RANDOMIZED CONTROLLED TRIAL OF TWO TELEMEDICINE MEDICATION REMINDER SYSTEMS FOR OLDER ADULTS WITH HEART FAILURE

A thesis submitted to Kent State University in partial fulfillment of the requirements for the Degree of Master of Arts

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CHAPTER I

INTRODUCTION

Over five million Americans suffer from congestive heart failure (HF), with an additional three million projected to suffer from HF by 2030 according to the American Heart Association (AHA, 2012). Heart conditions represent the most expensive class of diagnoses of direct health expenditures in the United States, with heart conditions costing greater than cancer, diabetes, or stroke (AHA, 2012). With total costs exceeding 95 billion dollars in 2008, HF is projected to cost 97 billion dollars by 2030 (AHA, 2012). Most of the cost that occurs when a patient fails to manage his or her complex treatment regimen can be attributed to rehospitalization (Granger et al., 2005; Kutzleb & Reiner, 2006). This complex treatment regimen includes symptom monitoring, restricting dietary and fluid intake, and properly managing multiple daily medications. The patient must not only adhere to his or her doctor’s multifaceted prescription for treatment, but also take appropriate corrective action when symptoms worsen. Improved self-management is thought to decrease rehospitalization. Benefits from improved chronic disease self-management could result in gains derived from fewer patient hospitalizations, shorter lengths of stay, and fewer outpatient visits (Katon et al., 1999; Katon et al., 2001; Katon et al., 2002; Ludman et al., 2003; Von Korff et al., 2003; World Health Organization [WHO], 2003). Meta-analyses reveal that interventions designed to improve medication adherence provide few effective results, with increases in adherence ranging from 4-11%
The Agency for Healthcare Research and Quality (AHRQ) advises that new studies should examine the element(s) that best improve medication adherence (2012). Branches of telemedicine, such as telehealth (using a standard home telephone line to transmit health information) and mHealth (using mobile technology to transmit health information), may represent two prospective avenues for targeting medication self-management. The present study aims to determine whether a telehealth (automated pillbox) or an mHealth (smartphone application) intervention improve medication adherence in older adults with systolic and diastolic HF.

**Overview of HF’s Burden**

HF affects 5.8 million people annually in the United States, and it is associated with decreased quality of life, and increased mortality, morbidity, and healthcare expenditures (Heart Failure Society of America et al., 2010; Lloyd-Jones et al., 2010). Twelve-month mortality for HF approaches 20% (Lloyd-Jones et al., 2009). Predictors of mortality among 48,612 individuals hospitalized with HF were age, systolic blood pressure, heart rate, creatinine, serum sodium, and the presence or absence of left ventricular systolic dysfunction (Abraham et al., 2008). Studies demonstrate that HF patients suffer from poor health-related quality of life, with increased HF severity, increased depressive symptoms, younger age, and poorer total recall memory contributing to poorer health-related quality of life (Pressler et al., 2010a).
Components of Effective HF Self-Management

Components of effective HF self-management include symptom monitoring, daily weighing, sodium and fluid restriction, and medication adherence. Although HF patients should minimize dietary sodium, patients frequently cannot estimate adherence to low-sodium diets potentially due to knowledge gaps that preclude accurate self-assessment of sodium use (Chung, Lennie, de Jong, Wu, Riegel, & Moser, 2008). Most patients with chronic cardiovascular disease, including HF, take multiple medications throughout the day (Coleman, Roberts, Sobieraj, Lee, Alam, & Kaur, 2012). Problems managing medication can lead to rehospitalization or death.

Between one-third and two-thirds of medication-related hospitalizations result from poor medication adherence (Osterberg & Blaschke, 2005). In a study of 282 adults over 70 years of age hospitalized due to HF, 142 patients and their families received a nurse-facilitated education intervention before discharge (Rich, Beckham, Wittenberg, Leven, Freedland, & Carney, 1995) while 140 received conventional care. Patients in the intervention group were significantly less likely to re-enter the hospital 90 days post-discharge: the number of readmissions for HF was reduced by 56.2% in the intervention group, which was significantly different from the readmissions for the control group, and the group’s average quality of life after 90 days improved more from baseline in the intervention group (1995). The intervention group’s reduction in hospital admissions represented a $460 per-patient cost reduction (1995). Altogether, this brief educational intervention appeared to improve HF self-management.
Adherence in HF

Generally in developed countries, the adherence rate to long term treatments for chronic illness is 50% (WHO, 2003). Studies have demonstrated that patients fail to fill 20% to 30% of their medication prescriptions and fail to take approximately 50% of their chronic-disease medications as prescribed (Bogner & de Vries, 2008; Bosworth et al., 2005). Non-white patients tend to display poorer adherence rates than white patients (Holmes, Luo, Hanlon, Elting, Suarez-Almazor, & Goodwin, 2012). One study of 209 HF patients found the median number of unique medications filled at a pharmacy within six months was 11 medications. The study reported that poor adherers more frequently discontinued and failed to fill their medications, and that they skipped doses to save money (Dunlay, Eveleth, Shah, McNallan, & Roger, 2011). Specifically, where full adherence is defined as having enough medication for every day for an entire year, the percentage of HF patients who attain full adherence may be as low as 10% (Monane, Bohn, Gurwitz, Glynn, & Avorn, 1994).

HF patients must achieve at least 88% adherence to maximize their chances of event-free survival (Wu et al., 2009). Studies of medication nonadherence have varied widely in observed adherence rates: one study found adherence rates ranged from 56-83% for different types of HF medications five years after an index HF hospitalization (Gislason et al., 2007). Murray and colleagues found low-income HF patients in the usual care group achieved medication adherence rates of 67.9% as opposed to 78.8% in patients who received education and monitoring from pharmacists (2007). Another study found 11% of HF patients took fewer than 80% of the prescribed pills of a single
monitored medication (Granger et al., 2005). Rates of medication adherence in HF vary by how adherence is defined and measured; these variations produce large ranges in adherence rates (Wu, Moser, Chung, & Lennie, 2008).

HF patients face many barriers to adherence including complex medication regimens, cost, and mild cognitive dysfunction. Many HF patients are prescribed antihypertensive and lipid-lowering medications. In cardiovascular disease patients prescribed antihypertensive and lipid-lowering medication, adherence rates are estimated to be at 50% or lower, and cardiovascular disease patients frequently discontinue these medications shortly after receiving the prescription (Wolf-Maier et al., 2004; Ansell, 2008; Ockene, Hayman, Pasternak, Schron, & Dunbar-Jacob, 2002). For example, the rate of nonadherence two years after being prescribed statins is as high as 75% (Chodick et al., 2008; Evans et al., 2009). Warfarin, a powerful blood thinner commonly prescribed to HF patients, was associated with a 22% nonadherence rate in one outpatient clinic sample over a median 139 days of electronic monitoring using MEMS caps readings (Cruess et al., 2010).

One large body of research has utilized pharmacist-led interventions targeting medication adherence in HF patients by increasing education and supervision of medication management. In a sample of 851 cardiovascular patients studied by Kripalani and colleagues on behalf of the Pharmacist Intervention for Low Literacy in Cardiovascular Disease Study Group, 50.8% made one or more clinically important medication errors within 30 days of hospital discharge (2012). Of the errors, 22.9% were serious and 1.8% were life-threatening (2012). Additionally, adverse drug events
occurred in 30.3% of the sample, and potential adverse drug events occurred in an additional 29.7% (2012). Patients who received pharmacist-assisted medication reconciliation (e.g., health literacy and cognitive-sensitive intervention counseling covering topics such as barriers to adherence, prescription labels, changes in regimens, and high-risk medications) did not demonstrate a reduction in clinically important medication errors compared to controls (2012). However, those who received the counseling tended to have fewer potential adverse drug events (2012). Another study of monthly pharmacist consultations across six months found such consultations improved medication compliance when the consultation and medication adherence measurement focused solely on one type of risky drug: loop diuretics (Bouvy, Heerdink, Urquhart, Grobbee, Hoe, & Leufkens, 2003). Another community pharmacist intervention consisted of one or two home visits in which pharmacists reviewed drugs and gave symptom self-management and lifestyle advice (Holland et al., 2007). This intervention did not lead to reductions in hospital admissions compared to care as usual (2007). Lastly, one nine-month pharmacist intervention produced improved medication adherence during the intervention, although it cautioned that a long-term intervention would likely be necessary for change because the effects dissipated upon follow-up (Murray et al., 2007).

Further, in one intervention study of adults with chronic HF, participants were assigned to either a physician-led remote telemedical management intervention program (e.g., portable devices for blood pressure, ECG, and body weight measurements connected to a personal digital assistant) or usual care (Koehler et al., 2011). Upon a median 26 month (minimum 12) follow-up, the remote telemedical management program
did not reduce all-cause mortality in ambulatory patients with chronic HF (Koehler et al., 2011).

Cognitive Dysfunction in HF

Besides all the typical challenges to optimal self-management of HF such as high medical costs, increased patient and family burden, and time-consuming doctors appointments, many adults with HF exhibit mild cognitive dysfunction. Estimates suggest 25-50% of patients with HF also experience mild cognitive impairment (Pressler, 2008). Therefore, telehealth interventions in this population must overcome the complication of cognitive dysfunctions in attention, memory, executive functioning, and global domains that lead to forgetting medication. One review suggested optimally effective medication adherence telehealth interventions targeting older adults with cognitive impairment should provide frequent continuous human interactions and contact, for example by telephone or televideo (Campbell, Boustani, Skopolja, Gao, Unverzagt, & Murray, 2012), as their dysfunctions may introduce additional challenges into the adoption and acceptance of an adequate medication adherence intervention.

The presence of mild cognitive impairment, subtle but observable deficits in one or more domains, in individuals with HF is approximately 53-58% (Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2006; Zuccala, Cattel, Manes-Gravina, Di Niro, Cocchi, & Bernabei, 1997). Moreover, memory dysfunction, and poorer global cognitive scores composed of the Mini-Mental Status Exam, working memory, psychomotor speed, and executive function all predict mortality in 166 stable outpatients with HF after 12 months with memory loss being the most predictive (Pressler, Kim, Riley, Ronis, & Gradus-Pizlo,
Furthermore, cognitive impairment is associated with poorer medication adherence in individuals with HF (Hawkins, Kilian, Firek, Kashner, Firek, & Silvet, 2012). In one study of a sample of community-dwelling older adults (not necessarily with heart failure), a composite of executive function and working memory tasks significantly predicted medication adherence (Insel, Morrow, Brewer, & Figueredo, 2006).

**Telemedicine Interventions**

Interventions for medication adherence are needed to ultimately reduce rehospitalization. Traditional health-promoting interventions have been investigated as potential adherence interventions across a myriad of conditions, including HF. When 78 randomized trials for adults with medical disorders were reviewed in a recent Cochrane review, no simple intervention (e.g., simplifying dose regimens, using adherence-promoting packaging) and few complex interventions effectively improved long-term medication adherence and health outcomes in adults (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008). Many health professionals most frequently utilize educational interventions to target medication adherence (Berben, Dobbels, Kugler, Russell, & de Geest, 2011). Also, switching to once daily and opposed to two and three times daily medication regimens has produced increased adherence in individuals with chronic cardiovascular diseases including HF (Coleman, Roberts, Sobieraj, Lee, Alam, & Kaur, 2012).

Telemedicine utilizes technology to measure and improve health through various modalities, such as the internet and telemonitoring devices like MEMS Caps. One review illustrated that although the literature appears to support Internet-based interventions
designed to improve medication adherence, most of these programs relied on self-reported adherence measures and therefore should be evaluated with caution (Linn, Vervloet, van Dijk, Smit, & Van Weert, 2011). One literature review of telemonitoring of heart failure compiled by Louis, Turner, Gretton, Baksh, & Cleland revealed some randomized controlled trials that demonstrated telemonitoring facilitates early detection of deterioration and reduced readmission rates as well as length of hospital stay (2003); another trial reviewed therein reduced mortality after six months of monitoring weight and symptoms although that study did not demonstrate reduced readmission rates (2003).

Medication reminding using telemedicine interventions may improve medication adherence. Two of the most promising sub-fields of telemedicine, telehealth (using a standard home telephone line to transmit health information) and mHealth (using mobile technology to transmit health information), may offer promise in targeting medication adherence across a variety of chronic illnesses.

Telehealth studies have targeted self-management for a variety of cardiovascular conditions. Numerous studies have investigated the use of telephone calls aimed to improve medication and treatment adherence. One program demonstrated 169 urban hypertensive African Americans experienced improvements on a measure of overall diet quality and in energy expenditure compared to controls after receiving once-weekly counseling messages via automated phone calls through a culturally adapted telecommunication system (Migneault et al., 2012). Another telehealth technology is a multi-compartment adherence device with reminder capacity which transmits data through a telephone connection; one feasibility study found subjects with HIV generally
found the device acceptable and useful, though 65% found the reminder chimes annoying (Haberer et al., 2012).

In another study utilizing a computer-controlled telephone system in which hypertensive patients called into their doctors weekly to report adherence and blood pressure, mean antihypertensive medication adherence and mean diastolic blood pressure improved significantly for those in the telephone system condition compared to controls (Friedman et al., 1996). Additionally, the program worked to improve diastolic blood pressure in nonadherent participants in the phone condition, while the control group demonstrated increases in diastolic blood pressure (1996). Ultimately, most of the telephone system users were satisfied with the system and most of the physicians at the 29 community sites ultimately integrated the telephone system into their practices as it was particularly cost-effect for nonadherent users of antihypertensive medication (1996). However, telehealth programs are limited by moderate effects.

It is important to note one study examining the use of a handheld device to promote medication adherence produced high adherence rates (nearly 90%), though it was paired with an attrition rate of 23% in a group of chronically ill patients (Heinrich & Kuiper, 2012). This study found a strong relationship between higher levels of education and low forgetting of medication (2012). Most individuals in this study did not have cognitive dysfunction and were judged to have adequate health-literacy (2012). This study paired reminding with a feedback mechanism, which was thought to promote purposeful medication-taking action in individuals who completed the study (2012).
**Telemedicine Interventions for HF**

Within telemedicine, mHealth interventions utilize cellular phones and smartphone applications to improve health behavior. Text messaging programs are one of the newest medication adherence improving methodologies because approximately 83% of adults in America own cellular phones and 73% of them use text messaging as a relatively inexpensive form of communication (Smith, 2011). Adults 65 and older send an average 4.7 texts per day (Smith, 2011). One study of 580 adults retrospectively observed significant adherence differences in the cohort that opted to receive text message medication reminders than in the matched control cohort for numerous medications, including antidiabetes medications and β-blocker therapy, suggesting text message reminder programs may help maintain high rates of medication adherence across time (Foreman et al., 2012). The findings suggested that participants who opted into a text message reminding program had higher adherence rates than those who opted out of receiving medication-specific text message reminder (2012). Furthermore, in this retrospective observational cohort analysis the text message reminder program assisted in preserving higher adherence rates over eight months (2012).

One study utilized a telemonitoring program administered via mHealth technology. In this program for 108 HF patients, the patients utilized a pharmacological treatment alone (control) against a pharmacological treatment plus a mobile phone-based telemonitoring patient terminal into which participants entered information, and values entered outside previously created parameters triggered an email sent to the study physician (Scherr et al., 2009). The participants transmitted their blood pressure, heart
rate, and body weight on a daily basis (Scherr et al., 2009). Ultimately, HF patients in the telemonitoring group demonstrated improved NYHA class by one class whereas controls did not (2009). Furthermore, significantly fewer telemonitoring participants were rehospitalized, and the individuals who returned demonstrated a statistically significantly shorter length of stay compared to controls (2009).

The present study is the first telemedicine study to utilize both telehealth and mHealth interventions for HF patients. It is also the first to target medication adherence in HF with telemedicine interventions. Additionally, it is one of the first feasibility and participant acceptability studies within this population.

**Study Aims**

The present research aimed to target two medication reminder systems with and without reminding. This study sought to evaluate adherence rates and participant acceptability of the devices. The present research aimed to evaluate two medication-reminding interventions, a smartphone application and an automated pillbox, in a pilot randomized clinical trial. Participant preferences for the interventions were assessed. The hypotheses were as follows:

1. Reminding would increase adherence compared to passive devices.
2. The smartphone would be rated higher than the pillbox.

Secondary aims are as follows:

1. Although mild cognitive dysfunction would be present, both groups would be able to use the devices following training during the second study visit according to direct observation.
2. Cognitive function would be associated with medication adherence.
CHAPTER II

METHODS

Participants

Older adults aged 45-90 years with HF confirmed by medical chart review were sought for this trial. Participants were required to: be English speaking; be New York Heart Association class II or III for three or more months; have a history of HF that has been managed by the patient for at least three months; have systolic HF with LVEF ≤40% documented using left ventricular angiography, nuclear wall motion study, or echocardiography, within 12 months of study enrollment or diastolic HF confirmed by chart diagnosis; be willing to allow a device attached to their telephone to be installed for the duration of the study; and live within 30 miles of Akron, Ohio. Participants could not: have a history of a neurological disorder or injury; have suffered moderate or severe head injury defined as >10 minutes of loss of consciousness; have past or current history of psychotic disorders or bipolar disorder; have a five year past or current history of alcohol or drug abuse defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Test Revision (DSM-IV) criteria; have a history of a learning disorder or developmental disability that interferes with functions of daily living as defined by DSM-IV criteria; have renal failure requiring dialysis; history of sleep apnea that is not being managed by continuous positive airway pressure (CPAP) therapy; have a history of
coronary artery bypass grafting within three months prior to enrollment; or be terminally ill (suspected to cease within the upcoming six months). Individuals with severe cognitive dysfunction were not included in this study.

**Description of the Sample**

Participants included 60 adults (65% male) averaging 69 ± 11 years of age (83% Caucasian). Demographic (Table 1), educational (Table 2) and comorbidities (Table 3) were similar between groups. Patients’ average Mini Mental Examination score was 28.67 ± 1.59, suggesting participants were oriented and not significantly demented.

Table 1

*Patient Demographic Characteristics by Device*

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>M (SD) for Smartphone Group</th>
<th>M (SD) for Pillbox Group</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69.04 (10.57)</td>
<td>69.63 (11.32)</td>
<td>48-89</td>
</tr>
<tr>
<td>Female (%)</td>
<td>32%</td>
<td>37%</td>
<td></td>
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Table 2

*Patient Highest Education Level Achieved by Device*

<table>
<thead>
<tr>
<th>Highest Education Level Achieved</th>
<th>Smartphone Group</th>
<th>Pillbox Group</th>
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</thead>
<tbody>
<tr>
<td>9-11th Grade</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Completed High School/GED</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Completed Technical or Trade School</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Completed Some College</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Completed Bachelors Degree</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Completed Masters Degree</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 3

*Patient Comorbidities by Device*

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>% for Smartphone Group</th>
<th>% for Pillbox Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>61%</td>
<td>50%</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0%</td>
<td>7%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>36%</td>
<td>30%</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>7%</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Apparatus**

**iPhone and iRx Reminder Application**

A third generation iPhone (Apple, Inc., Cupertino CA) was used as the medication reminder device in the mHealth condition. Every iPhone was equipped with a medication adherence application (iRx Reminder LLC, Akron OH) that reminded via text message or remained as a passive log. Each participant had a profile created on and controlled by an online secure control panel. By selecting the application icon, participants were directed to two possible screens. One screen contained a medication schedule. By selecting one of the times listed, participants viewed a list of pills they were scheduled to take at that time. On the same screen, participants had four button options: take all, skip all, and two snooze options. On the other screen, participants could view a list of their medications with information on each medication, including special instructions such as to take with a meal or before bedtime.

**Medsignals Box**

An automated pillbox (Medsignals, Austin TX) was used as the other medication reminder device. Each pillbox had four compartments, and patients’ pills were placed in
the compartments. Every pillbox was equipped with pre-programmed alarms at the time participants reported taking each of their pills, or they were equipped without alarms rendering them a passive adherence monitor. Each pillbox hooked into a phone line and participants were given instructions for how to refill each bin without recording a medication-taking event.

Measures

Medication Adherence

Following the intervention period, study personnel accessed online databases to which data was uploaded as it was collected via Wifi or 3G network connection (smartphone) or phone line connection (automated pillbox). Study personnel exported this data in Microsoft Excel. A daily adherence value was calculated by dividing the number of medication taking events (either a pill recorded as taken in the smartphone or a medication bin opened in the pillbox) by the number of medication taking events that were supposed to occur that day across all four medications (primary outcome measure). All 28 daily adherence values were entered into the analyses to preserve individual differences. All of the medications included were prescribed for one to three times each day, and as-needed medications were not selected for monitoring.
**Cognitive Dysfunction**

At the first assessment session, the following cognitive tests were administered: Modified Mini Mental Status Examination (used to screen for severe dementia and to characterize the sample; Teng & Chui, 1987); Rey Auditory Verbal Learning Tests; Rey-Osterrieth Complex Figure Test; Trail Making Test Parts A and B; Letter Number Sequencing; Frontal Assessment Battery; and the Stroop Color Word Test. Raw test scores were converted to T-scores using age and gender and, when possible, education. A cognitive dysfunction score was calculated by finding the mean of the T-scores of the following parts of the aforementioned tests: the delayed recall number correct of the Rey Auditory Verbal Learning Tests; the delayed recall of the Rey-Osterrieth Complex Figure Test; Trails B of the Trail Making Test Parts A and B; the final Letter Number Sequencing score; the total score of the Frontal Assessment Battery; and the color-words interference score of the Stroop Color Word Test.

**Rey Auditory Verbal Learning Test.** The Rey Auditory Verbal Learning Test begins with an examiner reading aloud a list of 15 words at 1 word per second. At the end of the list, the participant must recall as many of the words he or she can remember. The list is then read four more times with participants listing as many words after each reading of the list whether or not they already recalled those words. After the fifth reading, a distractor list is read after which the participant must recall as many of the items on the second list as possible. Immediately following the distractor items, the participant is told to freely recall as many items from the first list as possible. After twenty minutes, during which participants completed other neuropsychological testing,
they are asked to recall as many items from the first list they could remember. The total number correct of their delayed recall provided the delayed recall score incorporated into the measure of cognitive dysfunction. There is no time limit for the test. Norms were taken from Ivnik and colleagues (1992).

*Rey-Osterrieth Complex Figure Test.* Rey-Osterrieth Complex Figure Test is a test utilizing visuospatial abilities, memory, attention, and executive functions. First, individuals must copy a complex line drawing, and then must reproduce it from memory. After a 20 minute delay (administered following the delayed recall of the Rey Auditory Verbal Learning Test), participants are then asked again to recreate the line drawing on a blank sheet of paper from memory. The test discontinues when the participant gives up, notes they are done, or after five minutes. Norms were taken from Spreen & Strauss (1998).

*Trail Making Test.* Trail Making Test Parts A and B (Reitan, 1958) is a test sensitive to cognitive dysfunction tapping into processing speed, visual attention, executive functioning, and task switching. First, in Trails A, participants are given an example of connecting the dots between sequential circled letters, which they then do for 25 targets. Immediately following Trails A, in Trails B, the participant must switch from sequentially increasing number and letter targets (e.g., going from 1 to A to 2 to B to 3 to C) as quickly as possible. Time to completion was recorded. Norms were taken from Tombaugh (2004).

*Letter Number Sequencing.* Letter Number Sequencing (Wechsler, 1997) is a subtest of the Wechsler Adult Intelligence Scale (fourth edition). It utilizes attention span,
short-term auditory recall, processing speed, and sequencing. Participants are given a string of intermixed letters and numbers, which they must then repeat with numbers in chronological ascending order and then the letters in alphabetical order. The test is completed with strings increasing by one digit every four strings and there is no time limit. Norms were taken from Wechsler (1997).

**Frontal Assessment Battery.** The Frontal Assessment Battery (Dubois, Slachevsky, Litvan, & Pillon, 2000) assesses executive functioning through small tests of conceptualization, lexical fluency, motor skills, sensitivity to interference, and environmental autonomy. Participants accumulate points within each section, with partial credit given in most cases. Participants’ cumulative points score represents the final score. There is no time limit. Norms were taken from Appollonio et al (2005).

**Stroop Color Word Test.** The Stroop Color Word Test (Golden, 1978) examines attention and response inhibition. Individuals are first timed for how quickly they can read words that are the names of colors, then for naming the color (red, green, or blue) of four X’s, and then naming the color of the ink in which a non-congruent color word is printed. It is expected participants demonstrate slowing with each new trial. Norms were taken from Ivnik, Malec, Smith, Tangalos, & Petersen (1996).

**Mastery of the Intervention Following Training**

At the second study session, participants in all groups were taught how to use their assigned intervention (smartphone or pillbox). Following the training and an opportunity to ask questions, every participant was given a brief test of their ability to use the basic functions of the medication-related functions of the devices. Participants
demonstrated their knowledge of how the device was powered, how to use the device, how to open and close the pillbox bins (in the telehealth conditions), and how to open and use the smartphone application (in the mhealth conditions).

Device Ratings

A survey was created for this study to assess individuals’ evaluations of the device to which they were randomized. At the final study session, participants completed the questionnaire about their preference for the device they were assigned. The 14 items were summed into a total score reflecting their ultimate appraisal for the device. The range of possible scores was 14-70. Participants rated how much they agreed to each statement from strongly disagree to strongly agree. The statements assess factors such as helpfulness, improving quality of life, and satisfaction.

Design and Procedure

Enrollment began in June 2011 and ended in May 2012. Participants were enrolled from an outpatient hospital-affiliated cardiology clinic. Patient characteristics are summarized in Tables 1-3. The CONSORT chart in Figure 1 presents the flow of patients through the trial. Patient accrual from recruiting efforts and eligibility screening is presented in Figure 2.

The Institutional Review Boards of Kent State University and Summa Health System reviewed and approved the study procedures. Prospective participants were interviewed over the phone and were screened for eligibility. Prospective participants who were eligible according to their interview answers were asked for consent for study
Assessed for eligibility (n=80)

Excluded (n=20)
- Not meeting inclusion criteria (n=15)
- Refused to participate (n=5)
- Other reasons (n=0)

Enrollment

Randomized (n=60)

Allocated to smartphone intervention (n=30)
- Assigned to silent condition (n=15)
- Assigned to active condition (n=15)
- Started allocated intervention (n=30)

Lost to follow-up (n=1)
- Drop outs (n=1)
- Technology failure (n=2)
- Refused to use device (n=1)

Allocated to pillbox intervention (n=30)
- Assigned to silent condition (n=15)
- Assigned to active condition (n=15)
- Started allocated intervention (n=30)
- Did not start allocated

Lost to follow-up (n=1)
- Drop outs (n=0)
- Technology failure (n=0)
- Refused to use device (n=1)

Allocated to pillbox intervention

Intent to treat (n=28)
- Completers (n=26)

Allocation

Available for Analysis

Intent to treat (n=30)
- Completers (n=29)

Follow-Up

Figure 1. CONSORT Chart
Patient accrual from recruiting efforts and eligibility screening

Figure 2. Patient accrual from recruiting efforts and eligibility screening
personnel to complete a medical chart review to confirm appropriate diagnoses. Individuals who did not consent were disqualified from the study. Individuals who consented but did not meet appropriate inclusion criteria were disqualified, while individuals who consented and met appropriate inclusion criteria were notified of their eligibility. Participants who were eligible and who consented to participate scheduled all three assessments at that time. The study used a 2x2, open-label, randomized, open-label study design with a 1:1 allocation ratio. The sample size was largely determined by the pilot and feasibility nature of the trial. That is, the sample was limited to 60 participants to determine participant acceptance of the devices, patient ability to use the devices, and estimates of effect sizes that would aid in the design of a larger randomized clinical trial. Participants completed the first assessment session in the hospital’s center for clinical trials or in their home. After participants completed the first assessment session, which consisted of health interviews, cognitive testing, and psychosocial questionnaires, patients were randomized to the 2x2 design (pillbox x smartphone and reminding/active x passive/silent). Therefore, participants were randomized to 28 days of a smartphone with an application or automated pillbox designed to increase medication adherence with or without reminders using an order of assignment generated by random number. The study coordinator and one research assistant generated the random allocation sequence, enrolled participants, and assigned participants to interventions.

The device was installed in the participant’s home and participants were taught how to use the device during the second assessment session. After 28 days of monitoring,
the device was collected and participants completed additional questionnaires assessing health status, psychosocial factors, and acceptance of the intervention.

**Blinding**

Concealment of treatment allocation was not possible in this open-label trial. Participants and study personnel completed the first assessment session without knowledge of the group to which the participant would be assigned. Study personnel determined the participant’s condition prior to the second assessment session by procedures described above.

**mHealth Intervention**

One week after completing the first assessment session, study personnel arrived at the participant’s home. The participant was trained on how to use a third generation iPhone’s standard features (Apple, Inc., Cupertino CA), including the clock, calendar, text messaging, email, weather, camera, calculator, and notes, and learning was confirmed by a skills-based post-test. All participants were able to understand and use the smartphone. Afterwards, participants were trained on how to use the medication adherence application (iRx Reminder LLC, Akron OH). All participants were taught how to access the application, navigate the features within the application, and record a medication-taking event (taking a medication or skipping it). Participants in the silent (no reminder) condition were equipped with phones that did not provide reminders. Individuals in the active (reminder) condition were equipped with phones programmed to provide reminders and were taught about medication reminders that appeared via text
messages that linked to the medication adherence application. All participants were then tested on their ability to use the smartphone, and all participants were able to use the application following training. After testing, participants were allowed to load free applications onto the phone (e.g., games). Participants were given phone numbers of study personnel, whom they were encouraged to call for assistance. Participants then used the phone application for 28 days of monitoring.

**Telehealth Intervention**

Similar to the individuals in the smartphone application condition, one week after completing the first assessment session, study personnel arrived at the participant’s home where a 35-day supply (or as much as possible if less was available) was inserted into each of the medication bins of the Bluetooth-enabled automated pillbox (Medsignals, Austin TX). The pillbox was then installed into a telephone jack and electrical outlet, frequently in the kitchen or bedroom. The participant was then taught how to use the pillbox and was given a list to be kept next to the box of which medications were in which bin and refill instructions. Participants were quizzed on their ability to use the pillbox, and all participants demonstrated adequate understanding of the pillbox via direct observation by the research personnel. Participants then used the automated pillbox for 28 days of monitoring. Participants were given phone numbers of study personnel, whom they were encouraged to call for assistance.
Analysis Plan

The primary outcome measure was adherence across days per person post-intervention. Hierarchical Linear Modeling (HLM) analyses examined adherence between conditions and devices. Analyses were conducted based on both intent to treat with baseline values carried forward when post-intervention values were missing and completers, which were defined as individuals who not only completed the last assessment, but also were not hospitalized for at least one week, reported attempting to use the device through the study, and whose data were not lost due to technical failure. All analyses were conducted at the .05 level of significance. Data were analyzed using HLM 7 (student edition Scientific Software International, Skokie IL).

HLM (Bryk & Raudenbush, 1992) was primarily used to analyze data in the present study. HLM is appropriate because it can model relationships when several data points from each participant are present (Bryk & Raudenbush, 1992). However, unlike other techniques that aggregate data, it preserves intra-individual difference; here it modeled between-subject moderators of within-subjects relationships. Differences in HLM regression coefficients at level-1 for each participant are predicted by level-2 equations. Since multiple daily assessments of adherence (the continuous dependent variable) represent nested data, HLM is preferred over regression.

Furthermore, traditional estimations of power are not practical for HLM (Boyle & Williams, 2001). According to Kreft’s (1996) guidelines, power in HLM may be maintained when data is collected for at least three time points for each participant. Since each of the 60 participants’ adherence was monitored for four medications across 28
days, it is expected there should be enough statistical power as per the Kreft (1996) suggestions.

Moreover, a lack of a medication-taking event was considered non-adherence rather than missing data. Data was lost for two participants due to equipment failure, and these individuals were excluded from all analyses. Therefore, missing data was not a great concern in the present study with the exception of determining completers.

Adherence to four cardiovascular-related medications was tracked for each participant. Daily adherence percentage scores were calculated by comparing the number pills an individual took in a day to the number of pills the individual was prescribed to take per day. Every participant was monitored for 28 days. HLM analyses were used to determine whether the device or condition (reminding versus passive) resulted in a statistically significant dependent variable, adherence. An interaction term of device and condition was created in SPSS and entered into the HLM model.
CHAPTER III

RESULTS

Statistical Analyses Preparation

The current study utilized a time nested under person structure and an unconditional model. It was determined there was enough variability within individuals to use HLM, and the current model was appropriate compared to a baseline of model fit. A two level model was tested to determine if treatment condition and device type (level-2 predictors) predicted daily adherence (outcome) after controlling for the number of pills an individual was prescribed per day (level-1). An unconditional model confirmed variability in adherence exists between individuals.

Intent-To-Treat Analyses

The hypotheses were tested using the following intent-to-treat model:

Level-1 Model

\[
ADHERENCE_i = \pi_{0i} + e_i
\]

Level-2 Model

\[
\pi_{0i} = \beta_{00} + \beta_{01}*(DEVICE_i) + \beta_{02}*(DEVICE_{C_i}) + \beta_{03}*(CONDITIO) + r_{0i}
\]
Mixed Model

$$ADHERENCE_i = \beta_{00} + \beta_{01} \cdot DEVICE_i + \beta_{02} \cdot DEVICE_C_i + \beta_{03} \cdot CONDITIO_i + r_{ii} + e_{ii}$$

Data were normally distributed and no assumptions were violated. The unconditional model indicated variance in adherence exists between individuals and that the data was appropriate for hierarchical linear modeling, $x^2(54) = 2123.91, p < .001$. The intra-class correlation (ICC) was also calculated to determine which percentage of variance in adherence is attributed to the person level and which percentage is attributable to repeated measures level. The ICC was calculated by the following: $$ICC = \frac{\tau}{(\tau + \sigma^2)}.$$ In the current model, $\sigma^2 = 0.05195$ and $\tau = 0.06967$, which results in an ICC of 0.57. This result suggests that 57% of the variance in adherence is at the person level.

In the final model, device was not associated with medication adherence, $\pi[df=54]=0.17, p=.865$ (see Table 4). Additionally, condition was not associated with medication adherence, $\pi[df=54]=0.72, p=.477$ (see Table 4). There was no significant interaction between device and condition, $\pi[df=54]=-0.98, p=.333$. Please see Tables 5-7 for adherence means by device and condition.

**Completer Analyses**

The hypotheses were tested in completers using the aforementioned alarm by device type model. Individuals were excluded from completers analyses due to the following reasons: data was lost due to technical malfunctions, refused to use the device after beginning the intervention, and hospitalization for over a week during the
### Table 4

*Results of Intent-to-Treat Analyses*

Final estimation of fixed effects (with robust standard errors)

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t-ratio</th>
<th>Approx. d.f.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>For INTRCPT1, $\pi_0$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INTRCPT2, $\beta_{00}$</td>
<td>0.777613</td>
<td>0.062177</td>
<td>12.506</td>
<td>54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DEVICE, $\beta_{01}$</td>
<td>0.014955</td>
<td>0.087354</td>
<td>0.171</td>
<td>54</td>
<td>0.865</td>
</tr>
<tr>
<td>CONDITIO, $\beta_{02}$</td>
<td>0.062906</td>
<td>0.087870</td>
<td>0.716</td>
<td>54</td>
<td>0.477</td>
</tr>
<tr>
<td>DEV_COND, $\beta_{03}$</td>
<td>-0.134949</td>
<td>0.138060</td>
<td>-0.977</td>
<td>54</td>
<td>0.333</td>
</tr>
</tbody>
</table>

### Table 5

*Means for Adherence by Device Using Intent-To-Treat Analyses*

<table>
<thead>
<tr>
<th>Device</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pillbox</td>
<td>.80 (.33)</td>
</tr>
<tr>
<td>Smartphone</td>
<td>.76 (.36)</td>
</tr>
</tbody>
</table>

### Table 6

*Means for Adherence by Condition Using Intent-To-Treat Analyses*

<table>
<thead>
<tr>
<th>Condition</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>.79 (.36)</td>
</tr>
<tr>
<td>Passive</td>
<td>.78 (.33)</td>
</tr>
</tbody>
</table>

### Table 7

*Means for Adherence by Device and Condition Using Intent-To-Treat Analyses*

<table>
<thead>
<tr>
<th></th>
<th>Pillbox</th>
<th>Smartphone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>.84 (.32)</td>
<td>.73 (.39)</td>
</tr>
<tr>
<td>Passive</td>
<td>.76 (.33)</td>
<td>.79 (.33)</td>
</tr>
<tr>
<td>Total</td>
<td>.80 (.33)</td>
<td>.76 (.36)</td>
</tr>
</tbody>
</table>
intervention period. Data were normally distributed and no assumptions were violated.

The unconditional model indicated variance in adherence exists between individuals and that the data was appropriate for hierarchical linear modeling, $x^2(51) = 1154.22$, $p < .001$. The intra-class correlation (ICC) was also calculated to determine which percentage of variance in adherence is attributed to the person level and which percentage is attributable to repeated measures level. In the current model, $\sigma^2 = 0.05208$ and $\tau = 0.04020$, which results in an ICC of 0.44, meaning 44% of the variance in adherence is at the person level.

In the final model, device was not associated with medication adherence, $\pi[\text{df}=51]=0.81$, $p=.421$ (see Table 8). Additionally, condition was not associated with medication adherence, $\pi[\text{df}=51]=1.78$, $p=.081$ (see Table 8). There was no significant interaction between device and condition, $\pi[\text{df}=51]=-1.67$, $p=.101$ (see Table 8). Please see Tables 9-11 for adherence means by device and condition.

Table 8

Results of Completer Analyses

<table>
<thead>
<tr>
<th>Final estimation of fixed effects (with robust standard errors)</th>
<th>Coefficient</th>
<th>Standard error</th>
<th>t-ratio</th>
<th>Approx. d.f.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>For INTRCPT1, $\pi_0$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INTRCPT2, $\beta_{00}$</td>
<td>0.777309</td>
<td>0.062245</td>
<td>12.488</td>
<td>51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DEVICE, $\beta_{01}$</td>
<td>0.062043</td>
<td>0.076501</td>
<td>0.811</td>
<td>51</td>
<td>0.421</td>
</tr>
<tr>
<td>CONDITIO, $\beta_{02}$</td>
<td>0.121510</td>
<td>0.068306</td>
<td>1.779</td>
<td>51</td>
<td>0.081</td>
</tr>
<tr>
<td>DEV_COND, $\beta_{03}$</td>
<td>-0.181069</td>
<td>0.108392</td>
<td>-1.671</td>
<td>51</td>
<td>0.101</td>
</tr>
</tbody>
</table>
Table 9

*Means for Adherence by Device Using Completers Analyses*

<table>
<thead>
<tr>
<th>Device</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pillbox</td>
<td>.83 (.30)</td>
</tr>
<tr>
<td>Smartphone</td>
<td>.82 (.31)</td>
</tr>
</tbody>
</table>

Table 10

*Means for Adherence by Condition Using Completers Analyses*

<table>
<thead>
<tr>
<th>Condition</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>.85 (.30)</td>
</tr>
<tr>
<td>Passive</td>
<td>.80 (.31)</td>
</tr>
</tbody>
</table>

Table 11

*Means for Adherence by Device and Condition Using Completers Analyses*

<table>
<thead>
<tr>
<th></th>
<th>Pillbox</th>
<th>Smartphone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>.90 (.24)</td>
<td>.79 (.35)</td>
</tr>
<tr>
<td>Passive</td>
<td>.76 (.33)</td>
<td>.84 (.28)</td>
</tr>
<tr>
<td>Total</td>
<td>.83 (.37)</td>
<td>.82 (.31)</td>
</tr>
</tbody>
</table>

**Mastery of the Device Following Training**

Following an introduction to the device during the second study visit, each participant was tested on their ability to perform the necessary functions of the medication reminder system. In all groups, 100% of participants were able to use the device according to direct observation by study personnel. All participants demonstrated their knowledge of how the device was powered and how to use the device. Participants in the telehealth conditions were all able to open and close the pillbox bins. All
participants in the mHealth conditions demonstrated their ability to open and use the smartphone application.

**Medication Adherence**

According to intent-to-treat analyses, the overall adherence rate across all devices and conditions was 78% (see Table 7 for results for each arm of the trial). Overall, individuals with the pillbox adhered 80% of the time and individuals with the smartphone adhered 76% of the time. Those who received reminders adhered 79% of the time, and individuals with passive medication reminder systems achieved adherence rates of 78%.

According to completers analyses, the overall adherence rate across all devices and conditions was 82% (see Table 11 for results for each arm of the trial). Overall, individuals with the pillbox adhered 83% of the time and individuals with the smartphone adhered 82% of the time. Those who received reminders adhered 85% of the time, and individuals with passive medication reminder systems achieved adherence rates of 80% (Table 11).

**Cognitive Dysfunction**

In this sample, 27% of participants included in intent-to-treat analyses displayed cognitive dysfunction as demonstrated by a cognitive dysfunction score of a mean t-score of 35 or less on the compilation of neuropsychological testing. Cognitive dysfunction was not related to adherence in intent-to-treat analyses, \( r(56) = .00, p = .95 \). In the sample of completers, 26% displayed cognitive dysfunction as demonstrated by a cognitive
dysfunction score of a mean t-score of 35 or less. Cognitive dysfunction was also unrelated to adherence in the completers analyses, \( r(53) = .03, p = .86 \).

**Device Ratings**

Regardless of condition (reminding or passive), participants in intent-to-treat analyses overall strongly preferred the smartphone as compared to the automated pillbox, \( F(1, 55) = 14.84, p = .00 \). Participants who received smartphones (\( M = 48.74, SD = 13.88 \)) rated their device much higher than individuals who received pillboxes (\( M = 33.43, SD = 15.90 \)). The same was true for completers, \( F(1, 53) = 12.72, p = .00 \), where participants who received smartphones (\( M = 48.42, SD = 14.06 \)) rated their assigned device much higher than individuals who received pillboxes (\( M = 33.86, SD = 16.00 \)). At the conclusion of data collection, most participants who received a passive device spontaneously reported that a reminding function would likely improve the device.
This was the first evaluation of medication reminding in HF using telemedicine. All participants were able to use a smartphone or pillbox following brief training, despite mild cognitive dysfunction in approximately 26% of the sample. However, reminding had no effect on medication adherence. This finding did not support the hypothesis that reminding would increase adherence in both the smartphone and pillbox conditions. Participants strongly preferred the smartphone to the automated pillbox. Cognitive dysfunction was not related to adherence values. In fact, adherence values were unusually high. For completers, the median adherence was 90% for four medications over 28 days, and participants in the lowest quartile (< 71%) were evenly distributed between reminding (46%) and passive data collection (54%) conditions.

These findings are somewhat surprising given that previous studies have estimated adherence to long term therapies for patients with chronic illness in developed nations to be about 50% (Bogner & de Vries, 2008; Bosworth et al., 2005; WHO, 2003). Medication adherence research on HF illustrates a wide range of adherence values, with the majority of HF patients achieving suboptimal medication adherence (Gislason et al., 2007). Previous research has demonstrated HF patients must achieve 88% or greater adherence to maximize their chances for event free survival (Wu et al., 2009). In the
present study, the median adherence with a telemedicine intervention for completers was 90% over 28 days of monitoring.

Similar to previous literature (e.g., Haberer et al., 2012), although participants were willing to use the devices, they found some of the reminding features of the pillbox (i.e. alarms) annoying. It is very likely participants opened bins in the active condition merely to silence the alarms, effectively recording a medication taking event, without taking a pill. This study extends the literature on cardiovascular medication adherence by utilizing telehealth technologies.

The high adherence rates observed may be due to high levels of perceived social support. Or, participants may represent a well-managed sample that was largely adherent before the intervention, illustrating a selection effect. Studies published after this trial ended have suggested interventions using telehealth technologies use multiple months to minimize measurement reactivity followed by multiple months of monitoring (Cook, Schmiege, McClean, Aagaard, & Kahook, 2012). Additionally, it is promising that although cognitive dysfunction was present in the sample, all participants were able to use the telehealth devices. Moreover, participants’ desired levels of adherence were not studied; these factors are less frequently measured in commensurate literature. Although researchers and physicians hope HF patients aim for and achieve 100% adherence, it is more likely that few patients aim for adherence perfection, which would influence their motivation and health behaviors. These factors, namely patient adherence goals and motivation to adhere, must be measured in future studies and factored into interpretations of health behaviors and adherence rates.
Our results provide evidence that reminding alone does not necessarily improve adherence. Our results also provide evidence that patients prefer a less intrusive intervention; participants highly endorsed the smartphone, which may have blended into both their everyday lives as well as previously established medication reminder systems. Furthermore, adherence rates in the alarmed pillbox condition may have been inflated due to a desire to silence the alarms, obscuring true adherence rates. Dynamic interventions (administered to all medication takers where real-time adherence feedback targets nonadherers over the course of the intervention) may be especially comprehensive and promising (Cutrona et al., 2011). Within adherence literature, most researchers assume patients strive for 100% adherence rates. However, this likely does not fully capture participants’ intrinsic motivation to adhere to their medications.

This was one of the first studies to utilize two medication reminder systems for older adults with HF. Additionally, each device had both active and silent conditions. In accordance with suggestions from previous studies, this study measured cognitive dysfunction through a comprehensive neuropsychological battery targeting a variety of cognitive domains. Since study participants volunteered to learn to use the devices, their adherence may have been influenced by their interest in learning to use the device (Heinrich & Kuiper, 2012). Here, measurement reactivity due to a short monitoring period likely influenced results. Additionally, some telemedicine devices cannot capture overdoses, missed doses, or incorrect doses. In the present study, the smartphone application was unable to capture overdoses due to the design of the smartphone application. Participants may have been more receptive or resistant to using the new
system and although all participants enrolled knowing they would have to use a device provided by the research team, their willingness to fully adopt the device likely influenced the results. Most importantly, participants’ motivation to adhere to all their medications likely strongly influenced adherence rates; for example, some participants may only aim to adhere 80% of the time or only enough to minimize uncomfortable symptoms.

Conclusions

Nearly all patients were able to use a telemedicine intervention. Adherence rates were high, though not improved by reminding. Social support, established medication systems, ceiling effects from high baseline levels of adherence, and reactivity to measurement may have influenced findings. Future interventions should monitor longer to minimize reactivity. It appears ecological momentary assessment via smartphones in older adults is one viable telehealth technique for studying older adults with complex medical conditions. Unique features and innovation of the project include a new smartphone application, a novel telehealth tool in adherence research tested in a population with typically poor adherence that can result in exorbitant health and financial consequences via rehospitalization. Also, this randomized clinical feasibility study in older adults with systolic and diastolic heart failure is one of the first of its kind to utilize two telemedicine interventions. Despite pitfalls, this study provides significant promise for the future of improving adherence in patients with HF through telemedicine interventions.
APPENDIX 1

FINAL EVALUATION OF DEVICE

Note: “MRS” means medication reminder system.

On a scale of 1 to 5 where 1 is strongly disagree and 5 is strongly agree, rate how much you agree with the following statements:

I found the MRS easy to use. 1 2 3 4 5
The MRS helped me to remember my medications. 1 2 3 4 5
The MRS made my life easier. 1 2 3 4 5
I liked using the MRS. 1 2 3 4 5
I would recommend the MRS to a friend. 1 2 3 4 5
I have told people I know good things about this MRS. 1 2 3 4 5
I would buy this MRS for a loved one with HF if it were affordable. 1 2 3 4 5
Other people like me would find this MRS helpful. 1 2 3 4 5
Overall, I was satisfied with this MRS. 1 2 3 4 5
This MRS fulfilled my needs. 1 2 3 4 5
I would buy this product for myself if it were affordable. 1 2 3 4 5
This MRS improved my quality of life. 1 2 3 4 5
This product was well-designed. 1 2 3 4 5
The MRS was user-friendly. 1 2 3 4 5
REFERENCES
REFERENCES


pharmacotherapy in heart failure is associated with improved outcomes.

_Circulation, 116_(7), 737-744. doi: 10.1161/CIRCULATIONAHA.106.669101


