Adherence to Medical Treatments for Telemedicine Patients (Protocol)

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PROTOCOL

Background

1. Provide the scientific background, rationale and relevance of this project.

Proper adherence to prescribed medications is a fundamental requirement for effective health outcomes. The possible consequences of poor medication adherence include reduced effectiveness of treatments, deterioration of health conditions, longer recovery time, increased cost, irrecoverable damages to health, hospitalization, and even death. Despite the severe consequences, the medication adherence rate among patients is significantly low[1, 2, 3]. According to the World Health Organization (WHO), "Adherence to long- term therapy for chronic illnesses in developed countries averages 50%. In developing countries, the rates are even lower"[1]. Poor medication adherence is a public health problem, and WHO identifies it as a worldwide problem of striking magnitude. It causes about 33-69% of all the medication associated hospital admissions in the U.S.[4].

One of the main reasons for poor medication adherence is forgetfulness. People often forget to take medication at the appropriate time, and even sometimes take wrong dosages. Though forgetfulness is more prevalent in people with reduced cognitive ability such as the elderly, it is also very common to healthy and young people due to factors like daily routine, habits, and changes in medication regimen. Several studies show that medication adherence is improved significantly with the use of automated reminder systems[5, 6, 7].

A number of smart phone applications for medication reminder and tracking are available in app stores[8,9]. Researchers have also designed, developed and evaluated reminder systems using smart phones[10, 11]. However, smart phone apps are not convenient and effective enough for medication reminder and tracking. Though smart phones can be used by one hand when it is laid on or hung against some surfaces, most of the times users need to hold the phone by one hand and use it by another. Occupation of the hands for using the phones, and the attention required to use the apps justify that smartphone-based systems are significantly intrusive, and are not convenient, particularly for long-term and complex medication regimens. Also, a user is very likely to miss a reminder at home when the phone is far enough from his/her location at the time the reminder is given. For instance, a user may miss a reminder when he/she is busy in the kitchen, but the phone is in the bedroom far away from the user. Moreover, remainders may be missed while listening to songs, TVs or videos even if the phone is located near the user. In many situations like in meetings and classrooms, smart phones typically need to be kept silent, and users often forget to return the devices back to the non-silent mode when silence is not required any more. It is very likely that a user misses some reminders in such scenarios.

This study will test the feasibility of MedRem, a novel medication reminder and tracking system on wearable wrist devices, specifically with the Apple Watch 4. The study team will load the MedRem app onto two Apple Watch 4s for use during the study. As the device is

placed on the wrist, it is free from the above-mentioned limitations of smart phones. However, one of the major challenges in developing interactive systems for the wrist devices is their form factor. The touch screens available on these devices are tiny and much smaller compared to smart phones and tablet computers. MedRem enables user interactions by incorporating speech recognition and text-to-speech features along with clever interface design. The tiny display of the device is used for minimal inputs and outputs, while a user can retrieve and provide more information from/to the system through voice commands. Personalized models are built and updated over time to reduce errors in recognizing users' voice commands, and thus better user experience is provided.

Smart wearable devices like smart watches and wrist bands are usually enriched with many features like touch screens, microphones, sensors, Bluetooth and Wi-Fi. These devices are being used widely in healthcare applications including activity tracking, wellbeing monitoring, and reminders. Harmony is a hand wash monitoring and reminder system that uses inertial sensors of the smart watches in detecting hand wash activities of the wearer, and Bluetooth beacon-based localization technique to trigger reminders when required[12]. A diary-like system for diabetes patients is presented in another study that uses both smartphones and smartwatches to log information from and provide reminders to diabetes patients[13]. SPARK is a framework that combines smartphones and smartwatches together in monitoring symptoms of patients with Parkinson's Disease. It also supports physicians in providing tele-interventions to the patients[14]. Fabian et al. propose to show pictures of the drugs on the display of the wrist device to reduce confusion of the patients when multiple drugs need to be taken[15]. Some smartphone apps also synchronize reminders with smart watches[16]. However, these systems use only the small display of the wrist device, and therefore cannot provide detailed information related to a reminder using the wrist device only. Also, wrist devices used in the existing systems do not support rescheduling the reminders. Most of these reminders and tracking systems are aimed for specific group of patients or users. In contrast, MedRem is a general-purpose medication reminder and tracking system that can be customized according to the patient's needs. It combines speech recognition and text- to-speech technologies with intelligent interface design in providing reminders and tracking intakes.

One of the more complex issues in healthcare surrounds patient non-compliance with medical advice and treatment recommendations. Coupled with challenges in access to care faced by patients in rural or other underserved areas, the development of innovative solutions to chronic disease management is imperative. The UVA Center for Telehealth has long provided services to patients regardless of geographic barriers, and, in particular, for those facing serious health disparities. As is the case with traditional in-person services, clinicians are challenged to ensure (or monitor) that daily adherence to treatment is completed. The field of remote patient monitoring is growing, and new sensing and actuation technologies have the potential to monitor for adherence and to support interventions that improve adherence. The UVA School of Engineering and Applied Sciences and the UVA Center for Telehealth will collaborate on this study.

The proliferation of inexpensive sensing and actuation technology has the potential to bring improved health care to underserved areas. Telemedicine has made great strides in this regard. However, one of the most challenging problems is supporting patients in adhering to the (daily) treatments. Excellent remote health care will not work if the patients do not act on the advice and treatments. New, inexpensive, and easy to use technology (such as proposed here) has the potential to track adherence and, importantly, provide just-in-time, adaptive and learned interventions to increase adherence and thereby improve the health in rural communities. In this work we will focus on stroke patients, but the results of this work can be generalized to other medical conditions which will increase the future funding possibilities. Such solutions will not only improve health, but also reduce hospital readmissions. Underlying technical solutions will also have impact in producing robust and usable wearables and be a novel for voice processing in certain important contexts.

In this study, we will deploy the MedRem system to obtain a small amount of clinical and social acceptance data for a particular type of stroke patient. We will have two phases of deployment. In the first phase, we will deploy the system to control/test subjects. In the second phase, we will deploy the system in homes (each for 4 weeks) in order to collect some preliminary pre-pilot data. These systems will be deployed to stroke patients. Since this is a small study we will focus on stroke victims who are able to participate with a voice command home health system (i.e. no prohibitive cognitive impairments or language deficits), who have requirements for home- based therapy regimens (i.e. physical/occupational therapy), and who require medications for secondary stroke prevention (e.g. antithrombotic therapy to prevent ischemic stroke, stroke risk factor management with blood pressure, diabetes, cholesterol medications). We will identify patients by working with Dr. Andrew Southerland, a neurologist in the UVA Health System, who has extensive experience collaborating on mobile telehealth projects in stroke patients.

We will focus on the clinical value of improved rehabilitation by voice-based reminder interventions. The smart watch will identify exercise and provide the frequency and type of intervention for both medications and exercise. For exercise, we will interact with the patients (via audio on the watch) at specific times of the day to determine if they have completed that exercise. These messages will be prerecorded and loaded onto the MedRem app. We will also measure heart rate and heart rhythm using the smart watch's heart monitoring capabilities and inertial measurement units using the smart watch's accelerometer, gyroscope, and magnetometer.

Then, in future proposals other issues will be investigated including ability with respect to activity of daily living skills, attitudes, depression, anxiety, long-term use, and effect of reminders related to side effects. We would also extend the work to address caregiver issues of their own health and stress and anxiety. It is also possible to extend the use of the smart watches to assess the quality of the exercise regimen.

Objectives/Hypothesis

The purpose of this study (Phase 1) is to:

- determine the feasibility of the Apple Watch medication/exercise reminder system by deploying the system to two control subjects.

The purpose of this study (Phase 2) is to:

- assess the subjects' adherence to medications, exercise and checking heart rate (and quality of the exercise), with the use of MedRem
- assess the acceptance and usability of the MedRem system.

The hypothesis is that patients will use the system and that there are improvements in rehabilitation time and capability compared to averages for this population.

Study Design: Biomedical

1. **Will controls be used?** Yes.
   ►IF YES, explain the kind of controls to be used.
   We will test the system with two control patients.

2. **What is the study design?** Case series

3. **Does the study involve a placebo?** No.

Human Participants

Ages: ≥18 years
Sex: All
Race: All

Subjects- see below

1. **Provide target # of subjects (at all sites) needed to complete protocol.**
   Phase 1: 2
   Phase 2: 8

2. **Describe expected rate of screen failure/ dropouts/withdrawals from all sites.**
   Phase 1: 0%
   Phase 2: 20%

3. **How many subjects will be enrolled at all sites?**
   Phase 1: 2
   Phase 2: 10

4. **How many subjects will sign a consent form under this UVa protocol?**
   12. Phase 1 subjects will sign a Dry Run consent.

Inclusion/Exclusion Criteria

1. **List the criteria for inclusion**

Phase 1 (Controls)

- 18 – 75 years old
- Good general health (self-reported), with no history of CVA
- English-speaking
- Willingness and ability to comply with scheduled visits and study procedures

Phase 2 (Stroke Patients)

- 18 – 75 years old
- English-speaking
- Willingness and ability to comply with scheduled visits and study procedures
- Have requirements for home- based therapy regimens (i.e. physical/occupational therapy)
- Require medications for secondary stroke prevention (e.g. antithrombotic therapy to prevent ischemic stroke, stroke risk factor management with blood pressure, diabetes, cholesterol medications).
- Have a Modified Rankin Scale for Neurologic Disability (MDS) of 2 – 4

2. List the criteria for exclusion

Phase 1 (Controls)

- Pregnant women, fetuses, neonates, children, prisoners, cognitively impaired, non-English speaking subjects
- Prohibitive cognitive impairments or language deficits
- Does not have wireless internet connection at home

Phase 2 (Stroke Patients)

- Pregnant women, fetuses, neonates, children, prisoners, cognitively impaired, non-English speaking subjects
- Have a Modified Rankin Scale for Neurologic Disability (MDS) of 0-1 or 5
- Prohibitive cognitive impairments or language deficits
- Significant weakness, dystonia, or spasticity that will prevent proper use and response to the Apple Watch device
- Live in nursing home or rehabilitation facility
- Does not have wireless internet connection at home

3. List any restrictions on use of other drugs or treatments. n/a

Statistical Considerations

1. Is stratification/randomization involved? No.

2. What are the statistical considerations for the protocol?

Phase 1:

The objective of Phase 1 is to determine the feasibility of the Apple Watch medication/exercise reminder system by deploying the system to two control subjects.
The primary endpoint of this phase to assess the usability of the system and to work out any technical problems. The usability will be assessed by the 'Test Patient MedRem Usability Survey.' (see attached)

Phase 2:
The objective of Phase 2 is to determine the effectiveness of the Apple Watch medication/exercise reminder system by deploying the system to stroke patients. The goal is to assess the clinical value of improved rehabilitation by voice-based reminder interventions.

The primary endpoint of this phase is to assess the patients' adherence to medications and exercise. Adherence will be measured by patient responses to questions prompted by the MedRem System.

The secondary endpoint of this phase is to assess the acceptance and usability of the system. Acceptance and usability will be measured by the Intervention Patient MedRem Usability Survey (see attached). Steps taken and distance covered data will also be collected from the Apple Watch.

3. Provide a justification for the sample size used in this protocol.
2 control subjects will suffice in determining the feasibility of the device software.

8 study subjects will suffice in determining the effectiveness of the device software. We will aim to recruit 10 subjects, accounting for a dropout rate of 20%.

4. What is your plan for primary variable analysis?
The primary variable will be analyzed by counting whether the patient responded to the MedRem system prompts and whether the patient confirms that the medication was taken or therapy exercise was completed.

5. What is your plan for secondary variable analysis?
The secondary variable will be measured based on the survey results. We will also analyze the steps taken, and distance covered data collected from the Apple Watch.

6. Have you been working with a statistician in designing this protocol? No.

7. Will data from multiple sites be combined during analysis? No.

Study Procedures-Biomedical Research

1. What will be done in this protocol?

Phase 1:

The MedRem system will be deployed to two control subjects who will interact with the system by responding to medication and exercise reminder prompts. Subjects will be provided with oral and written information regarding the watch and MedRem system. Test subjects will not take any sham medications or exercise regimens, but will be provided a sham reminder schedule. They will simply respond verbally to prompts and press a button on the watch when finished speaking as if they are taking the medication or doing the exercise. After one week of interacting with the system, the study team will follow up with the subject and determine the functionality of the system by asking survey questions. If changes need to be made, the subject will interact with the system for one more week to test out the new changes. At the end of each week of the testing period, the subject will respond to a survey over the phone (see attached 'Test Patient MedRem Usability Survey').

Phase 2:

After a patient is identified, recruited, and consented, the study team will introduce the MedRem system to the stroke patient. The patient will be thoroughly trained before taking the device home, and will be given written information and instructions for the AppleWatch and the MedRem system. A member of the study will have to come to the patient's home to connect the apple watch to the patient's home wifi. The subject will be asked to wear the watch while awake during their daily activities. Subjects will be given contact information for a member of the study team to be available by telephone if they have questions once they begin to use the watch. The subject's physician and physical therapist, who are also members of the study team, will collect all medications and treatment regimens for the subject and give that information to the programming team. The programming team will upload the medication and treatment regimens to the MedRem system. The licensed providers, on the study team, will review the list of medication and physical therapy exercises before the information is sent to the subject's MedRem system on their Apple Watch.

The subject's medication will be set by time of day they have specified in discussion with their health care provider. As above, the provider will review the medication regimen before it is sent to the subject. The MedRem app will ask each subject at the specified time if they have taken their medication and the specific name of the medication will appear on the MedRem app. For exercise regimens, the MedRem app will ask at specific times of the day if the subject has performed their exercise. The MedRem system will also ask the subject to check their heart rhythm using the Applewatch twice a day at specified times. Patients will respond verbally to the Medrem app and will press a button to indicate a finished response. The heart rhythm will not be stored in the MedRem database but the time stamp from each ECG taken will be recorded. All ECGs will be deleted once a timestamp is documented.

Each week, a member of the study team will follow-up with the patient to see how well the system is working and if any reminders need to be adjusted for time of day. The app is controlled remotely, so the computer science study team member who is the subject's health care provider can make any adjustments without having to physically

see the patient. The study team will also confer with the patient's physician if any adjustments to their medication or exercise regimen need to be made. All adjustments will be assigned and reviewed by their subject's licensed provider using the same review process as stated above. The study team will administer the 'Intervention Patient MedRem Usability Survey' over the phone at the end of each week of the study period. After one month, the study team will call the patient and administer a survey over the phone (see attached). At the end of the study period, the patient will return the device at their next follow-up appointment in the Neurology clinic.

At the end of study participation, a licensed health care provider will assist the subject to transition to a conventional method for keeping track of medications and exercise routines.

2. If this protocol involves study treatment, explain how a subject will be transitioned from study treatment when they have completed their participation in the study. n/a

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