A. Study Purpose and Rationale

Diabetes mellitus is the most common and serious chronic disease in the United States. There are nearly 26 million Americans with dabetes, 30% of which are aged 65 and older.[1] California in particular has the highest incidence of new diabetes cases and nearly 4 million people estimated to be suffering from the disease.[2] The costs of caring for this disease are astronomical and are estimated to exceed more that $24 billion in California and $174 billion nationally.[1,2]

Despite the availability of effective treatment, diabetes remains poorly controlled. Fewer than 7% of diabetic patients meet treatment goals for lipids, blood pressure, and glycosylated hemoglobin A1c.[3,4] Elderly patients with diabetes have higher rates of mortality, congestive heart failure, myocardial infarction and stroke as compared to age-matched controls without the disease.[5] Moreover, despite evidence that the mortality rate is decreasing over time, the rate of complications is remaining the same.[6] As a result, the average number of lifetime complications per patient is increasing as patients are living longer. With the incidence of diabetes rapidly rising, this is a fatal combination for the economic wellbeing of our health system.

Poor adherence to recommended self-management guidelines is well-recognized as a significant barrier to effective glycemic control. Improved outcomes have been associated with better adherence to medications, blood sugar self-monitoring, diet and lifestyle changes, and appointment attendance.[7-14] Barriers include time constraints, knowledge deficits, denial, limited social support, inadequate resources, and low self-efficacy.

A major challenge in chronic disease self-management, particularly in older Americans, is social isolation.[15] Elderly diabetic patients with poor social support have twice the mortality rate of those with adequate support.[16] Furthermore, though families and friends often want to help their loved ones better manage their conditions but do not know how to act or when to act. Studies consistently show that patients with empowered caregivers or peers have better outcomes.[17]

Mobile phones are an ideal platform for supporting chronic diseases like diabetes because they are ubiquitous, low-cost, reliable, real-time, and versatile; and unlike most technologies, actually enjoy greater usage amongst racial/ethnic minorities. In self-management, mobile phones can help individuals remember to do various health-related activities and record them, and also help others in their personal wellness ecosystem to review ongoing health patterns and respond quickly to changes in health status.

In Spring of 2010, we pilot-tested a mobile phone-based diabetes self-management program in urban African Americans using a precursor to our Care-Smarts software in which automated, personalized text messages were sent to participants with medication, foot care, and appointment reminders and text messages were received back on adherence. Participants were registered in SMS-Care after querying them on their preferences (e.g., timing, frequency, and content of messages) and began receiving text messages the following day. Each participant received a daily medication reminder (e.g., “Time to take your diabetes medications”), a daily or semi-weekly question about medication adherence (e.g., “How many times did you take your medication?”), and a weekly question about foot care (e.g. “How many times did you check your feet this week?”). Weekly telephone interviews were conducted by a certified diabetes educator (CDE) to obtain feedback on the participants’ experience and, if necessary, make adjustments to their personalized SMS-Care program. The participant could elect to change the content or timing of messages and add or remove messages.

Eighteen participants from the South Side of Chicago, a low-income urban African-American community, completed the four-week pilot. The average age was 55 and the average number of years with diabetes was eight. Half of the participants were initially very or somewhat uncomfortable with the text messaging function of their

cell phones. On average, each participant exchanged approximately 220 text messages with SMS-Care during the one-month pilot. Participants responded to messages 80 percent of the time and on average responded within 6 minutes. The majority of participants strongly agreed that the system was easy to use, helped them to avoid missing medications and increased the frequency of foot self-examinations. Diabetes self-efficacy, as measured using a validated survey instrument, improved following the intervention ($p<0.01$) while the number of missed medications decreased.

Using a technology platform widely available across socioeconomic groups, our study demonstrated an improvement in diabetes self-management by empowering patients to better manage their chronic diseases. Through simple reminders and automated two-way messaging the software helped patients feel supported in the everyday tasks required to keep their diseases under control. Because we targeted a low-income, underserved population; it also suggested that we had found an intervention that worked for the "least common denominator", which gave us hope that our technology could be scaled broadly across diverse communities around the country.

A key lesson from this work was that the messages alone were not what sustained patients' interest and engagement with the system. Rather it was the combination of the messaging plus interaction with a certified diabetes educator that reinforced their commitment to self-care goals. This human element encouraged patient engagement with the system and added an additional layer of support for their daily self-management. In this proposal, we aim to heed this lesson by engaging and empowering a significantly underutilized resource, informal caregivers, (who we call "health buddies"). Using health buddies, rather than professional health care providers, avoids creating an additional strain on the health care system, which we believe will improve the scalability of this intervention.

Historically, peers have been an underutilized resource in the management of patients with chronic diseases like diabetes. In this project, we propose to develop the novel concept of an "mbuddy" or mobile health buddy. Our goal is to utilize health information technology to enable the health buddy to take active part in co-managing the diabetes condition of the subject. We believe because this program does not rely on health care providers it will be more readily scalable and implementable in diverse settings. In this proposal, we aim to leverage our success developing and piloting a patient-centered mobile phone-based diabetes intervention into patient and health buddy co-management tool that uniquely serves the challenges faced by older Americans. mBuddy has two distinct advantages over currently available mobile health solutions:

- One, by engaging patients and their informal caregivers (or "health buddies"), mBuddy will decrease reliance on the health care system and be able to be implemented in diverse communities. Implementing mobile health in clinics and hospitals requires integrating data systems and modifying provider workflows, both of which present enormous barriers, and as a result adoption of mobile health technologies has been slow. In our previous work, by focusing on patient empowerment rather than the transmission of health information, we demonstrated an improvement in diabetes self-efficacy that was sustained even after participants stopped receiving messages from the system. At the same time, from extensive interviews with participants, we learned that having regular personal interaction with someone who was engaged with the system (for the pilot this was a diabetes educator) was critical for participant buy-in. By leveraging an underutilized member of a patient's care team – his/her health buddy – mBuddy will empower patients without creating an additional burden on the health care system.

- Two, through its use of novel algorithms based on theoretical models of behavior change, empowerment, and persuasive technology, the mBuddy platform maximizes patient engagement in self-management of chronic disease. Unlike most mobile health interventions, which require a care manager to review and respond to health information transmitted by the patient, mBuddy will be fully automated. It's lack of dependence on professional

health care staff will make mBuddy less expensive and easier to implement across a range of health care settings. Additionally, mBuddy is specifically built for basic mobile phones and does not require participants to have smart phones, data plans, or regular access a computer or the Internet. This will make mBuddy available and accessible to anyone with access to a mobile phone.

B. Study Design and Statistical Analysis

100 patients meeting inclusion/exclusion criteria, once consented, will participate in a non-blinded randomized control trial. Patients in the intervention group will be enrolled in individually tailored message programs focusing on specific self-management domains of diabetes. Patients will receive messages consisting on average of a daily reminder message, a daily question to which the user is requested to answer and a weekly educational message related to self-care. Example messages include “Exercising is very important for your help. Try to walk at least 30 minutes today!” and “Did you take remember to take your diabetes medications today?” Patient responses will be stored and used by mBuddy algorithms to determine further messaging content and frequency. After two weeks, mBuddies will also begin receiving messages consisting of two types of messages: the same weekly educational message received by the patient and messages specifically in response to patient feedback. These messages tell the mBuddy how the patient is doing and provide a recommendation of how the mBuddy should further engage the patient. For example, if the patient is responding “no” to medication adherence questions, the mBuddy will receive a message asking him/her to discuss with the patient why the patient is not taking the medication. Some examples are shown below:

1. Patient responds they exercised 0 minutes over the past 3 days. Our system triggers a message to buddy: "Consider giving patient X a call to encourage them to get some more exercise." This alert would also generate follow-up messages to both the patient and mBuddy asking to confirm mBuddy involvement.

2. Patient responds everyday that they took their medication. The system prompts the buddy who gets a message: "Congratulate patient X for taking all her medications. Let him/her know this is really important."

3. Patient has not responded to any messaging in 2 days. This triggers a message to the buddy: "Patient X is not responding to our messages. Give her a call to let her know you think this is important for her health.”

Patients in the control group will be scheduled to receive weekly culturally-tailored messages via automated voice or SMS with content intended to reinforce self-care goals. Both intervention and control group patients will be given educational pamphlets emphasizing optimal self-management of diabetes.

On enrollment, participants will complete questionnaires to obtain demographic information (e.g., age, gender, ethnicity, education, insurance, etc.), historical cellular phone usage, and adherence to self-management goals. Patients will then complete a version of the validated 4-item Diabetes Self-efficacy Scale (DSES) and a quality of life assessment (SF-8) tool. Patients in the intervention arm will also complete the instrument designed during phase 1 to identify their stages of change within the diabetes self-care domains. The patient’s selected mBuddy will complete a survey on caregiver burden and diabetes comprehension.

On completion of the trial, each participant will complete surveys to assess their comfort level with the Care-Smarts system, satisfaction with the pilot and adherence to ADA guidelines. Participants in the intervention group will additionally be asked to report on their satisfaction with the mBuddy component of the trial. The DSES, SF-8 and caregiver burden surveys will again be administered. Once patients complete their follow-up CVMG appointment, data on blood pressure, hemoglobin A1C, and weight will be obtained from the clinic. Two months

after completion of the trial, each participant will be contacted by phone. Participants will again be queried on their adherence to ADA guidelines and the DSES, SF-8 and caregiver burden surveys will be administered.

Data Analysis

The primary outcome of this study is change in glycosylated Hemoglobin A1c (Hgb A1c). Hgb A1c provides a 90 day average of a patient's daily blood sugar levels. Studies have shown a direct relationship between the average Hgb A1c and rate of micro- and macro-vascular complications. Patients with better controlled diabetes have shorter hospital stays and reduced complications when hospitalized.

This study is designed to detect a 0.5% absolute reduction in Hgb A1c, with a statistical power of 80% at the 5% level of significance. With an estimated effect size of 0.5 and a standard deviation of 0.5, this calculates to 20 patients per group or a total of 40 patients combined. We will be enrolling 100 patients or 50 per group to ensure significance and protect against drop-out rates. Chi-square tests will be used to compare between trial arms and pre-post data.

Secondary outcomes include self-efficacy (DSES), caregiver burden (???), and quality of life (SF-8). Survey data will be obtained at three time points: on enrollment, on completion of trial, and two months post-trial. Pre-post analyses will be conducted as well as control vs intervention using Wilcoxon sign-rank tests.

Measures of feasibility will include enrollment rate, completion rate, and process metrics (e.g., participant response rate, response timing).

C. Study Procedures

D. Study Drugs

No drugs will be used during this trial.

E. Medical Devices

No medical devices will be used.

F. Study Questionnaires

1. Demographic info
2. Cell phone usage and comfort level
3. Adherence to ADA guidelines
4. Diabetes Self-efficacy Scale
5. SF-8
6. Stage of Change
7. Caregiver Burden (Zarit Burden Interview from American Family Physician)
8. Pilot Satisfaction

G. Study Subjects

Inclusion criteria include: (1) patients with type II diabetes, (2) Hemoglobin A1c > 8.0%, (3) aged 60 or older, (4) on at least one diabetes specific medication (an oral hypoglycemic or insulin) which has been stable over the past

three months, (5) at least a fifth grade reading level in English(??), (6) have regular access to a cell phone, (7) are of self-identified African-American or Hispanic origin, (8) and are community dwelling . In addition, patients need to enter the study with a mBuddy who is at least 18 years of age, has access to a personal cell phone, and has at least a fifth grade reading level in English.

H. Recruitment of Subjects

Patients will be recruited from the practices of Dr. Rodney Hood and Dr. Richard O. Butcher at the CareView Medical Group (CVMG). The combined practices of Drs. Hood and Butcher care for an estimated 8000 patients of which 25% are over 60 and have type II diabetes, and serves a predominantly African American (50%) and Hispanic (40%) population. Patients meeting inclusion/exclusion criteria will subsequently be consented and randomized to either the intervention or control arm.

J. Potential Conflict of Interest

Jonathan Dick is co-founder of mHealth Solutions, the maker of CareSmarts.

K. Location of Study

CareView Medical Group, San Diego, CA

L. Potential Risks

The major risk of the proposed study is loss of confidentiality, but this risk is low given the protections planned (see below). If a participant were to lose their phone or to let another person borrow it, older messages sent by the system may identify him or her as having diabetes. Additional risks relate to the possibility of misunderstanding the purpose and content of text messages sent to and from mBuddy. Messages sent to remind patients to take their medication or monitor their glucose may be misunderstood. In addition, patients may falsely assume that urgent messages sent to mBuddy will be reviewed by their health care provider.

<u>Adequacy of Protection Against Risks</u>

Recruitment and Informed Consent: Individuals participating in focus groups and pilot testing be asked to provide written informed consent for participation and consent to be recorded. All research protocols and informed consent will be reviewed by the Claremont Graduate University Institutional Review Board.

<u>Protection against Risk</u>

All project staff will complete training in the conduct of human subjects research. Documents and participant information obtained for research purposes will be strictly maintained according to IRB standards to ensure confidentiality at all times. All documents with participant names will be kept in locked file cabinets or a password-protected file. Only study staff listed on the IRB application materials will have access to the information. Patient health identifiers will be kept in a password-protected file.

The mBuddy will operate on a secure server and all identifying data will be encrypted. Access to mBuddy will only be available to the data manager and to researchers. The server will be password protected, and a log of all access of identifying data will be kept.

There is the potential that the content of the messages, if read by another person, will reveal PHI. Thus medication names will not be used unless specifically requested by the participant. Generic terms like “pill”, “dose” and “reminder” will be used to remind patients to take their medication.

Patients will have access to research assistants to troubleshoot any technical difficulties they may experience using the phones throughout the study. Patients will be instructed that mBuddy is not an emergency reporting system and that clinical issues regarding their care management should be directed to their physician (and not the researchers/staff in this study).

M. Potential Benefits

Patients and health buddies who take part in the focus groups may learn more about barriers to optimal self-management of chronic illness and thereby, respectively, improve their own self-management and practice patterns. For example, in our previous work, many patients noted that they didn’t know how important routine foot care was to preventing diabetic foot complications.

Participants in the pilot study may benefit directly from participation in two ways. First, based on our experience piloting our previous software, mBuddy may help them to manage their diabetes via reminders to take medications, check their feet for wounds and eat a low-glycemic diet. Second, the participant will receive unlimited text messaging during their participation. There is no control arm for the pilot study so all participants will receive the intervention.

N. Alternative Therapies

O. Compensation of Subject

Patients will be compensated $20/month to cover costs of text messaging.

P. Costs to Subject

None

Q. Minors as Research Subject

N/A

R. Radiation or Radioactive Substance

N/A

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