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# Optimizing Medication Reminders Using a Decision-Theoretic Framework

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**Abstract**

*We discuss a new approach to patients' adherence to enhance to their medication-taking regimen by developing a context-aware alerting system that would optimize the expected utility of alerts. Each patient's instantaneous context is assessed using a real-time sensor network deploying a variety of sensors. The alerts are generated to optimize the expected value to the patient. This paper is focused on the initial assessment of the utility of alerts, including the tradeoff between effectiveness and annoyance.*

***Keywords:***

Medication adherence, Artificial intelligence, Machine learning, Home monitoring, Reminders

## Introduction

Medication adherence, defined as adherence to a plan mutually agreed upon between a patient and his or her primary clinician, is key in therapy as well as in clinical trials of new drugs. Insufficient adherence to the planned medication regimen can obviously have a significant impact on the efficacy of care. Population-based studies of medication taking in aging patients and in those with chronic diseases have shown that medication non-adherence leads to increased hospitalization and mortality [1-4]. One population-based study found that drug-related visits accounted for 12.6% of all emergency room visits, with 19% of these visits being directly related to medication non-adherence [5]. Non-adherence is of particular concern in clinical drug trials, where good adherence is essential to accurately assessing the safety and efficacy of the drug [6, 7].

Since more than 3 billion prescriptions worth $203 billion are dispensed annually in the USA [8], strategies to improve medication adherence have the potential to both reduce health care costs, and to significantly improve health outcomes. In a meta-analysis of intervention studies to improve medication adherence, McDonald and colleagues found that most studies had only a modest effect, and the most successful studies involved a variety of interventions including information, self-monitoring, counseling, and reminders. These interventions included behavioral, cognitive, and social aspects, and no single characteristic of the interventions led to improved adherence or outcomes [9]. Kripalani and colleagues also found that although 54% of interventions led to some improvement in adherence, only very small improvements, if any, were seen in clinical outcomes[10]. Thus, while it is clear that strategies to improve adherence are needed, it is still not obvious which strategies are most effective.

Prior research studying patients' adherence to medication taking regimens has been plagued by technical limitations. Even the measurement of adherence has been a difficult problem because of the researchers' frequent reliance on subjective reports of the patients' behaviors [11, 12] or on pill counts [11, 13, 14]. These reports are often unreliable because of patients' memory lapses and sometimes because of their unwillingness to admit missing medications. These problems are exacerbated in older populations because of the combination of typically complex medication-taking regimens and a frequent decline in cognitive abilities, such as memory and executive functions [15, 16].

Two problems must be solved in order to improve patients' adherence to their medication plans. The first one concerns our ability to assess objectively any individual's adherence to their plan. The second problem involves the development of effective and acceptable alerting and reminding systems.

We and other researchers have demonstrated the feasibility of automatically assessing medication taking behaviors [13, 17]. This assessment is generally based on various technological solutions whereby sensors detect the opening and closing of medication containers. The differentiating feature of the technology investigated in our prior study is that the medication dispenser is wirelessly connected to a local area network and permits medication-taking behaviors to be monitored in real time. As described below, this feature is important in order to make the alerting system aware of the patients' medication-taking behaviors. We note that this type of assessment techniques is limited to sense only patients' interactions with the medication dispenser. Although opening the dispenser does

not guarantee medication taking, this technique is more reliable than the approaches based on self-reports or pill counts.

With very few exceptions [18], most of the existing reminding and alerting systems generate alerts at fixed time points prescribed by the medication taking regimen. Although these have been shown to be useful, they frequently fail to achieve adherence for a variety of reasons, mostly associated with the patients' context and concurrent activities. For example, if the patient is involved in various concurrent activities such as sleeping, telephoning or is not near the medication dispenser when the alert is generated, he may not respond to the alert. In addition, if the alerting system is not aware whether or not the patient took the medication, it cannot generate follow up alerts.

To mitigate these problems, we have recently prototyped and investigated a context aware system and compared it to a time based approach [19-21]. The investigated system used a variety of sensors situated in the patients' homes and interconnected by a real-time sensor network designed to assess their state, and used a rule-based approach to infer the patients' state and to generate context aware alerts. The results of this rather limited study suggested the potential of context-based reminding, but the study was limited by the choice of the type and intensity of alerts.

The key challenge for this work is to develop techniques and supporting technology that would remind the patient at times when the patient could act on the reminder, and that the reminder would be most effective and minimally annoying. It would not be hard to generate alerts that would be effective in forcing the medication-taking behavior. For example, one could theoretically install extreme alerts such as a siren used in emergency vehicles that would be very difficult to ignore. The problem is that most patients would not tolerate such annoying devices and would turn them off. The selection of the most effective alerts is, therefore, a compromise between the benefits of the intensity of alerts and their annoyance.

Since the medication-taking behavior is a stochastic process, this optimization can be conveniently cast in a decision-theoretic framework. This paper describes a decision-theoretic framework to implement such a system based on a state representation of the activities of the patient, the prompting actions and the patient's responses. The state of the patient is inferred from a variety of sensors that represent indirect measurements of his or her activities. Therefore, a framework appropriate for optimization should be based on a partially observable, possibly Markov, decision process (POMDP) [22]. However, for the sake of simplicity we illustrate the approach using a simpler, one step maximizing utility approach. The main focus of this paper is to describe the general approach, the theoretical framework and its feasibility, with a particular focus on utility assessment. The ability to assess the utility of the alerts is a key problem in making this approach feasible.

## Utility-Based Medication Adherence Framework

### Metrics of Adherence

There are numerous ways to describe the degree of adherence. For example, the most frequent metric for adherence is the probability of taking medications within and interval $\pm 90$ minutes of the prescribed time. Another, more sensitive metric is the average deviation from the nominal time. The metrics should also include deviations in the type of medication or the dose, i.e., taking the wrong amount or wrong drug. For the purpose of this paper, we focus on the temporal deviations.

### Context and State Assessment

One of the key components of a principled, expected utility-based approach involves a representation of the patient's activity that would in turn enable one to estimate the probability that he will take the medication. For the sake of computational simplicity, i.e., computability, we assume that a patient's activities can be categorized into a small number of discrete states, $q$. The state of a patient is inferred from a set of contextual measurements implemented as sensors located in the patient's home. The set of sensors may include a variety of devices ranging from passive motion sensors, contact switches, to range measuring systems. The contextual measurements are then used in combination with an appropriate model to infer the state of the patient and ultimately the likelihood of taking a medication.

### Explicit Costs and Benefits

As described in the introduction, one of the most important knowledge acquisition and representation tasks in designing a medication reminding system has to do with the explicit incorporation of the costs and benefits associated with all actions that the reminding system might perform. For example, simply detecting that a patient in the home has probably forgotten to take an evening dose of a particular drug does not necessarily imply that a loud alarm should ring. Factors to consider in designing a protocol for reminding include:

- Reminder Intensity - Reminders can be delivered via various media at various stimulus intensities and modalities (text / light display on medication caddy → text / soft beep → louder beep on watch → text message on cell phone → phone message → phone call). Each of these approaches to reminding is associated with a different level of annoyance to the user and different probability of being noticed and attended to.
- Length of time since target time – Reminding too early or too late has a higher cost that reminding on time. However, reminding prior to when the user was going to take the medication anyways has a fairly high annoyance cost.
- Importance of the specific medication – It is more important to remind a user of a critical drug (e.g., anticoagulant) as compared with a noncritical pill (e.g., vitamin). Higher annoyance factors will be tolerated for more critical medications. In addition, for some medications, the

timing is more critical (e.g., 4 times / day) versus others that could be taken any time of day.

- Context for the user – Reminders that account for a user's location and availability to take the medication will be far more successful than a strictly time-based reminder. For example, there is a high utility for reminding when the user is near the medication caddy and when they are occupied with conflicting activities (e.g., sleeping, visiting with others, in the middle of a meal).

Our approach to medication reminding is cast in an expected utility framework for determining when and with what type or "media" and intensity or "strength" to remind a user to take a medication. More formally, the general expression for the expected utility has the form

$$\bar{U}[A,C] = \sum_{q=1}^{M} p(q \mid A,C) u_q(A,C), \qquad (1)$$

where $\bar{U}$ is the expected utility of an alerting action $A(t)$ when the patient is in state $q$ and context $C(t)$. $A(t)$ is one of possible actions generated by the alerting system and may include visual and auditory modalities as well as different alert intensities. We note that one of the possible actions is $A = \varnothing$ or "do nothing." The context $C(t)$ is a vector that represents all available measurements including motion sensors, for all times $t' \le t$. In general, the state of a patient is related to the instantaneous activity, such as sleeping, but in may also be an abstract representation of sensor data.

The probability that the patient is in state $q$ given an action and contextual measurements is denoted by $p$. This embodies the two levels of uncertainty: (1) uncertainty due to the indirect measurements of the patient's state and (2) the uncertainty of taking the medication, given the state. Within the expected utility framework in Equation (1), the latter uncertainty is incorporated in the utility $u_q(A,C)$.

To illustrate the approach, we assume that the patient is in one of two states: $q = 0$ and $q = 1$ representing the failure and success in taking the medication, respectively. When the patient is in state 1, the time $T$ when he takes the medication is a random variable with a probability distribution $F_1(T)$. Assuming that the only available sensor is the medication dispenser, that indicates that a medication was not taken by time $t$, it is possible to compute the probability that the patient is in the "forgetting" state by

$$\Pr\{q = 0 \mid T > t\} = \frac{p_0}{1 + (1 - p_0)[1 - F_1(t)]}, \qquad (2)$$

demonstrating that as time increases and medication is not taken, the probability that the patient will forget increases and consequently, the expected utility of an alert increases. With information from additional sensors, it is possible to increase the number of possible states and improve the accuracy of this assessment.

**Estimation of Time Probability Distribution**

As shown in Equation (2), an essential component of the maximum utility calculation is the probability distribution of times that the medication is taken without prompting. In order to implement this approach, it was necessary to estimate this distribution by monitoring individuals taking medications without any alerts. Such estimates were obtained in a baseline condition of a prior study [19, 20]. Because of the cyclic nature of time, i.e., daily periodicity, we developed a novel approach to the density estimation process. For the purpose of the present discussion, however, we performed a maximum likelihood fit using beta distributions.

## Empirical Estimation of Alert Utilities

The goal of this laboratory study is to estimate the utility of alerts and prompts. The utility assessments includes the benefits (positive utility) representing the effectiveness of reminding the patient to take his or her medication, as well the cost (negative utility) associated with the alert annoyance and failure to achieve the desired result. Our current study was designed to investigate several modalities, device form-factors and signal intensities of the prompting systems. The main dependent measures were subjective judgments in response to the various system reminders. In addition to the demonstrated prompts, subjects were asked to rate a number of other prompting devices

**Methodology**

In order to approximate real-life distractions, we introduced new methodology based on dual task. The dual task consisted of a background continuous activity (watching a comedy show) which was occasionally interrupted by the primary task. The computer generated the video as well as the signals that triggered the alerts.

When an alert was generated, the participants' task was to notice the alert and to respond to the alert by walking over to a medication dispenser and opening a specific compartment. The medication dispenser was designed to record both the time of the interaction and the specific compartment that was opened. The collected information comprised quantitative as well as qualitative data. In addition to the objective data (time duration and the identity of the medication tracker compartment that was opened), the participants were asked to judge the annoyance of the alerts generated by the devices included in the experimental part of the study. In addition, following the active experiment, they were asked to rate several devices that were not part of the experiment. The different devices were presented as much as possible in random order for different subjects.

**Prompting Devices**

The prompting devices used in this experiment were selected to cover a wide range of form factors and modalities. We used a combination of commercially available devices and our enhanced alerting devices. The following is a list of these devices and the corresponding modality:

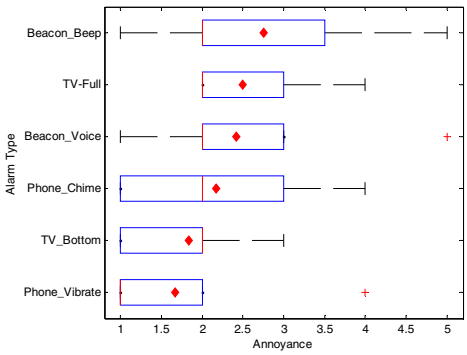


*Figure 1- A box plot of the annoyance ratings of different device for 10 subjects.*

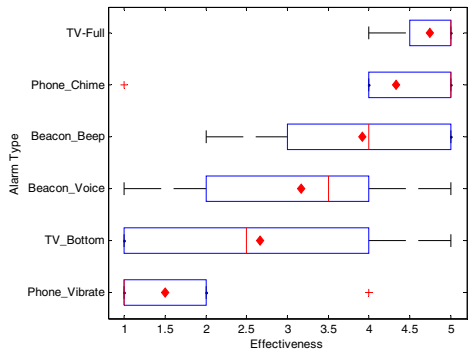


*Figure 2- A box plot of the effectiveness ratings of different devices.*

1. Vibrating modality, e.g., watch
    a. Adult version of a watch
    b. Pediatric version of a watch
    c. Vibrating Pendant
    d. Vibrating mobile telephone
2. Auditory alert watch with informational display indicating the action to be performed as a part of the secondary task.
3. Medication dispenser with audio-visual alert mechanism
    a. Visual alerts only
    b. Sounds only
4. PDA with auditory and visual (text) alerts and messages
5. Cell phone with voice and/or text messages
6. Office phone alerts
7. Television set (captioned message or full screen)

**Procedure**

The participants were recruited from a pool of elderly subjects participating in other, ongoing experiments. They were introduced to the study using a brief video in which an experimenter described the purpose, the task, and the procedure. During the video introduction, the participants were asked to adjust the level of the audio to a comfortable level – this was also used to assess their hearing. During the introduction, the participants also learned to use the remote control that enabled them to start and stop the television show. Following this introduction, the participants were consented.

The experiment was initiated by the participants using the remote control that started the television show. The participants were presented the alerts, namely the alert modality and type of signal in a pseudo-random order to reduce the potential of sequential effects. Following the experimental procedure described in the Methodology section above, the participants were asked to rate the devices in several ways including rank-ordering, as well as using a Lickert scale. In particular, they were asked to rate the effectiveness of each alert and its annoyance. In order to ascertain that the participants paid attention to the television show, they were also asked to answer a number of questions about selected details of the show.

## Results

In this section we first analyze the data from the empirical utility assessment study and then combine them with the data from our prior study [19, 20]. The results of the annoyance ratings, combined across subjects are shown in Figure 1. Similarly, Figure 2 represents the summary of the effectiveness ratings that appeared to be consistent with subjects' behaviors during the study. Although there appears to be some agreement, there is clearly significant inter-subject variability. A large component of this variability was due to the differences in individual preferences as ascertained by their comments and responses to questionnaires. Using the estimates of the utility and probability distributions from our pilot studies, we simulated a variety of alerting situations in order to determine important details of a potential implementation. An example of such an issue is the notion of a *refractory period*. In particular, after the system issues an alert, the instantaneous annoyance due to potential repetition of the same alert is significantly higher. The actual value of this increase and its temporal course of the refractory period needs to be investigated in a spate study.

## Conclusion

We have developed a new decision-theoretic framework and approach to optimize reminding and alerting using contextual information. Our data from several pilot experimental studies, in combination with this theoretical framework, suggest that an optimal, utility-based approach is possible and may improve medication-taking adherence. Additional improvement could be gained by including aspects such as the refractory period and the utility of interruption [23]. However, this study offers evidence to show the feasibility of integrating home monitoring data to infer patient context for reminding systems and also demonstrates the importance of incorporating patient preferences for alerts and reminders. Future directions for work in this area include linking medication adherence data

with personal health records and electronic medical records for broader health management use.

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