A Study of Medication-Taking and Unobtrusive, Intelligent Reminding

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Abstract

Poor medication adherence is one of the major causes of illness and of treatment failure in the United States. The objective of this study was to conduct an initial evaluation of a context-aware reminder system, which generated reminders at an opportune time to take the medication. Ten participants aged 65 or older, living alone and managing their own medications, participated in the study. Participants took a low-dose vitamin C tablet twice daily at times that they specified. Participants were considered adherent if they took the vitamin within 90 minutes (before or after) of the prescribed time. Adherence and activity in the home was measured using a system of sensors, including an instrumented pillbox. There were three phases of the study: baseline, in which there was no prompting; time-based, in which there was prompting at the prescribed times for pill-taking; and context-aware, in which participants were only prompted if they forgot to take their pills and were likely able to take their pills. The context-based prompting resulted in significantly better adherence (92.3%) as compared to time-based (73.5%) or no prompting (68.1%) conditions ($p < 0.0002$, $\chi^2 = 17.0$). In addition, subjects had better adherence in the morning than in the evening. We have shown in this study that a system that generates reminders at an opportune time to take the medication significantly improves adherence. This study indicates that context-aware prompting may provide improved adherence over standard time-based reminders.

Key words: *home health telemonitoring, telehealth, information management*

Introduction

Poor medication adherence is one of the major causes of illness and of treatment failure in the United States (U.S.). Bedell et al.[1] found that 76% of prescription and nonprescription medicines are taken incorrectly. This is particularly true for the aging. More than 75% of people aged 65 and older take prescription medication, and on average they take three or more medications a day.[2,3] Unfortunately, more than 50% of these individuals are nonadherent to their medication regimen,[4,5] which can lead to increased hospitalization and drug side-effects.[6] With more than 3 billion prescriptions worth $203 billion dispensed in the U.S. annually,[7] it is clear that tools to help people take their medications properly can be of tremendous benefit. Furthermore, the benefit of such tools extends beyond the management of medication adherence in patient populations. Clinical trials to assess the safety and efficacy of new drugs necessarily rely on proper medication adherence by study participants to obtain accurate data.[8,9] Most interventions to improve medication compliance are complex and require frequent contact between a patient and a nurse or caregiver.[10–13] Thus, methods to both accurately assess medication adherence and to encourage optimal adherence are of considerable interest.

Existing methods of tracking medication adherence suffer from a number of drawbacks. Pill counts, the mostly commonly used method, overestimate adherence.[14–16] So does self-report of adherence.[14,17,18] The widely used Medication Event Monitoring System (MEMS, Aardex Ltd.) provides excellent information about adherence, but has several shortcomings. The MEMS cap is difficult to open for arthritic hands,[19–21] and it does not accommodate the use of pill boxes for sorting medications into daily doses,[22] as are commonly used by the elderly[23] or when taking multiple drugs.[22] MEMS also does not report adherence in real-time, so rapid intervention cannot take place.

Reminders and aids to adherence vary in their usefulness.[12,24–26] In general, multimodal methods that incorporate behavioral feedback

DOI: 10.1089/tmj.2009.0033

appear to be the most effective at improving adherence outcomes.[27] However, most successful interventions appear to require active intervention by a human monitor, and in general, simple time-based prompting is not as effective as reminders that are behaviorally integrated into a person's daily activities.[23] With this in mind, we hypothesized that a system which generates reminders at an opportune time to take the medication will lead to improved adherence as compared to time-based reminders. To examine this hypothesis, we have developed a medication tracking and reminding system that allows both measurement of adherence, and real-time, context-aware reminders.[28] The objective of the present study was to evaluate whether or not such context-aware reminders may improve adherence as compared to time-based reminders. It should be noted that the research system used in this study is more complex than would ultimately be necessary for a context-aware medication reminder system, since it was also used to develop the inference algorithms needed to determine when prompting is appropriate. There are technical challenges inherent in deploying such a research system to a large number of homes that we have been addressing in related studies. This report summarizes the results of our initial evaluation in a small group of community-dwelling elders.

Materials and Methods

PARTICIPANTS

Ten participants aged 65 or older were selected from a pool of participants in an earlier study of medication adherence in which they were considered "poor adherents" (missing more than 20% of prescribed doses during a twice-daily vitamin regimen over a 5-week period).[29] All participants lived independently and alone in one of two retirement communities and were currently managing their own medication regimen on a daily basis. All participants provided written informed consent (Oregon Health & Sciences University Institutional Review Board #1682). Participants were functionally independent, and were screened for dementing illness with the Mini-Mental State Examination[30] (exclusionary score <24) and the Clinical Dementia Rating scale[31] (exclusionary score >0).

ASSESSMENTS

Age and years of schooling were collected for each participant. Cognitive function was assessed using the Alzheimer's Disease Assessment Scale–Cognitive Subtest (ADAS-Cog).[32,33] The ADAS-Cog has been used to differentiate the stages of Alzheimer's disease from mild to severe,[34] and there exist published norms for this test in a range of ages of elderly adults.[33] In addition, we also collected delayed word-list recall scores,[35] scores on both parts A and B of the Trail Making Test,[36] scores on the Geriatric Depression Scale,[37] and scores on the Cumulative Illness Rating Scale.[38]

MEDICATION MONITORING AND REMINDING SYSTEM

In order to provide context-aware prompting to participants when they missed taking their medications on time, we created a medication monitoring and reminding system that unobtrusively collected data about the participants' activities and medication adherence, and used this information to prompt at appropriate times.[28] *Table 1* shows the components of the system and their purpose. The prompting was controlled by an inference engine, which used dynamic Bayesian inference[39,40] to "learn" an individual's activities from the sensor data and then to make a decision to prompt based on those activities.

PROCEDURES

Participants were asked to take a low-dose (250 mg) vitamin C tablet twice daily at 12-hour intervals (e.g., 7 AM and 7 PM); the times were selected by the subject during the initial interview. Participants were considered adherent if they took the vitamin

Table 1. Equipment Used in Each Home to Enable Context-Aware Prompting

ITEM	LOCATION	PURPOSE	DETAILS
Motion sensors	1 per room	Detecting location of participant in the home	X10 model MS14A (x10.com)
Contact sensors	Outside doors	Detecting when participant left the home	X10 model DS10A (x10.com)
Phone sensor	Phone line	Detecting when participant was on the phone	Detects on-hook and off-hook events
Bed sensors	Beneath the mattress	Detecting movement in bed	Tactex model STLBT1 (Vancouver, CA)
Laptop computer	In the home	Collecting data from the wireless devices	CTL laptops, model U553W
7-day reminder in the home pillbox	In the home	Collecting time of pill-taking	Intel research device
Activity beacon	In the home	Alerting the participant to take their pill through visual and auditory prompts	Intel research device
Messaging watch	1 per person	Send the participant a message when it was time to take their medication	Microsoft research device

within 90 minutes (before or after) of the prescribed time. We used the medication tracking and reminding system to assess how different forms of prompting (no prompting, time-based prompting, and context-aware prompting) affected adherence in this group, using a three-period repeated-measures design. During the no-prompting phase (10.7 ± 4.4 weeks), participants received no reminders to take their vitamins. During time-based prompting (10.1 ± 3.3 weeks), participants were reminded to take their vitamin by the auditory beep and visual alarm on the MedTracker device, which would prompt for 10 seconds every minute for 3 minutes at the specified dose times. During context-aware prompting (8.4 ± 4.2 weeks), prompting occurred only when the system inferred that participants were likely to miss taking their vitamin, and at a time when the participant was likely able to take the pill. The generation of the prompting events (signals), consistent with the inference, was governed by the following set of rules:

1. Prompt at the closest location to the participant, using either the MedTracker itself or the closest activity beacon.
2. Never prompt outside the adherence window (90 minutes before and after the time to take the vitamin).
3. Don't prompt if the vitamin has already been taken within the current window.
4. Don't prompt if the participant is not home. Resume if the participant returns home before the window ends.
5. Don't prompt if the participant is in bed. Wait until they are out of bed to prompt.
6. Don't prompt if participant is on the phone. Wait until they are off the phone to prompt.
7. Don't prompt before the time the user usually takes the pill (estimated from their baseline data). The only exception to this is if the participant appears to be leaving the home prior to their regular pill-taking time.
8. If it is less than 20 minutes left until the adherence window expires, start prompting, disregarding all other rules (except 2–4).

In the case of the context-aware prompting, participants were prompted both by the visual and auditory alarms on the MedTracker, and by the flashing and audio message of the beacon (*Table 1*).

Analysis

We defined "adherent" as taking the vitamin within a 3-hour window around the selected time—90 minutes before the time and 90 minutes after the time. Adherence to regimen was measured as the percentage of pills taken within this window. Consistent with past studies of medication taking, an adherence of 80% or greater was considered good adherence.[41–43]

The effect of prompting strategy on adherence was assessed using a mixed model design, with subjects as a random factor and prompting strategy as a fixed factor, with the weeks of monitoring as a repeated measure within each prompting strategy.

We constructed a one-way analysis of variance (ANOVA) based on nested beta-binomial residuals for the adherence data. This analysis is more appropriate for binomial data than the usual Gaussian-based ANOVA (particularly for very high or low adherence rates), and accounts for the variation between subjects (random effect) with a beta distribution on the underlying adherence rate.[44] We constructed three nested beta-binomial models for this analysis. The simplest used a single distribution to model all the data (two parameters), and hence assumed that the adherence rates were independent of the prompting strategy. The second model allowed the mean population rate to depend on the prompting strategy but constrained the variances, resulting in four model parameters. The third model removed the constraint on the variances, resulting in six free parameters. We fit the models by maximum likelihood and compared them using a likelihood ratio test. We estimated the 95% confidence intervals from the distribution of means computed on 2,000 bootstrap replicates from the original data, each fit by maximum likelihood to the model selected by the ANOVA. Multiple comparisons were made using the Bonferroni criterion.

Results

Ten subjects (mean age 82.7 ± 6.4, 9 females, 1 male, mean education 16.3 ± 2.2 years) participated in the study. Cognitive and health measures for these subjects are shown in *Table 2*. Two subjects dropped out of the study prior to the introduction of the first

Table 2. Group Characteristics (Mean ± Standard Deviation)

PARTICIPANTS	ALL SUBJECTS	SUBJECTS WITH COMPLETE DATA
Number	10	7
ADAS-Cog	6.6 ± 5.9	6.2 ± 5.4
Delayed recall	7.3 ± 3.2	7.3 ± 2.8
GDS	2.0 ± 1.7	2.2 ± 1.7
CIRS	18.8 ± 3.49	19.0 ± 3.35
TMT-A (secs)	120.8 ± 44.9	114.7 ± 41.9
TMT-B (secs)	132.7 ± 46.2	132.0 ± 52.6

ADAS-Cog, Alzheimer's Disease Assessment Scale–Cognitive Subtest; GDS, Geriatric Depression Scale; TMT-A, Trail Making Test A; TMT-B, Trail Making Test B; CIRS, Cumulative Illness Rating Scale.

prompting intervention (1 due to illness, 1 chose not to continue). Another subject was removed from the study due to violation of the protocol. In other cases, only partial data were available due to withdrawal after the time-based prompting (2 subjects). Thus, complete data were available for only 7 subjects. One final subject had only partial data during the baseline phase due to technical issues. The data from that subject were included in the analyses below, since it allowed us to look at differences between time-based and context-based prompting. There were no differences in any of the neurocognitive measures between the subjects used for analysis and the complete group (*Table 2*).

The best fit to the adherence data resulted from the second ANOVA model, in which the population mean adherence rates depended on the prompting strategy but the variances were constrained. For most subjects, their adherence was quite variable week to week. The mean adherence rates (estimated in the ANOVA) and their 95% confidence intervals was 68.1% [57.5–80.5] for the baseline condition. During this period, only 1 subject achieved good adherence (>80%). Although subjects did better overall during the time-based prompting phase, only 2 subjects obtained an average weekly adherence of over 80%. The mean adherence rate was 73.5% [68.0–78.6] for time-based prompting. Notably, during the context-aware prompting phase, most subjects achieved excellent adherence, and the mean adherence was 92.3% [84.7–97.0].

The differences in the mean adherence rates for each prompting strategy were significant at $p < 0.0002$ ($\chi^2 = 17.0$). *Figure 1* shows the estimated beta distributions corresponding to each of the three prompting conditions. Context-aware prompting had a clear advantage over the baseline and time-based prompting; not only is the mean adherence rate higher, but the variation is less than for the baseline or time-based prompting populations. There was also a small difference between subjects ($F_{6,169} = 2.7$, $p < 0.02$).

The mean difference in adherence during context-based prompting as compared to the no-prompting phase was 24.1%, and between context-based and time-based was 14.4%. A box plot of overall, morning, and evening adherence (*Fig. 2*) reveals some interesting details of the participants' adherence during the study. In particular, evening adherence was consistently worse than adherence in the morning during all prompting phases; however, the difference between morning and afternoon adherence under context-based prompting was much less.

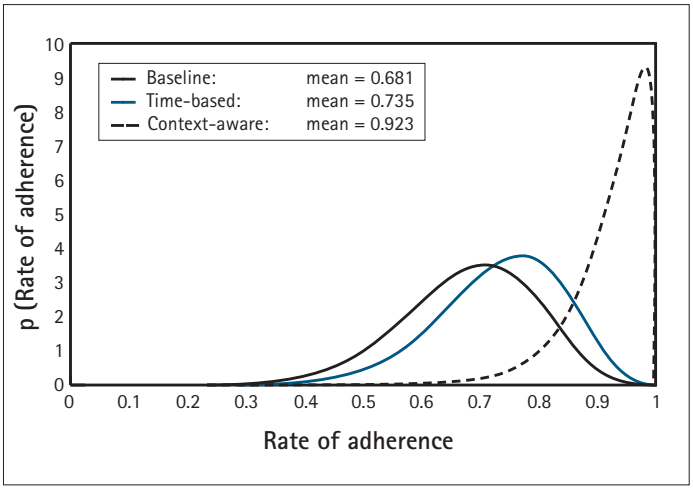

Fig. 1. Estimated Beta distributions corresponding to each of the three prompting conditions.

Discussion

We have shown in this study that adherence to a medication regimen can be improved through the introduction of electronic reminders, and in particular that a system that generates reminders at an opportune time to take the medication significantly improves adherence. With context-based prompting, reminders

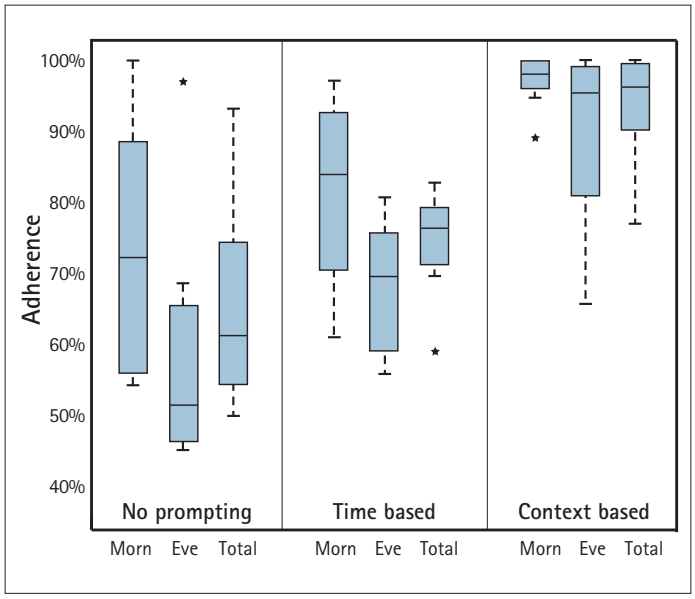

Fig. 2. Box plot of weekly morning, evening, and overall adherence rates under each of the prompting conditions. Asterisks indicate the value of outliers.

occurred only when the system inferred that participants were likely to miss taking their vitamin, and at a time when the participant was likely able to take the pill. Although simple time-based reminders were somewhat effective at improving our participant's adherence, the context-based system led to excellent compliance: 86% of participants showed good adherence during that phase of the study, as compared to only 17% during the no-prompting and time-based phases of the study. To our knowledge, this is the first study to demonstrate the efficacy of a context-based medication reminder system.

Many interventions have been proposed for improving medication adherence.[12,13,24] Recently, a number of electronic devices that sound an alarm and dispense medication[45] when a pill should be taken have become commercially available. Unfortunately, like a wrist-watch alarm, all of these devices require the user to be present to hear the alarm. More recently, Sterns and Mayhorn proposed a pill-dispensing Personal Digital Assistant (PDA), which led to improved adherence in a population of young adults during the third month of a 3-month field trial.[46] Because subjects carried the PDA during the day, they were able to take the medication from the device when prompted. However, this approach has the drawback that the user must remember to carry the device, and in some populations, including the elderly, this may pose an unacceptable burden. The system used in our study did not require the user to carry any devices, but rather monitored their movements and medication taken unobtrusively and determined when prompting should be done.

Our study had some limitations. The sample size is this exploratory study was very small, and as a consequence we were unable to conduct the study as a cross-over study. Therefore, we cannot know for sure that adherence simply improved over time for some of our participants. However, subjects were followed for several months in each phase of the study, and we did not see trends within individual phases. Our finding of somewhat increased adherence during the time-based prompting phase is also consistent with other studies of time-based prompting. The small sample size also makes it difficult to draw general conclusions about the efficacy of our approach in a large population. Nonetheless, the results of the current study are extremely promising.

This study has important implications for elders living independently in the community. Medication mismanagement in the elderly is a significant health issue, both financially and in terms of increased hospitalization[47] and drug side-effects.[6] Many elders would prefer to remain in their homes, and yet there are few effective tools available for managing the large number of medications taken by this population. The results of the current study suggest that a context-aware medication reminding system could lead to improved medication adherence in this population. Further investigation in a larger study of community-dwelling elders is needed to confirm the potential of this approach.

Acknowledgments

The authors thank Intel Corporation for their support of this research. Dr. Kaye is funded for research by the Department of Veteran's Affairs by a Merit Review grant, and National Institutes of Health (NIH) grants #AG008017, #AG024059, #AG024978, #AG026916, #AG024826, #AG10483, and #AG024904. Dr. Hayes' effort on this research was funded by Oregon Opportunity.

Disclosure Statement

This study was funded by Intel Corporation, a company that may have a commercial interest in the results of this research and technology. Kofi Cobbinah, Terry Dishongh, Janna Kimel, Michael Labhard, Jay Lundell, Umut Ozertem, Matthai Philipose, Kevin Rhodes, and Sengul Vurgun were Intel employees at the time of this study. In addition, Tamara Hayes has a significant financial interest in Intel Corporation. This potential conflict has been reviewed and managed by OHSU. Jeffrey Kaye and Misha Pavel do not have any competing financial interests in this study.

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Received: March 18, 2009
Accepted: April 10, 2009