

*Implementation Brief* ■

## A Two-way Messaging System to Enhance Antiretroviral Adherence

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**Abstract** Failure to adhere to complex antiretroviral regimens can lead to resistance and treatment failure among HIV-positive persons. In this study of the feasibility of an automated two-way messaging system to improve adherence, participants received multiple short daily messages designed to remind, educate, encourage adherence, and solicit responses concerning side effects and self-reported adherence. Twenty-five participants remained in the study for a median of 208 days, receiving 17,440 messages and replying to 14,677 (84%). Participants reported missing one or more doses on 36% of 743 queries and reported medication side effects on 26% of 729 queries. Participants expressed high satisfaction with the messaging system and reported that it helped with medication adherence. The study suggests that it is feasible to use an automated wireless two-way messaging system to communicate with HIV-positive patients over an extended period of time.

■ *J Am Med Inform Assoc.* 2003;10:11–15. DOI 10.1197/jamia.M1047

A better understanding of HIV pathogenesis and viral dynamics, the availability of highly active antiretroviral therapy (HAART), and viral load and resistance assays have given clinicians and patients the ability to manage HIV infection and have resulted in dramatic decreases in the numbers of AIDS-related deaths and opportunistic infections.<sup>1,2</sup> The effectiveness of HAART, however, depends on strict adherence to often complex medication regimens. In

fact, adherence levels of 95% may be needed to achieve the best virologic outcomes.<sup>3,4</sup> Subtherapeutic dosing accelerates the development of resistant viral strains, which has serious implications for both individual and public health.<sup>5-7</sup>

Few behavioral interventions, such as providing education, counseling, or additional supervision, have demonstrated efficacy in increasing adherence.<sup>8</sup> The expanding field of medical technology, however, holds great potential for behavioral health promotion interventions. Studies using communicating devices, such as pagers, alarms, and telephones, though generally small and uncontrolled, show promising results.<sup>9</sup> Alarm devices have been shown to increase adherence.<sup>10,11</sup> For example, Frick et al. found that 82% of women on a once-daily regimen who were randomized to use an alarm device were  $\geq$  95% adherent compared with 36% of the women without an alarm.<sup>10</sup> Erickson et al. used pagers with tailored messages to remind patients to take their asthma medications and found that patients felt comfortable using the pager, easily learned the features, readily integrated the use of the pager into their daily routines, generally perceived the messages as very useful, and showed improvement in self-reported adherence to both oral and inhaled medications.<sup>12</sup> In another

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Financial support for the two-way messaging system was provided by Talaria, Inc.

Disclosure: Drs. Madigan and Dunbar own stock in Talaria, Inc.

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Received for publication: 11/06/01; accepted for publication: 08/09/02.

er small study among elderly patients, adding a programmable pager increased mean medication adherence from < 60% to 95%.<sup>13</sup> Other studies, including a review of computer-generated interventions by Revere and Dunbar,<sup>9</sup> have also shown significant improvement through pagers.<sup>14,15</sup>

This study combines an automated paging system with a two-way messaging feature to provide not only continual support, education, and encouragement to adhere, but also to solicit patient-reported rates of adherence, side effects experienced, and impressions of the pager. Our literature search did not identify any published studies using two-way pager technology, nor has the use of pagers been previously studied among the HIV-positive population.

## Methods

### Setting

We conducted the study from December 1997 to December 1998 in a university-affiliated primary care HIV/AIDS clinic in Seattle, Washington. The clinic serves a medically underserved population of approximately 950 HIV-infected persons, 72% of whom are Caucasian, 67% men who have sex with men, 24% injection drug users, and 9% women. Approximately 88% of the clinic population receives full or partial funding for health care services from public sources, and approximately 90% get their medications filled at the on-site pharmacy. A preliminary internal look at the clinic's on-site pharmacy refill records in 1998 showed that our clinic population had a mean adherence level of 74%, which is below the currently desired level of 95%. The study was approved by the University of Washington's Institutional Review Board, and all participants provided written informed consent.

### Participant Enrollment and Training

A convenience sample of participants was selected for inclusion based on their being on HAART, being willing to carry a pager, and receiving their medications from the clinic pharmacy. After enrollment, each participant described daily work, food, sleep, and medication schedules to the pharmacist so that a daily medication schedule could be written and the pagers programmed with an appropriate schedule of messages and questions with multiple-choice replies. The functioning of the pager and the nature and purpose of the messages were also demonstrated. Participants were told to telephone or page the inves-

tigator with technical concerns, call the clinic for medical concerns, and dial 911 for emergencies.

The study was planned to run for 3 months; however, in response to participants' enthusiasm, it was extended beyond 6 months.

### Equipment

The participants received two-way alphanumeric pagers with programmable silent or audible alerts and the capability of both sending and receiving short text messages. Participants could utilize the pagers for personal use as well if they so desired. The messages could be 20 lines long but only four lines of text could be viewed concurrently. Participants could respond to a message easily with a canned response or by composing their own replies using a crude "soft key" interface. The investigators used a commercially available proprietary software operating on a Microsoft Windows NT personal computer to enter, edit, and store messages for delivery to the pagers (Talaria, Inc., Seattle, WA). The proprietary software enabled the investigator to create an algorithm of the number and type of messages sent to each participant each day (e.g., 2 reminder messages for a twice-daily regimen, 1 entertaining message, and 1 assessment of side effects experienced) and to download and save hundreds of generic messages, which could then be individualized quickly and efficiently to create a panel of pages at baseline that covered the entire duration of the study. In addition to loading outgoing messages, the investigator could review the incoming replies using a custom-built web interface that organized messages by patient, time, or content. To maintain constant contact with study participants, an investigator carried a special pager equipped with a screen and miniature keyboard designed to send and receive e-mails. This pager enabled participants to communicate with an investigator 24 hours per day.

In addition to the manual daily message review, an automated filter operated in real time 24 hours per day. Incoming messages (replies) passed through proprietary software that detected "call me" messages or other replies identified by investigators as needing immediate attention, which were then automatically forwarded to the investigator's pager.

The system recorded into a database the content of all outgoing messages and replies and the exact time that messages were sent and replies received. This record enabled us to calculate "response time," defined as the time between message delivery and

reply, and “response rate,” defined as the percentage of messages answered. The messages within the database were classified by content.

### Messages

The participants were sent between 3 and 8 messages daily via the two-way pagers, depending on their dosing schedules. Clinical messages included reminders to take all medication doses and to follow medication dietary requirements. If multiple medications were to be taken at the same time, each medication was specified. Other messages provided information or questions about medication adherence, sleeping habits, mood, stressful events, medication side effects, food intake, drug use, and messaging system use. Some messages were designed to be educational, such as those describing appropriate dietary habits, enhancing awareness of important side effects, and emphasizing the importance of adherence. The effectiveness of this education was not evaluated, however. Participants also received entertainment messages in the form of jokes, news bulletins, and quizzes. Message content varied from day to day and was individualized to address patients by name, to use drug names familiar to the participant (brand vs. generic), and to employ other question sets appropriate for the medication regimen.

All messages requested acknowledgment, and approximately one-half of the messages requested that the participant select a reply from a multiple-choice list sent with the message. Messages were phrased as a statement (e.g., “Good morning, JR. Time for your indinavir.”) or as a question (e.g., “Good morning, JR. Time for your indinavir. Any problems with your medications over the weekend?”), followed by a choice of answers (“Took all on time”; “Took all, but not all on time”; “Missed one dose”; “Missed more than one dose”).

The first 10 study participants completed a written satisfaction survey weekly for 4 weeks and then at 8 and 12 weeks. They were asked to rate their attitudes to the messaging system using 10-point scales (better/worse, comforting/annoying, helpful/unhelpful, convenient/inconvenient, useful/useless, and more cared for by clinic/less cared for by clinic). Subsequent enrollees were not required to complete this questionnaire, because the responses were almost uniformly positive.

Intermittently, queries were sent to monitor ongoing attitudes toward the messaging system. In addition,

all participants received via pager a four-question survey about the pager 3 weeks before the end of the study. Participants were also asked in an exit interview whether they would continue this service if it were offered to them.

### Observations

We enrolled 25 HIV-positive persons into the study. Eighty-eight percent of participants were male and 64% Caucasian. We did not ask about employment status, nor did patients report any problems with the pagers related to employment. Mean age was 39 years, and mean CD4+ cell count was 358 cells per mm<sup>3</sup>; 80% had an undetectable HIV-1 RNA (< 500 copies per ml). The majority of patients were taking a twice- or thrice-daily regimen, which was typical for the clinic population during the period of study. Participants remained in the study for a median of 208 days (range: 11–398). Nineteen participants used their pagers for at least 3 months. Six participants dropped out of the study prematurely due to disliking the pager (2), leaving town (1), living in an area with inadequate wireless reception (1), experiencing a personal crisis (1), or dying (1).

Over the course of the study, the system sent 17,440 messages via the pagers, and the participants replied to 14,677 (84%; range: 62–100%). The multiple-choice feature of the pager enabled quick and easily rated replies. Ten of the participants used the custom message feature a few times, and four participants used it extensively.

Results below are based on the 19 of 25 participants (76%) who remained in the study for 3 months or more. The median response time was 6.0 minutes (range: 3.5–24.6). Fifty-eight percent (430 of 743 queries) of responses indicated perfect adherence over the past few days, and 36% (268 of 743 queries) indicated one or more missed doses. Seventy-nine percent (11 of 14) of participants reported that the pager improved adherence to their medication regimen.

The lowest response rates followed questions about drug use; 13 of 61 replies reported regular alcohol or marijuana interference with adherence, and 4 of 30 replies confirmed recent “hard” drug use. Sixty responses were sent describing a recent stressful event, and 11 requesting to talk to someone. Participants reported side effects in response to 187 (26%) of 729 semiweekly queries. The most common side effects reported were nausea and diarrhea (45 and 34 reports, respectively).

Satisfaction with the messaging system remained high throughout the study: 47% percent of pager replies indicated that participants "loved it." Twelve of the 14 participants (86%) who completed an exit interview expressed a desire to continue using the pagers. The most valued pager features were the medication reminders and the content of the entertaining messages. Participants disliked the size of the pager and felt that it was too large. We did not assess the extent to which people used the pagers for personal communication; thus, we cannot comment whether that feature contributed to their satisfaction with the pager.

### System Maintenance

The pager system was extremely robust. The only sustained system downtime was for a scheduled software upgrade. Two pagers failed and were replaced. Thirty minutes per day of investigator time were spent reviewing messages, and approximately one day per month was used to load new message schedules.

### Discussion

This study demonstrates the feasibility and limited staff support necessary for two-way pagers to deliver education, support, and reminders directly to patients as well as to assess self-reported adherence. Findings indicate that patients liked the pager and believed that the system helped them to improve medication adherence. Participants reported that the most appealing aspects of the pagers were the medication reminders and the entertaining messages. The high level of satisfaction may stem from participants' embracing the pager technology because they themselves contributed to the design of their paging schedule and could use it for other purposes such as personal paging. This convenience sample was chosen based on willingness to participate. Consequently, we may have selected a more acquiescent group, which may have contributed to the high level of pager acceptability. Given that the majority of participants had never used a pager or computer previously, however, we do not believe that we selected a more technologically savvy group.

Participants were more than willing to respond to pager-mediated queries, as shown by the frequent and prompt response rate (84% of 17,440 queries). Participants did, however, show a low response rate to personal questions about illicit drug use. Consequently, this type of question was removed midway through the study.

In addition to collecting real-time self-reported medication adherence information, which is comparable to that identified through a phone survey,<sup>16</sup> the two-way pagers can collect real-time information about the presence of side effects, symptoms of disease, and mood—all potentially alterable and adherence-modifying factors. Consequently, two-way pagers offer the potential to identify factors that contribute to non-adherence as the factors present themselves and before medication resistance develops.

New wireless technologies might enhance medication adherence by allowing customization of the intervention to meet patients' specific needs, which addresses the problem of forgetting as well as providing support and education. In addition, the automated paging system provides the advantage of personalized messages but does not require extensive staff time commitment for maintenance, even if the volume of participants is increased. Future research is needed to identify subgroups of HIV-positive persons most likely to benefit from this type of technological intervention. Finally, this study captured only self-reported adherence rates, which often overestimate adherence. Additional research is needed to determine whether pagers can reliably capture adherence data, similar to medication event management systems (MEMS) or pharmacy refill records, and whether this approach is cost-effective.

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