FEASIBILITY AND ACCEPTABILITY OF A SYSTEMCHANGE™ INTERVENTION TO IMPROVE MEDICATION ADHERENCE IN OLDER ADULT STROKE SURVIVORS: A PILOT RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Purpose: The purpose of this study is to evaluate the feasibility, intervention mechanism, and potential effectiveness of the SystemCHANGE™ (Change Habits by Applying New Goals and Experiences) intervention in older adult, non-adherent ischemic stroke patients. This pilot intervention study will guide future protocol refinement of a fully powered study.

Significance: There has been a striking increase in the number of stroke survivors in the past two decades. Of the nearly 800,000 people who survive their first stroke each year, the risk of recurrent stroke is 15% over five years and highest in the first six months after having a stroke, emphasizing the need for early initiation of appropriate prevention therapies. The patient's ability to adhere to a medication regimen is a key variable in preventing recurrent stroke events. Adherence intervention studies have proven marginally effective for individuals with acute and chronic illnesses, and ineffective for stroke survivors. This pilot study is the first to evaluate SystemCHANGE™ to enhance MA in stroke survivors. Data from this study will guide future protocol refinement of a fully powered study.

Methods: An innovative 2-month SystemCHANGE™ intervention to enhance antithrombotic medication adherence (MA) in 30 older non-adherent stroke survivors recruited from a Midwestern neurology office using an RCT design with an attention-control group. SystemCHANGE™, grounded in the socio-ecological model, sought to systematically improve MA behaviors by identifying and shaping routines, involving supportive others in routines, and using medication-taking feedback through small patient-led experiments. Medication-taking feedback was provided, and MA was measured by electronic monitoring. The difference between the two groups during the one-month maintenance phase evaluated the efficacy of the intervention. Descriptive statistics for social support perceived health and personal systems behaviors was calculated for pre- and post-intervention measurements. Trends in medication non-adherence differences between the two groups were identified.

APPROVAL PAGE

The faculty listed below, appointed by the Dean of the College of Nursing and Health Studies, have examined a dissertation titled "Feasibility and Acceptability of a SystemCHANGE™ Intervention to Improve Medication Adherence in Older Adult Stroke Survivors: A Pilot Randomized Controlled Trial," presented by Jennifer Lynn Wessol, candidate for the Doctor of Philosophy degree**,** and certify that in their opinion it is worthy of acceptance.

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CHAPTER 1

INTRODUCTION

The research was a pilot randomized controlled trial (RCT) testing the feasibility and acceptability of a SystemCHANGE™ (Change Habits by Applying New Goals and Experiences) intervention on antithrombotic medication adherence (MA) as assessed electronically by the Medication Event Monitoring System ([MEMS®] WestRock, USA and Switzerland) in older adult stroke survivors. Chapter one provides a review of the literature related to MA in older individuals who have experienced a stroke. To offer meaningful context, the prevalence of cerebrovascular disease (stroke) is presented. To build toward MA interventions in the stroke survivor, a background of MA is presented. Included in chapter one is the definition of adherence as well as the measurements of MA and barriers to MA, followed by an overview of interventions used in MA research. Finally, the theoretical underpinning and conceptual framework of the SystemCHANGE™ intervention is presented. Chapter two is a manuscript published in the *Journal of Neuroscience Nursing* titled "A Systematic Review of Randomized Controlled Trials of Medication Adherence Interventions in Adult Stroke Survivors" that systematically appraises RCT interventions to improve MA in adult stroke survivors (Wessol, Russell, & Cheng, 2017). Chapter three addresses the methods used in this research. Chapter four present the results of this study, and finally, chapter five discusses the results, conclusions, and direction for future research.

Aims and Research Questions

The goal of this study was not hypothesis testing; rather, data and feedback from participants was used for protocol refinement and the formulation of a power analysis for a fully powered study. To test the feasibility and acceptability of a SystemCHANGE™

intervention on antithrombotic MA in older adult stroke survivors, the study's specific aims were as follows.

Aim 1

Aim 1 was to evaluate the feasibility of a large-scale SystemCHANGE™ intervention and an educational intervention in older adult, non-adherent stroke survivors to improve antithrombotic MA through formalizing the protocols, validating recruitment and randomization procedures, and providing data for a power analysis.

Research Questions of Aim 1

1. How can the study protocol be refined?
2. How many potential participants meet excluded criteria?
3. How many participants are necessary to recruit and assess to identify 30 non-adherent older adult stroke survivors.
4. How many participants are needed to conduct a fully powered study?
5. What is the attrition rate?
6. How feasible is it for the participant to be involved in the intervention?
7. To what extent can adequate fidelity to the intervention be maintained?
8. What is the extent of missing data?

Aim 2

Aim 2 was to test the acceptability of a two-month SystemCHANGE™ intervention and a two-month attention control educational intervention on antithrombotic MA in older adult, non-adherent stroke survivors.

Research Questions of Aim 2

1. What are the intervention and survey demands of the participant?

2. How much time is required by the participant for the intervention and surveys?
3. Do the study participants intend to continue the intervention after the end of the study?
4. Do the participants stay in the assigned groups, e.g., not want to move from control group to treatment group?
5. Do participants know that they are in the treatment group or control group at the end of the study?
6. Do the participants feel the time spent per session is too long, too short, or just right?
7. Do the participants feel the time spent in the study was too long, too short or just right?
8. Do the participants feel the measures were too extensive?
9. Any other suggestions for improving the study?

Exploratory Aim 1

Exploratory aim 1 was to explore the role of potential mediators (e.g., social support and perceived health) and moderators (e.g., systems thinking and adherence level) of antithrombotic medication adherence in older adult stoke survivors in the SystemCHANGE™ intervention and those in the attention control education intervention.

Research Questions of Exploratory Aim 1

What is the role of potential mediators and moderators of antithrombotic medication adherence in older adult stoke survivors in the SystemCHANGE™ intervention and those in the attention control education intervention?

Exploratory Aim 2

Exploratory Aim 2 was to evaluate the difference between the SystemCHANGE™ interventions to the attention control education intervention on antithrombotic MA in this population.

Research Question of Exploratory Aim 2

What is the difference between the SystemCHANGE™ intervention and the education interventions' effect on antithrombotic MA?

Stroke

Definition and Classification

A stroke occurs when there is an interruption of blood supply to a focal area of the brain characterized by a neurological deficit lasting 24 hours or more (Bader, Littlejohns, & Olson, 2016; Hickey, 2009). Classification of stroke is determined by the mechanism of the focal brain injury and the type and localization of the vascular lesion and is divided into two kinds of events: ischemic or hemorrhagic. Ischemic stroke is attributed to a vascular cause whereby an artery is occluded, causing a cerebral infarction (Hickey, 2009; Sacco et al., 2013). The underlying causes of ischemic strokes can be classified into five categories: large-artery atherosclerosis; cardio-embolic; small-vessel disease; other determined cause such as dissection, hypercoagulable states, or sickle cell disease; and cryptogenic infarcts (Adams et al., 1993; Marnane et al., 2010). A hemorrhagic stroke is attributed to the weakening of the cerebral artery wall whereby blood leaks into the subarachnoid space or brain parenchyma that is not caused by trauma (Hickey, 2009). The main underlying cause of intracerebral hemorrhagic stroke is small vessel disease secondary to hypertension, while ruptured aneurysms are the preeminent cause of subarachnoid hemorrhage (Donnan, Fisher,

Macleod, & Davis, 2008). Regardless of the mechanism, when there is an interruption of blood flow to the brain, irreversible brain cell death starts to occur within three to five minutes resulting in the occurrence of a stroke (Bader et al., 2016).

Prevalence

By 2030, the percentage of Americans age ≥ 65 will increase from 15% to 21%; translating to a projected 1 in 5 Americans in this age group (Colby & Ortman, 2015). Because of the aging population, the incidence of stroke is projected to increase 20.5% between 2012 and 2030 (Nelson, Whitsel, Khavjou, Phelps, & Leib, 2016). Between 2015 and 2035, the direct medical costs related to stroke is projected to more than double from $36.7 billion to $94.3 billion; the majority of the projected increase will be in those ≥ 80 years of age (Benjamin et al., 2018; Nelson et al., 2016). There has been a striking increase in the number of stroke survivors in the past two decades (Feigin et al., 2014). Of the nearly 800,000 stroke survivors each year, the risk of recurrent stroke is 15% over 5 years, emphasizing the need for initiation of appropriate prevention therapies (Arsava et al., 2016; Benjamin et al., 2018; Feng, Hendry, & Adams, 2010; Shaya et al., 2006).

Over the course of three decades, risk factor control targeting control of hypertension, hyperlipidemia, and tobacco contributed significantly to the improved 10-year post-stroke survival (Lakshminarayan et al., 2014). As a result, in 2008 stroke declined from the third to the fourth leading cause of death in the United States (Towfighi & Saver, 2011). The decline in stroke death rates continued over the next six years when the Centers for Disease Control and Prevention (CDC) reported stroke dropped to the nation's fifth leading cause of death (Kochanek, Murphy, Xu, & Arias, 2014). Looking at death rates in a different perspective, from 2004 to 2014, the age-adjusted stroke death rate decreased 28.7%, and the actual

number of stroke deaths declined 11.2% (Benjamin et al., 2018). Despite the improvement in post-stroke survival, stroke continues to be the most common cause of long-term disability that includes mobility and speech problems, which frequently result in dependency on others in activities of daily living (Benjamin et al., 2018; Kernan et al., 2014).

Modifiable Risk Factors

An international case-control study of 6,000 individuals suggested that 10 potentially modifiable risk factors explained 90% of the risk of stroke (O'Donnell et al., 2010). Identified risk factors were history of hypertension, current smoking, abdominal obesity, diet (low fruit and fish consumption), physical activity, diabetes mellitus, alcohol intake, psychosocial factors, cardiac causes (thromboembolism) and increased levels of apolipoproteins (Kernan et al., 2014; Meschia et al., 2014; O'Donnell et al., 2010). Findings showed that hypertension was an important risk factor for both ischemic and hemorrhagic strokes; more so in intracerebral hemorrhagic stroke (Boan, Lackland, & Ovbiagele, 2014; De Simoni, Hardeman, Mant, Farmer, & Kinmonth, 2013; Lawes, Bennett, Feigin, & Rodgers, 2004; O'Donnell et al., 2010; Towfighi, Markovic, & Ovbiagele, 2014). Large RCTs and meta-analyses have identified several medications (antithrombotic, antihypertensive (Go et al., 2014; Lawes et al., 2004), and HMG-CoA reductase inhibitors (Amarenco & Labreuche, 2009; Bang, Saver, Liebeskind, Pineda, & Ovbiagele, 2008; Sanossian, Saver, Navab, & Ovbiagele, 2007) which significantly reduce the risk of vascular events such as stroke; however, few trials directly address the role of drugs in secondary prevention among persons with stroke (Kernan et al., 2014). Drawing on primary prevention data, the American Heart Association/American Stroke Association (AHA/ASA) recommends antithrombotic therapy and reduction of both blood pressure and cholesterol

levels in the prevention of recurrent stroke (Arnan, Burke, & Bushnell, 2014; Kernan et al., 2014). This study focused on improving adherence to antithrombotic medications: aspirin (acetylsalicylic acid), Plavix® (Clopidogrel Bisulfate), Aggrenox® (aspirin-dipyridamole), Xarelto® (rivaroxaban), Pradaxa® (dabigatran), or Coumadin® (Warfarin Sodium).

Medication Adherence

Background

Adherence is defined by the World Health Organization (WHO) as "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider" (Sabaté, 2003, p. 3). Vrijens et al.'s (2012) ABC taxonomy considers the sequence of steps a patient must undertake to be defined as "adherent to treatment": (a) initiation, (b) implementation, and (c) persistence. Once home after hospitalization, the individual who has experienced a stroke must initiate the new medication regimen by filling his/her prescription and taking the first dose (Vrijens et al., 2012). Once the prescription is initiated, he/she must implement the regimen by following the prescription dosing regimen including taking the medication at the prescribed time. After implementation, the patient may stop taking the medication. Persistence is the time from initiation until discontinuation, also known as the duration of therapy (Vrijens et al., 2012). Non-adherence occurs when medication is either not initiated, initiation is delayed, prescription dosing regimen is not followed, or the medication is discontinued before completing the regimen (Vrijens et al., 2012). The patient's ability to maintain a medication regimen is a key variable in preventing recurrent stroke events (Brown & Bussell, 2011; Lager et al., 2014). That being said, there is not an empirically established rate of adherence which is needed to prevent recurrent stroke (Brown & Bussell, 2011; Culig

& Leppée, 2014; DiMatteo, Giordani, Lepper, & Croghan, 2002; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Kripalani, Yao, & Haynes, 2007; Lager et al., 2014; McDonald, Garg, & Haynes, 2002; Osterberg & Blaschke, 2005; Roter et al., 1998). There are studies which provide direction for establishing a rate of adherence. For example, Gehi, Ali, Na, & Whooley (2007) conducted a study in patients with coronary artery disease that concluded that if patients only took 75% or less of their medications as prescribed, the risk of stroke was fourfold higher than patients who were 100% adherent. An analysis of the persistence of use of warfarin sodium, aspirin, or clopidogrel bisulfate on stroke recurrence in a Maryland Medicaid population showed that stroke recurrence was 57% less likely if patients consistently took medications over time, e.g., were persistent (Shaya et al., 2006). Closely adhering to dosing regimen is important to achieve full anticoagulant effects (Camm et al., 2012; Furie et al., 2012; Held, Wolf, & Hennerici, 2013; Manolis & Poulimenos, 2013; Pudusseri, Shameem, & Spyropoulos, 2013). When considering the short half-life of the new antithrombotic agents such as dabigatran, rivaroxaban, and apixaban, missing only one dose can lead to a significant loss of anticoagulant effects (Camm et al., 2012; Held et al., 2013; Pudusseri et al., 2013). As a result, the patient would be without any anticoagulation protection from recurrent stroke event. Therefore, very high levels of MA (e.g. $\geq$ 97%) are required to achieve full anticoagulant effects.

Measures

Adherence can be measured through subjective or objective measures (Brown & Bussell, 2011). Measuring MA subjectively involves collecting data from the patient, or through collateral reporting from family members or healthcare providers (Brown & Bussell, 2011; Culig & Leppée, 2014). Objective measures used in MA are obtained by measurement

of physiologic markers (i.e., blood pressure, lipid levels), pill counts, or data from pharmacy refill records (Brown & Bussell, 2011; Osterberg & Blaschke, 2005). MA can also be objectively measured through biochemical measurements. Objectively measuring biochemical measures is accomplished through testing for the presence of drug levels/drug metabolites in the patient's blood or urine (Brown & Bussell, 2011; Osterberg & Blaschke, 2005). Lastly, MA can be objectively measured using an electronic monitoring device (EMD).

There are advantages and disadvantages to the different measures. For example, self-reported measurements are less expensive and easy to use but have limitations including whether or not the participant understands the questions, potential for inaccurate reporting (recall bias), and their willingness to disclose information (Osterberg & Blaschke, 2005; Sabaté, 2003). Objective measures such as blood pressure can be influenced by many factors other than MA, and pill counts assume the pills have been taken as directed (MacLaughlin et al., 2005; Osterberg & Blaschke, 2005). Pharmacy refill data can be an effective and inexpensive method for assessing MA when using a closed pharmacy system or claims data bases (Balkrishnan, 2005; Osterberg & Blaschke, 2005). That said, the information is limited to filling and refilling prescriptions, and it fails to yield information about whether patients take medications as prescribed (Osterberg & Blaschke, 2005; Sabaté, 2003). Testing for drug levels/drug metabolites in the blood or urine is expensive and can be inconvenient for patients. Moreover, only a limited number of medications can be monitored in this way. The bioavailability and completeness of absorption of the medication, as well as the rate of metabolism and excretion, are factors that make it difficult to correlate drug concentrations in blood or urine with adherence (Neiheisel, Wheeler, & Roberts, 2014). Electronic monitor

devices (EMDs) provide a precise, quantifiable measurement of adherence by capturing the three indicators of adherence: percent of dose taken, percent of days the correct number of doses taken, and the percent doses taken on time (Neiheisel et al., 2014). Despite the precise nature of the data provided by EMDs, there is no verification that the medication was actually taken (Bosworth, Oddone, & Weinberger, 2006; Neiheisel et al., 2014). Finally, EMDs are expensive, and the cost can be prohibitive to use (Osterberg & Blaschke, 2005; Sabaté, 2003).

The EMD utilized in this study was the MEMS® cap (WestRock, USA & Switzerland), which is a medication vial cap that electronically records the date and time that the bottle is opened. Three indicators of adherence as assessed by MEMS® are: 1) dose-count, which is the percentage of prescribed doses taken; 2) dose-days, which are the percentage of days the correct number of doses taken; and 3) dose-time, which is the percentage of doses taken on schedule (Vrijens et al., 2012). The MEMS® cap has been used with older study participants with success. In a study that examined 73 older renal transplant patients' perceptions of electronic medication monitoring, study participants reported the MEMS was practical, and they could not describe any instances in which using the MEMS® cap was difficult (Russell et al., 2009).

Barriers

Literature describing MA barriers in those experiencing a stroke is discussed in this section. The dimensions of health as described by WHO were used to organize the barriers. The dimensions include: patient-related, health system, social/economic, therapy- related, and condition related dimension (Sabaté, 2003). Patient-related barriers include low health literacy, forgetfulness, decision to omit doses, poor self-management, health beliefs (lack of

awareness of the severity of their illness), patient representations of their illness, ability to read and understand medication instructions, and perceived medication side effects (Coetzee et al., 2008; Gellad, Grenard, & Marcum, 2011; Sabaté, 2003). Socioeconomic barriers include lower education level, lack of support systems, and lack of transportation (Brown & Bussell, 2011; Sabaté, 2003).

Health system barriers include: failure to recognize medication non-adherence in patients, poor transitions of care, prescribing complex medication regimens, limited office visit time, failing to adequately explain the benefits and side effects of a medication, not considering the cost of medications, and poor therapeutic patient-provider relationships. Other considerations are limited access to health care, switching to a different formulary, and having prohibitively high costs for drugs, copayments, or both (Brown & Bussell, 2011; Sabaté, 2003). Therapy-related barriers include complex regimens and medication side effects (Brown & Bussell, 2011; Sabaté, 2003). Also important to consider is maintaining a medication regimen that does not have any unpleasant symptoms, even without strict compliance to a medication regimen (Jimmy & Jose, 2011).

Finally, condition-related barriers include disease-specific factors (Brown & Bussell, 2011; Sabaté, 2003). Disease-specific factors such as the location of a stroke may serve as an indicator of adherence (Coetzee et al., 2008). For example, a stroke that occurs in the middle cerebral artery (MCA) territory can cause residual symptoms, such as poor planning and conceptual ability, working memory difficulties (and other related executive functioning impairments), impaired self-awareness, attention, and receptive aphasia (Bader & Littlejohns, 2010). A stroke survivor may have one or more barrier to optimal adherence (Bosworth et al., 2006). Residual impairment should be assessed by the health care provider, as

non-adherence is likely; stroke survivors' ability to follow a medication regimen may be affected (Coetzee et al., 2008).

Medication Adherence Interventions

Categories

There are three categories of MA interventions: educational, affective, and behavorial. Educational interventions are patient-centered, focusing on conveying information about a disease or medication to the patient (Roter et al., 1998). Educational intervention methods can be delivered individually or in a group setting. Delivery of educational content can be achieved through audiovisual, oral (in person or by telephone), or written communication (either mailed, emailed, or given personally) (Peterson, Takiya, & Finley, 2003). Affective interventions focus on improving adherence through targeting feelings, emotions, or social support. Affective interventions are delivered through counseling, family support, or supportive home visits (Roter et al., 1998). Behavioral interventions focus on changing medication taking behavior through changing the patient's skill level or routines (Peterson et al., 2003; Roter et al., 1998). Behavioral interventions include simplifying the medication regimen, packaging changes such as the use of blister packs, patient contracts, calendars, pill boxes, self-monitoring, and email or telephone refill reminders (Peterson et al., 2003).

Medication Adherence Interventions across Chronic Illness

There is growing evidence to suggest that because nearly 50% of stroke survivors are non-adherent with medication regimens, "effective ways to help people follow medical treatments could have far larger effects on health than any treatment itself" (Haynes, Ackloo, Sahota, McDonald, & Yao, 1996, p. 20). Historically, interventions that focused on the

individuals' intention and/or motivation have had little effect on improving MA (Conn et al., 2009; Kripalani et al., 2007; Matteson & Russell, 2010; McDonald et al., 2002; Peterson et al., 2003; Roter et al., 1998). For example, Roter (1998) completed a meta-analysis that examined the effects of adherence intervention outcomes from 153 studies from 1977 to 1994. This meta-analysis concluded there was not a significant difference in improvement of MA between the outcomes of behavioral and educational interventions. Behavioral and educational interventions had a greater impact on indirect measures of MA (Weighted mean Effect Size [ES] = 0.83) than educational interventions (Weighted mean ES=0.35). Interventions that used a combination of educational, behavioral, and/or affective interventions showed larger effects than single-focused interventions (Roter et al., 1998). A meta-analysis by Conn et al. (2009) synthesized 33 randomized controlled trials that evaluated interventions to improve MA in older adults. Random effects models were used to estimate overall mean ES for MA, knowledge, health outcomes, and health services utilization. Findings suggested that interventions focusing on behavioral rather than cognitive processes yield better MA outcomes (ES=.67 and ES=.48, respectively). In the same meta-analysis, interventions that included disease and drug education were less effective than interventions without education. Surprisingly, these interventions had an adverse effect on MA; however, the effect was not statistically significant. Despite the evidence emphasizing behavior-based interventions, such as forming habits and self-management, there continues to be a need for further research identifying effective interventions to increase MA.

Medication Adherence Interventions in Stroke Survivors

A qualitative comparison of 13 high and 13 low adherers to medication revealed two main themes: the importance of a stable medication routine and beliefs about medication and treatment, particularly the perceived necessity versus concerns about possible harmful effects (Chambers et al., 2011). High adherers reported remembering to take their medication and seeking support from both family and health professionals. The high adherence group also had a realistic understanding of the consequences of non-adherence and believed their medicine did them more good than harm. Low adherers reported forgetting their medication, sometimes intentionally not taking their medication and receiving poor support from medical staff. Low adherers reported they disliked taking their medication and had limited knowledge about the purpose of taking the medication and often disputed its benefits. These findings suggested appropriate medication and illness beliefs, coupled with a stable medication routine, could be helpful in achieving optimal MA in stroke patients. Interventions designed to target both intentional (beliefs about treatment, particularly the perceived necessity of medication versus concerns about possible harmful effects) and non-intentional (failure to actively remember, or in some cases physically manage, to take their medicine as prescribed) adherence may help improve MA in stroke patients (Chambers et al., 2011; Clifford, Barber, & Horne, 2008). The SystemCHANGE™ intervention addresses both of these areas.

Two systematic reviews of interventions to improve MA in adult stroke survivors have been published. First, Lager et al. (2014) completed a systematic review of 26 RCT intervention studies for improving modifiable risk factor control in the secondary prevention of stroke. Thirteen of the studies included the measured outcome of adherence to secondary

prevention medications, of which six studies tested educational and behavioral interventions and seven involved organizational interventions. Although delivery of the education in each study was in different formats, the results were the same; there were no demonstrable difference between the intervention and control groups (Lager et al., 2014). For this reason, the study tested a behavioral intervention that focuses on problem-solving and goal-setting rather than education. Specifically, a self-management intervention called SystemCHANGE™ was tested for feasibility and acceptability in increasing MA rates in older individuals who have experienced a stroke.

Self-Management Medication Adherence Interventions

Self-management is the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002). Patients who self-manage medication regimens do so by establishing and repeating routines concerning taking medication (Alemi et al., 2000; Lorig & Holman, 2003; Matteson & Russell, 2013; O'Carroll, Chambers, Dennis, Sudlow, & Johnston, 2014). Medication-taking behavior can be affected by multi-level environmental processes. Forming medication routines by making the act of taking medication a habit shows promise in improving adherence (Haslbeck & Schaeffer, 2009; Russell, 2010). Interventions such as SystemCHANGE™ address self-management by directing the stroke survivor to reflect on his/her habits and identify possible changes that can be made in daily routines, thereby improving medication-taking behavior (Moore et al., 2006; Ruppar, Conn, & Russell, 2008; Russell, 2010).

SystemCHANGE™ Intervention

SystemCHANGE™, an innovative intervention for effecting health behavior change, is based on Bronfenbrenner's Social Ecological Model (SEM) and Deming's Plan-Do-Check-Act (PDCA) cycles. SystemCHANGE™ is a systems-focused intervention that seeks to change behavior that focuses on patients' personal systems rather than on their motivation or intention (Alemi et al., 2000; Moore et al., 2009; Russell, 2010). Researchers have used the SystemCHANGE™ intervention to increase and maintain physical exercise (Moore & Charvat, 2002), improve sleep hygiene (Webel, Moore, Hanson, Patel, et al., 2013), reduce stress (Lundeen, Fisher-Pai, & Neuhauser, 2001), lower asthma attacks (Alemi & Neuhauser, 2004), improve eating behaviors (Alemi, Pawloski, & Fallon, 2003), weight management (Plow et al., 2013), enhance care of those with hypertension (Hebert & Neuhauser, 2004), and improve MA (Matteson-Kome, Winn, Bechtold, Bragg, & Russell, 2014; Sanders & Van Oss, 2013). At the patient level, improving medication-taking behavior through identifying steps that comprise daily routines improved adherence to medication regimens (Moore et al., 2009; Russell, 2010).

Conceptual/Theoretical Framework

Many behavior theories describe, explain, and predict health behavior. These theories are used to underpin new health behavior change interventions to improve MA (Bosworth et al., 2006; Riekert, Ockene, & Pbert, 2014). Typically, behavioral theories used in MA interventions aim to enhance knowledge through education, attitude through counseling, and behavior through skills training. However, even for multi-faceted interventions, meta-analyses find small effect sizes. For example, Peterson et al. (2003) reported an overall ES of the combined interventions to improve MA was 0.08 correlation coefficient (r). Similarly,

Lawrence et al. (2015) reported there was no significant difference in odds of an individual complying with medication post-treatment in intervention group compared to control (OR 1.10). There is a need for theory-driven interventions that focus on multiple environmental levels rather than the individual (Conn, Enriquez, Ruppar, & Chan, 2016; Ruppar, 2010; Russell, Ruppar, & Matteson, 2011). For this study, the SystemCHANGE™ intervention uses Bronfenbrenner's Social Ecological Model (SEM) to identify routines and Deming's Plan Do Check Act Model (PDCA) to incorporate medication taking in an existing routine (Moore et al., 2006). The following paragraphs provide a description of Bronfenbrenner's SEM and Deming's PDCA, followed by the conceptual framework of the SystemCHANGE™ intervention.

Bronfenbrenner's Social Ecological Model

Bronfenbrenner's SEM is a grand theory originally developed to describe the relationship between an active, growing person and the changing properties of the immediate settings in which the developing person lives (Bronfenbrenner, 1977). Although the SEM was developed to address how the environment affects the development of children, the multilevel approach translates well with MA by addressing etiologic influences of health and behavior that contribute to adherence (Bronfenbrenner, 1977). The major assumption of this model is a reciprocal relationship between levels (Bronfenbrenner, 1977, 1979). Changes in the social environment are affected by and effect individual behavior (Bronfenbrenner, 1977, 1979). Because of reciprocity, interventions that focus on one level should be evaluated at multiple levels (McLeroy, 2006; McLeroy, Bibeau, Steckler, & Glanz, 1988).

Four core principles of the SEM are identified. The first core principle is that there are multiple influences on specific health behaviors, including factors at the intrapersonal,

interpersonal, organizational, community, and public policy levels (Bronfenbrenner, 1977; Stokols, 1992). The second core principle is that influences on behaviors interact across these different levels. The third core principle is that ecological models should be behavior-specific, identifying the most relevant potential influences at each level (Bronfenbrenner, 1977; Stokols, 1992). The final core principle is that to establish long-term improvements in health behavior, interventions that target more than one level are the most effective (Bronfenbrenner, 1977; Stokols, 1992; Stokols, Allen, & Bellingham, 1996).

This theory goes beyond identifying variables for non-adherence by addressing the environment, behavior, physiology, and health outcomes at multiple levels: patient-, micro-, meso-, exo-, and macro-system levels (Bronfenbrenner, 1977). The idea that behaviors both shape and are shaped by the social environment is also emphasized (Bronfenbrenner, 1977; Stokols, 1992). The patient-system considers characteristics of the person including demographics, knowledge, self-efficacy, and medication beliefs (Bronfenbrenner, 1977; McLeroy et al., 1988; Yach, 2002). Next, the microsystem considers interpersonal relationships and the immediate environmental setting, including relationships with family and social support (Bronfenbrenner, 1977; McLeroy et al., 1988; Yach, 2002). Next, the mesosystem address the interrelations among settings such as family, health care provider, and employer (Bronfenbrenner, 1977; McLeroy et al., 1988; Yach, 2002). The exosystem considers indirect environmental settings that the person does not actively participate in but nonetheless have an impact on his or her immediate environment (Bronfenbrenner, 1977; Bronfenbrenner & Morris, 1998). Finally, the macrosystem refers to larger institutional systems of a culture or subculture, such as the economic, social, education, healthcare, legal, and political systems (Bronfenbrenner, 1977; McLeroy et al., 1988). In this study, the

SystemCHANGE™ intervention was implemented with the stroke survivor at the individual-, micro-, and meso- system levels, not at the exo- or macro- system levels (Moore et al., 2006; Ruppar et al., 2008; Russell, 2010).

Deming's Plan Do Check Act Cycle

The PDCA model was first presented by Dr. Edward Deming, an American expert in quality management, in the 1950s (Deming, 1952; Moen & Norman, 2006). It sought to influence workflow and processes to optimize productivity and decrease system error in the manufacturing sector (Deming, 2013; Gidy, Jilcha, Beshah, & Kitaw, 2014). The PDCA cycle is extensively used in quality management. It is the process of finding and solving problems and is applicable for the continuous improvement of the management of medical quality (Ghosh & Sobek II, 2015; Langley, 2009; Redick, 1999). In the 1990s, the concept of the PDCA cycle was introduced to the field of medical quality management by American experts and since, has been widely used in many aspects of healthcare quality control (Bushell, 1992; Saxena, Ramer, & Shulman, 2004; Taylor et al., 2014).

Deming's PDCA model is made up of four stages for improvement or change (Deming, 2013). In the "Plan" stage, a definition of the problem, possible causes, and solutions are hypothesized (Deming, 2013; Moen & Norman, 2010). Next is the "Do" stage, whereby solutions are developed and carried out. The "Check" stage evaluates the results of the plan. As part of evaluating the results, the individual determines if the goal was achieved (Deming, 2013; Moen & Norman, 2010). The final stage, "Act," identifies what was learned in the "Check" step. The person takes action based on what was learned in the "Check" step (Deming, 2013; Moen & Norman, 2010). If the change was successful, the solution would

be standardized. If the change was not successful, this information would inform a new PDCA cycle (Deming, 2013; Moen & Norman, 2010).

Conceptual Model of SystemCHANGE™

The theoretical underpinnings of the SystemCHANGE™ intervention are Bronfenbrenner's SEM and Deming's PDCA cycles. Figure 1.1 shows the integration of the SEM, Deming's PDCA model, and SystemCHANGE™ into a conceptual model. The first phase of the SystemCHANGE™ intervention is primarily influenced by the SEM, while the second and third phases of SystemCHANGE™ are mainly influenced by Deming's PDCA.

The purpose of the first phase of the SystemCHANGE™ intervention is to evaluate the person's individual-, micro-, and meso- systems to identify recurring routines to which taking medication can be added. First, the important people to medication taking are identified. Next, the immediate environment is evaluated: identification of recurring life routines and social support. Then, the individual system is evaluated, and life cycles are identified. Finally, evaluation is performed regarding the interrelations among major settings in the mesosystem such as the patient's ability to access medications (e.g., through pharmacy mail order or picking up meds at a pharmacy), and access to care. The second phase of the SystemCHANGE™ model begins once the identification the individual's existing routines is complete.

In the second phase of the SystemCHANGE™ intervention, the SystemCHANGE™ coach assists the patient in developing possible solutions to improve MA (sharing what worked from previous research and the literature). After identifying a possible solution, the third phase of the conceptual model begins.

The third phase of the SystemCHANGE™ intervention is where the stroke survivor implements the solution identified in step two. This phase is primarily influenced by Deming's PDCA Model. A chain of steps, or routine, where the desired change is to occur is identified (Plan). Once a plan is agreed upon, the proposed individual systems solution is incorporated in a person's existing routine through small experiments of change (Do). Medication taking is tracked using a medication event monitoring cap. Next, the SystemCHANGE™ coach and patient evaluate medication-taking data using an electronic monitoring printout (Check). Lastly, data are evaluated to see if a change was indeed effective (Act) (Alemi & Neuhauser, 2005; Berben, Dobbels, Engberg, Hill, & De Geest, 2012; Matteson-Kome et al., 2014; Russell, 2010). Identifying possible solutions and conducting small experiments can be repeated until optimal adherence is achieved (Plow et al., 2013; Russell, 2010).

SystemCHANGE™ is markedly different from cognitive behavioral theory (Russell et al., 2011). The current study implemented the intervention at the patient's individual-, micro- and meso- system levels, not at the exo- or macro- system level of large system or community. This is a paradigm shift in interventions because it is a systems thinking approach that focuses on the individual's personal-, micro-level systems rather on altering motivation or intention (Moore & Charvat, 2002). SystemCHANGE™ supports patient-designed, interventionist guided, small experiments using Deming's PDCA cycle.

Improving MA with a SystemCHANGE™ intervention depends on the patient's ability to formulate daily routines concerning taking medicines (Moore et al., 2006). In doing so, the person's personal-, and micro-level systems are addressed rather than his/her motivation or intent to improve adherence (Russell, 2010; Russell, Conn et al., 2011). The

conceptual model represented in Figure 1.1 is the foundation for the research study. Evaluating existing routines in a person's individual-, micro-, and meso- systems to discover where mediation taking can be incorporated is what makes the SystemCHANGE™ intervention innovative. The end goal is for medication taking is for it to become integrated into the daily routine and not dependent on memory alone.

Innovation

This study has great potential to move stroke survivor adherence science forward. The study: (a) Supports patient-designed, interventionist-guided, small experiments using SystemCHANGE™, based on Brofenbrenner's SEM (Bronfenbrenner, 1977, 1979) and integrating Deming's PDCA cycles (Deming, 2013), which combine to move beyond existing interventions' focus on cognitive-behavioral skills; (b) proposes the first evaluation of SystemCHANGE™ in stroke survivors to improve MA; (c) has potential, based upon previous work, to have a "dose" impact, which, if supported in this pilot study, could hold promise as a translatable intervention for use by healthcare providers in practice settings (Matteson-Kome et al., 2014; Russell, Conn et al., 2011); and (d) has potential clinical significance, based on Russell, Conn's TIMElink study's effect size of 1.4, which translates into about an 11% improvement in MA (Russell, Conn et al., 2011).

Conclusion

Chapter one defined stroke and described MA and MA interventions. The theories used to underpin the SystemCHANGE™ intervention and the conceptual framework of the SystemCHANGE™ intervention were reviewed. Based on the gap identified in the reviewed literature, an MA intervention study to improve MA in stroke survivors should include a theory-based behavior change intervention, an RCT study design, and a reliable and valid

measure of MA. Therefore, moving the field forward requires performing a randomized controlled trial utilizing a personal system focused intervention directed toward non-adherent stroke survivors objectively measured by electronic monitoring. The strengths of this pilot study are establishing the feasibility and acceptability of the innovative SystemCHANGE^{TM} intervention in a previously unstudied population, including a non-adherent sample, using a randomized controlled design, and measuring adherence using electronic monitoring. The primary investigator has experience with the population and intervention. This pilot study is significant in that it could establish the feasibility and potential effectiveness of the intervention for a future, fully powered study. Chapter two is a manuscript that systematically appraises RCT interventions to improve MA in adult stroke survivors.

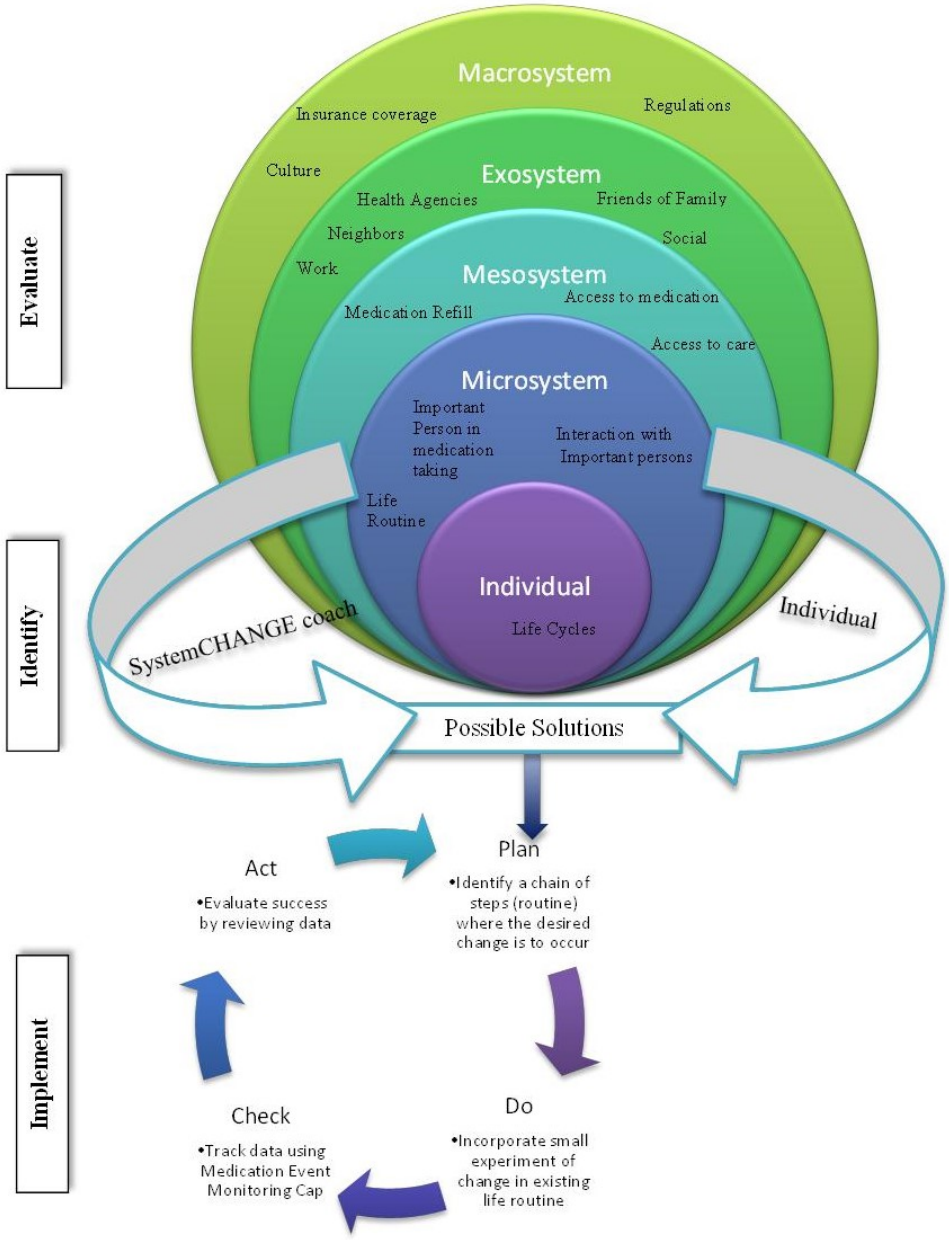


Figure 1.1. Conceptual Model of SystemCHANGE™.

CHAPTER 2

LITERATURE REVIEW: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS OF MEDICATION ADHERENCE INTERVENTIONS IN ADULT STROKE SURVIVORS

This chapter is a published article in the *Journal of Neuroscience Nursing:* "A Systematic Review of Randomized Controlled Trials of Medication Adherence Interventions in Adult Stroke Survivors" (Wessol et al., 2017).

Background: Stroke survivors are at an increased risk for recurrent stroke. Despite recommendations to avoid recurrence from the American Heart Association/American Stroke Association, medication adherence (MA) in persons with chronic conditions such as stroke is only 50%. Purpose: The aim of this study was to synthesize randomized controlled trial intervention studies designed to increase MA in adult stroke survivors.

Search Methods: The Cumulative Index of Nursing and Allied Health Literature, PsycINFO, PubMed, and Excerpta Medica database from January 1, 2009, to December 31, 2015, were searched. Study Selection: This study reviewed randomized controlled trials evaluating MA interventions in stroke survivors. Data Extraction: Two reviewers independently assessed all full-text articles, and those not meeting the inclusion criteria by both researchers were excluded. Results: This review included 18 studies involving 10,292 participants. Overall, the strength of the included studies was strong. Statistically significant results were reported in 5 of the 18 (28%) studies. Of these, 3 used cognitive/behavioral interventions to increase MA, whereas 2 studies used an educational-based intervention. Conclusions: Despite some isolated success, most MA interventions in stroke survivors do not show statistically significant improvement. Future MA research must address the lack of

consistent use of objective measurement tools and focus on the long-term benefits of MA interventions.

Keywords: intervention, medication adherence, non-adherence, stroke, systematic review

Introduction

More than 6.6 million people in the United States have survived a stroke (Mozaffarian et al., 2016). Stroke incidence is projected to increase 20.5% because of aging between 2012 and 2030 (Mozaffarian et al., 2016). Of the 800,000 people who survive their first stroke, the risk of recurrent stroke is 15% for 5 years and highest in the first 6 months after having a stroke, emphasizing the need for early initiation of appropriate prevention therapies (Mozaffarian et al., 2016; Shaya et al., 2006). Adherence to a medication regimen is key in preventing recurrent stroke events (Simpson et al., 2006).

Medications are prescribed to treat modifiable stroke risk factors with the intent of reducing the risk of recurrent stroke (Hankey, 2014; Kernan et al., 2014). It is estimated that MA in people with chronic conditions such as stroke is only 50%. Many survivors of a stroke are at risk for poor outcomes, including recurrent stroke and decreased quality and length of life (Lichtman et al., 2010).

Although medication non-adherence impacts stroke survivors' outcomes, only two systematic reviews (SR) of RCT interventions, addressing modifiable risk factors have been published (Lager et al., 2014; Lawrence et al., 2015) but they failed to address the effectiveness of MA interventions. The purpose of this paper is to synthesize RCT intervention studies designed to increase MA in adult stroke survivors.

Methods

The review was conducted as described in a protocol registered with PROSPERO (CRD42015016437). A search of CINAHL, PsycINFO®, PubMed®, and EMBASE® was conducted to identify studies that tested the efficacy of interventions to improve MA in adult stroke survivors. RCT filter was used with the PubMed® and EMBASE® databases. Combination of terms: "stroke," "ischemia," "ischemic," "intraparenchymal hemorrhage," "subarachnoid hemorrhage," intracerebral hemorrhage," "cerebral stroke," "vascular accident," "adherence," "compliance," "persistence," "concordance," "non-adherent," "non-adherent," "noncompliant," "non-compliant," "risk factor," and "secondary prevention" were used. Additional studies were located through ancestry.

Search Method and Study Selection

Inclusion criteria for eligible studies were as follows: (1) published from January 1, 2009, to December 31, 2015; (2) included adults (≥ 18 years old) who were ischemic and/or hemorrhagic stroke or transient ischemic attack survivors; (3) were RCTs aimed at improving MA. The flow of studies through the SR is displayed in (see Figure 2.1).

Full-text articles were assessed for eligibility when a decision of exclusion could not be made based on title and abstract alone. Two reviewers (J.W. and C.R.) independently assessed all full-text articles, with those not meeting the inclusion criteria excluded. Abstracted data included author/year, purpose/design/theory, sample/setting, intervention description (timing, dose, and duration), measures/outcomes, results, methodological strengths/weaknesses, and quality assessment. Data are displayed in Table 2.1.

Results

Sample/Setting

Eighteen studies, with a total of 10,292 participants were included. Sample size ranged from 30 (Sides et al., 2012) to 3821 (Peng et al., 2014). The mean age of intervention participants was 65 years, with a range of 56.03 (Evans-Hudnall et al., 2012) to 73.2 years (Johnston et al., 2010); the mean age of control participants was 64.87 years, with a range of 49.65 (Evans-Hudnall et al., 2012) to 72.4 years (Johnston et al., 2010). Attrition rates ranged from 0% (Mackenzie et al., 2013) to nearly 29% (Peng et al., 2014); most (n=12, 66%) had less than 20% attrition (Allen et al., 2009; Evans-Hudnall et al., 2012; Flemming, Allison, Covalt, Herzig, & Brown, 2013; Hedegaard, Kjeldsen, Pottegård, Bak, & Hallas, 2014; Kamal et al., 2015; Kim, Lee, & Kim, 2013; Kronish et al., 2014; Mackenzie et al., 2013; McAlister et al., 2014; O'Carroll, Chambers, Dennis, Sudlow, & Johnston, 2013; Sides et al., 2012; Slark, Khan, Bentley, & Sharma, 2013). Percent of male participants ranged from 40% (Kronish et al., 2014) to 97% (Damush et al., 2015). Seven studies were performed in the United States (Allen et al., 2009; Damush et al., 2015; Evans-Hudnall et al., 2012; Flemming et al., 2013; Johnston et al., 2010; Kronish et al., 2014; Sides et al., 2012).

Intervention Description

Dose of the interventions spanned from approximately an hour (O'Carroll et al., 2013; Sides et al., 2012; Slark et al., 2013) to 9 hours (Kronish et al., 2014). Eight (44%) studies did not report the dose of the intervention. Follow-up time ranged from 2 months (n=2, 12%) (Kamal et al., 2015; Nayeri, Mohammadi, Razi, & Kazemnejad, 2014) to 12 months (n=4, 22%) (Flemming et al., 2013; Hedegaard et al., 2014; Peng et al., 2014; Wolfe

et al., 2010); with 3 month follow-up being the most common (n=5, 31%) (Johnston et al., 2010; Kim et al., 2013; O'Carroll et al., 2013; Sides et al., 2012; Slark et al., 2013).

Study Results

Significant results were reported in 5 of the 18 (28%) studies (Hohmann, Neumann-Haefelin, Klotz, Freidank, & Radziwill, 2013; Johnston et al., 2010; Kamal et al., 2015; Nayeri et al., 2014; O'Carroll et al., 2013). Of these five intervention studies, three used Cognitive/Education and Behavioral interventions to increase MA (Johnston et al., 2010; Kamal et al., 2015; O'Carroll et al., 2013). The intervention O'Carroll et al. (2013) used focused on establishing a better medication-taking routine, using an implementation intentions approach to develop an individually tailored plan whereby patients write down when and where they will take their medication using the format of an "if-then" plan ("If it is time X in place Y and I am doing Z, then I will take my pill dose"). In contrast, Johnston et al. (2010) used a provider-targeted educational intervention whereby physicians used standard discharge order set and template incorporating statin prescriptions regardless of cholesterol level, or antihypertensive/warfarin use in patients with atrial fibrillation. A behavioral intervention was used by Kamal et al. (2015) implemented a text message system to deliver content about medication taking importance with reminders.

Two studies used cognitive/educational intervention. Nayeri et al. (2014) used a four-step, family-centered educational program including a needs assessment, family education, follow-up phone conversation, and care coordination. Hohmann et al. (2013) used a patient-targeted intervention using a clinical pharmacist to provide detailed medication information at discharge.

Quality Assessment

Study quality scoring is found in Table 2.2. This 27-item scale assesses the characteristics of RCTs, using 5 subscales: reporting, external validity, bias, confounding, and power. The maximum score was 32. Internal consistency has been reported as (KR-20: .89) and inter-rater reliability was good (r = .75) (Downs & Black, 1998).

Discussion

We systematically reviewed RCT studies designed to increase MA in adult stroke patients. Five of 18 (28%) reported statistically significant improvements in adherence outcomes, which is comparable to documented success rates in general adherence intervention literature ranging from 11% (Peterson et al., 2003) to 38% (Haynes et al., 2008). Results were also comparable to those found in SRs of MA interventions targeting specific populations with chronic conditions, for example, reporting MA rates of 24.8% (DiMatteo, 2004) and 54.1% (Kripalani et al., 2007).

Educational and behavioral interventions were not generally associated with improved MA. Different MA measures with varied reliability and validity were used in the educational and behavioral intervention studies. For example, Kamal et al. (2015) measured MA with the Morisky Self-report of Adherence Scale at baseline and 2 months, whereas Nayeri et al. (2014) used a researcher-developed "Adherence to the Therapeutic Regimen (ATR)" questionnaire at 2 months. O'Carroll et al. used a combination of methods to measure adherence, including Medication Adherence Report Scale at baseline and 3 months and Medication Event Monitoring System (MEMS®) at 3 months. Johnston et al. (2010) assessed adherence through review of medical records, where adherence was defined as documentation of a filled statin prescription, documentation of a filled warfarin prescription,

or an International Normalized Ratio blood test 6 months after discharge. Finally, Hohmann et al. (2013) determined MA via primary care physician report of current medication list. The use of different measurement of MA over varying timeframes contributes to the lack of conceptual clarity, making it difficult to compare methods and results across studies (Roter et al., 1998). Most of the studies (Evans-Hudnall et al., 2012; Johnston et al., 2010; Kamal et al., 2015; Kim et al., 2013; Nayeri et al., 2014; O'Carroll et al., 2013; Sides et al., 2012; Slark et al., 2013) focused on short-term adherence (≤ 3 months); where long-term results (≥ 12 months) were only presented in four studies (Flemming et al., 2013; Hedegaard et al., 2014; Peng et al., 2014; Wolfe et al., 2010). Because adherence rates decrease over time, long-term MA may be overestimated (Bushnell et al., 2011).

The Downs and Black quality scoring of included studies are found in Table 2.2. Overall the strength of the included studies was strong. Reporting scores ranged from 4 to 8, with a mode score of 6. A limitation in study reporting is not clearly describing the intervention, making it challenging to assess the potential risk of bias or for intervention replication. External validity is also a limitation. With scores ranging from 0 to 3 and a mode score of 1, the likelihood of findings being effective in other settings/populations is unknown. For this reason, low generalizability may contribute to a failure to translate interventions into practice. Overall internal validity was good. Internal validity (bias) scores ranged from 2 to 5, with a mode of 3. Internal validity (confounding) scores ranged from 2 to 6, with a mode of 4. Power scores ranged from 0 to 5, with a mode of 0. Power is a limitation because, in the 7 studies (39%) that scored 0, it is uncertain whether the findings were due to the intervention or due to chance sample sizes that varied dramatically with a range of 30 to

3,821 participants. Although power varies with the precision of measures, nearly half of the 18 studies (n = 7) did not have sufficient power to detect a clinically important effect.

Strengths and Limitations

This SR has several limitations. We conducted an SR of the peer-reviewed literature but did not include studies from "gray literature," such as agency reports, doctoral dissertations, abstracts, or conference proceedings, which may introduce a publication or time-lag bias. In addition, only English-language studies were included. Because of this, studies in other languages may have been omitted. Third, the reporting of MA is not universal; therefore, MA was measured using different tools, which can confound the results/conclusions.

Conclusion

This SR of MA interventions in adult patients with stroke have not shown intervention effectiveness comparable with previously published SRs (Lager et al., 2014; Lawrence et al., 2015). Most interventions did not show significant improvement in MA (Conn, Ruppar, Enriquez, Cooper, & Chan, 2015; Demonceau et al., 2013; Lager et al., 2014; Van Camp, Van Rompaey, & Elseviers, 2013). Despite these results, one must consider the World Health Organization's statement that increasing adherence may have a greater effect on health than any new medical treatment (Sabaté, 2003). Ergo, health care providers must recognize that poor MA contributes to suboptimal clinical outcomes. Cognitive/education, whether delivered at the patient, family or provider is a suitable strategy (Hohmann et al., 2013; Nayeri et al., 2014). Although this may be true, patient education alone rarely improves MA (Conn et al., 2009; Haynes et al., 2008; Kripalani et al., 2007; Van Camp et al., 2013). MA interventions that incorporate behavioral (Kamal et al., 2015) or a

combination of cognitive/educational and behavioral interventions (Johnston et al., 2010; O'Carroll et al., 2013), with support resources and innovative tools may have the most impact on maintaining a medicating regimen, but intervention details are lacking which make determination difficult. Addressing medication non-adherence challenges researchers to test new, innovative approaches to MA behavior change; improving MA across various settings. Such evidence-based interventions could contribute to reducing the number of recurrent strokes and contributing to a reduction in healthcare costs (Simpson et al., 2006). Future MA research must also address the lack of consistent use of objective measurement tools as intervention effectiveness may be skewed by imprecise measurement of MA. Finally, research must focus on long term benefits of MA interventions in stroke survivors.

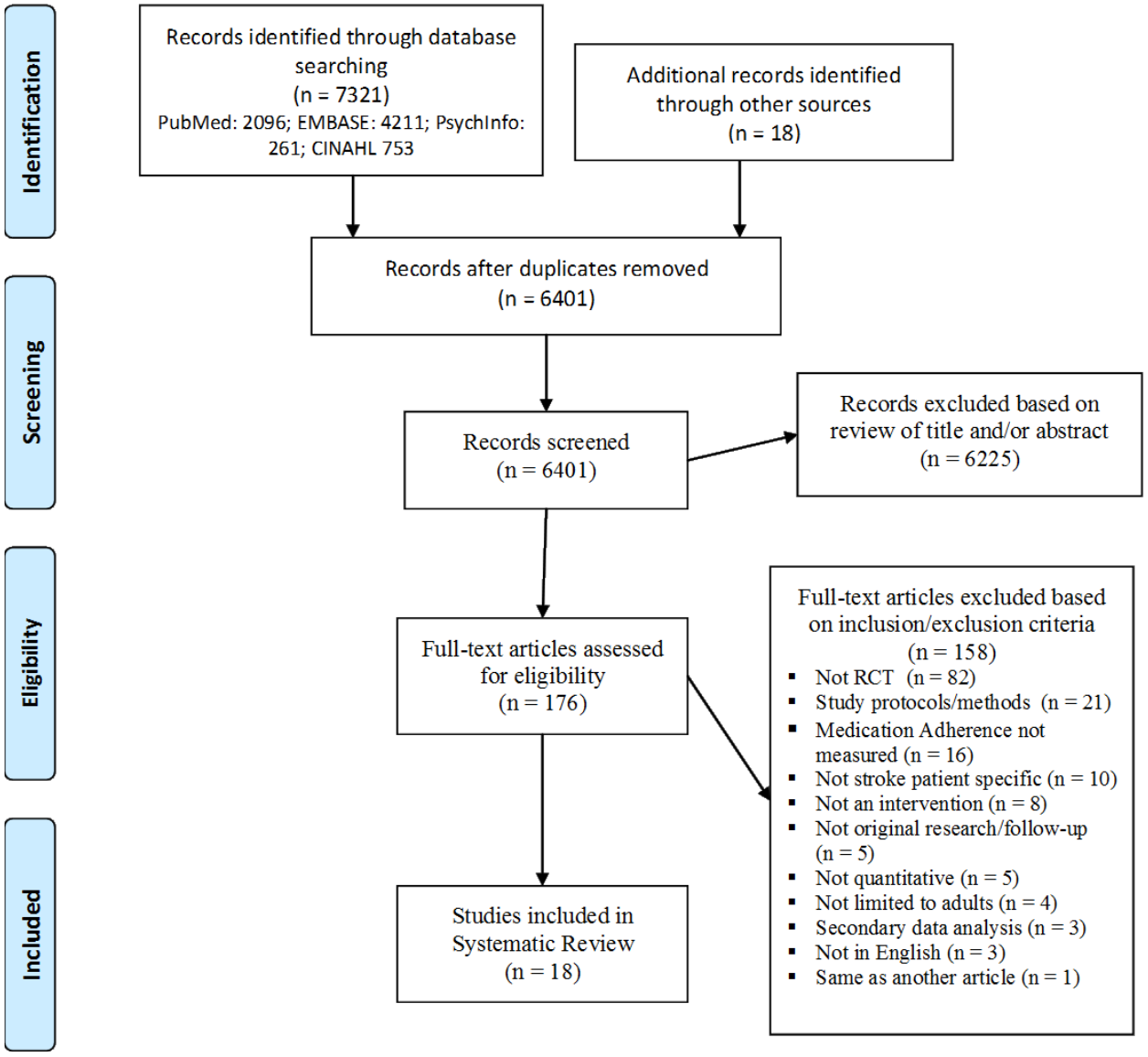


Figure 2.1. PRISMA Flow Diagram. n denotes the number of published studies.

Table 2.1

Evidence Table: Participant Details and Study Characteristics

Author Year	Intervention type Theory	Measure MA outcome
Allen 2009	**Intervention:** Cognitive/Education & Behavioral - Self-management **Control:** Usual/routine care **Theory:** Wagner's model for chronic illness care	**MA tool:** Investigator-generated questionnaire **No Significant MA Results**
Damush 2015	**Intervention:** Cognitive/Education & Behavioral - Self-management **Control:** Attention Control – education pamphlets and general phone calls **Theory:** Self-Efficacy	**MA tool:** Medication Possession Ratios **No Significant MA Results**
Evans-Hudnall 2012	**Intervention:** Cognitive/Education & Behavioral - Self-care **Control:** Usual/routine care **Theory:** NR	**MA tool: S**elf-report **No Significant MA Results**
Flemming 2013	**Intervention:** Cognitive/Education & Behavioral –Motivational Interview **Control:** Usual/routine care **Theory:** NR	**MA tool:** Self-report **No Significant MA Results**
Hedegaard 2014	**Intervention:** Cognitive/Education & Behavioral -Motivational Interview **Control:** Usual/routine care **Theory:** NR	**MA tool:** Medication Possession Ratio **No Significant MA Results**

Table continues

Author Year	Intervention type Theory	Measure MA outcome
Hohmann 2013	**Intervention:** Cognitive/Educational – Pharmacist-led education **Control:** Usual/routine care **Theory:** NR	**MA tool:** Primary care physician report of current medication list **Significant MA Results:** Adherence rose from 83.3% (C) to 90.0% (I) (P=0.01) Antithrombotics (83.8% C versus 91.9% I [P=0.033]) Statins (69.8% C versus 87.7% I [P<0.001]). **Effect size:** d= 0.0829
Johnston 2010	**Intervention** Cognitive/Education & Behavioral -Standardized discharge orders, templates **Control:** Usual/routine care **Theory:** NR	**MA tool:** Review of medical records **Significant MA Results:** Patient-level, improvements in treatment rates at intervention hospitals were attributable to increased use of statins (OR, 1.29; p =0.02) and improved blood pressure control (OR, 1.27; p = 0.03). **Effect size:** d= 0.1404
Kamal 2015	**Intervention:** Behavioral - Automated Short Messaging Service **Control:** Usual/routine care **Theory:** Health Belief Model and Social Cognitive Theory	**MA tool:** Morisky MA Scale **Significant MA Results:** Mean difference in adherence score between intervention & usual care group was 0.54 (95 % CI; 0.22–0.85) (p = <0.01) adjusted for all other variables **Effect size:** d=0.616
Kim 2013	**Intervention:** Cognitive/Educational – Web-based education **Control:** Usual/routine care **Theory:** NR	**MA tool:** Self-report **No Significant MA Results**

Table continues

Author Year	Intervention type Theory	Measure MA outcome
Kronish 2014	**Intervention:** Cognitive/Education & Behavioral - Peer-led workshops **Control:** Usual Care (Delayed Intervention) **Theory:** Chronic Disease Self-Management Program (Chronic Care Model)	**MA tool:** Morisky MA Scale and Antithrombotic pill count. **No Significant MA Results**
McAlister 2014	**Intervention:** Cognitive/Education - Intensive pharmacist case management **Control:** Attention Control - Monthly education and reinforcement of risk factor modification, and blood pressure measurement **Theory:** NR	**MA tool:** Self-report **No Significant MA Results**
MacKenzie 2013	**Intervention:** Cognitive/Education & Behavioral - Motivational interviewing **Control:** Attention Control – same as intervention except no health care provider initiated contact. **Theory:** Self-efficacy & Self-managed care	**MA tool:** **S**elf-report and pharmacist review of prescription refills **No Significant MA Results**
Nayeri 2014	**Intervention:** Cognitive/Education - Education & care coordination **Control:** Usual/routine care **Theory:** Adult Learning Theory	**MA tool:** Adherence to the Therapeutic Regimen (ATR) questionnaire **Significant MA Results:** Intervention group: Levels of adherence in the Adherence to Medication Regimen significantly higher ($p = < 0.000$) **Effect size:** d= 4.53

Table continues

Author Year	Intervention type Theory	Measure MA outcome
O'Carroll 2013	**Intervention:** Cognitive/Education & Behavioral – Two sessions to establish medication taking routine **Control:** Attention control: Two meetings with RA **Theory:** Leventhal's Self-Regulation Theory	**MA Tool:** Screening: pre/post Intervention: Medication Adherence Report Scale Intervention: Medication Events monitoring System **Significant MA Results:** - Percentage of doses taken on schedule: mean difference, 9.8%; 95% CI (0.2, 16.2); p=0.048 - MARS score: mean difference, 0.61; 95% CI (0.1, 1.2); p=0.027 **Effect size:** d= 0.691
Peng 2014	**Intervention:** Cognitive/Educational - lifestyle modification algorithm - written and web-based educational material **Control:** Usual/routine care **Theory:** NR	**MA tool:** Percentage adherence defined as total number of measures performed divided by total number of eligible patients **No Significant MA Results**
Sides 2012	**Intervention:** Cognitive/Educational -Medication Coaching **Control:** Usual/routine care **Theory:** NR	**MA tool:** Self-report **No Significant MA Results**
Slark 2013	**Intervention:** Cognitive/Education - Risk awareness **Control:** Usual/routine care **Theory:** MRC approach to complex interventions (Theory of Change)	**MA tool: S**elf-report **No Significant MA Results**

Table continues

Author Year	Intervention type Theory	Measure MA outcome
Wolfe 2010	**Intervention:** Cognitive/Education & Behavioral –Self-management **Control:** Usual/routine care **Theory:** Medical Research Council Framework for the development and evaluation of complex health service interventions	**Medication adherence tool:** Self-report: patient Interview **No Significant MA Results**

Table 2.2

Quality Scoring

	Allen et al.	Damush et. al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
Reporting																		
1. Is the hypothesis/aim/ objective of the study clearly described? yes=1 no=0	1	1	1	1	1	1	0	1	1	1	0	1	1	1	0	1	1	1
2. Are the main outcomes to be measured clearly described in the Introduction or Methods section? yes=1 no=0	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1
3. Are the characteristics of the patients included in the study clearly described? yes=1 no=0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4. Are the interventions of interest clearly described? yes=1 no=0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	1

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described? yes=2 partially=1 no=0	2	1	1	0	0	0	1	0	0	0	0	0	0	1	1	0	1	0
6. Are the main findings of the study clearly described? Yes=1 no=0	0	1	0	1	1	0	1	0	1	0	1	0	1	0	1	1	1	1
7. Does the study provide estimates of the random variability in the data for the main outcomes? Yes=1 no=0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1
8. Have all important adverse events that may be a consequence of the intervention been reported? Yes=1 no=0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
9. Have the characteristics of patients lost to follow-up been described? Yes=1 no=0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0
1o. Have actual probability values been reported(e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001? yes=1 no=0	1	1	1	1	0	1	1	0	1	1	1	1	0	1	1	1	1	1
External validity																		
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited? yes=1 no=0 UTD=0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited? yes=1 no=0 UTD=0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
Internal validity - bias																		
13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? yes=1 no=0 UTD=0	1	0	1	0	1	0	1	0	1	0	1	0	1	1	0	1	0	1
14. Was an attempt made to blind study subjects to the intervention they have received? yes=1 no=0 UTD=0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
15. Was an attempt made to blind those measuring the main outcomes of the intervention? yes=1 no=0 UTD=0	1	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
16. If any of the results of the study were based on "data dredging", was this made clear? yes=1 no=0 UTD=0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? yes=1 no=0 UTD=0	1	1	1	0	1	1	1	1	1	1	0	1	0	1	1	0	1	1
18. Were the statistical tests used to assess the main outcomes appropriate? yes=1 no=0 UTD=0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
19. Was compliance with the intervention/s reliable? yes=1 no=0 UTD=0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
20. Were the main outcome measures used accurate (valid and reliable)? yes=1 no=0 UTD=0	1	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
Internal validity - confounding																		
21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? yes=1 no=0 UTD=0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time? yes=1 no=0 UTD=0	1	0	1	0	1	0	1	0	1	1	1	1	1	1	1	0	0	1
23. Were study subjects randomized to intervention groups? yes=1 no=0 UTD=0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al.	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? yes=1 no=0 UTD=0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? yes=1 no=0 UTD=0	1	1	1	0	0	0	1	0	0	0	0	0	0	0	1	0	1	1
26. Were losses of patients to follow-up taken into account? yes=1 no=0 UTD=0	0	0	1	1	1	1	1	0	1	1	1	1	0	1	0	0	1	0

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

Table continues

	Allen et al.	Damush et. Al	Evans-Hudnall et al	Flemming et al.	Hedegaard et al.	Hohmann et al.	Johnston et al.	Kamal et al.	Kim et al.	Kronish et al.	McAlister et al.	MacKenzie et al.	Nayeri et al.	O'Carroll et al.	Peng et al.	Sides et al.	Slark et al.	Wolfe et al.
Power																		
27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%? Sample sizes have been calculated to detect a difference of x% and y% Scoring based on size of smallest intervention group.(scored 0-5). Size of the smallest intervention group: <n1 = 0 n1- n2 = 1 n3 - n4 = 2 n5 - n6 = 3 n7 - n8 = 4 n6+ = 5	3	4	4	0	0	5	5	5	0	4	0	1	5	0	5	0	5	0

Answers were scored 0 or 1, with the exception of one item (#5) in the Reporting subscale, which was scored 0 to 2, and the item on Power, which was scored 0 to 5.

CHAPTER 3

METHODOLOGY

Background of SystemCHANGE™

The behavior change intervention (SystemCHANGE™) is designed to assist individuals and families to change their daily routines by considering how the immediate environment (family, work, and school routines) affects healthy living behaviors. SystemCHANGE™ focuses on system redesign of daily routines using a series of small, self-designed experiments. Six manuscripts have been published using the SystemCHANGE™ intervention to increase the adoption and maintenance of health promoting behaviors in diverse populations including adults following cardiac events (Moore et al., 2006; Moore & Charvat, 2002), kidney transplant recipients (Russell, Conn et al., 2011), HIV patients (Webel, Moore, Hanson, Patel, et al., 2013), and patients with inflammatory bowel disease (Matteson-Kome et al., 2014). The health behaviors addressed in these studies included exercise (Moore & Charvat, 2003; Moore et al., 2006), medication adherence (Matteson-Kome et al., 2014; Russell, Ruppar et al., 2011), and sleep duration (Webel, Moore, Hanson, Patel et al., 2013). Of these six manuscripts, three studies delivered the intervention in a group setting (Moore et al., 2006; Moore & Charvat, 2002; Webel, Moore, Hanson, Patel et al., 2013), two studies delivered the intervention to an individual (Matteson-Kome et al., 2014; Russell, Conn et al., 2011), and one manuscript was a case study (Moore, Jones, & Alemi, 2016). Table 3.1 displays SystemCHANGE™ studies.

Significant results were reported in two of the five (40%) studies (Moore et al., 2006; Russell, Conn et al., 2011). The remaining studies showed an improvement in measured outcomes; however the improvements were not statistically significant. Moore et al. (2009)

Table 3.1

SystemCHANGE™ Studies

Study	Population	Intervention	Results
Moore & Charvat (Moore & Charvat, 2002) Using the CHANGE Intervention to Enhance Long-Term Exercise **Design:** Pilot post-assessment-only **Purpose:** Pilot to determine the effectiveness, feasibility and acceptability of CHANGE intervention.	Adults recovering from a myocardial Infarction **Age $\bar{X}$:** 58.0 **N:** 16	**Delivery:** Group **Outcome:** Exercise - Number of minutes of exercise - Number of minutes swimming - Number of minutes exercised within the target heart rate	CHANGE intervention group performed considerably more exercise than persons in the control group.
Moore et al. (Moore et al., 2006) Effects of a CHANGE Intervention to Increase Exercise Maintenance Following Cardiac Events **Design:** RCT **Purpose:** Test the effectiveness of CHANGE (Change Habits by Applying New Goals and Experiences), designed to increase exercise maintenance in the year following a cardiac rehabilitation program	Cardiac patients who had a recent cardiac event **Age:** I: 62.5 ± 11.4 C: 62.3 ± 10.8 **N:** 250	**Delivery:** Group **Primary Outcome:** - Exercise - Exercise maintenance – number of months participants continued to exercise after intervention - Exercise amount – number of hours - Intensity compliance – amount of time spent exercising in the target heart rate zone	The CHANGE group continuing to exercise longer as compared to the usual-care group (Log Rank Test = 4.81, p = .02)

Table continues

Study	Population	Intervention	Results
Russell, Conn et al., 2011 Taking Immunosuppressive Medications Effectively (TIMELink): A Pilot Randomized Controlled Trial in Adult Kidney Transplant Recipients **Design:** Pilot RCT **Purpose:** To determine the feasibility and efficacy of a six-month continuous self-improvement intervention versus an attention control management in medication non-adherent adult kidney transplant patient	Renal transplant recipients. **Age $\bar{X}$:** 51.5 I: 55 C: 44 **N:** 30	**Delivery:** Individual **Primary Outcome:** - Feasibility of the intervention - Immunosuppressive medication adherence **Duration:** 6 months	- Statistically significant difference between groups over the entire six-month period (t11 = 2.33, p = 0.0396). - Continuous self-improvement intervention effect size was large (Cohen's d = 1.4; r = 0.6).
Webel, Moore, Hanson, Patel, et al., 2013 Improving sleep hygiene behavior in adults living with HIV/AIDS: a randomized control pilot study of the SystemCHANGE™–HIV intervention **Design:** Pilot RCT **Purpose:** To test the feasibility of a novel, evidence-based intervention SystemCHANGE– HIV on sleep outcomes. **Trial registration number**: NCT01256814 **Published Protocol:** Webel, Moore, Hanson, & Salata, 2013	HIV patients Age ≥ 21 years old **Age $\bar{X}$:** **I:** 49.1 **C:** 47.8 **N:** 43	**Delivery:** Group **Primary Outcome:** - Feasibility of the intervention - Sleep duration and quality - Quality of Life **Duration:** 10 weeks	- Results suggest that a refined SystemCHANGE–HIV intervention may improve objectively-measured sleep outcomes. - An increase of 10 minutes per night is an improvement over a previous sleep hygiene intervention in our target population.

Table continues

Study	Population	Intervention	Results
Matteson-Kome et al., 2014 Improving maintenance Medicating Adherence in Adult Inflammatory Bowel Disease Patients: A Pilot Study **Design:** Pilot RCT **Purpose:** To evaluate the feasibility, intervention mechanism, and potential effectiveness of the CSI intervention in adult non-adherent participants in a mid-western IBD clinic	Non-adherent adults with inflammatory bowel disease **Age $\bar{X}$:** 44.8 **N:** 19	**Delivery:** Individual **Primary Outcome:** - Feasibility of the intervention - Potential effectiveness of the intervention on improving medication adherence **Duration:** 3 months	- The change in the medication adherence score for the CSI group was not statistically significant (P=0.14) though the trends were in the anticipated direction. - Effect size = 1.9
Moore et al., 2016 Family self-tailoring: Applying a systems approach to improving family healthy living behaviors **Design:** Case Study **Purpose:** To describe a new model of health behavior change, SystemCHANGE			

used the SystemCHANGE™ intervention to address exercise maintenance problems in 250 individuals who had had a recent cardiac event (myocardial infarction, coronary artery bypass surgery, and/or angioplasty). This study found no differences in the amount, frequency, or intensity of exercise. Instead, the intervention was effective in reducing the probability of stopping exercise in the year following completion of a cardiac rehabilitation program (Log Rank Test = 4.81, p = .02). The intervention in Russell, Conn et al.'s (2011) pilot study focused on identifying the kidney transplant recipient's life routines, important people, and possible solutions to enhance medication taking. The mean medication adherence score for the intervention group (n = 8) was significantly higher than the attention control group's (n = 5) mean medication adherence score (p = 0.03). The intervention effect size (Cohen's *d*) was large at 1.4. Thus, the intervention shows promise as an effective and feasible approach to improve medication adherence in adult kidney transplant recipients.

This pilot study builds on previous SystemCHANGE™ studies (Matteson-Kome et al., 2014; Russell, Conn et al., 2011) that have shown MA can be improved by systematically building medication taking into existing routines so that medication is in the right place at the right time. Currently, there are eight studies in progress (including this study) testing the SystemCHANGE™ with exercise/activity, MA, and health promotion registered in Clinicaltrials.gov. These studies are in various stages of completion: Five studies are completed with no study results available, one is active but not recruiting, two studies are recruiting, and one study is recruiting by invitation. The studies in progress will provide valuable information on the use of the SystemCHANGE™ intervention in addressing medication adherence, exercise, weight loss, and health eating habits. A list of SystemCHANGE™ studies in progress is found in Table 3.2.

Table 3.2

SystemCHANGE™ Studies in Progress

Study	Population	Intervention	Results
Long-term Exercise in Older Cardiac Patients **Design:** RCT with three intervention arms **Purpose:** To test two theoretically distinct behavior change interventions against a usual care group to increase lifestyle exercise after a cardiac event. **Principal Investigator:** Shirley Moore, PhD **Trial registration number:** NCT02323919	Cardiac patients **Age:** ≥ 55 years old **N:** 420	**Delivery:** group **Primary Outcome:** Objectively measured hours of exercise/month **Duration:** 1 year	Completed No study results available
SystemCHANGE: An Intervention for Medication Change in Adult Kidney Transplant Patients (MAGIC) **Design:** RCT **Purpose:** To determine whether the SystemCHANGE™ intervention is more effective than the attention control group in improving MA in adult kidney transplant recipients **Principal Investigator:** Cynthia L. Russell PhD, RN **Trial registration number:** NCT02416479 **Published Protocol:** (Russell et al., 2016)	Renal transplant patients **Age:** ≥ 18 years old **N:** 190	**Delivery:** Individual **Primary Outcome:** immunosuppressive medication adherence rates **Duration:** 4 years	Active, not recruiting

Table continues

Study	Population	Intervention	Results
A Clinical Trial of SystemCHANGE™ to Improve Exercise, Diet and Health in HIV-Infected Adults **Design:** RCT **Principal Investigator:** Allison Webel, PhD, RN **Purpose:** To test an intervention to improve and maintain exercise in HIV-infected adults. **Trial registration number:** NCT02553291	HIV patients **Age:** ≥ 18 years old **N:** 109	**Delivery:** six weekly group sessions, followed by monthly telephone booster **Primary Outcome:** Exercise **Duration:** 6 months	Completed, No study results available
Examining the Efficacy of a SystemCHANGE™ Weight Management Intervention in Stroke Survivors **Design:** RCT, parallel-group **Purpose:** To examine a novel behavior change approach - SystemCHANGE™ - to promote weight loss and improve health and function in stroke survivors. **Principal Investigator:** Matthew A. Plow, PhD **Trial registration number:** NCT01776034 **Published Protocol:** (Plow et al., 2013)	Stroke survivors **Age:** 30 to 75 years old **N:** 45	**Delivery:** 12 face-to-face group sessions over 3 months **Primary Outcome:** body weight and patient-reported and objective outcomes of health and function. **Duration:** 6 months	Recruiting

Table continues

Study	Population	Intervention	Results
Ideas Moving Parents and Adolescents to Change Together (IMPACT) **Design:** RCT with three intervention arms **Purpose:** To compare the effects of three distinct behavioral obesity management interventions on BMI in overweight/obese middle school, urban youth. **Principal Investigator:** Elaine Borawski, PhD **Trial registration number:** NCT01514279 **Published Protocol:** Moore, Borawski, Cuttler, Ievers-Landis, & Love, 2013	6th graders who are overweight or obese **Age:** 11-15 years old **N:** 360	**Delivery:** Face to face family level interventions at 2 week intervals over the first 12 months followed by rotating monthly group face-to-face meetings and phone calls **Duration:** 4 years	Enrolling by invitation
Increasing Activity Post-Kidney Transplant With SystemCHANGE™ (CHANGE) **Principal Investigator:** Tara O'Brien, PhD, RN **Trial registration number:** NCT03191630	Renal transplant patients **Age:** ≥ 65 years old	**Delivery:** Group **Duration:** 1 year	Recruiting

Table continues

Study	Population	Intervention	Results
SystemCHANGE™ Stroke: A Systems Approach to Healthy Living after Stroke **Design:** RCT **Purpose:** To examine the effectiveness of SystemCHANGE^{TM}-Stroke compared to enhanced usual care to improve healthy eating, physical activity, and medication adherence in Thai post-stroke patients **Principal Investigator:** Vilailert Kompton PhD(c), RN	Stroke Survivors **Age:** 18-80 **N:** 110	**Delivery:** Community **Duration:** 3 months	Dissertation complete
Impact of SystemCHANGE™ Intervention on Medication Adherence in Older Adults With Heart Failure: A Pilot RCT **Design:** Pilot RCT **Purpose:** To evaluate the acceptability and feasibility of a SystemCHANGE™ intervention to improve medication adherence in older adults with heart failure. **Principal Investigator:** Angela Andrews, PhD(c), RN **Trial registration number:** NCT03162848	Heart failure patients **Age:** ≥ 65 years old **N:** 30	**Delivery:** Individual **Duration:** 5 months **Primary Outcome:** - Test feasibility - Medication adherence	Completed, No study results available

Table continues

Study	Population	Intervention	Results
Randomized Controlled Pilot Study of a SystemCHANGE™ Medication Adherence Intervention in Older Adult Stroke Survivors **Design:** Pilot RCT **Purpose:** To evaluate the feasibility and acceptability of using a SystemCHANGE™ intervention in older adult stroke survivors to improve medication adherence. **Principal Investigator:** Jennifer Wessol, PhD(c), RN **Trial registration number:** NCT03211130	Ischemic stroke survivors **Age:** ≥ 50 years old	**Delivery:** Individual **Duration:** 5 months **Primary Outcome:** - Test acceptability and feasibility - Medication adherence	Completed

Methods: Design

A pilot RCT, single-masked (participants), design with repeated measures using the SystemCHANGE™ and attention-control intervention in older adult stroke survivors with medication non-adherence documented by electronic monitoring was conducted. During a 2-month screening phase, MA was electronically monitored. The Medication Event Monitoring System (MEMS®) has a weak intervention effect in the first 30 days of use (De Geest et al., 2006; Denhaerynck et al., 2008). For this reason, the first 30 days of MEMS® data from the analysis was eliminated. Closely adhering to dosing regimen is important to achieve full anticoagulant effects (Camm et al., 2012; Furie et al., 2012; Held et al., 2013; Manolis & Poulimenos, 2013; Pudusseri et al., 2013). Because of this, an adherence rate of ≥ .97 was used. Adherent participants (adherence rate of ≥ .97% after screening) (Camm et al., 2012; Furie et al., 2012; Held et al., 2013; Manolis & Poulimenos, 2013; Pudusseri et al., 2013) exited the study (Russell et al., 2006). The SystemCHANGE™ intervention has shown treatment effect at one month (Matteson-Kome et al., 2014; Russell, Conn et al., 2011) thus, the SystemCHANGE™ intervention was delivered for two months. The non-adherent participants (adherence score < .97) entered the study's 2-month intervention phase and were randomized into the treatment or attention-control condition. During the intervention phase, the PI visited both groups of participants at home at baseline and telephoned them three times (one week, one month, and two months). Baseline Social Support Appraisal Index, System Thinking Scale, and Perceived Health surveys were assessed. A one-month maintenance phase followed the intervention phase. Electronic medication monitoring continued, but no intervention was delivered to either group. Participants were followed in the study for a total of five months (two months screening, two

months intervention, and one month maintenance). Final measurements of MA, Social Support Appraisal Index, System Thinking Scale and Perceived Health survey were obtained at the end of the intervention (see Figure 3.1).

Setting

This study was conducted in the Kansas City, Missouri and Kansas City, Kansas areas. Study visits occurred in the participant's home for the baseline home visit and then telephone calls were made for one week, one month, and two months in both groups.

Sample

A convenience sample of 30 older adult stroke survivors from Saint Luke's Neurological Consultants, affiliated with Saint Luke's Health System, a comprehensive stroke center, was sought for enrollment in the screening phase of this pilot study. This program provides care for over 25 patients a month who are ≥ 50 years of age. The number of potential participants necessary to screen to enroll 30 participants was unknown. Based on a previous study (O'Carroll et al., 2013), 36 participants needed to be approached to consent 30 participants, of which 47% (14) would have a MA rate < .97. Of the 14 participants who were eligible for the intervention, 90% consented to enter the intervention and 95% completed the intervention phase (13 participants), and 93% completed the study (12 participants) (O'Carroll et al., 2013). Based on O'Carroll et al.'s (2013) study, it was proposed 14 participants would enter the intervention phase: seven participants in the SystemCHANGE™ intervention group and seven participants in the attention control group. The recruitment and eligibility rates in this pilot study provided valuable data for designing a larger study.

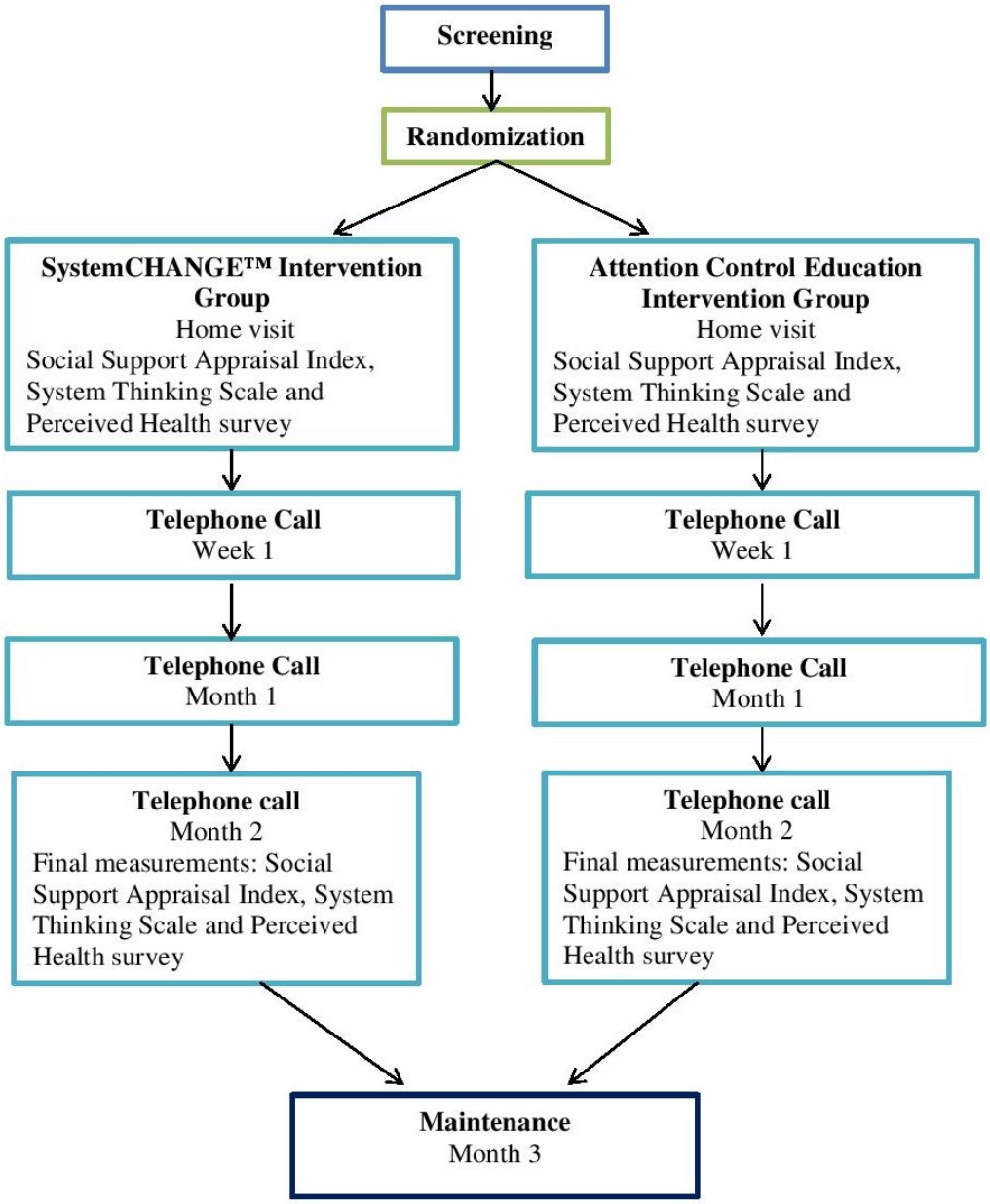


Figure 3.1. Participant Flow Chart

Study inclusion criteria were as follows:

1. Participants were age ≥ 50 years old at time of study entry.
2. Participants received post-stroke care with Saint Luke's Neurology.

3. Participants were prescribed at least 1, once a day, antithrombotic medication.
4. Participants were able to provide informed consent.
5. Participants were able to open an electronic cap.
6. Participants were able to self-administer medications.
7. Participants had or had access to a telephone.
8. Participants had no cognitive impairment as determined by a score of 4 or greater on The Six-item Screener (SIS) (see Appendix A) (Callahan, Unverzagt, Hui, Perkins, & Hendrie, 2002; Unverzagt et al., 2011).

Sample Size

Due to the exploratory nature of this study, the sample size was limited to 30 participants. This study was not powered for statistical tests of significance.

Randomization

Participants were randomly assigned to treatment or attention-control group on a 1:1 ratio using computer-generated block randomization. Non-adherent participants (MA < .97) were sequentially assigned after the screening phase. Adherent participants (MA ≥ .97) exited the study.

Participant Attrition

Attrition was monitored and reasons for those who exited the study were documented. Participant burden was minimized by conducting all study activities by phone, mail/email, or during home visits. To thank participants progressively for their time and participation, participants received a $10 honorarium for completing the screening and $10 for completing the intervention phases. Participants received a thank you of $20 upon completing the study. The PI mailed these honoraria at the end of each phase.

Fidelity

Fidelity was first addressed by training the PI to deliver the SystemCHANGE™ intervention using a well-defined protocol. Strategies for achieving proficiency in the delivery of the SystemCHANGE™ include training for intervention delivery in which (a) the philosophical underpinnings of the intervention were discussed, (b) intervention procedures were covered in detail, and (c) the PI had an opportunity to practice the necessary skill sets needed for the intervention (Bellg et al., 2004). The PI delivered the intervention to all participants following the checklist; thus the variance in intervention delivery was reduced.

Second, treatment fidelity strategies were implemented to the participants' receipt of treatment. Receipt of treatment "involves processes that monitor and improve the ability of patients to understand and perform treatment-related behavioral skills and cognitive strategies during treatment delivery" (Bellg et al., 2004, p. 448). During screening, the PI assessed the participants' ability to use the MEMS® cap prior to consent. Then, MEMS® use and *MEMS® Diary* use were assessed using the *MEMS® Use Form* to ask about MEMS® use at the screening one week and one month telephone calls. At the home visit, the PI evaluated the participants' comprehension of the intervention using the teach-back method to check for understanding.

SystemCHANGE™ Training

The PI delivered the SystemCHANGE™ intervention and the attention control intervention at the UMKC campus and via video conference with the experts (Dr. Cynthia L. Russell, Debbie Clark, and Courtney Miller) on 11/28/2017 and 12/12/2017. To preserve intervention integrity, simulation and role play were used until the PI was able to apply the protocol consistently, as judged by the expert using the SystemCHANGE™ protocol

checklist. To ensure the highest level of PI protocol knowledge and skills, training sessions also included role playing of disruptive situations for both interventions, and delivering both interventions for a different behavior change such as exercise or diet. The experts provided the PI feedback on performance, and the PI retrained as necessary until she achieved 100% intervention protocol integrity.

Measures/Instruments

To meet this pilot study's aims, each of the following surveys included evaluation questions to be used for protocol refinement and the formulation of a power analysis for a fully powered study. The research instruments used are described in the following sections. Copies of the instruments can be found in the appendices.

Cognitive Function

Cognitive function was measured with The Six-item Screener (SIS) (see Appendix A), which is a global measure of cognitive status that assesses 3-item recall and orientation to year, month, and day of the week (Callahan et al., 2002). Scores range from 0 to 6 with a score of 4 or fewer correct indicative of cognitive impairment (Callahan et al., 2002). The SIS has been validated against clinical diagnoses of dementia and mild cognitive impairment (74% sensitivity and 80% specificity for both groups combined vs. cognitively normal elders) (Callahan et al., 2002; Unverzagt et al., 2011).

Demographic Information

Demographic information was collected (see Appendix B) including age, sex, race, ethnicity, marital status, employment status, date stroke, treatment(s) received, income, insurance coverage, number and type of other medication, and pillbox use.

Social Support

Social support was measured using The Social Support Appraisals Index (SS-A) (see Appendix C), which is a 23-item self-administered, self-report scale measuring the degree to which a person feels cared for, respected, and involved with family and friends (Vaux et al., 1986). The participants' responses were strongly agree, agree, disagree, or strongly disagree with each statement. Total scores range from 23 to 92. Questions that were negatively stated (#3, 10, 13, 21, and 22) were reversed. Then total and subscale scores were computed by summing scores for relevant items: (i) total score = all 23 items, (ii) family subscale = sum of 8 "family" items, (iii) friend subscale = sum of 7 "friend" items. Low scores indicate high levels of support conversely; high scores indicate low levels of support (Vaux et al., 1986). The scale had good reliability and validity (Cronbach α coefficients .90, .81, and .84) (Vaux et al., 1986). The SS-A showed stability over a six-week interval, with reliability scores of .80. Convergent validity was demonstrated with significant associations to seven other appraisal measures. Adequate concurrent and divergent validity with other perceived support measures was demonstrated and showed predicted associations with measures of theoretically related support network resources (antecedents) and psychological well-being (consequences) (Vaux et al., 1986).

Perceived Health

Perceived health status was measured by one question, "How is your health in general?" (see Appendix D). Participants select excellent, very good, good, fair, poor, or very poor. Perceived health status reflects people's overall perception of their health, including both physical and psychological dimensions (Bowling, 2005). The question has good reliability and validity (Bowling, 2005).

Personal Systems Behaviors

Personal Systems Behaviors was measured by Systems Thinking Survey (adapted for patients) (see Appendix E), a 20-item scale using a 5-point Likert scale. The tool was developed by Drs. Dolansky and Moore and measures personal system behaviors perceptions. It has good reliability and construct and discriminate validity. Test-retest was 0.74 and Cronbach's Alpha was 0.89 (Dolansky, Moore, Singh, & Alemi, 2010). The tool discriminated between those receiving high and low or no SystemCHANGE™ training (p=0.05 and 0.01, respectively) (Dolansky et al., 2010).

Medication Adherence

Medication adherence was measured using the MEMS®cap (MEMS 6 TrackCap without LCD display) (see Appendix F), which is a medication cap containing a battery and microelectronics that record the date and the time of each cap removal to create a medication "event" ("MEMS® Cap Versatile Adherence Monitoring Cap," 2016). It measures the three indicators of adherence: (a) dose-count, percentage of prescribed doses taken; (b) dose-days, percentage of days correct number of doses taken; and (c) dose-time, percentage of doses taken on schedule (Vrijens et al., 2012). Self-reported MA uses recall memory, which is unlikely to be accurate enough to provide valid data regarding the exact timing of doses (Vrijens et al., 2012). MEMS® caps are waterproof and have been shown to be reliable in temperatures ranging from -20°C to 70°C and in up to 95% humidity ("MEMS® 6: Medication Event Monitoring System," 2003). A unique serial number is printed on each MEMS® cap. The cap has a battery life of 36 months from initialization; up to 3,800 medication events (cap openings) can be stored; it is accurate to within 2 minutes per month; and it has a reported failure rate of 2% ("MEMS® 6: Medication Event Monitoring System," 2003). Data stored on the MEMS cap are downloaded via a specialized cap reader (Wireless

Reader) to a computer, where it is stored in proprietary data management software (PowerView, Aprex Corp., Union City, CA, USA) that facilitates data cleaning and calculation of medication adherence rates.

Participants used the MEMS® cap with one, once-a-day oral antithrombotic medication. The PI instructed participants to: (a) place medication into the MEMS® bottle, (b) not take it from any other containers, and (c) place all new medication refills into the bottle. If a participant stored medications in a pillbox, the PI provided small colored disks or "Tic-Tacs" to place in the pillbox. In previous work, Tic-Tacs have successfully reminded participants to remove the medication from the MEMS® bottle (Russell, Conn et al., 2011). Participants were instructed on using the *MEMS® Diary* (see Appendix G). The instructions included to document: (a) any accidental cap openings, (b) openings when no medication was ingested, and (c) when a medication was removed early and taken on time.

Wireless Reader

MEMS® cap transfers data by telemetry to the Wireless Reader that downloads, encrypts, and transmits it via wireless circuits to a central database ("MEMS® Cap Versatile Adherence Monitoring Cap," 2016). The participants' data could be reviewed by the PI via a secure website.

Intervention

Screening

After consent was obtained, the PI completed MEMS® pill bottle training using an 11-step script as follows.

1. This is the MEMS cap and bottle. The cap has a small electronic chip in the top that records the date and time the cap is removed. We will presume that this is the time you took your medicine.
2. Please remove the cap from the MEMS bottle. You will just simply twist the cap off.
3. You will put one of your medications that you take once a day into the MEMS pill bottle and for the next two months you will take your medicine from the MEMS bottle. The cap will monitor how many times per day you opened the pill bottle and took your medicine. Please continue to carry out your normal medication taking routine. Please do not change how you take your medications. We want to know more about how you normally take your medications. We want to see your natural medication taking patterns. You can talk about which medicine they would like to put in the bottle at this time.
4. There may be times when you open the MEMS but don't take a pill, for example if you are refilling your bottle or taking your medicines out early to take later. You will use the MEMS Diary Form for the times you open your bottle but did not take a pill. For example, if you are going out for the evening and put your medications in your purse or pocket you would make a note of the date, time and explanation of why you removed the medicine early. This form is important and will need to be returned with the MEMS pill bottle at the end of this study. Please keep the MEMS Diary Form with your MEMS pill bottle.
5. If the patient takes more than one antithrombotic medication daily, use a coin flip to determine which antithrombotic medication to monitor with the MEMS Cap.

6. Do you use a pillbox for your medications? If yes, we've sent you some Tic-Tacs. You can place them in your pillbox at the day and time you would take your medication (name of medicine going in the MEMS). These Tic-Tacs will remind you to take a pill from your MEMS bottle so you do not forget.
7. You must put your antithrombotic medication in the MEMS pill bottle. You cannot keep it in the pill box and then open and close the MEMS pill bottle as if you were taking the medication. We call this "triggering the MEMS" and you cannot do this because it will not document your medication taking correctly.
8. Please write on the MEMS diary today's date, the time and the explanation of what happened in the columns. Write "MEMS pill bottle training" because you opened the bottle and did not take the medication.
9 Please write the name of your antithrombotic medication and any other details on the pill bottle with the black felt tip pin provided. Please do not write on the cap.
10. Do you have any questions? In order for me to know that I have explained this correctly will you tell me how you are going to use the MEMS Cap and bottle to take your antithrombotic medication?
11. I will call you in one week to check on your progress. Please feel free to contact me if you have any questions. Assure that the participant has your contact information.

After MEMS cap training was complete, the participant used the MEMS® cap to track medication taking for two months. During the 2-month screening phase, the PI contacted the participant at 1 week and Month 1 to assess correct MEMS® use and MEMS® Diary using the MEMS® Use Form (see Appendix H) by asking: Do you have any questions about using

the MEMS® cap and bottle? Tell me about how you are using it; Is the use of the colored disks/Tic-Tacs making it any more difficult to take the antithrombotic medications?; Are you taking your medications directly from the MEMS® medication bottle for each dose? (e.g., not triggering the cap or routinely taking several doses at once); Tell me about how you are using the diary. If the participant responded in any way that indicated that the MEMS® cap or MEMS® Diary was being used incorrectly, the PI re-educated the participant.

After the 2-month screening period, the PI contacted the participant to assess MEMS® use using the MEMS® Use Survey (see Appendix I) by asking: 1) Tell me what you think of the MEMS caps. 2) Do you think that the MEMS caps had a negative, neutral, or positive overall effect on your medication taking routine? 3) How practical do you think using the MEMS caps on a daily basis was for you? 4) Describe any instances when you think using the MEMS® cap and MEMS® Diary as directed was difficult. The participant was asked to return the MEMS® or MEMS® Diary through the mail in the postage paid envelope provided by the PI.

This procedure has been used successfully in other studies (Russell, Conn et al., 2011; Russell et al., 2016) with no loss of MEMS® caps or data. Once the cap was received, the PI downloaded the data from the MEMS® cap to the secure, cloud-based data platform, medAmigo™. The medAmigo™ data platform processes participant data using predefined algorithms to present a comprehensive picture of the participants' adherence. Whenever notations appear in the *MEMS® Diaries*, the PI used the information to correct MEMS® data in medAmigo™. For example, if a participant made an entry on his/her MEMS® Diary that state "Filled bottle, no dose taken," the PI retrieved the MEMS® cap data on the medAmigo secured website and made edits to the dosing history. The event was located, deleted, and a

comment was noted, “Filled bottle.” If the participant noted on the MEMS® Diary that the antithrombotic was not taken for an extended period of time for an illness such as influenza, a surgery/procedure such as dental procedure, or IVC filter removal, the consecutive days were labeled as non-monitored. Participants whose MA rate was ≥ .97 exited the study, and those whose rate was < 97 continued to the 2-month intervention phase. The PI randomized participants whose medication adherence score was < .97 into the treatment group or the attention-control group. At the home visit (described in the next section) the MEMS® cap and bottle were returned to the participant by the PI. A $10 thank-you gift card was mailed to the participant at the end of the screening period.

SystemCHANGE™ Intervention

The planned baseline home visit was approximately 65 minutes. Table 3.3 provides an overview of the intervention delivered during the home visit and the telephone call at one week, one month, and two months. The PI mailed/emailed the MEMS® report to the participant prior to the one-month and two-month calls. If adherence was the same or lower, the PI encouraged the participant to try another solution from the *Solution Assessment Scale* (see Appendix J). The maintenance phase began after the two-month intervention; the PI encouraged the participant to continue using the MEMS® cap and diary during the maintenance phase.

At the end of the intervention phase, PI ended the SystemCHANGE™ intervention by discussing the participant’s improvements. The PI encouraged the participant to continue to use the MEMS® for the one-month maintenance phase. At the end of the maintenance phase, the PI reminded the participants to return the MEMS® cap and diary in the mail. They were also asked about the practicality of using the MEMS® cap.

Table 3.3

Summary of SystemCHANGE™ Intervention

Timing	Method/Content
Screening	MA electronically monitored for two months.
Intervention: Baseline	Home visit with participant and important person if applicable (65 minutes): Review MEMS® from screening, Describe Intervention, Identify important people, Routines, Cycles of Routines, and Possible Solutions, install the wireless reader. A time to speak by telephone at 1 month is scheduled.
Week 1	Phone call: PI asks if the participant has implemented the solution. A time to speak by telephone at 1 month is scheduled.
Month 1	Phone call: Mail or email weekly MEMS® report to the participant. Discuss if solutions helped; if not identifies new solutions.
Month 2	Phone call: Mail or email weekly MEMS® report to the participant. Close the intervention by discussing participant's improvements. Encourage participant to continue using the MEMS® cap and diary during the maintenance phase.

SystemCHANGE™ Intervention Phase

Home visit. The PI began by introducing herself and asking participant how things have been since last meeting. The PI then prepared to set up the Wireless Reader by asking the participant, "Where do you usually get the best cell service/reception?" and asked for a place near the best cell service/reception to plug in the Wireless Reader. The PI explained that the Wireless Reader would be reviewed later in the home visit.

After introductions and the Wireless Reader was plugged in, the PI and participant sat at a table where the participant and PI could easily work together with the laptop. The first 20 minutes of the home visit involved the participant completing three surveys (Social Support Appraisal Index, Systems Thinking Scale, and Perceived Health) on the PI's

touchscreen laptop. The participant was asked if assistance with entering data was preferred. If assistance was requested, questions were read to the participant and answers selected on the computer screen. The PI reminded the participant that there were no right or wrong answers to the surveys. First, the Social Support Appraisal Index was introduced by the PI by stating, "Below is a list of statements about your relationship with family and friends. Please indicate how much you agree or disagree with each statement as being true." The survey consisted of 23 questions:

1. My friends respect me.
2. My family cares for me very much.
3. I am not important to others.
4. My family holds me in high esteem.
5. I am well liked.
6. I can rely on my friends.
7. I am really admired by my family.
8. I am respected by other people.
9. I am loved dearly by my family.
10. My friends don't care about my welfare.
11. Members of my family rely on me.
12. I am held in high esteem.
13. I can't rely on my family for support.
14. People admire me.
15. I feel a strong bond with my friends.
16. My friends look out for me.

17. I feel valued by other people.

18. My family really respects me.

19. My friends and I are really important to each other.

20. I feel like I belong.

21. If I died tomorrow, very few people would miss me.

22. I don't feel close to members of my family.

23. My friends and I have done a lot for one another.

Then, the Systems Thinking Scale was opened and introduced to the participant by stating, "Now I would like to talk to you about your systems thinking. Please read each of the statements and indicate the frequency of agreement with the statement about when I (you) want to make any improvement in your life...." The Systems Thinking Scale consisted of 20 questions:

1. I seek everyone's view of the situation.
2. I look beyond a specific event to determine the cause of the problem.
3. I think understanding how the chain of event occur is crucial.
4. I include people in my family to find a solution.
5. I think recurring patterns are more important than any one specific event.
6. I think of the problem at hand as a series of connected issues.
7. I consider the cause and effect that is occurring in a situation.
8. I consider the relationship among people in my environment.
9. I think that systems are consistently changing.
10. I propose solutions that affect the environment, not specific people.
11. I keep in mind that proposed changes can affect the whole system.

12. I think more than one or two people are needed to have success.

13. I keep my goals in mind.

14. I think small changes can produce important results.

15. I consider how multiple changes affect each other.

16. I think about how different people might me affected by the improvement.

17. I try strategies that do not rely on my or others memory.

18. I recognize system problems are influenced by past events.

19. I consider the past history and culture of my family.

20. I consider that the same action can have different effects over time, depending on the state of the system.

Lastly, the Perceived Health Survey was opened and introduced by the PI by stating, "Please read the statement and select the best response that indicates your current perceived health." The Perceived Health Survey consisted of one question: How is your health in general? After the completion of the third survey, the participant was reminded that the surveys would be repeated at the completion of the intervention, in two months.

After the three surveys were completed, SystemCHANGE™ specific slides (see Appendix K) were shown and reviewed with the participant to help them understand the principles of SystemCHANGE™. The SystemCHANGE™ specific slides start with an overview of MA with the statements, "Everyone has challenges with taking their medications on time every day" and "We'd be surprised if you took your medication on time every day." The intent of the SystemCHANGE™ intervention is also described with the following statement: "The SystemCHANGE™ intervention is meant to help you focus on changing your medication taking routines and make medication taking an effortless habit by trying

'small experiments.'" The slides then describe the four steps of the SystemCHANGE™ intervention:

1. Exploring habits around medication taking time and task.
2. Trying a small experiment that changes medication taking habits.
3. Tracking medication taking with the MEMS® cap.
4. Evaluate how the change is working with the MEMS® cap medication taking report.

After reviewing the SystemCHANGE™ slides, the participant was asked if they had any questions. The teach-back method was used to check for understanding by asking; "To make sure I've done a good job of explaining this to you, tell me in your own words what SystemCHANGE™ is." A copy of the SystemCHANGE™ slides were provided to the participant, and she was encouraged to place them on the refrigerator with the MEMS® report. This "storyboard" approach was intended to be a visual reminder to increase awareness of medication taking and engage family and friends in the process (Russell et al., 2016).

Once understanding of the SystemCHANGE™ intervention was established, the PI introduced the MEMS® report (see Appendix L) by stating, "This is a report that shows your medication taking from the MEMS cap for the past one month. You used the MEMS cap for two months; however studies have shown the most recent one month are a better example of how you really take your medications. Let me help you understand this report." The PI showed the participant the personal MEMS® report from the last one month of the screening period. The PI oriented the participant to the report, pointing out the participant information (generic name of the medication being monitored, the range of dates for the report), general

information (the number of monitored days, number of prescribed doses, number of doses taken), taking information (% prescribed number doses taken, % days number of doses taken), and hours (interdose intervals and % prescribed doses taken on schedule), days (x-axis), times (y-axis), 6-hour medication taking goal (green bar), blue dots for each time the MEMS® cap was opened with a presumed medication ingestion, red triangles for missed doses, and gray bar when both doses are missed on a day. The PI then discussed the overall MA score with the participant as well as the reported MA rate for each day of the week. The PI then asked, "What is your adherence goal?" For those who stated an adherence goal below 100%, the PI helped the participant understand the goal should be 100%, and the PI could help them reach that goal. Any corrections to the report made from the MEMS® Diary were discussed. The PI used an encouraging approach with phrases such as "opportunities for improvement" and "possibilities for doing better" when discussing the report with the participant.

Once the MEMS® report was discussed, the PI introduced the *Important People Form* (see Appendix M). The PI asked the participant to identify the important people who are involved in the medication taking processes. The PI noted that this is a person who lives, works, or is around much of the time and can make a difference in medications processes. If a person was identified, then the PI, using the *Important People Form* as a guide, asked the following seven questions of the participant.

1. Does this person keep house with you?
2. Do you need to consider this person's schedule when you are deciding the best time to take your medications?

3. Does this person help you in carrying out daily living activities (bathing, eating, cleaning, washing clothes, commuting, etc.?
4. Can this person's decisions affect time, medication availability, or other resources needed for taking your medications?
5. Does this person's decision affect whether your medications are available for you to take?
6. Do you see each other on a daily basis?
7. Does this person affect how and when you socialize with others?

The participant answered "yes" or a "no" for each question related to the identified person. The PI discussed with the participant that it is not important whether this person is liked or not, and that this person may or may not also take medications. If the participant identified more than one person who shapes the medication taking process, the steps would be repeated for each person identified. If an important person was not identified, the *Important People Form* was not completed.

Next, the participant's routines were identified using the Life Routines Form (see Appendix N). The PI asked the participant to identify routines that occur daily, weekly, or monthly, focusing on the impact each has on medication taking using the Life Routines Form. Daily routines were assessed first. The participant was asked to go through a typical day starting with waking up. The PI wrote down each event described by the participant on the Life Routines Form. Next, the participant described the activities that occur weekly starting with Monday, then Tuesday, until all of the days of week were discussed. The PI wrote down each event on the *Life Routines Form*. Finally, the PI asked the participant to identify routines that happen monthly. After discussing routines that occur daily, weekly,

and monthly, the PI and participant discussed activities that occur at different times. The periodic events were listed on the *Life Routines Form* with the average time of occurrence. Finally, the PI and participant checked that all major living activities (eating, cleaning, sleeping, shopping, commuting, work) were listed even if the activities did not occur with specific periods. The most likely time for the occurance of major living activities were listed as well as any activity that was part of obtaining medications or taking medications (e.g., obtaining a refill prescription from the transplant team, picking up medications from the pharmacy, paying for medications, placing medications in an organizer, placing medications around the house), included events and activities that prevent the participant from taking medications or taking medications on time. Examples include getting home too late from work, or forgetting because of sleeping late on a weekend morning, include social activities. For example, eating out or going to a movie may affect medication taking, include any rituals associated with medication taking (e.g., brushing teeth, making coffee, watching a TV show.)

Then the PI used the Life Routines Form to document the participant's descriptions of the frequency, activity, and the activity's impact on medication taking. The PI then read these notes back to the participant and guided the participant in looking for a stable activity which builds daily activities. The PI placed the collaboratively identified routines (daily, weekly, monthly) into the Cycles Form (see Appendix O). This graphic format helps participants understand the relationship between routines and how they work against changing medication behavior. The PI discussed daily, weekly and monthly cycles with the participant and noted how, for example, a routine such as sleeping late on weekends or working impacts medication timing.

Once life routines were identified, the PI and participant collaboratively considered possible environmental changes to enhance medication-taking routines during the home visit. The PI and participant used the Solution Assessment Scale for deciding whether the possible solution was a favorable one. The Solutions Assessment Scale is formatted using a single-item technique called a Visual Analog Scale. The Visual Analog Scale method uses lines, the lengths of which are taken to denote the continuum of some experience (Amico et al., 2006). The lines are horizontal, with stops ("anchors") at right angles to the line at both extremes representing the limits of the experience. The left end of the Solutions Assessment Scale is labeled "Systems Oriented," and the right end of the scale is labeled "Personal Effort/Motivation." Using the Solutions Assessment Scale, the participant made a mark to determine if the solution identified is systems oriented or based on improving personal effort or motivation. The PI encouraged the participant to prioritize one solution for implementation.

The participant was instructed to use the MEMS® Reader to send their MEMS® information each month to the PI. The PI showed the participant how to set the MEMS® on the Wireless Reader and told them it turns blue when it is working. The PI informed the participant that the PI would call them on the telephone and walk them through the steps when the participant was sending the MEMS information to the PI. The home visit ended with the PI and participant arranging a time for the PI to telephone the participant in one week to determine if the participant had implemented the solution identified.

The PI telephoned the participant one week after the home visit to assess correct MEMS® use using the MEMS® Use Form and asks them if the identified solution had been implemented, which the PI documented in REDCap® (Research Electronic Data Capture).

The PI encouraged the participant to continue using the MEMS®, and both agreed upon a telephone call in one month.

SystemCHANGE™ intervention: One-month call. The PI printed the MEMS® report, mail/emailed it to the participant, and telephoned the participant on the scheduled day and time to discuss it. The PI asked the participant: 1) Have there been any changes in their antithrombotic medication since the last month; describe the medication changes and 2) If there were medication changes, has this affected the medication that is being used with the MEMS® cap? The PI reviewed the MEMS® report with the participant. The PI used the Evaluation of SystemCHANGE™ Goals (see Appendix P) to ask the participant: 1) Tell me what you are learning about medication taking. 2) Do you think that the changes to your routines that you have made are changing your medication-taking? 3) Do you need to make other changes to your medication taking routines? The PI encouraged the participant to continue to use the solution identified during the home visit if appropriate. To keep the participant focused on the goal, the PI encouraged the participant to post medication-taking results in a prominent place for friends and family to see, assuming the participant is comfortable with a "storytelling" approach. The participants was encouraged to celebrate steps made toward improving medication taking because this would make the participant more committed and solidify the behavior change**.**

SystemCHANGE™ intervention: 2-month call and beginning of maintenance phase. At the end of Month 2 of the intervention phase, the PI brought closure to the adherence intervention by discussing the improvements that the participant made over the previous two months. The PI asked the participant: 1) if there were any changes in their antithrombotic medication since the last month and to describe the medication changes, and

2) If there were medication changes, did this affect the medication that was used with the MEMS® cap? The participant was also asked to complete the surveys Social Support Appraisals Index, Perceived Health, and Systems Thinking via telephone call, which was entered directly into REDCap® by the PI. The participant was asked to respond to four questions on The Medication Event Monitor (MEMS®) Use Survey. The PI introduced the four questions by saying "As you know, we are interested in knowing more about using the MEMS® caps. Thinking about how you used the MEMS® caps. . . "

1. Tell me what you think of the MEMS® caps.
2. Do you think that the MEMS® caps had a negative, neutral, or positive effect on your medication taking routine? Describe this to me.
3. How practical do you think using the MEMS® on a daily basis was for you? Describe what you mean.
4. Describe any instances when you think using the MEMS® as directed was difficult.

The responses were entered directly into REDCap® by the PI. The PI encouraged the participant to continue to use the MEMS® cap and diary for the next one month during the maintenance phase. A $10 thank-you gift card was mailed to the participant at the end of the intervention phase, after the PI received the MEMS® cap in the mail.

SystemCHANGE™ study completion: 3-month call. The PI contacted the participant via a telephone call. The PI mailed the participant a mailer to return the MEMS® cap and diary. A twenty-dollar thank-you gift card was sent to the participant when the MEMS® cap and *MEMS® Diary* were received in the mail.

Attention-Control Intervention

The PI, who is an experienced stroke nurse, delivered the attention control intervention. Table 3.4 shows the 2-month attention-control intervention. The stroke materials were developed by the Saint Luke's Marion Bloch Neuroscience Institute and are given to every stroke patient before dismissal. The PI called participants at Week 1, Month 1, and Month 2 to review chapter(s) from the book and answered questions about them. If the control participant raised questions about medications or medication-taking, PI referred them to their Neurologist. Interval, frequency, and setting of the home visit and telephone calls were all exactly the same for the intervention and control groups.

At the end of the intervention phase, PI closed the attention control intervention by reviewing the stroke information the participant reviewed during the previous month. The participants continued to use the MEMS® for the one-month maintenance phase. At the end of the maintenance phase, the PI reminded the participants to return the MEMS® cap and diary in the mail. They were also asked about the practicality of using the MEMS® cap.

Attention-Control Intervention Phase

Home visit. The PI began by introducing herself and asking the participant how things had been since last meeting. After introductions, the PI and participant sat at table where the participant and PI could easily work together with the PI's laptop. The PI then introduced the surveys to the participant. The first 20 minutes of the home visit involved the participant completing three surveys (*Social Support Appraisal Index,* Systems *Thinking* Scale, and *Perceived Health*) on the PI's touchscreen laptop. The participant either completed the surveys on his/her own or the PI read them to the participant and the participant pointed to the answer. The PI reminded the participant that there was no right or

wrong answers to the surveys. First, the *Social Support Appraisal Index* was introduced by the PI by stating "Below is a list of statements about your relationship with family and

Table 3.4

Summary of Attention-Control Intervention

Timing/ Content from "Stroke Education for Patients and Families?	Method/Content
Screening	MA electronically monitored for two months
Baseline: "Stroke Risk Factor Reduction," "Stroke Facts"	Home visit: with participant and important person if applicable (65 minutes): Education provided in person by PI at participant's home. A time to speak by telephone at 1 month is scheduled.
Week 1:	-Phone call: PI asks if the participant has any questions about chapters reviewed at the home visit - A time to speak by telephone at 1 month is scheduled.
Month 1: "Rehabilitation and Recovery"	Phone call: PI contacts participant for brief educational review and discussion of any questions.
Month 2: "Nutrition"	Same as Month 1.

friends. Please indicate how much you agree or disagree with each statement as being true."

The survey consisted of 23 questions:

1. My friends respect me.
2. My family cares for me very much.
3. I am not important to others.
4. My family holds me in high esteem.
5. I am well liked.

6. I can rely on my friends.
7. I am really admired by my family.
8. I am respected by other people.
9. I am loved dearly by my family.
10. My friends don't care about my welfare.
11. Members of my family rely on me.
12. I am held in high esteem.
13. I can't rely on my family for support.
14. People admire me.
15. I feel a strong bond with my friends.
16. My friends look out for me.
17. I feel valued by other people.
18. My family really respects me.
19. My friends and I are really important to each other.
20. I feel like I belong.
21. If I died tomorrow, very few people would miss me.
22. I don't feel close to members of my family.
23. My friends and I have done a lot for one another.

Then, the *Systems Thinking* Scale was opened and introduced to the participant by stating, "Now I would like to talk to you about your systems thinking. Please read each of the statements and indicate the frequency of agreement with the statement about when I (you) want to make any improvement in your life...." The *Systems Thinking* Scale consisted of 20 questions:

1. I seek everyone's view of the situation.
2. I look beyond a specific event to determine the cause of the problem.
3. I think understanding how the chain of event occur is crucial.
4. I include people in my family to find a solution.
5. I think recurring patterns are more important thank any one specific event.
6. I think of the problem at hand as a series of connected issues.
7. I consider the cause and effect that is occurring in a situation.
8. I consider the relationship among people in my environment.
9. I think that systems are consistently changing.
10. I propose solutions that affect the environment, not specific people.
11. I keep in mind that proposed changes can affect the whole system.
12. I think more than one or two people are needed to have success.
13. I keep my goals in mind.
14. I think small changes can produce important results.
15. I consider how multiple changes affect each other.
16. I think about how different people might me affected by the improvement.
17. I try strategies that do not rely on my or others memory.
18. I recognize system problems are influenced by past events.
19. I consider the past history and culture of my family.
20. I consider that the same action can have different effects over time, depending on the state of the system.

Lastly, the Perceived Health Survey was opened and introduced by the PI by stating, "Please read the statement and select the best response that indicates your current perceived health."

The Perceived Health Survey consisted of one question: How is your health in general? After the completion of the third survey, the participant was reminded that the surveys would be repeated at the completion of the intervention, in two months.

After the three surveys were completed, the PI introduced the educational materials titled "Stroke Risk Factor Reduction" and "Stroke Facts." The PI reviewed the following topics while referencing the educational material: "Stroke Risk Factor Reduction": how modifiable risk factors can be managed, facts about stroke, risk factors for stroke, and signs of a stroke. "Stroke Facts": what is a stroke, what are the symptoms of a stroke, what are the types of stroke, what medications reduce the risk of ischemic stroke, and are strokes are diagnosed. The home visit ended with the participant and PI discussing a telephone call in one week to check on any further questions related to the materials, and the mailing of the second educational material in one month. A telephone call was scheduled to discuss the second material. The PI telephoned the participant to discuss any further questions related to the first educational material. The PI encouraged the participant to continue using the MEMS®, and both agreed upon a telephone call in one month to review the second educational material, "Rehabilitation and Recovery."

Attention-control intervention: One-month call. The second educational material was reviewed by the participant prior to the scheduled telephone call. The PI asked the participant via telephone call 1) if there were any changes in their antithrombotic medication since the last month and was asked to describe the medication changes; 2) If there were medication changes, has this affected the medication that is being used with the MEMS® cap? The PI briefly reviewed the educational material with the participant from the chapter titled, "Rehabilitation and Recovery" that included the following topics: What are the effects

of a stroke, recovering from a stroke, and what to expect after a stroke. The PI encouraged the participant to continue using the MEMS®, and both agreed upon a telephone call in one month to review the third educational material "Nutrition."

Attention-control intervention: 2-month call and beginning of maintenance phase. The third educational material was reviewed by the participant prior to the scheduled telephone call. The PI asked the participant via scheduled telephone call 1) if there have been any changes in their antithrombotic medication since the last month and was asked to describe the medication changes; 2) If there have been medication changes, has this affected the medication that is being used with the MEMS® cap? The PI briefly reviewed the educational material from the chapter titled "Nutrition" with the participant that included the following topics: healthy food choices and sodium-free flavoring tips.

At the end of Month 2 of the attention-control intervention phase, the PI brought closure to the attention-control intervention by discussing the overall knowledge gained over the course of the two months. The PI asked the participant: 1) if there were any changes in their antithrombotic medication since the last month and to describe the medication changes 2) If there were medication changes, did this affect the medication that was being used with the MEMS® cap? The participant was also asked to complete the surveys Social Support Appraisals Index, Perceived Health, and Systems Thinking via telephone call which was entered directly into REDCap® by the PI. The participant was asked to respond to four questions on The Medication Event Monitor (MEMS®) Use Survey. The PI introduced the four questions by saying, "As you know, we are interested in knowing more about using the MEMS® caps. Thinking about how you used the MEMS® caps. . ."

1. Tell me what you think of the MEMS® caps.

2. Do you think that the MEMS® caps had a negative, neutral or positive effect on your medication taking routine? Describe this to me.
3. How practical do you think using the MEMS® on a daily basis was for you? Describe what you mean.
4. Describe any instances when you think using the MEMS® as directed was difficult.

The PI encouraged the participant to continue to use the MEMS® cap and diary for the next one month during the maintenance phase. The PI reminded the participant that the MEMS® cap and diary were returned to the PI via the mail at the end of the one-month maintenance phase. A $10 thank-you gift card was mailed to the participant at the end of the intervention phase, after the PI received the MEMS® cap in the mail.

Three-months attention-control study completion. The PI contacted the participant via a telephone call. The PI mailed the participant a mailer to return the MEMS® cap and diary in. A $20 thank-you gift card was sent to the participant when the MEMS® cap and MEMS® Diary were received in the mail**.**

Procedures

Institutional Review Board approval was obtained from Saint Luke's Health System (see Appendix Q) and a Request to Rely was obtained from the University of Missouri-Kansas City (UMKC). Refer to Appendix R for a summary of the SystemCHANGE™ procedures.

Recruitment

The following recruitment steps were followed: The list of scheduled patients for the day was evaluated by Dr. Karin Olds or Dr. Crandall and the PI. Scheduled patients who did

not meet inclusion criteria based on age, diagnosis, known not to self-administer medications, or not prescribed a once-a-day antithrombotic were not approached for study participation. The remaining scheduled patients were approached by Dr. Karin Olds or Dr. Crandall during their scheduled follow-up appointment and asked if they would like the PI to explain the study in further detail. For those who agreed, the PI approached the stroke survivors and discussed possible participation in the study. Those who agreed to discuss participation with the PI continued the recruitment process in a private area in the Saint Luke's Neurology office. The PI provided an overview of the study. For those who were eligible but declined to be in the full study, the PI asked them if they would consent to supply demographics only. If so, only demographic data were collected. If the participant consented to the study, inclusion criteria were reviewed, and the cognitive screening exam was administered. If the participant was eligible to proceed, demographic information was gathered, and the participant received MEMS® cap and diary training. The PI also abstracted demographic information from the electronic medical record.

Study Contacts

The study had three phases: the screening phase, the intervention phase, and the maintenance phase. Study participation in the screening phase involved the initial contact after a scheduled neurology appointment and three telephone calls. Study participation in the intervention phase involved one home visit and three telephone calls for those in the SystemCHANGE™ intervention group and in the Education intervention group. An outline of study procedures for the SystemCHANGE™ intervention and Educational intervention is shown in Appendix R and Appendix S respectively.

Screening

After obtaining consent, the PI contacted each participant by telephone one week and one month after entering the screening phase of the study to assess MEMS® cap use using the MEMS Use Form. The PI also addressed questions, comments, or problems the participant may have had related to the MEMS® cap or MEMS® diary. This approach has been successful in improving MEMS cap usage in other MA studies (Matteson-Kome et al., 2014; Russell, 2010).

At the end of the second month, the PI called the participant to assess MEMS® use using the MEMS® Use Survey. The participant was reminded to return the MEMS® cap and MEMS® Diary in the mail using the postage-paid envelope provided by the PI. If the postage-paid envelope had been misplaced, a new postage-paid envelope was mailed to the participant.

Randomization

Once the PI received the MEMS® in the mail, participants with adherence scores < .97 were randomized to either the SystemCHANGE™ intervention or the attention control education intervention. To ensure balanced distribution to each intervention arm, a computer-generated block randomization with a block size of four was used (Polit & Beck, 2017).

Intervention

Following randomization, non-adherent participants were contacted by telephone to schedule a day and time for the PI to conduct a home visit. During the home visit, the participants randomized to the SystemCHANGE™ intervention and the education

intervention completed baseline measures: Social Support Appraisal Index, System Thinking Scale, and Perceived Health Survey.

SystemCHANGE™ intervention. During the home visit, the SystemCHANGE™ participants then received the intervention that included SystemCHANGE™ slides, review of MEMS® report, Important People Form for medication taking (if applicable), Life Cycles Form, Solutions Assessment Scale, and setting up the Wireless Reader . Upon completion of the intervention, the participant and PI arranged a time for the PI to telephone the participant in one week and in one month. The one-week telephone call was when the PI and participant discussed any questions related to the home visit.

Telephone calls. One-month call: The participants received the MEMS report in the mail/email prior to the one-month call. The participants were informed of their MA rate verbally, and the MEMS report provided a graphical display for feedback on their level of adherence. The participant and PI arrange a time for the PI to telephone the participant in one month. Two-month call: The participants received the MEMS report in the mail/email prior to the two-month call. The participants were informed of their MA rate verbally, and the MEMS report provided a graphical display for feedback on their level of adherence. During this call, the Social Support Appraisal Index, System Thinking Scale, and Perceived Health Survey were completed.

Attention-control education intervention. During the home visit, the attention-control participants received the intervention that included a discussion of the following chapters: "Stroke Risk Factor Reduction" and "Stroke Facts" from the Saint Luke's Marion Bloch Neuroscience Institute Stroke Education for Patients and Families. Upon completion of the intervention, the participant and PI arranged a time for the PI to telephone the

participant in one week and in one month. The one-week telephone call was when the PI and participant discussed any questions about chapters reviewed at the home visit.

Telephone calls. One-month call: The PI contacted the participant and discussed the following chapter "Rehabilitation and Recovery" from the Saint Luke's Marion Bloch Neuroscience Institute Stroke Education for Patients and Families. The participant and PI arranged a time for the PI to telephone the participant in one month. Two month call: The PI contacted the participant and discussed the following chapter: "Nutrition" from the Saint Luke's Marion Bloch Neuroscience Institute Stroke Education for Patients and Families. During this call, the Social Support Appraisal Index, System Thinking Scale, and Perceived Health Survey were completed.

Data Analysis

The UMKC School of Nursing and Health Studies biostatistician assisted the PI with analysis for this study. All statistical tests were conducted using SPSS V23 statistical package (SPSS Inc., Chicago, IL) and alpha level was set at 0.05.

Demographics

Demographics were summarized using descriptive statistics. Age was described using mean, standard deviation (SD), and range. Categorical data (gender, educational level, employment status, ethnicity, stroke etiology, the number of previous strokes, time since the last stroke, and medication) were described using percent of each group.

Aim 1

Aim 1 was to determine the feasibility of the SystemCHANGE™ intervention compared to an educational intervention in older stroke survivors to improve MA on a larger scale through formalizing the protocol, validation of recruitment and randomization

procedures, evaluating the intervention effect, and providing data for a power analysis. Participants' responses to questions, that were entered in RedCAP®, about their study participation and intervention experience were evaluated for themes. All feasibility data – enrollment rates, reasons for study exclusion, visit duration, and participant evaluations were used to refine the intervention protocol and in the design of follow-up trials.

Aim 2

Aim 2 was to pilot test the acceptability of a two-month SystemCHANGE™ intervention compared to a two-month attention control education intervention on MA in older adult, non-adherent stroke survivors by implementing the intervention and obtaining participant feedback on intervention protocol. Time was quantified, and perceived effort and practicality required by the participant for completion of survey instruments and each intervention step were evaluated. The PI analyzed open-ended questions for the frequency of themes.

Exploratory Aim 1

Exploratory Aim 1 was to explore the role of potential mediators and moderators of antithrombotic MA in older adult stoke survivors. Descriptive statistics for social support perceived health and personal systems behaviors were calculated for pre- and post-intervention measurements.

Exploratory Aim 2

Exploratory Aim 2 was to evaluate the effect of the intervention on MA. Trends in medication non-adherence differences between the two groups were identified. The difference between baseline and 2- and 5-month medication non-adherence scores were also examined and used to calculate effect size of the intervention.

Security Plan for Data

Participants were assigned a unique code number that the PI used for identification and linkage of all data and data forms. All data were entered and stored in the password-protected REDCap® data system. All electronic medication monitoring data, identified only by the participants' unique code number, was encrypted and sent wirelessly to the MEMS database. Only aggregate data were reported. All data analysis was completed by the PI and UMKC School of Nursing and Health Studies biostatistician. The UMKC School of Nursing and Health Studies biostatistician only had access to a subject number with no key to participants' identities.

REDCap®

The Center for Health Insights of the University of Missouri-Kansas City (UMKC) was used as a central location for data processing and management. Vanderbilt University, with collaboration of a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap® data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Center for Health Insights. The iterative development and testing process result in a well-planned data collection strategy for individual studies. REDCap® servers are housed in a local data center at the University of Missouri-Kansas City, and all web-based information transmission is encrypted. REDCap® was developed specifically around HIPAA-Security guidelines and is recommended to UMKC researchers by both the Privacy Office and Institutional Review Board. REDCap® has been disseminated for use locally at other institutions and currently supports 240+

academic/non-profit consortium partners on six continents and over 26,000 research end-users (www.project-redcap.org, accessed June 5, 2017).

Human Subjects Protection

Risk/Benefit Assessment

The study received IRB review and approval from Saint Luke's Hospital and a request to rely from UMKC prior to participant enrollment. This and the use of informed consent generally assisted in the protection of study participants.

Several strategies were developed to address the risks associated with use of the MEMS® caps. At the beginning of the screening phase, the participant received specific instructions regarding the use of the MEMS® cap and bottle. The participant transferred the designated drug to the bottle with the attached MEMS® cap. They were instructed how to refill the bottle with pills in order to replenish the bottle when needed. If a participant was using a pill box, the study staff trained the participant to use the colored marker or "Tic-Tac" to remind them to take their medication from the MEMS® bottle. Patients who wished to use a pill box or pocket doses were allowed to do so, and their adherence data were adjusted accordingly.

When carrying out the intervention in participants' homes (or neutral meeting place), the PI had a "buddy system" in place, whereby the PI informed a friend or colleague of the time, place, and duration of the interview, and arranged to call them once the interview was finished. If the researcher had not called by a certain time, the friend or colleague would then have sought assistance.

If the PI suspected abuse or neglect of the study participant, the PI would have reported the incident to the Missouri Department of Health and Senior Services (DHSS) to

investigate. The PI would have called the hotline at 800-392-0210. The hotline operates 365 days per year from 7 a.m. to 12 a.m. Any participants who reported the DHSS event would have been immediately withdrawn from the study, and IRB would have been notified.

The PI had completed CITI training, and thus was trained to protect participant confidentiality. The PI devised a plan with the participants for appropriate means of making contact with the participant. For example, what phone numbers they might use and whether they may leave a message or text message. Participants were assigned a study number on the signed consent, and all collected data were marked with study number only. The informed consent forms with participant name matched to study number were stored separately from the study data in a locked file cabinet in the PI's home office. Only appropriate study staff had access to study data. Only aggregate data were reported.

Ethical concerns arise whenever beneficial treatment effects are anticipated and some participants are assigned to a control group, especially if the control group receives no intervention. In this study, even control participants received an attention intervention, also considered low risk, which could have increased their MA.

The study procedures were performed parallel to the medical care plan; therefore study participation would not introduce direct medical or physical risk to the patient. To further reduce possible physical risk, the PI was trained regarding situations when they should refer the participant to the neurology office, forward information to the neurology office, or contact the neurology office directly. The PI was responsible for overseeing general project safety issues.

The evaluation of the risk-benefit ratio for this study involved minimal risk for the participant enrolled that was outweighed by a potentially large benefit for all stroke

survivors. Potential personal participant benefits and potential societal benefits support the appropriateness of the study.

Participants' Rights and Risks

Adverse events related to using MEMS® were unlikely. However, the PI asked participants during each telephone encounter if they had experienced any MEMS®-related problems with taking their medications. Any perceived problems were documented exactly as the participant presented them in REDCap®. The PI probed with follow-up questions. Any significant events would have been shared immediately with the Neurologist. Any participants who appeared to have experienced an adverse event related to using the MEMS® would have been immediately withdrawn from the study, and IRB would have been notified.

Major adverse events during this study were not anticipated. If the PI had been unable to contact a participant in normal channels, the PI would have made extraordinary efforts to contact the participant to determine if an adverse event had occurred. Appropriate notification of IRB would have occurred. No interim analysis of the data was performed since untoward effects were of such low risk.

Adverse Event reporting would have been followed using the Saint Luke's Health System's IRB. Any adverse event (an unfavorable and unintended event, symptom or disease that is associated with the study and not described by the investigator in the consent procedure) must be reported to the IRBs in writing within five working days. Any Serious Adverse Event (an event that is life-threatening regardless if associated with the study) must be reported immediately to the IRBs. All adverse events, serious and non-serious, would have been fully documented on the appropriate report form(s). For each adverse event, the

PI would have provided the onset, duration, intensity, treatment required, outcome, and action taken.

Privacy and Confidentiality

Participants' privacy were protected in several ways: 1) The PI recruited from the Saint Luke's Neurology office during a regularly scheduled stroke follow-up visit; 2) The home visit was completed in the participant's home or neutral meeting place of their choice; 3) All other study activities were conducted over the telephone.

There were several mechanisms to ensure the confidentiality of data collected from the participants. All paper files were stored in locked file cabinet in the PI's home, and electronic files were stored in password-protected files in REDCap®. REDCap® is a browser-based, metadata-driven software solution and workflow methodology for designing clinical and translational research databases and is designed to comply with HIPAA regulations. Furthermore, both paper and electronic files were identified only by a participant's ID number. Identifying information on the signed consent linking participants to their study ID number was retained off-site in a locked cabinet accessible only by the PI.

The data were entered and stored directly into REDCap®. The Center for Health Insights of the University of Missouri-Kansas City (UMKC) was used as a central location for data processing and management. Vanderbilt University developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap® data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Center for Health Insights. The iterative development and testing process results in a well-planned data collection strategy for individual studies.

REDCap® servers are housed in a local data center at the University of Missouri-Kansas City, and all web-based information transmission is encrypted. REDCap® was developed specifically around HIPAA-Security guidelines. REDCap® has been disseminated for use locally at other institutions and currently supports 900+ academic/non-profit consortium partners on six continents and over 138,000 research end-users (www.project-redcap.org). Only the PI had access to the password.

CHAPTER 4

RESULTS

Feasibility and acceptability pilot studies address the uncertainties that need to be clarified, as well as the processes and procedures that need to be implemented before a future fully powered trial can be planned. The purpose of this pilot study was to test the feasibility and acceptability of a two-month SystemCHANGE™ intervention in non-adherent older adult stroke survivors. The secondary aims were to evaluate whether the intervention had any effect on perceived health, systems thinking, and MA. This chapter is divided into four major sections. The first section summarizes the sample of participants who entered the screening phase of the pilot study. The second section of this chapter addresses the feasibility of the SystemCHANGE™ intervention and attention control education intervention. This summary includes a description of how the study protocol can be refined, how many participants met inclusion criteria, the number of participants needed to screen to identify 30 non-adherent participants, how many participants are needed to conduct a fully powered study, attrition rate, the feasibility of the participant to be involved in the intervention, and the extent of missing data. The third section of this chapter addresses the acceptability of a two-month SystemCHANGE™ intervention and attention control education intervention in this population. Included in this summary are a description of the intervention and survey demands on the participants, time required for the intervention and surveys, intent of the participant to continue the intervention after the end of the study, participants' feedback on the time spent in the study and the length of each session, and suggestions for improving the study. Finally, the exploratory aims are addressed.

A total of 30 participants entered the study screening phase, and 28 completed the study screening phase. Two participants were eligible to be randomized into the study, one in the treatment group and one in the control group. The enrollment data is presented in Figure 4.1: Enrollment Data Using CONSORT guidelines.

The screening sample population was 46.7% (14/30) male and 63.3% (19/30) female. Ages ranged from 50 to 84 years, with a mean of 64.8. Half the participants used a pillbox to organize their medications. Table 4.1 displays Screening Phase Demographics.
The participants took an average of 7.77 (SD=3.191) prescribed medications (including Aspirin), with a range of 3 to 15. The number of over-the-counter medications taken (excluding Aspirin) on a regular basis averaged 1.9 (SD=0.8), with a range of 1 to 4. Table 4.2 shows Characteristics of Screening Phase Sample: Continuous Variables.

Feasibility

Protocol Refinement

Once the participant consented to participate in the study, the PI collected demographic information and completed the Six Item Screener. PI obtained the demographic information from the electronic medical record for six participants (20%); they did not verbally answer the demographic questions. When completing the Six Item Screener, eight (26.7%) participants commented they had just completed similar questions during their scheduled office visit. After all questions about the study were answered and data were collected, each participant was given a blue, handled bag with the signed copy of the consent, postage-paid mailer, MEMS® cap and bottle, and MEMS® diary. The participants stated it

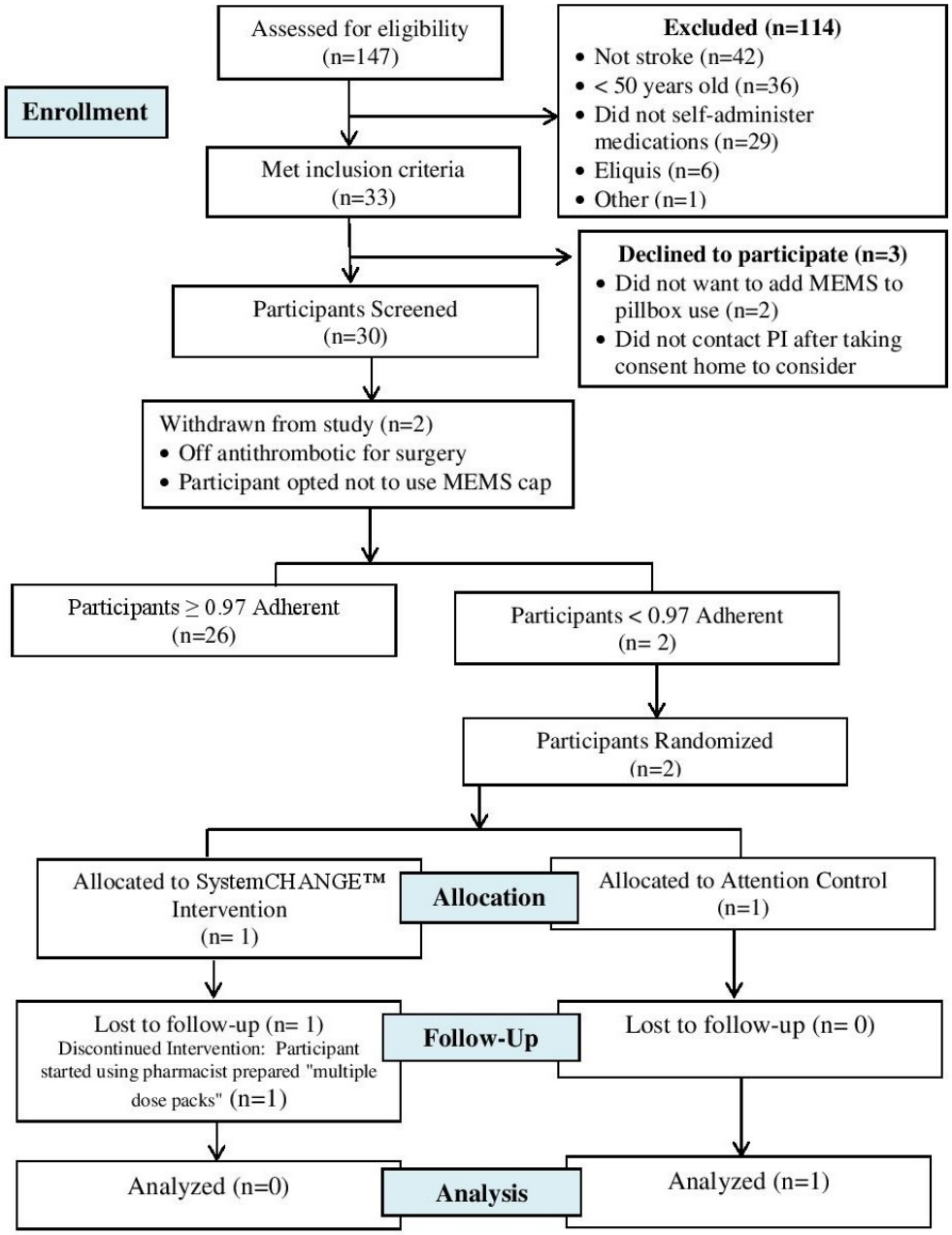


Figure 4.1. Enrollment Data Using CONSORT Guidelines

Table 4.1

Screening Phase Demographics

Characteristics	Screening Sample n (%)
Gender: n (% male)	14 (46.7)
Ethnicity	
Caucasian	19 (63.3)
African-American	7 (23.3)
Multiracial	2 (6.7)
Latino or Hispanic	1 (3.3)
American Indian	1 (3.3)
Marital Status	
Married	21 (70)
Divorced	3 (10)
Widowed	3 (10)
Never married	2 (6.7)
Living with someone	1 (3.3)
Employment Status	
Retired	13(43.3)
Employed full time	11 (36.7)
Disabled	4 (13.3)
Employed part-time	2 (6.7)
Date of Most Recent Stroke	
< 1 month ago	1 (3.3)
1 – 3 months ago	16 (53.3)
4-6 months ago	6 (20)
10-12 months ago	1 (3.3)
1-5 years ago	5 (16.7)
> 5 years ago	1 (3.3)
Antithrombotic	
Aspirin & Plavix®	12 (40)
Aspirin	10 (33.3)
Rivaroxaban (Xarelto®)	4 (13.3)
Warfarin (Coumadin®)	3 (10)
Clopidogrel (Plavix®)	1 (3.3)

Note. n = 30

Table 4.2

Characteristics of Screening Phase Sample

Characteristics	Mean (SD)	Median	Range
Age at Time of Entering Study	64.8 (9.496)	64	50 - 84
Number of Previous Strokes	1.43 (.568)	1	1 - 3
Number of Prescribed Medications	7.77 (3.191)	7	3 - 15
Number of OTC Medications (excluding Aspirin)	1.9 (.803)	2	1 - 4

Note. OTC: Over-the-Counted; SD: standard deviation
Continuous Variables (n=30)

was nice to have the handled bag to keep everything together. Of the 30 participants who entered the screening, two participants misplaced the postage-paid mailer. New mailers were sent by the PI to those who misplaced the original mailer.

The SystemCHANGE™ intervention and attention control education intervention were effectively delivered to the study participants. During the home visit, the PI used the SystemCHANGE™ protocol/education protocol to maintain fidelity of the intervention. When applying the protocol, the PI discovered the participants were comfortable completing the Support Appraisal Index, System Thinking Scale, and Perceived Health Survey on the PI's touchscreen laptop. When asked "Did you have any difficulty understanding any of the questions that were asked?" at the end of each survey, both participants answered "no." The SystemCHANGE™ participant commented she would prefer the PI to stay seated and available to answer questions as she was completing the three questionnaires instead of

getting up to check on the Wireless Reader. The participant randomized to the attention control education intervention preferred a public meeting location rather than her home for the home visit.

The telephone contacts at 1 week, 1 month, and 2 months were feasible. Each telephone contact was scheduled in advance during the prior contact with the participant. Both participants asked the PI for a text reminder of the upcoming call a day in advance so they would not forget about the call. The MEMS® training included the statement, "You must put your antithrombotic medication in the MEMS pill bottle. You cannot keep it in the pill box and then open and close the MEMS pill bottle as if you were taking the medication. We call this 'triggering the MEMS,' and you cannot do this because it will not document your medication taking correctly." Despite this education, the participant in the SystemCHANGE™ intervention deviated from the MEMS® cap protocol when she "triggered" the MEMS® to indicate taking her antithrombotic, but did not store her antithrombotic in the MEMS® bottle once she started receiving her medications in "multi-dose packs" from CVS pharmacy. The CVS multi-dose packs is an optional service offered by CVS Pharmacy in which all medications are organized into packs and labeled according to the date and time when they are to be taken. This deviation from the MEMS cap protocol resulted in the participant being withdrawn from the study by the PI one month and two weeks after the home visit of the intervention.

Potential Participants Who Met Inclusion Criteria

One hundred forty-seven patients were screened over 16 office visit days between November 28, 2017, and February 5, 2018. Each day, the PI and neurologist (Dr. Olds or Dr. Crandall) assessed the list of scheduled patients; patients who did not meet inclusion criteria

were identified based on age, diagnosis, and known history by Dr. Olds and Dr. Crandall. The enrollment data is presented in Figure 4.1: Enrollment Data Using CONSORT guidelines.

Number of Participants Necessary to Recruit and Assess to Identify 30 Non-adherent Older Adult Stroke Survivors

A total of 28 participants completed the screening phase to identify the two eligible non-adherent participants who could be randomized into the intervention phase of this pilot study. This is a non-adherence rate of 7% (2/28) (see Figure 4.1: Enrollment Data Using CONSORT Guidelines). Thus, 440 participants would have had to be screened to achieve this study's goal of 30 non-adherent participants.

Participants Needed to Conduct a Fully Powered Study

The number of participants who were non-adherent (n=2) was not sufficient to conduct a power analysis.

Attrition Rate

The attrition rate of screening was 6.6% (2/30). Two participants (6.6%) withdrew from the screening phase. One participant was taken off his antithrombotic medication for a surgery that resulted in a prolonged hospital stay. The second participant withdrew from the study because she had difficulty adding the MEMS® cap to pillbox use. When asked to explain "difficulty," the participant stated her bathroom was small and the area where she kept her pillbox was small; adding the MEMS® bottle to the area was too crowded. She also stated it was difficult to remember to take her antithrombotic from the MEMS bottle when all her other medications were in the pill box. The Tic Tac didn't really help because it was the

size of one of her pills. She would place all her pills, including the Tic Tac, in her hand and take all them at once.

Two participants entered the intervention phase with one participant randomized to the SystemCHANGE™ intervention and one participant randomized to the attention control education intervention, and one participant completed the study. Two participants did not complete the screening phase of this study.

Feasibility for the Participant to be Involved in the Intervention

At the completion of the intervention, both participants were asked for their perceptions of their respective intervention's burden. The feasibility of the SystemCHANGE™ intervention was found to be positive and without significant participant burden.

The participant in the SystemCHANGE™ intervention reported "very little" for the amount of time required for participation, and she had positive comments regarding her experience. The participant reported she had no significant inconvenience with her participation or with medication taking. During the 1-month telephone call, the participant was asked, "Do you think that changes to your routines that you have made are changing your medication taking?" She reported, "I really didn't change my routines. I just moved the pill bottle next to my bathroom sink." When asked, "Tell me what you are learning about medication taking?" she replied, "I'm learning that moving the medication bottle to a new location makes it easier for me to take it because it's there where I need it."

The participant in the attention control education intervention reported the "right amount" for the amount of time required for participation. She had no significant inconvenience with her participation or with medication taking. During the telephone calls,

the participant and PI discussed the assigned chapter. The participant stated she "liked being able to ask questions when I don't feel rushed. . . . the nurse at the hospital went over this book during my hospitalization but I just couldn't process the information."

Extent to which Adequate Fidelity to the Interventions Can Be Maintained

Fidelity is the extent to which the implementation of an intervention is faithful to its plan (Polit & Beck, 2017). There were two components of the interventions that were monitored for fidelity: the initial home visit in the participant's home and the subsequent telephone contacts. The SystemCHANGE™ intervention and attention control education intervention have four "components," including the home visit, 1-week telephone call, Month 1 telephone call, and a Month 2 telephone call. The dose of an intervention refers to each intervention contact or component (Conn & Chan, 2016). The dose of the SystemCHANGE™ intervention and attention control education intervention has two elements, "intended dose" and "delivered dose." The "intended dose" is defined as the number of participants intended to get the four SystemCHANGE™ intervention or attention control education intervention components. The "delivered dose" of the SystemCHANGE™ intervention and attention control education intervention is the number of components that were actually delivered, divided by the number of participants intended to receive the specific component of the SystemCHANGE™ intervention or attention control education intervention. The timing of the SystemCHANGE™ intervention and attention control education intervention components, or delivered dose timing, was defined as ± 2 days from the targeted intervention delivery date. Table 4.3 shows the SystemCHANGE™ intervention dose delivered to the intervention participant ,and Table 4.4 displays the Attention Control Education Intervention dose delivered to the attention control participant.

Table 4.3

Dose of SystemCHANGE™ Intervention

SystemCHANGE™ Component	Intended dose	Delivered Dose (%)	Delivered Dose Timing (%)
Home visit	1	1 (100%)	1 (100%)
Week 1 telephone call	1	1 (100%)	1 (100%)
Month 1 telephone call	1	1 (100%)	1 (100%)
Month 2 telephone call	1	0	0

Table 4.4

Dose of Attention Control Education Intervention

Education Component	Intended dose	Delivered Dose (%)	Delivered Dose Timing (%)
Home visit	1	1 (100%)	1 (100%)
Week 1 telephone call	1	1 (100%)	1 (100%)
Month 1 telephone call	1	1 (100%)	1 (100%)
Month 2 telephone call	1	1 (100%)	1 (100%)

Extent of Missing Data

The participant in the SystemCHANGE™ intervention completed the screening phase and 1-month and 11 days of the 2-month intervention. All data collected at the home visit including the Social Support Appraisal Index, Perceived Health Question, and Systems Thinking Survey, were entered into REDCap® by the participant using the PI's touchscreen laptop computer by the participant. However, the surveys were not completed at the 2-month telephone call due to the early withdrawal (19 days) of the participant.

The participant in the attention control intervention completed the 2-month screening phase, 2-month intervention phase, and 1-month maintenance phase of the study. All data collected at the home visit including *Social Support Appraisal Index, Perceived Health Question,* and *Systems Thinking Survey*, were entered into REDCap® by the participant using

the PI's touchscreen laptop computer by the participant. The *Social Support Appraisal Index, Perceived Health Question,* and *Systems Thinking Survey* data were collected at the 2-month telephone call. Printed copies of the surveys were left with the participant at the home visit. The participant was able to read along and see the choice of responses as the survey questions were read to the participant. The survey responses were entered into REDCap® by the PI.

Acceptability

Survey Demands and Time Requirements

The two participants' responses to completing the *Social Support Appraisal Index, Perceived Health Question,* and *Systems Thinking Survey* were positive, and both participants felt that the amount of time it took to complete the surveys of *Social Support Appraisal Index* (7 and 8 minutes)*, Perceived Health Question* (< 1 minute), *Systems Thinking Survey* (5 and 7 minutes) was acceptable. The participants did not voice any concerns or state that completing the surveys on the PI's laptop was burdensome. The participant in the attention control education intervention phase of the pilot study stated that completing the three surveys over the phone was more difficult than completing the surveys on the PI's touchscreen laptop, despite having a printed copy of the surveys available when answering the survey questions.

The initial home visit for the SystemCHANGE™ intervention was 54 minutes, and the home visit for the attention-control education intervention was 61 minutes. After completing the *Life Routines Form*, the participant in the SystemCHANGE™ intervention stated, "It would have been easier if I could have wrote down my routine myself, that way I could have filled in where I got things out of order easier." The 1-week follow-up telephone

call was 8 minutes and 6 minutes for the SystemCHANGE™ intervention and education intervention respectively. The 1-month telephone call was 13 minutes and 11 minutes for the SystemCHANGE™ intervention and education intervention respectively. The 2-month telephone call was 8 minutes for the education intervention. Lastly, the 3-month telephone call for the education intervention was 17.6 minutes.

Participants' Intent to Continue the Intervention

The participant who entered the SystemCHANGE™ intervention exited the study after one month and 11 days. She was withdrawn from the study due to the use of "multiple dose packs" from CVS pharmacy. Even so, she continued to use the SystemCHANGE™ intervention solution in addition to the "multiple dose packs."

Participants' Intent to Stay in the Assigned Groups

There was one participant randomized to the SystemCHANGE™ intervention and one participant randomized to the attention control education intervention. Neither participant expressed a desire to move to the other group.

Participants' Knowledge of Which Treatment they are in at the End of the Study

The participant randomized to the SystemCHANGE™ group was asked upon the exit of the study if she was in the intervention group or the control group. She replied, "I really do not know. My consent stated I would be randomized to either the SystemCHANGE™ intervention or an education intervention. I know I received the SystemCHANGE™ intervention, but I don't know it was the treatment or control." The participant in the education intervention could not determine if she was in the intervention group or the control group.

Do the Participants Feel the Time Spent per Session Was Too Long, Too Short, or Just Right?

The participant in the SystemCHANGE™ intervention reported "just right" for the amount of time required for each session: 54 minutes for the home visit, 8 minutes for the Week 1 telephone contact, and 13 minutes for the Month 1 telephone contact. The participant in the education intervention reported the time spent per session was "just right" for each session: 61 minutes for the home visit, 6 minutes for the Week 1 telephone contact, 11 minutes for the Month 1 telephone contact, and 10 minutes for the Month 2 telephone contact.

Do the Participants Feel the Time Spent in the Study Was Too Long, Too Short or Just Right?

The participant in the SystemCHANGE™ intervention reported the time in the study was "too long." She stated "the screening period was what made the study feel so long. One month of screening would have been perfect." The participant in the attention control education intervention stated the intervention was "just right." She went on to say the monthly telephone contacts "broke up" the time so that it didn't feel like five months.

Do the Participants Feel the Measures were Too Extensive?

Neither participant felt the measures were too extensive. The participant in the SystemCHANGE™ intervention stated having the MEMS® cap record the date and time she took her medication was nice because keeping a journal of when she took her medication would have been arduous. The participant in the attention control education intervention stated it would have been easier if the device used to electronically monitor her medication taking were more similar to using a pillbox so she could keep all of her medications together.

Participant Suggestions for Improving the Study

The participant in the SystemCHANGE™ intervention suggested that medication adherence should be measured with something that would not have excluded her from the study. When the PI asked her to explain what she meant, the participant stated she would have liked to have completed the study and recommended measuring MA with an electronic pillbox or electronic monitoring system that includes multi-dose packs. The participant also stated she would have liked to "have a version of this intervention as part of the Stroke Support Group meeting" she attends at Saint Luke's Hospital. The participant in the attention control education intervention recommended the surveys completed at the 2-month telephone call would be easier to complete if the surveys "could be completed using Survey Monkey" rather than answering the questions verbally. She also stated she "would have like knowing what her adherence score was each month."

Exploratory Aims

What is the role of potential mediators and moderators of antithrombotic MA in older adult stoke survivors in the SystemCHANGE™ intervention and those in the attention control education intervention?

Two participants entered the intervention phase of this study. Because of this, exploratory research questions could not be addressed.

What is the difference between the SystemCHANGE™ intervention and the education interventions' effect on antithrombotic MA?

Two participants entered the intervention phase of this study. Because of this, the difference between the interventions could not be determined.

CHAPTER 5

DISCUSSION

This pilot study achieved its objective of assessing the feasibility and acceptability of implementing a SystemCHANGE™ intervention and attention control education intervention in non-adherent adult stroke survivors. This chapter discusses the results of the study in relation to the study aims, existing literature, and conceptual framework. It also addresses the study's strengths and limitations as well as the implications for clinical practice and future research.

Feasibility

The SystemCHANGE™ intervention and attention control education intervention were effectively delivered to the study participants without any report of undue burden to the participants. Feasibility of the SystemCHANGE™ intervention was found to be positive and without significant participant burden, which was also the case in a similar kidney transplant sample (Russell, 2010). A primary goal of any intervention study is to maximize the dose of the intervention while minimizing the participant burden. The participant was active in identifying her existing habits and suggesting ways to place her medication in the right place at the right time.

Recruiting and Attrition

The screening sample population was comparable to the general stroke population of 48% male (Hall, Levant, & DeFrances, 2013). Participants' ages ranged from 50 to 84 years, with a mean of 64.8, which is comparable to the Adherence eValuation After Ischemic stroke–Longitudinal (AVAIL) study that evaluated 2,457 ischemic stroke or TIA patients in the AHA/ASA GWTG-Stroke registry who were discharged from 106 hospitals, where the

average age was 67 years old (Bushnell et al., 2011). Half the participants in this study used a pillbox to organize their medications. The participants took an average of 7.77 (SD=3.191) prescribed medications, with a range of 3 to 15. The number of over-the-counter medications taken (excluding Aspirin) on a regular basis averaged 1.9 (SD=0.8), with a range of 1 to 4. This is comparable to the stroke population in the AVAIL study where stroke survivors took 4–10 medications (Bushnell et al., 2011). Recruiting from the offices of Saint Luke's Neurology was effective. Of the 30 participants who entered the screening phase, two participants (6.6%) did not complete the screening phase of this study. This is comparable to previous studies with similar designs that have reported attrition rates between 6.4% (O'Carroll et al., 2013) and 13% (Evans-Hudnall et al., 2012). The screening sample, however, was not generalizable to the stroke population as a whole due to the majority of participants having had his/her most recent stroke one to six months prior to the pilot study.

Screening Adherence Rate

The results of previous studies evaluating post-stroke secondary prevention MA vary widely. The adherence rate in the screening phase of this study was 93%. This is similar to adherence rates of a study that used secondary data analysis that objectively measured adherence using prescription refill data for up to two years following a stroke event where MA at 3 months was 89% for warfarin and 96% for any antiplatelet drug (Glader, Sjolander, Eriksson, & Lundberg, 2010). In the Preventing Recurrence of Thromboembolic Events through Coordinated Treatment (PROTECT) study, antithrombotic MA rates of 98% were reported in 128 patients at one year of follow-up (Ovbiagele, Kidwell, Selco, Razinia, & Saver, 2005). The PROTECT study, however, was a single-center quality improvement

initiative that focused on evidence-based tools and algorithms for stroke prevention strategies.

The adherence rate in the screening phase of this study is higher than previous studies that included only non-adherent stroke survivors for intervention. O'Carroll et al.'s (2013) study identified 355 stroke survivors to participate in an MA interventional study, of which 190 participants (69%) were adherent at baseline and did not participate in the intervention phase of the study. Eighty participants were excluded for other reasons such as using a dosette box and requiring assistance with medication taking. A dosette box is a pill organizer that has separate compartments for the days of the week or times of day. The adherence rate is also much higher than published systematic reviews of MA in stroke survivors of 50% (Al AlShaikh, Quinn, Dunn, Walters, & Dawson, 2016; Bridgwood et al., 2018; Lawrence et al., 2015; Wessol et al., 2017). Additionally, the adherence rate in this pilot study is also higher than those found in systematic reviews of MA intervention targeting specific populations with chronic conditions in general adherence intervention literature ranging from 11% (Peterson, Takiya, & Finley, 2003) to 38% (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008). Adherence rates were also higher than those found in SRs of MA interventions targeting specific populations of older adults (59%) (Conn et al., 2009) and chronic conditions (24.8% and 54.1%, respectively) (DiMatteo, 2004); Kripalani, Yao, & Haynes, 2007).

The high adherence rates in this pilot study may be attributed to the multiple layers of stroke-specific education that the stroke survivors received from direct care nurses, advanced practice nurses, neurologists, neurointensivists, and hospitalists once they were admitted to Saint Luke's Hospital. Stroke survivors also receive a printed medication list and

prescriptions at dismissal. This is consistent with a 10-year longitudinal study by Thrift et al. (2014) that reported the most important factor associated with persistent MA was having a prescription at discharge from the hospital. In the same longitudinal study, the use of antithrombotic agents declined with each successive year (92% at discharge, 78% at 10 years; $P< 0.001$). In the AVAIL study, MA decreased from 76% at three months (Bushnell et al., 2010) to 66% at one year (Bushnell et al., 2011). Accordingly, the high adherence rate may be attributed to the disproportionately high number of participants (16/30; 53%) recruited whose most recent stroke event was three to six months prior to entering this study.

The multiple layers of stroke-specific education that are addressed at Saint Luke's Hospital include education about stroke and modifiable risk factors, starting at admission through day of dismissal. When a patient presents to the emergency room, the patient is specifically asked questions about their medical history, medication history, and surgical history, which includes if he/she takes anti-platelet or anticoagulation medications. Once a stroke is diagnosed, the education continues throughout the hospitalization. The treatment team is multidisciplinary to encompass all areas of stroke care and includes neurology, neurointensivists, hospitalists, rehabilitation, and pharmacy. This team works collaboratively to deliver the best care with the overarching goal of producing outstanding patient outcomes. These outcomes are defined by Clinical Practice Guidelines and are included in stroke-specific certification measures set by The Joint Commissions. At Saint Luke's Hospital of Kansas City, every stroke patient receives "Saint Luke's Marion Bloch Neuroscience Institute Stroke Education for Patients and Families" (stroke book). The stroke book fulfills The Joint Commission stroke education requirement that stroke patients receive education materials that address activation of the emergency medical system, need for follow-up after

discharge, medications prescribed at discharge, risk factors for stroke, and warning signs and symptoms of stroke (Joint Commission, 2018). The stroke book is used by all disciplines in the stroke program including the primary nurse, advanced practice registered nurses, and therapy teams to educate the patient; it has content about what medications reduce the risk of ischemic stroke and information specific to anticoagulants and antiplatelet agents. Added to the use of the stroke book, the patient care plan is initiated using mutually agreed upon goals of the healthcare professionals and the stroke patient. When the patient is dismissed, he/she receives a current medication list and an after-visit summary that includes the antithrombotic which the patient will take. This layering of education at Saint Luke's Hospital may be a contributor to high adherence rates in this study.

Acceptability

Consistent with prior SystemCHANGE™ intervention studies to improve MA, participants accepted the intervention (Matteson-Kome et al., 2014; Russell, 2010; Russell et al., 2018). The ability to deliver the intervention in the patient's home indicates the participants' acceptance of having a research nurse in the home. The recommendation of the SystemCHANGE™ intervention participant to "have a version of this intervention as part of the Stroke Support Group meeting" indicates that the intervention may more broadly translate in a group (Plow et al., 2013) or community setting (Komton, 2018).

Strengths

This pilot study is the first to focus on non-adherent adult stroke survivors, use electronic monitoring of adherence, and test the innovative SystemCHANGE™ intervention. The strengths of this study include the ability to recruit and retain (screening phase) older adult stroke survivors. An additional strength of this study was the use of a maintenance

phase. This study's focus on non-adherent stroke survivors at baseline was another strength, in that it prevented ceiling effect and evaluated the effectiveness of the intervention in the population of people who would be in need of adherence improvement.

In the 18 intervention studies reviewed to improve MA in adult stroke survivors, only one used electronic monitoring as the adherence measure (O'Carroll et al., 2013). Measuring MA via electronic monitoring is more expensive than self-report, but the information gleaned from the data is vital to the SystemCHANGE™ intervention because it allows the PI and participant to evaluate the three indicators of adherence: percent of dose taken, percent of days the correct number of doses was taken, and the percent doses taken on time (Neiheisel et al., 2014) using the MEMS® printout.

Effective interventions to improve MA in people with chronic illness are needed to bridge the research and practice gap (Haynes et al., 2008; Nieuwlaat et al., 2014). The World Health Organization (WHO) recommends that patients need to be supported rather than blamed for not taking medications as prescribed. Furthermore, the WHO suggests that integrating MA with a daily habit may improve MA (Sabaté, 2003). Russell, Ruppar, and Matteson (2011) recommend shifting attention to evaluate the ecological influences on MA, focusing on the individual- and micro-systems to identify possible solutions to have medication in the right place at the right time. Systematic reviews found behavioral interventions with self-monitoring and feedback were effective (Conn, Ruppar, Chase, Enriquez, & Cooper, 2015; Demonceau et al., 2013; Kripalani et al., 2007; Ruppar, Delgado, & Temple, 2015). This pilot study contributes further evidence that MA interventions based on participants' individual- and micro-systems have potential to shape medication-taking behaviors.

Limitations

The results of this study must be interpreted with caution because of the small sample size and the use of a convenience sample. The use of a convenience sample introduces the potential for selection bias because it is uncertain whether the sample studied is representative of the target population. For the findings of the study to be generalizable to the population as a whole, the sample must be representative of the population from which it is drawn (Polit & Beck, 2017). The sample in this study was biased to those whose most recent stroke was one to six months prior. The PI chose a specific disease population, non-adherent adult stroke survivors, to pilot test the SystemCHANGE™ and attention control education intervention. This study was not intended to have adequate power to perform hypothesis testing. Even so, the small sample size did not allow the PI to fully evaluate the frequency of responses to determine feasibility and acceptability of the intervention. The study could not determine the differences within and between the SystemCHANGE™ and attention intervention group. Additionally, the sample was not large enough to determine the effect size, nor was it large enough to conduct a power analysis to determine the sample size of a fully powered study. The MEMS® Cap is not a direct measure of MA because it is assumed when the bottle records an opening, the participant ingested the medication. Also, the MEMS® may have a Hawthorne effect; however, the PI excluded the first month's data during the screening period, thereby minimizing this effect.

Future work should include a larger sample size with greater diversity to explore differences between adult stroke survivors with varying date of most recent stroke. Study participants took a variety of antithrombotic medications, each of which may have varying influences on MA due to side effect profiles or cost. A larger sample would permit the

evaluation of covariates such as specific antithrombotic medication, medication class, level of disability, and varying times since most current stroke. The results from this study would be further strengthened by a longer duration of electronic monitoring for determining adherence rates, as a longer monitoring period would provide a complete picture of MA patterns.

Implications for Future Research

This study indicates recruiting older adult stroke survivors is feasible. Additional pilot testing is needed to determine the effect size for further testing in a larger randomized controlled trial. Additional research is needed to determine the role of potential mediators (e.g., social support and perceived health) and moderators (e.g., systems thinking and adherence level) of antithrombotic MA in adult stoke survivors. The role of environmental and system factors on medication adherence continues to require further study.

Additionally, future work should address the effect of the SystemCHANGE™ intervention in diverse stroke populations, such as stroke survivors with varying levels of disability and cognitive function. Also, including adult stroke survivors aged 18 and older should be considered to identify the age group(s) that is most non-adherent. Equally important, future work should include adult stroke survivors who have been prescribed antithrombotic therapy for varying time frames.

Conclusion

In conclusion, this study adds support to earlier findings that MA interventions based on participants' individual- and micro- systems have potential to shape medication-taking behaviors in adult non-adherent stroke survivors. The feasibility and acceptability evaluation

has shown the intervention protocol to be well received by the participants in this study, who did not view the study as burdensome or disruptive to their lives.

Future research will require pilot testing that includes participants with varying time since most recent stroke and multiple recruitment sties to increase generalizability and to fully evaluate the frequency of responses to determine feasibility and acceptability of the intervention. Then a fully powered study could be conducted with a design and sample size with adequate power for tests of statistical significance and the ability to analyze for subgroup differences. Variables such as the number of medications, number of daily doses, baseline adherence rate, and time since the most recent stroke event could be studied. There is evidence, however, to support targeting the individual- and micro-systems to establish habits as one component of interventions to improve antithrombotic medication adherence.

APPENDIX A

THE SIX ITEM SCREENER (SIS)

I am going to mention three things to you: apple, table, penny.

Now I'd like to ask you several questions:
1. What day of the week is it?
2. What month is it?
3. What year is it?

Thank you.

Now I'd like for you to tell me the three things that I mentioned to you earlier.
4. Apple
5. Table
6. Penny

Evaluation of Survey:

Time Taken to Administer Survey (in minutes): _____
Did you have any difficulty understanding any of the questions that were asked? Yes No
If yes, which ones did you have difficulty understanding?
Please suggest how the question(s) could have been asked so that they were clearer to you.

Scoring: The participant receives 1 point for each correct answer in questions 1-3 and 1 point for each of the three things that are recalled for a total score of 6. If 3 or more questions are missed, the Pp does meet inclusion criteria.

APPENDIX B

DEMOGRAPHIC INFORMATION

Gender: □ Male □ Female □ Binary
Age: □ 50-59 □ 60-69 □ 70-79 □ 80-89 □ 90-99
Educational Level: □ grade school □ some high school □ high school □ some college □ college graduate

Marital Status: □ married □ divorced □ never married □ living with someone

Employment Status: □ employed full time □ employed part-time □ disabled □ unemployed □ retired

Ethnicity: □ White □ Hispanic or Latin □ Black or African American □ Native American or American Indian □ Asian / Pacific Islander □ Other

Etiology of Stroke:

□ Ischemic (blocked artery) □ Transient ischemic attack (TIA) □ Hemorrhagic (brain bleed) □ Both ischemic and hemorrhagic □ Unknown

Number of previous strokes:

□ 1 □ 2 □ 3 □ 4 □ > 5

When did you have your stroke?

□ < 1 month ago □ 1 – 3 months ago □ 4- 6 months ago
□ 7 – 9 months ago □ 10 – 12 months ago □ 1- 5 years ago □ > 5 years ago

MEMS®

Date of MEMS® start:_____MEMS® number:_____

Medication:

Antithrombotic medications:

□ Aspirin □ Clopidogrel (Plavix®) □ Dipyridamole (Aggrenox®)
□ Rivaroxaban (Xarelto®) □ Dabigatran (Pradaxa®) □ Warfarin (Coumadin®)

- Medication taking time for antithrombotic medication: _____
- Do you use a pillbox for your medications? □No(0) □Yes(1)
- Number of current prescribed medications (excludes vitamins, over-the-counter medications _____
- Number of over-the-counter (non-prescription, **excluding Aspirin**) medications taken on a regular basis in the last 3 months, such an analgesics, allergy medications, etc. (A regular basis can be considered medications taken more than once per week.)_____

APPENDIX C

SOCIAL SUPPORT APPRAISALS INDEX (SS-A)

Below is a list of statements about your relationship with family and friends. Please indicate how much you agree or disagree with each statement as being true. (Using the scale below, circle one number corresponding to each statement.)

1 STRONGLY AGREE
2 AGREE
3 DISAGREE
4 STRONGLY DISAGREE

1. My friends respect me	1	2	3	4
2. My family cares for me very much	1	2	3	4
3. I am not important to others	1	2	3	4
4. My family holds me in high esteem	1	2	3	4
5. I am well liked	1	2	3	4
6. I can rely on my friends	1	2	3	4
7. I am really admired by my family	1	2	3	4
8. I am respected by other people	1	2	3	4
9. I am loved dearly by my family	1	2	3	4
10. My friends don't care about my welfare	1	2	3	4
11. Members of my family rely on me	1	2	3	4
12. I am held in high esteem	1	2	3	4
13. I can't rely on my family for support	1	2	3	4
14. People admire me	1	2	3	4
15. I feel a strong bond with my friends	1	2	3	4
16. My friends look out for me	1	2	3	4
17. I feel valued by other people	1	2	3	4
18. My family really respects me	1	2	3	4
19. My friends and I are really important to each other	1	2	3	4
20. I feel like I belong	1	2	3	4
21. If I died tomorrow, very few people would miss me	1	2	3	4
22. I don't feel close to members of my family	1	2	3	4
23. My friends and I have done a lot for one another	1	2	3	4

Evaluation of Form:

- Time Taken to Administer Survey (in minutes): _____
- Did you have any difficulty understanding any of the questions that were asked? Yes No
If yes, which ones did you have difficulty understanding?
- Please suggest how the question(s) could have been asked so that they were clearer to you.

APPENDIX D

PERCEIVED HEALTH QUESTION

We are interested in how you view your health. Please place a check mark in the box below the word that best describes your health.

	Excellent	Very good	Good	Fair	Poor	Very Poor
How is your health in general?						

Evaluation of Form:
Time Taken to Administer Survey (in minutes): _____
Did you have any difficulty understanding the question? Yes No
If yes, please suggest how the question could have been asked so that it was clearer to you.

APPENDIX E

SYSTEMS THINKING SURVEY

Instructions:
Please read each of the statements and place an "x" in the answer box that indicates the frequency of agreement with the statement:

When I want to make an improvement:	**Never**	**Seldom**	**Some of the time**	**Often**	**Most of the time**
1. I seek everyone's view of the situation.					
2. I look beyond a specific event to determine the cause of the problem.					
3. I think understanding how the chain of events occur is crucial.					
4. I include people in my family to find a solution.					
5. I think recurring patterns are more important than any one specific event.					
6. I think of the problem at hand as a series of connected issues.					
7. I consider the cause and effect that is occurring in a situation.					
8. I consider the relationships among people in my environment.					
9. I think that systems are constantly changing.					
10. I propose solutions that affect the environment, not specific people					

Systems Thinking Scale Continued

When I want to make an improvement:	Never	Seldom	Some of the time	Often	Most of the time
11. I keep in mind that proposed changes can affect the whole system.					
12. I think more than one or two people are needed to have success.					
13. I keep my goals in mind.					
14. I think small changes can produce important results.					
15. I consider how multiple changes affect each other.					
16. I think about how different people might be affected by the improvement.					
17. I try strategies that do not rely on my or others memory.					
18. I recognize system problems are influenced by past events.					
19. I consider the past history and culture of my family.					
20. I consider that the same action can have different effects over time, depending on the state of the system					

Evaluation of Form:

Time Taken to Administer Survey (in minutes): _____

Did you have any difficulty understanding any of the questions that were asked? Yes No

If yes, which ones did you have difficulty understanding?

Please suggest how the question(s) could have been asked so that they were clearer to you.

APPENDIX F

MEDICATION EVENT MONITORING

APPENDIX G

MEDICATION EVENT MONITOR (MEMS) DIARY

Write down any time that you accidentally open the MEMS, if you don't get the MEMS cap on tight, if you remove pills before time to take them, or any other situation that you think we should know about. This is very important so that we know when your MEMS may have been opened when you didn't take a pill. This diary will need to be returned to us when you return your MEMS caps.

Date	Time	Explanation of what happened

APPENDIX H

MEMS® USE FORM

Medication Event Monitor (MEMS) Phone Calls
PI Makes Notes for Phone Calls on This Form

Day 7 +/- 2 days

1. Do you have any questions about using the MEMS or MEMS diary? Tell me about how you are using them.

2. Is the use of the colored disks/Tic-Tacs making it any more difficult to take the antithrombotic medicines? Please tell me more about using the colored disks/Tic-Tacs.

1 Month

3. Do you have any questions about using the MEMS or MEMS diary? Tell me about how you are using them.

4. Is the use of the colored disks/Tic-Tacs making it any more difficult to take the antithrombotic medicines? Please tell me more about using the colored disks/Tic-Tacs.

APPENDIX I

MEMS® USE SURVEY

Medication Event Monitor (MEMS) Phone Calls
PI Makes Notes for Phone Calls on This Form

As you know we are interested in knowing more about using the MEMS® caps. Thinking about how you used the MEMS® caps:

1. Tell me what you think of the MEMS® caps.

2. Do you think that the MEMS® caps had a negative, neutral or positive effect on your medication taking routine? Describe this to me.

3. How practical do you think using the MEMS® on a daily basis was for you? Describe what you mean.

4. Describe any instances when you think using the MEMS® as directed was difficult.

APPENDIX J

SOLUTIONS ASSESSMENT SCALE

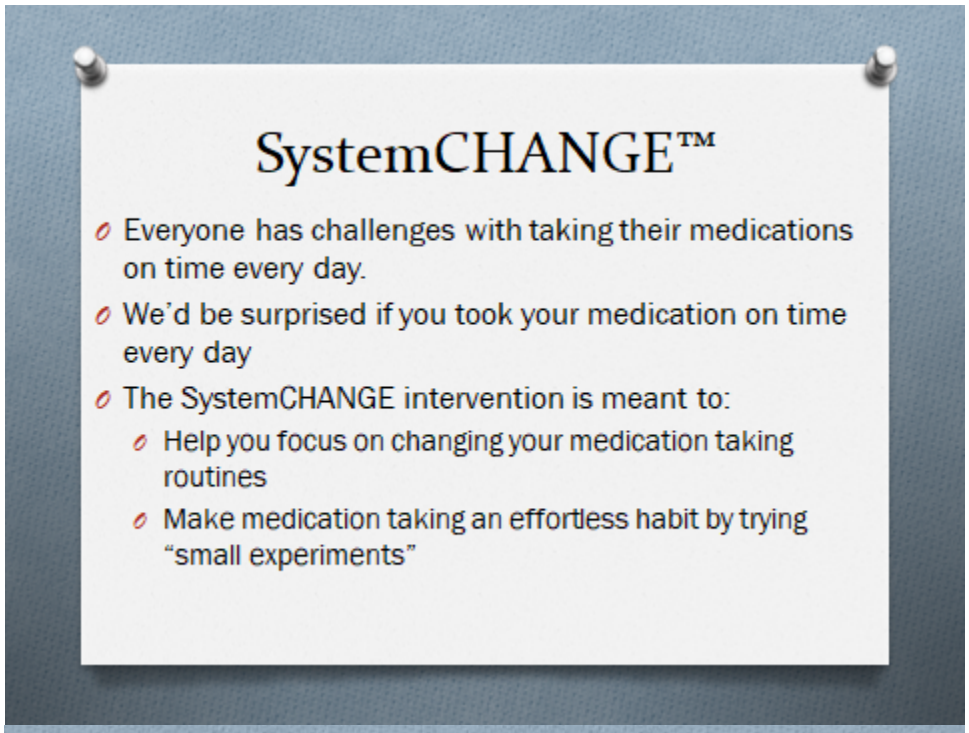
Solutions Assessment Scale

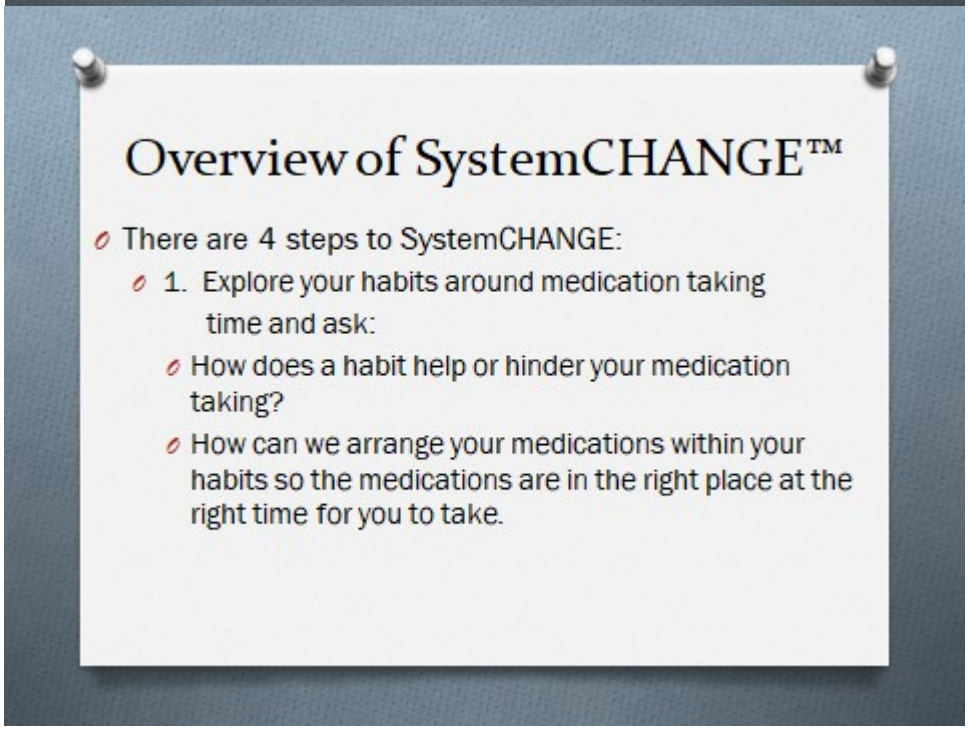
Systems Oriented ___ ___ ___ ___ ___ ___ Personal Effort/Motivation

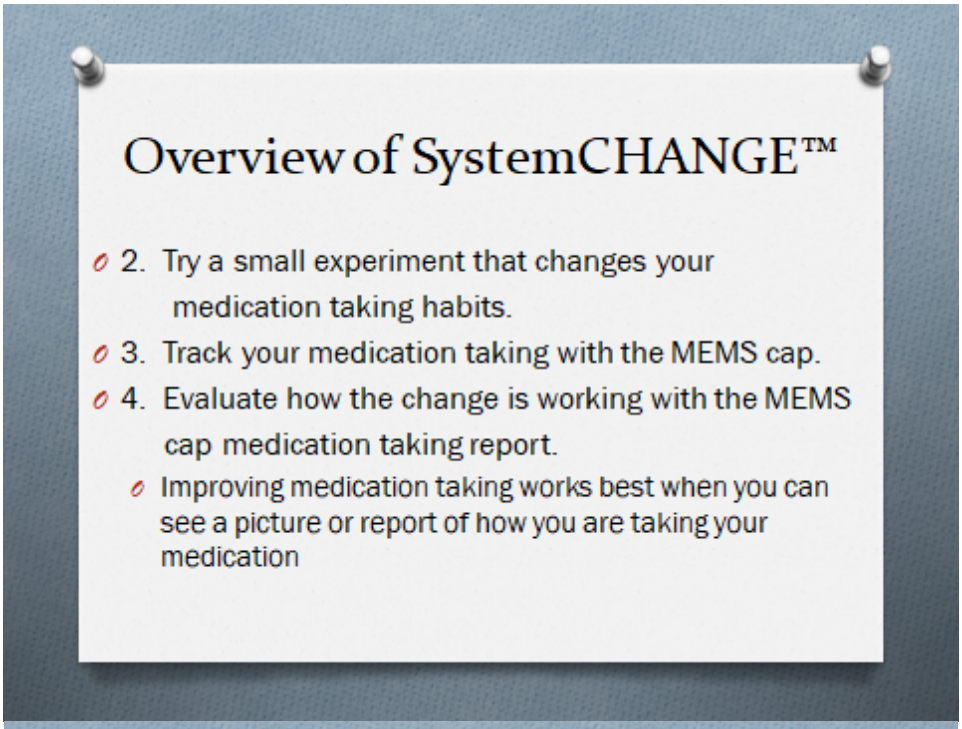
Evaluation of Survey:
Time Taken to Administer Survey (in minutes): _____
Did you have any difficulty understanding any of the questions that were asked? Yes No
If yes, which ones did you have difficulty understanding?
Please suggest how the question(s) could have been asked so that they were clearer to you

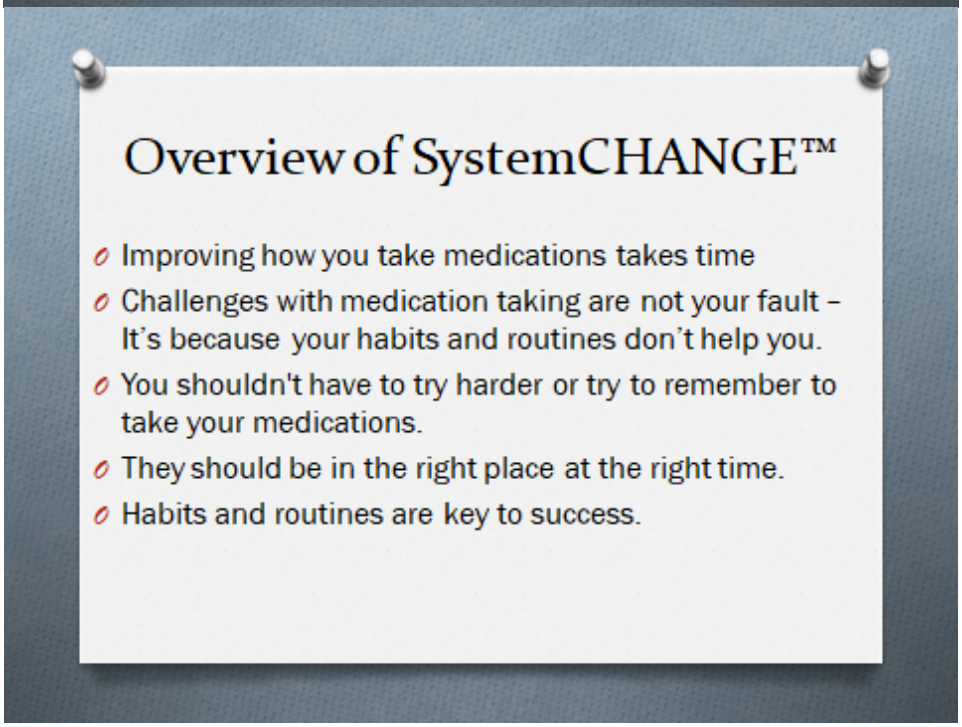
APPENDIX K

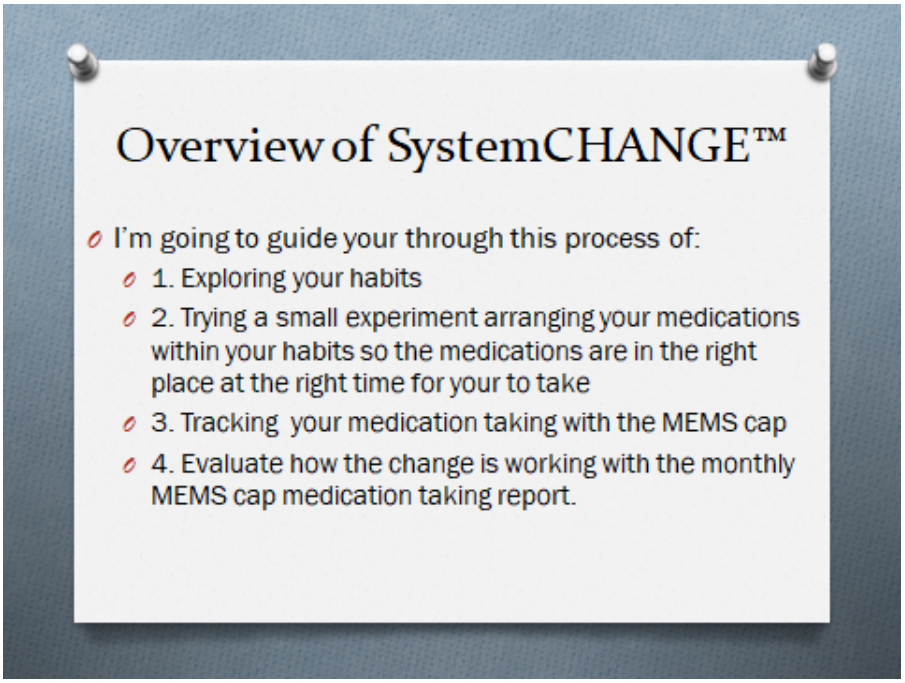
SYSTEMCHANGE™ SPECIFIC SLIDES






Overview of SystemCHANGE™
2. Try a small experiment that changes your medication taking habits.
3. Track your medication taking with the MEMS cap.
4. Evaluate how the change is working with the MEMS cap medication taking report.
Improving medication taking works best when you can see a picture or report of how you are taking your medication


Overview of SystemCHANGE™
Improving how you take medications takes time
Challenges with medication taking are not your fault – It's because your habits and routines don't help you.
You shouldn't have to try harder or try to remember to take your medications.
They should be in the right place at the right time.
Habits and routines are key to success.

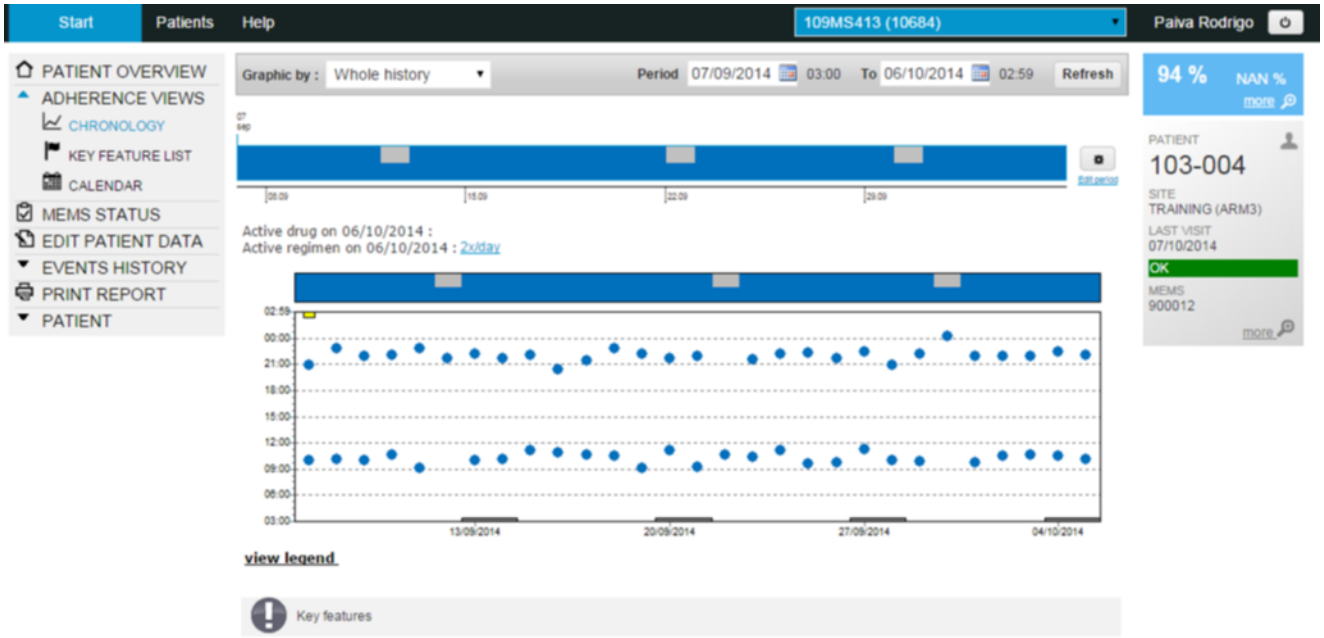

Overview of SystemCHANGE™
I'm going to guide your through this process of:
1. Exploring your habits
2. Trying a small experiment arranging your medications within your habits so the medications are in the right place at the right time for your to take
3. Tracking your medication taking with the MEMS cap
4. Evaluate how the change is working with the monthly MEMS cap medication taking report.


Questions?

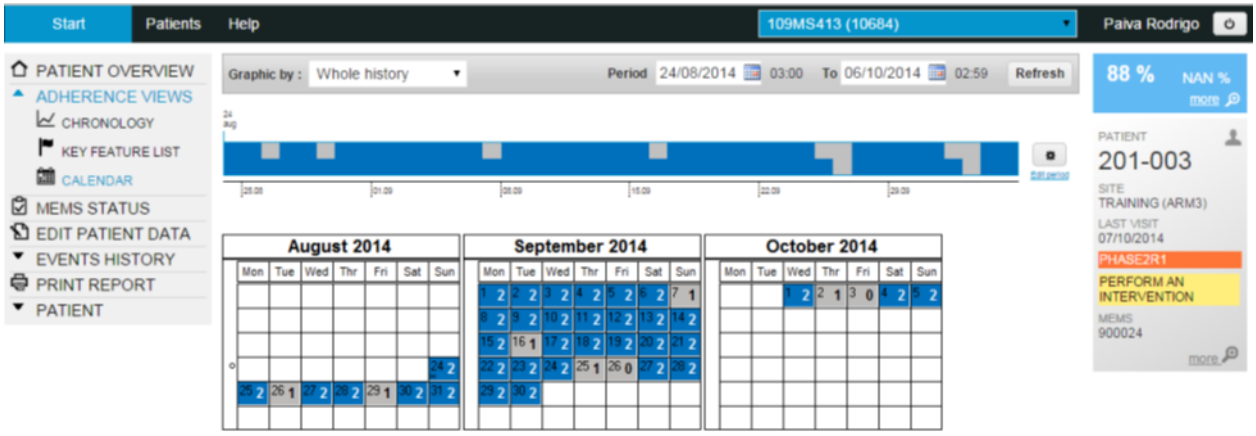
APPENDIX L

SAMPLE MEMS® REPORT

MEMS Chronology plot



MEMS Calendar



APPENDIX M

IMPORTANT PEOPLE FORM

Adapted from Alemi (Alemi & Neuhauser, 2005)

Important People Form		
Name of person (first name/relationship to you):	Yes	No
1. Does this person keep house with you?		
2. Do you need to consider this person's schedule when you are deciding the best time to take your medications?		
3. Does this person help you in carrying out daily living activities (bathing, eating, cleaning, washing clothes, commuting, etc.)?		
4. Can this person's decisions affect time, medication availability, or other resources needed for taking your medications?		
5. Does this person's decision affect whether your medications are available for you to take?		
6. Do you see each other on a daily basis?		
7. Does this person affect how and when you socialize with others?		
Total number of yes responses		

Evaluation of Form:
Time Taken to Administer Survey (in minutes): _____
Did you have any difficulty understanding any of the questions that were asked? Yes No
If yes, which ones did you have difficulty understanding?
Please suggest how the question(s) could have been asked so that they were clearer to you.

APPENDIX N

LIFE ROUTINES FORM

Adapted from Alemi (Alemi & Neuhauser, 2005)

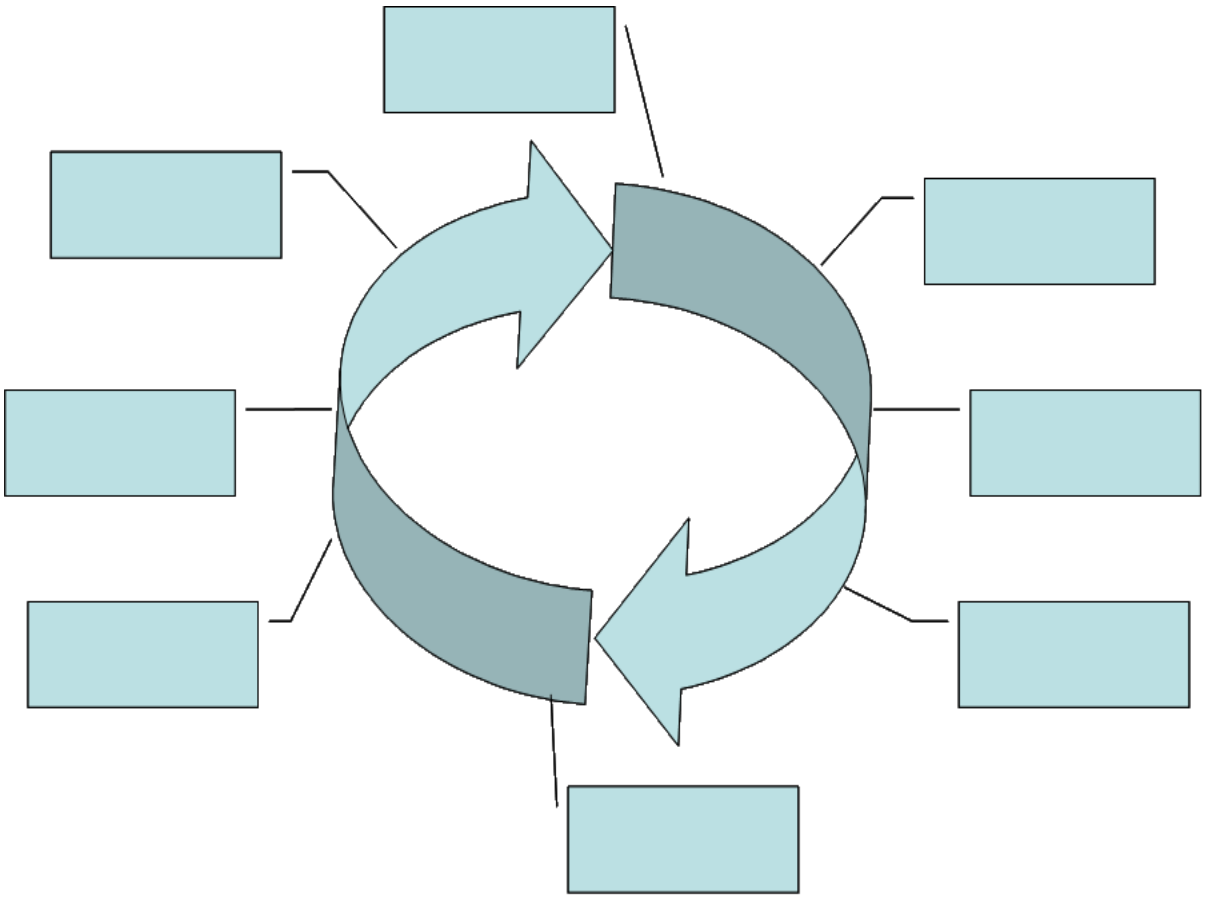
Life Routines Form		
Repeat time (daily, weekly, monthly, other)	***Routine (include any event that repeats over time, even if not at specific periods)***	***Impact on medication taking***

Evaluation of Form:
Time Taken to Administer Survey (in minutes): _____
Did you have any difficulty understanding any of the questions that were asked? Yes No
If yes, which ones did you have difficulty understanding?
Please suggest how the question(s) could have been asked so that they were clearer to you.

APPENDIX O

CYCLES FORM

Adapted from Alemi (Alemi & Neuhauser, 2005)



APPENDIX P

EVALUATION OF SYSTEMCHANGE™ GOALS FORM

Medication Event Monitor (MEMS®) Phone Calls
PI Makes Notes for Phone Calls on This Form

Tell me what you are learning about medication taking?

Do you think that changes to your routines that you have made are changing your medication taking?

Do you need to make other change to your medication taking routines?

APPENDIX Q

SAINT LUKE'S HEALTH SYSTEM IRB APPROVAL LETTER

Saint Luke's
HOSPITAL OF KANSAS CITY

4401 Wornall Road
Kansas City, MO 64111
816-932-2000

November 17, 2017

Jennifer Wessol, RN
4401 Wornall Road
Kansas City Mo 64111

Re: IRB# 17-154:
Feasibility and Acceptability of an SC intervention to Improve Medication Adherence in Older Adult Stroke Survivors: A Pilot Randomized Controlled Trial"
Approval of Initial Submission

Dear Jennifer Wessol, RN:

Please be advised that the above-referenced research was reviewed by the IRB Chair on 11/16/2017. The IRB concluded that your study is ***approved*** under expedited categories 5 &7.

Attached please find the final stamped and dated copy of the approved informed consent. You may now begin your research.

The IRB has determined that the ***continuing review*** of your research must occur annually. Your next continuing review must occur by 11/15/2018. It is your obligation to not let your IRB approval lapse, which will occur automatically on 11/15/2018. Please submit your continuing review materials to the IRB Office two months (60 days) before your approval would lapse.

We remind you that there are numerous ***investigator obligations*** that are applicable during the conduct of research. You are required to:

- Adhere to the Investigational New Drug (IND) Application and Investigational Device Exemption (IDE) regulations, if applicable. *See* 21 CFR Parts 312 and 812.
- Adhere to the human subject protections regulations and best practices in the conduct of research. *See* 21 CFR Parts 50 and 56 and 45 CFR Part 46 and International Conference on Harmonization E-6.
- Promptly report unanticipated problems that occur during the research to the IRB. *See* 21 CFR 56.108(b) and 45 CFR 46.103 and ICH E-6.
- Not make any changes to your research, including your protocol and the informed consent documents, without prior IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects. *See* 21 CFR 56.108 and 45 CFR 46.103.
- Maintain adequate, accurate, and complete study records. *See* 21 CFR Parts 312 and 812.
- Continuously oversee and monitor the conduct of your research for both data integrity and subject safety. *See* 21 CFR 56.111 and 45 CFR 46.111.
- Make sure your IRB approval does not lapse. *See* 21 CFR 56.109 and 45 CFR 46.109.
- Abide by all applicable Saint Luke's Health System policies and procedures.

Saint Luke's
HOSPITAL OF KANSAS CITY

4401 Wornall Road
Kansas City, MO 64111
816-932-2000

The IRB Office is available as a resource to you. Please let us know if you have any questions.

Sincerely,

Jennifer Murray
IRB Administrator

APPENDIX R

SUMMARY OF SYSTEMCHANGE™ INTERVENTION

Timing	Day	Office Visit	Home Visit	Phone Call	Method/Content
Screening	0	✓			- The PI will describe the intervention and obtain informed consent. - The PI will collect **demographic** information and complete the **Six Item Screener.** - Instruct participant on **MEMS® cap** and **MEMS® diary** use. - The PI will ask participant preferred communication method (email, text, phone).
	7±2			✓	- Assess correct MEMS® use and MEMS® diary use after training and use **MEMS® Use Form** to ask about MEMS® use
	30±2			✓	- Contact participant and follow the **MEMS® Use Form** to ask about MEMS® use.
	60			✓ ✓	Administer the **MEMS® Use Survey** PI will have the participant return the **MEMS® cap** and diary through the mail.
Intervention	60		✓		- **Introduction** - Briefly describe intervention (5 minutes) - Review **MEMS® reports** (5 minutes) - Ask preferred method to receive MEMS® reports - **The Social Support Appraisal** (5 minutes), - **Perceived Health Status Question** (2.5 minutes) - **Systems Thinking Scale** (10 minutes). - **Important People Form** (10 minutes)- Identify important people involved in medication taking. - **Life Routines Form** (10 minutes): Identify routines or habits that occur daily, weekly, or monthly focusing on their impact on medication taking. - **Cycles Form** (10 minutes): PI and participant collaboratively identified routines - **Solution Assessment Scale** (2.5 minutes): Collaboratively consider possible environmental changes that enhance medication-taking routines. - **Install Wireless Reader** (5 minutes): The PI installs the MEMS® wireless reader and teaches the participant how to use it. - A time to speak by telephone in 1 month is scheduled.

Timing	Day	Office Visit	Home Visit	Phone Call	Method/Content
	63±2			✓	PI asks if the participant has any the SystemCHANGE™ intervention and asks if the solution has been implemented. - A time to speak by telephone at 1 month is scheduled
	90±2			✓	Mail or email **MEMS® report** to the participant, Discuss if solutions helped if not identifies new solutions.
	120			✓	Mail or email **MEMS® report** to the participant. Close the intervention by discussing participant's improvements. Encourages participant to continue using the MEMS® cap and diary during the maintenance phase. - The **Social Support Appraisals Index, Perceived Health** and **System Thinking Survey** will be administered.
Maintenance	120				Participants will continue using the MEMS® cap and diary; there will not be any intervention or feedback.
	150			✓	Participants will be asked to mail the MEMS® cap back.

APPENDIX S

SUMMARY OF EDUCATION INTERVENTION

Timing	Day	Office Visit	Home Visit	Phone Call	Method/Content
Screening	0	✓			- The PI will describe the intervention and obtain informed consent. - The PI will collect **demographic** information and complete the **Six Item Screener.** - Instruct participant on **MEMS® cap** and **MEMS® diary** use. - The PI will ask participant preferred communication method (email, text, phone).
	7±2			✓	The PI will contact participant and follow the **MEMS® Use Form** to ask about MEMS® use.
	30±2			✓	The PI will contact participant and follow the **MEMS® Use Form** to ask about MEMS® use.
	60			✓	PI will have the participant return the **MEMS® cap** and diary through the mail.
Education Intervention	60		✓		- **Introduction** (5 minutes) - Briefly describe intervention (5 minutes) - Review **MEMS® reports** (5 minutes) - **The Social Support Appraisal** (5 minutes), - **Perceived Health Status Question** (5 minutes), - **Systems Thinking Scale** (10 minutes). - **Education** provided in person by PI. Discuss Chapters: "Stroke Risk Factor Reduction," "Stroke Facts" - A time to speak by telephone at 1 month is scheduled
	63±2			✓	PI asks if the participant has any questions about chapters reviewed at the home visit - A time to speak by telephone at 1 month is scheduled
	90			✓	Discuss chapter: "Rehabilitation and Recovery."
	120			✓	Discuss chapter: "Nutrition." Close the intervention by encouraging participant to continue using the MEMS® cap and diary during the maintenance phase. - The **Social Support Appraisal Index, Perceived Health** and **System Thinking Survey** will be administered.
Maintenance	120				Participants will continue using the MEMS® cap and diary; there will not be any intervention or feedback.
	150			✓	Participants will be asked to mail the MEMS® cap back.

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VITA

Jennifer Wessol was born August 18, 1972, in Kansas City, Missouri. She was educated at Park Hill High School in Kansas City, Missouri. She then pursued undergraduate studies and was awarded a Bachelor of Science in Nursing degree in 1995 from Avila College in Kansas City.

In addition to the pursuit to obtain a Ph.D. in nursing, Mrs. Wessol has spent over 20 years as a direct care nurse. She has worked at Baptist Medical Center as a float pool and telemetry nurse. She has been employed at Saint Luke's Hospital for 20 years in critical care positions, including cardiac catheterization lab, critical care float pool, and most recently as a Code Neuro Nurse.

Mrs. Wessol entered the University of Missouri-Kansas City School of Nursing and Health Science Ph.D. program with an ardor for nursing research focused on improving the lives of adult stroke survivors. Upon completion of the Doctor of Philosophy degree, Mrs. Wessol plans to continue working as a Code Neuro Nurse, researching, and teaching future nurses.