.2. SMS system description

Programming for the SMS-CASI schema was based in the principals and on the structure of eHealth Behavior Management model, which describes the use of technological tools (e.g., SMS, computers, mobile phones) as incorporated into the trans-theoretical (stages of change) model, to increase personal involvement and self-efficacy (see Fig. 3). The eHealth Behavior Management model was important for this study because one of our major goals was increasing adherence to the biomedical and behavioral protocols of the study.

Starting at the enrollment visit, participants indicated the time of the day they wanted to receive the SMS reminder. Participants were encouraged to match the time of the reminder with the time of the day they expected to self-administer a product dose. A password, corresponding to an abbreviated version of their study site and participant ID (e.g., PT15 for participant number 15 in Pittsburgh, PA), was used to initiate the SMS-CASI when prompted. Participants had to answer only one survey question regarding their use of study product by sending a number (0–90). Upon receipt of the number of times of product use, the system generated a final message indicating that that day's session had been completed (see Fig. 4).

2.2.3. SMS-CASI system architecture and programming

SMS-CASI systems for each country were programmed at a central location in the United States. The software program used was then federated by downloading it to each country's computer system and text messages were sent and received via a Global System for Mobile