# Stroke Self-Management: Effect on Function and Stroke Specific Quality of Life

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## 1.0 Background

**Epidemiology of Stroke.** Stroke is a high volume medical condition. On average, one United States citizen experiences a stroke every 45 seconds. Stroke affects 700,000 persons each year in the U.S of which 200,000 are recurrent episodes.  Stroke is the third leading cause of death, produces the greatest number of hospitalizations for neurological disease and is the leading cause of adult acute-onset and long-term disability in the United States. Up to 50% of stroke survivors have some functional disability within 6 months of an ischemic stroke event. Veterans surviving stroke are even more vulnerable to functional disability given the recent reductions in rehabilitation facilities and the fragmentation of acute stroke care services. Stroke is estimated to affect at least 15,000 veterans each year with estimated costs of $111 million for acute inpatient care, $75 million for post acute inpatient care, and $88 million for follow-up care over 6 months post stroke.

Within the VA, approximately 60,000 patients had a primary outpatient encounter for stroke during fiscal year 2010 (FY10). Data from the Office of Quality and Performance (OQP) Stroke Special Study demonstrate that more than 5,000 veterans were admitted to a VA facility for acute ischemic stroke in FY07 and another 5000 veterans with a transient ischemic attack (TIA) or mini-stroke, were admitted in a VA facility or received care at an urgent clinic or emergency department in VA. One year post-stroke mortality for VA inpatients is approximately 20%; and 30% of veterans with stroke are discharged to non-community, institutional settings. The total VA cost of stroke treatment was almost $315 million in FY05, with a cost per patient of over $18,000. Moreover, patients who have had a stroke or a transient ischemic attack (TIA) are at risk for recurrent stroke and death. Over 12% of those with stroke or TIA will experience another stroke within a year. A recent study of Canadian TIA survivors reported a 22% rate of recurrent vascular events. Although some stroke risk factors are not modifiable (e.g. age), many stroke risk factors are modifiable (e.g., hypertension, and physical inactivity). Modifiable risk factors are most effectively managed through a combination of lifestyle and medication management and thus require strategies that target and support behavioral modification and the uptake of prescribed therapies by clinical providers.

**Stroke Prevention Efforts**. Although many stroke risk factors are modifiable, most patients with stroke or TIA do not have adequate control of their stroke risk factors. Data from the National Behavioral Risk Factor Survey indicated only 3% of adults living in the US reported healthy lifestyle characteristics (e.g., nonsmoking; healthy weight; regular physical activity; and consumption of five fruits and vegetables per day). In a recent randomized trial of high-dose folate vitamin therapy in patients with recent stroke, stroke survivors in the trial continued lifestyle practices that elevated their stroke risk (e.g., cigarette smoking). Many studies have documented inadequate control of blood pressure after vascular events.  Despite knowledge of the methods and impact of risk reduction, providers may not aggressively counsel or treat patients with behavioral or medical interventions for stroke prevention.

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**Current VA Secondary Stroke Programs**.  With the exception of the Bay Pines VAMC in Florida, we are aware of no systematic or standardized programs or support available in VHA to improve guideline adherence for stroke risk factor management.  Although some programs exist to support specific risk factor management (e.g. diabetes, or hypertension), these are not routinely targeted to veterans with recent stroke or TIA. Further, there is less support for management of behavioral risk factors and for improving stroke survivors' education and self-management practices. Yet, educating stroke survivors on stroke risk management is mandated by the VA/DoD stroke rehabilitation guidelines, championed by the American Stroke Association, and included in the JC criteria for stroke care. We have chosen to implement this program within a year of the stroke/TIA event given our previous experience in our pilot study. This time period provides a sufficient timeframe to harness a patient's motivation to change after stroke. In addition, our preliminary data from stroke survivors suggest that stroke survivors are ready to make lifestyle changes after their stroke hospitalization and have transitioned to home (see section C).

**Evidence-based Tools to Manage Stroke Risk Factors.** Research of existing stroke risk factor management tools revealed two systematic programs: the American Stroke Association (ASA) (a division of the American Heart Association, AHA) Get with the Guidelines (GWTG) Program and the Stroke PROTECT (Preventing Recurrence of Thromboembolic Events through Coordinated Treatment) program. Both programs are based upon the AHRQ, clinical guidelines for stroke, as are the VA/DoD guidelines for stroke rehabilitation.  During acute care for stroke, one of the recommended goals is to begin therapies for prevention of recurrent stroke.

**American Stroke Association (ASA).** The Get With the Guidelines Program (GWTG) is a hospital-based quality improvement program developed to improve care for patients with cardiac disease and stroke and to obtain a 20% reduction in heart disease, stroke, and risk by 2020. The GWTG Stroke program focuses on implementing guidelines for acute stroke treatment and ischemic stroke prevention. The program identifies local champions to lead the hospital's team to implement the guidelines prior to patient discharge as research has shown that patients are more likely to comply with medication prescriptions at 6 months if medications are started during hospitalization.  For ischemic stroke prevention, providers target smoking cessation counseling, lipid and cholesterol levels, anti-thrombotics, weight and exercise management, atrial fibrillation, and diabetes management. The stroke module has been rolled out to over 1392 hospitals since 2003 and the Bay Pines VAMC is the only VA hospital included in part because of the external data reporting requirements.  No data has been released to date specifically on secondary stroke risk factor management.

Most recently, the Scientific Council for the AHA published a set of clinical guidelines that promoted physical activity participation among stroke survivors to enhance functional status and minimize disability.  Although these guidelines and the complimentary physical activity monitoring tools are available from the ASA, there is no specific effort to provide them to veterans with recent stroke or TIA.

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We have incorporated the ASA risk factor management support materials into our stroke self-management program.

 **Patient Self-Management programs**. During the past several decades, patient-self management (PSM) programs have been developed to foster self care among patients with chronic disease.  Variation exists in terms of the program components, location of the program with the health care system and staff involvement.  Experts define PSM as strategies that enable the patient's ability to monitor and manage daily health and symptoms, to problem-solve to overcome barriers encountered, to modify lifestyle risk factors, and to communicate with clinical providers as active collaborators in defining and adhering to health and therapeutic goals.

The evidence on the effectiveness of (PSM) programs varies across chronic conditions. Randomized controlled trials of PSM programs have demonstrated improvements in outcomes for chronic medical conditions including asthma; low back pain; hypertension; arthritis; and diabetes. In addition, PSM programs offer patients options and strategies for coping with chronic medical conditions in order to function daily and maintain health-related quality of life. Patients with chronic disease are often left on their own to cope and manage their symptoms in between medical visits.

In summary, although a couple of hospital based quality improvement programs exists, there are no evidence based stroke self-management programs available to implement in VHA for patients surviving stroke and TIA.

**Deliverables to Veteran Health Administration**.  We have developed a stroke self-management program using core elements of a generic, evidence-based chronic disease program and infused the program with stroke specific elements based upon the input of key VA stroke stakeholders through a formal development evaluation. The programs include standardized manuals for the program provider and for the stroke/TIA survivor along with patient support materials (see Appendices 1 and 2). We have already fielded requests by front line VA nurses for stroke education materials. If our program demonstrates efficacy and later effectiveness, our ultimate goal is to assist the VHA in becoming a leader in high quality stroke care by implementing a stroke self-management for veterans with stroke and TIA in VHA inpatient and outpatient services in order to reduce functional disability, reduce stroke risk factors, and improve stroke specific quality of life. With future implementation across VA facilities nationwide in mind, we will upload all program materials into the VA Stroke QUERI toolkit that is available online and promoted in our dissemination efforts to clinical neurology providers in VA. <u>Thus, the deliverables to the VA from the proposed project are: 1) an evidence-based stroke self-management program including its standardized materials for VA providers and patients; 2) a formative evaluation of patient barriers and facilitators to stroke self-management.</u>

The audience for the information generated as a result of this study includes VA researchers, managers, clinicians, nurses, social workers, health psychologists and veterans themselves along with their caregivers. VA researchers, particularly health services and implementation researchers (including QUERI investigators)

will use our findings about stroke self management and risk factor reduction to inform the design of implementation projects including the use of tailoring strategies based upon resources and staffing. VA managers will use our data to plan similar projects or to extend risk factor management and self-management program to other high risk groups of veterans.  As the patient medical home interest in VA becomes more widespread in VA, the standardized program provides an opportunity for specialized outpatient care to collaborate with primary care services. Clinicians may use our data to stimulate and inform efforts at their own facility to increase stroke risk factor management and patient post stroke self-management and potentially reduce the occurrence of future strokes. Veterans will find our stroke self-management program and support materials helpful in defining the best care after stroke and improving their management of risk factors and maintain their community roles. In addition, the additional support from the program may increase Veteran stroke patient satisfaction with VHS. **Significance for the Veteran Health Administration**. Stroke affects at least 60,000 veterans each year and this number will likely increase as the veteran population ages. According to the ASA, the prevalence of stroke is expected to double by 2020 with the increased proportion of older adults nationwide. Our previous QUERI work indicates that stroke risk factors are often undermanaged by VHA. Our proposed study provides VHA with an evidence-based tool for implementing VA/DoD guidelines on secondary stroke prevention. Moreover, the proposed project will evaluate the program in 3 facilities with small, medium and large volume of stroke patients that will enable us to plan the tailoring of the program to accommodate the structure of VA neurological services across VHA. Furthermore, as VHA sets up its Patient Care Medical Home Labs with a focus on patient self-management and behavioral health, our stroke self-management program offers a standardized program with support materials for health psychologists and care managers to use for stroke survivors in outpatient care.

**Preliminary Studies**
 **Prior work that informs this project**. We have conducted several studies that provide critical background and data that led to the development of our stroke self-management program, inform this project, and illustrate how this project is a natural next step in our goal to improve the quality of care for veterans with stroke. In addition, our recently completed pilot study of our stroke self-management program provides key insight into the design and delivery of our proposed intervention. Dr. Damush has also conducted a successful study of a self-management intervention for primary care patients with low back pain, which informs our design of the lifestyle modification module.
 **Randomized controlled trials**. Dr. Damush was a co-investigator on a stepped care project for veteran and non-veteran patients with musculoskeletal pain of the low back, hip or knee and with depression.  Dr. Damush developed the pain self-management protocol, trained the nurse case managers, and directed the implementation of this portion of the intervention. From this study, we bring the experience of delivering a medication and lifestyle modification program in the VA outpatient care setting adjuvant to primary care services. The co-investigator,

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Dr. Williams, has recently completed an NIH-funded study investigating the effectiveness of an antidepressant case-management intervention vs. usual care in the treatment of post stroke depression. From this study, which completed enrollment of more than 400 stroke survivors and 250 family caregivers, we have gained important knowledge and experience that inform our study design in terms of identifying stroke patients at the time of hospitalization, successfully following them for as long as nine months post-stroke, interacting with our existing VA clinic systems to conduct the study, and detecting and managing symptoms in the post-stroke period. Moreover, IU Health Methodist Hospital in Indianapolis was one of the study sites for which our Research Coordinator, Ms. Gloria Nicholas, BSN, was the lead case manager. From this experience we have maintained a professional relationship with this local site which has become a primary stroke center certified by the Joint Commission and has agreed to be a local site for this proposed project.

**Qualitative Research**. Our team has also used focus groups to assist in the design and evaluation of primary care-based interventions. We completed 12 focus groups of veteran stroke survivors (6 groups had strokes and the other 6 had TIAs) at Indianapolis and Houston VAMCs. We queried participants and their family caregivers on stroke risk reduction practices, preferences, barriers encountered, provider assistance, and use of existing tools to assist with this management. Participants discussed their awareness and use of nutrition/dietician services, blood pressure home monitoring machines, smoking cessation preferences, and medication adherence strategies, lack of physical activity, anger management classes, and stress management techniques. The stroke survivors indicated that they were more willing to change behavior and manage stroke risk factors after the stroke, indicating that experiencing a stroke was indeed a teachable moment for stroke risk factor management.

**Patient readiness to change** – Across the groups, stroke survivors discussed what risky behaviors they stopped after experiencing a stroke as the stroke became a teachable moment. Indeed, some veterans who reported experiencing multiple stroke events said those events influenced them to change their behaviors. In sum, we have a multidisciplinary team with extensive experience in interview and focus group conduct and analysis, and intervention development. Finally, our team is experienced in conducting focus groups and semi-structured interviews for stroke research, including some recent examples that directly inform our design.

**Stroke Self-Management Pilot Study**

As a secondary objective of a VA IIR on the Detection and Treatment of Post-Stroke Depression (PI – Williams LS and Co-PI – Damush TM), we pilot tested our stroke self-management program at two VAMCs (Indianapolis and Gainesville, Florida). The objective was to pilot test the effect of a self-management intervention to help patients manage post-stroke symptoms.

Design. We employed a prospective, randomized, outcome-blinded design to assess the impact of a self-management program vs. usual care among veteran stroke survivors at the two facilities. Outcomes were assessed by trained interviewers blinded to treatment assignment. Participants were identified during

admission for ischemic stroke and were randomized in blocks of four, stratified by site and by receipt of inpatient rehabilitation (as a marker of stroke severity), to the patient self-management intervention or usual care intervention. Enrollment took place within a month of stroke discharge. Participants were consented using standard procedures in compliance with local IRB and VA guidelines.

Intervention: The program applied theoretical concepts of Bandura's Self-Efficacy to the intervention components: Verbal Persuasions (e.g. doctor recommendations), Social Modeling/Vicarious Experiences (e.g., learning from other stroke patients experiences), Past Achievements (e.g., smoking relapse), and Reinterpretation of Sensations/Physical State (e.g. use of distraction and relaxation methods to thwart depression and anxiety). Participants received 6 biweekly telephone sessions to deliver the stoke self-management program or a placebo telephone call program that mimicked the intervention schedule. Sessions targeted primary outcomes of stroke self-management, and secondary outcomes of self-efficacy. The self-management program followed a standardized manual (placebo call simply asked how the patient was doing), and interviews were conducted at 3 and 6 months with a booster call at 4.5 months. We based our self-management intervention on the Stanford Self-Management Program, a program centered on enhancing patient self-efficacy to manage symptoms.

Based upon the underlying theory and the results of our formative evaluation, we created a menu of stroke self-management topics that were incorporated into a 6-session program with a written standardized manual delivered bi-weekly primarily by telephone. The topics included: expectations after stroke; negative/positive thinking; addressing fears; meaningful activities; follow up medical visits; communication with providers and caregivers; adapting/coping with disabilities; medication adherence; physical activity to improve mood and energy; access to community resources; and stroke risk factor modification. Each session targeted building self-efficacy using goal setting and behavioral contracting. Each patient was coached to choose at least one specific goal to work on in each session, including the specifics of when, where, and for how long they would do the specific behavior. Patients rated their confidence in carrying out each behavior and were encouraged to only select behaviors that they rated a 7 out of a possible 10 (completely confident in doing). In the follow-up telephone calls, patients received individualized feedback about their progress toward their selected goal(s) and were encouraged to continue to work on the chosen behavior or to select or add a new behavior goal.

Enrollment, consent and other patient variables were collected at baseline (prior to hospital discharge or within four weeks of discharge). Outcomes were collected via telephone at three months and six months post-enrollment. Patients assigned to usual care received stroke education pamphlets and a general stroke education session at enrollment, and phone calls to assess stroke

symptoms (with no self-management training) at identical time points as intervention patients as an active attention control.

**Results**. We enrolled 63 veterans with stroke into the pilot program (41 from the INVAMC and 22 from the GVVAMC). The intervention and control groups did not differ on age, race, sex, or on percent living alone. The groups also did not differ on the admission NIH Stroke Scale (3.3 intervention vs. 3.3 control) indicating the participants had on average minor stroke severity. Although not statistically different, the intervention group had slightly higher baseline depression symptom scores than the control group (mean PHQ9 6.5 vs. 4.2).

Stroke Self-Management Intervention Processes. Of the six planned sessions, the average number of sessions completed by the intervention group was 5.0 and the average number of attention sessions completed by the control group was 5.7. The session rates completed did not differ by site. The most frequent activities reported in the behavioral plans by those in the intervention were the following: became active around the home; walked in the community; took pills as doctor recommended; ate healthy foods and eliminated unhealthy foods; practiced other physical activity and listened to relaxation CD.

Self-efficacy. Baseline mean score for the self efficacy measure of Communicating with Physician in the intervention group was 8.5 vs. 8.9 in the control group ($p > 0.05$). Mean change from baseline was significantly different between groups at the second follow up visit (intervention group with mean increase in confidence of 0.5 points vs. control group mean decline of 0.8 points. Model based estimates controlling for intervention group and visit also showed a significant difference in mean self efficacy of communicating with a physician at the $2^{nd}$ follow up visit (p-value = 0.0231).

Self-Management behaviors. Participants in the intervention group reported an increase in time spent in aerobic activity compared to the control group. At 3 months the intervention group demonstrated a mean increase in 47.6 minutes in intervention compared to a mean decrement of 3 minutes in the control group (p = 0.13); this effect was sustained at 6 months (increase in 24.4 minutes in the intervention group compared to increase of 4 minutes in control group, p = 0.50), although these differences were not statistically significant.

Stroke Specific Quality of Life. At baseline, subjects in the intervention group had significantly lower (worse) mean scores for several SSQOL scales including Mobility, Thinking, Energy, and Work as well as SSQoL overall score. This imbalance is likely due to the relatively small sample size in this pilot study. Mean change from baseline in SSQoL Family roles (baseline intervention mean score = 3.6 and control mean = 4.2) was significantly different between groups at the 3 month follow up visit. On average subjects in the Intervention group showed an improvement of 0.5 points, while subjects in the control group showed a decline of 0.3 points. Model based comparisons at this time point were also different; however, this difference was only marginally significant with p-value 0.052.

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Mean change from baseline for SSQoL Social roles scores (baseline intervention mean score = 3.1 and control mean = 3.6) was significantly different between groups at the first follow up visit (intervention group improved by 0.3 points vs. control group decreased by 0.4 points). Model based comparisons also showed a similar difference at the first follow up visit with p-value = 0.04. Similar estimates of mean change from baseline of SSQoL Work scores were also significantly different between groups at the 6 month visit.
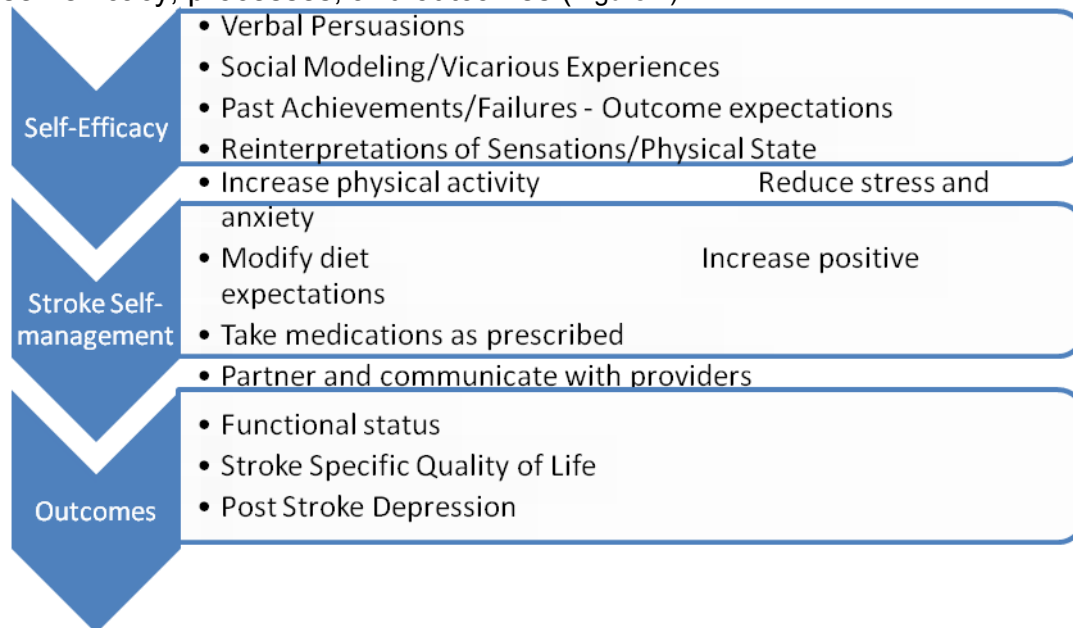
**Self-management intervention impact and context.** This study is one of the first to test the efficacy of a stroke self-management program that was developed with input from key stakeholders (i.e., veterans with stroke, caregivers, and clinical providers of stroke care). Currently, there are no other published results from a stroke specific self-management program. Our process measures indicate that offering a stroke self-management program after stroke is feasible. However, recruiting strictly from the acute stroke phase can limit the reach of this program into the veteran population, especially for VA facilities that provide less acute inpatient stroke care but may provide significant stroke rehabilitation or follow-up care. Although our sample size limited our statistical power to detect an intervention effect, we observed consistent differences in patient self-efficacy and stroke specific quality of life suggesting that the program has the potential to improve the quality of life of veterans with stroke. We employ this data to design and evaluate the efficacy of a more focused stroke self-management program (this proposed IIR).

**Conclusions/Impacts**. The results of this study demonstrate feasibility in participating in a self-management program for veteran stroke survivors. Veterans with stroke may have some unique needs for self management support for some issues including feeling confident and comfortable enough to leave the home and participate in the community after stroke. A lack of transportation services and difficulty with reading and writing after stroke may produce challenges in the process of learning self-management. Thus, we offer our program both in person and by telephone to meet the delivery needs of the veteran.

| LESSONS LEARNED FROM PREVIOUS RESEARCH | IMPLICATIONS FOR THE PLANNED INTERVENTION |
|---|---|
| Reasons for refusal to participate included needing time to adjust before participating in a program | Extend the recruitment period from 4 weeks to 12 months post stroke to account for the patient's readiness to change. |
| Short- term improvements in self-management reverted back to baseline after program ended | Extend the program from 3 months to 6 months to foster behavioral change. |
| Family role, Social role, and Work role functioning improvements were associated with intervention assignment. | Establish these outcomes as our primary outcomes of the trial and target the intervention to increase focus on these roles. |

| Reading and writing after stroke may be problematic for some stroke survivors. | Created a behavioral checklist to simply goal setting form. |
|---|---|
| Walking and working around the home were the most frequently report physical activities | Promote these activities in the exercise and physical activity component of the intervention. |
| Cell phone minute use to interact with staff was problematic for some veterans | Provide compensation for completing research assessments. |
| Stroke survivors desire for fellowship from similar stroke survivors. | Include monthly stroke support group during months 4-6. |

**C4. Theoretical Framework**. We employ the principles of Social-Cognitive theory [51] to guide the development of the intervention elements that target patient self-efficacy, processes, and outcomes (Figure 1).



**C.4b  Social Cognitive Theory and Patient Self-Management**: We will base our self-management intervention on the Stanford Self-Management Program, a program centered around enhancing patient self-efficacy to manage symptoms.[29,38] Self-efficacy, defined as the level of confidence in one's ability to perform a specific behavior, is a concept within social cognitive theory and is the link between knowledge and action.[51]  Patients may possess health knowledge, but may perceive themselves as incapable of performing health behaviors. According to social cognitive theory, a person's behavior is predicted by the confidence in ability to perform a specific behavior in a given situation and the outcome expectations of behavior performance.[51,52]  Bandura suggests that we are constantly processing, evaluating, and reevaluating information about our strengths and weaknesses, which form the basis for perceptions of abilities (i.e., self-efficacy). We evaluate even more when we encounter problems or new situations. Self-efficacy, in turn, affects the behaviors we choose or avoid and the amount of effort put forth to perform those behaviors (e.g., treatment adherence).

Self-efficacy perceptions are influenced by a variety of cognitive determinants, including: 1) verbal persuasion; 2) past experiences or performance accomplishments; and 3) vicarious experiences or learning through observation of events or other people. We will specifically address these cognitive determinants in our self-management program.   Physiological states

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also provide information to the person that may affect self-efficacy so we will assess patient-perceived symptoms as potential mediators of the intervention. In addition, we will employ this framework to guide our outcomes measurement and planned evaluations.

## Research Design and Methods

| STROKE SELF-MANAGEMENT STUDY DESIGN AND EVALUATION | | | | | | |
|---|---|---|---|---|---|---|
| RECRUIT | BASELINE | RANDOMIZE | INTERVENTION (6 months) | 3 MONTHS | 6 MONTHS | 12 MONTHS |
| | ASSESSMENT | | CONTROL | ASSESSMENTS | | |

**Study timeline (see Gantt Chart):** The study is planned for four years. We will devote our efforts to start up and training during the first 3 months of year 1 and then proceed with recruitment during Months 4 – 30. We will conduct follow up assessments through Month 42. We will finish year four with analyses of the intervention and a summative evaluation to guide our next phase of implementing the stroke self-management program.

### 2.0    Rationale and Specific Aims

Stroke is prevalent, costly and associated with increased long term disability, morbidity and mortality. Despite advances in the prevention and acute management of stroke, many patients do not receive high quality stroke care and there is wide variation in the transitional points of care across the continuum of stroke. Veterans with a stroke or transient ischemic attack (TIA) are at elevated risk for future vascular events within 90 days and death within the year. The VA/Department of Defense (DoD) and Joint Commission (JC) stroke clinical care guidelines promote the management of risk factors to prevent secondary stroke events. Yet, there are no post stroke programs designed and systematically offered to reduce this risk, and increase stroke, specific quality of life among veterans after discharge from VA.

Our previous research with key VA stakeholders, veterans and their caregivers, identified the recovery period after stroke as stressful and taxing as they attempt to self-manage their health with residual disabilities, navigate the VHA healthcare system, and cope with the loss of functioning and roles (family, social, work) and the consequential social isolation.

While disease specific programs exist for chronic conditions such as diabetes or specialty clinics are available for specific conditions (e.g., hypertension, anti-coagulation), to our knowledge, there are no published evaluations of stroke-specific self-management programs. Thus, we lack an evidence-based program to address the identified needs of veterans with stroke/TIA. We developed and pilot tested a stroke self-management

program that incorporated the general core elements of the Stanford University Chronic Disease Self-Management program and added stroke specific elements based on the results of our formative developmental evaluation with key VA stroke stakeholders. Our pilot test study demonstrated positive trends in self-efficacy, self-management and risk management behaviors, and stroke specific quality of life. We plan to incorporate the lessons learned from the pilot study to more rigorously test the effect of a stroke self-management program on functioning, stroke specific quality of life, and risk factor management in a randomized controlled trial. Our ultimate goal is to establish an evidence-based stroke self-management program to implement in VHA. The specific aims of this project are:

Primary Aim 1. To determine the effect of a stroke self-management program on stroke specific quality of life at 3, 6, and 12 months.

Secondary Aim 2. To determine the effect of a stroke self-management program on process factors: self-efficacy and self-management behaviors at 3, 6, and 12 months.

Secondary Aim 3. To conduct a summative evaluation at 12 months to understand patient barriers and facilitators to stroke self-management.

To evaluate these specific aims, this study will test the following hypotheses:
Hypothesis 1. Compared to subjects randomized to usual care, participants with stroke/TIA who are randomized to the stroke self-management intervention will demonstrate better stroke specific functioning and quality of life at 3, 6, and 12 months.
Hypothesis 2. Compared to subjects randomized to usual care, participants with stroke/TIA who are randomized to the stroke self-management intervention will report.

## 3.0   Inclusion Criteria
- age 18 or older,
- acute diagnosis of ischemic stroke or TIA within past 12 months,
- able to speak and understand English,
- no severe cognitive impairment,
  Our language and cognitive screening strategy is identical to that which we have successfully employed in our NIH-funded post-stroke depression study and our pilot study.  The cognitive screening is designed to allow patients with moderate cognitive and language effects of stroke to be included in the study. This is important because these stroke effects are critical impairments that impact patients and their families and may also impact the success of the intervention.  Cognitive screening will be done with Short

Portable Mental Status Questionnaire which assesses short- and long-term memory and orientation. This screener has been validated in a study of older community dwelling adults and we have also successfully used this screener in our VA study of PSD. All patients with a score > 6 will be enrolled, as this score has previously identified patients without severe dementia, which would decrease reliability of self-reported symptoms and satisfaction, while allowing the inclusion of patients with cognitive effects of stroke. Language screening will be done with the **National Institutes of Health Stroke Scale**, commands and language questions. Patients with significant language comprehension (commands score > 0) or receptive language deficits (aphasia score $\geq$ 2) will be excluded.

- access to a telephone,
- willing to follow-up in VA/IU Health/Wishard outpatient care,
- willing to attend all individual phone and group meetings during the 6 month intervention,
- life expectancy of at least 6 months as defined by the patient's treating clinical provider,
- No documented personality disorder diagnosed by a health professional,
- Ability to self-manage,
- No active alcohol and/or substance abuse,
- No end stage renal disease on dialysis.

## 4.0 Enrollment/Randomization

We will obtain written consent and enroll patients into this randomized controlled trial. Patients interested in participating in the study will be consented using standard procedures in compliance with local Institutional Review Board, HIPAA guidelines and VA R & D Committees. Patients would be given the opportunity to be consented via telephone and sign the written informed consent statement and HIPAA form by mail. All patients will receive a copy of the informed consent form, written in 6th grade English or less, and will be given time to read it or have it read to them and to ask questions.  For all potential study subjects, permission to discuss the study with the patient will be obtained from the attending physician prior to recruitment.  Methodist, Wishard, Roudebush, and Jesse Brown patients, who do not wish to participate in this study, will be excluded. Our investigators have extensive experience in recruiting stroke / TIA survivors for studies and are well-integrated into the local clinical and research culture at their respective facilities.

Indianapolis study team would also assist Jesse Brown study site to recruit, consent, administer assessments and conduct study intervention with Jesse Brown patients over the phone and via mail.

Retrospectively - We will use a modification of Reker's high specificity algorithm to identify patients hospitalized with acute ischemic stroke. Specifically, primary position admission ICD-9 codes related to ischemic strokes and TIAs (DXPRIME from PTF main) have been demonstrated to have at least 88% sensitivity and 90% specificity for identifying patients with acute ischemic stroke. These ICD-9 codes will be extracted from PTF main to identify the study sample in the VA and from INPC (Indiana Network for Patient Care) data by Regenstrief for the Methodist and Wishard patients. We will apply this algorithm retrospectively to identify Roudebush veterans meeting the study criteria during the past 12 months during the beginning of recruitment phase given that we are recruiting prospectively up to 12 months post discharge. We will add time since stroke event at baseline as a covariate in the analyses to control for this time effect. We have used these criteria successfully in past qualitative and administrative data research.

 Prospectively - Subjects will be identified during their stroke/TIA admission at Methodist Hospital, Wishard Hospital and Roudebush.   Indianapolis study personnel at each site will conduct daily screenings of neurology, medicine, and rehabilitation admissions (including review of electronic medical record and/or written admission logs and verbal contact with providers) to identify all patients with acute ischemic stroke/TIA at Methodist, Wishard and Roudebush VAMC.

We will obtain written consent and enroll retrospective and prospective patients into this randomized controlled trial at Methodist, Wishard and Roudebush. Patients interested in participating in the study will be consented using standard procedures in compliance with local IU Institutional Review Board, HIPAA guidelines and Roudebush VA R & D Committees. Patients would be given the opportunity to be consented via telephone and sign the written informed consent statement and HIPAA form by mail. All patients will receive a copy of the informed consent form, written in 6th grade English or less, and will be given time to read it or have it read to them and to ask questions prior to being consented.

We will use a stratified block randomization scheme. Randomization will be conducted with each stratum defined by site and stroke/TIA diagnosis. With each stratum, participants will be randomized by blocks of size 8. In other words, we will randomly assign equal number of participants in each block into the intervention or control group (i.e. 4 in intervention and 4 in control group). Randomization by blocks is used to ensure balanced number of subjects in two arms.

For the exit focus groups, we will take a random sample of approximately 25% of the study intervention subjects from each site and invite those participants o participate in an exit focus group. A total of up to 108 intervention subjects from Methodist, Wishard, Roudebush and Jesse Brown will be invited.  We plan to hold -up to 9 groups with  6-10 participants per focus group. At each site, one group will consist of subjects who completed all of the 12 week stroke self-management program to best understand compliance and motivation and the

other group will consist of subjects who completed less than the 12 week program to best understand their barriers. Two groups will be comprised of Jesse Brown participants, two groups will target Methodist participants, two groups will be comprised of Wishard participants and the remaining two groups will be comprised of participants from Roudebush VAMC.  Each focus group will meet once for up to two hours.  Sessions will be held in a conference room located at Jesse Brown VA, Roudebush VA, Wishard Hospital and at Methodist hospital, so that the location is easily accessible and familiar.  In the past, we have made transportation arrangements for participants and will do the same for participants in this study. Participants will be reminded by telephone one week before, and again two days before the focus group.

## 5.0    Study Procedures

Before study activities commence approval from IU IRB will be obtained followed by Roudebush VAMC Research and Development Committee approval.  Once all the necessary regulatory approvals are obtained we will commence this study. We will conduct a randomized controlled trial comparing subjects randomly assigned to the stroke self-management intervention to subjects randomly assigned to usual care. Subjects from both groups will be assessed at baseline, 3, 6, and 12 months. The stroke self-management program will be delivered over 6 months (12 weeks biweekly sessions followed by 12 weeks of bimonthly telephone and group support sessions). Usual care participants will receive written stroke risk factor materials. Our primary outcomes will be stroke specific quality of life and our secondary outcomes will be stroke self-management, self-efficacy, functioning, and post stroke depression. Additionally, we will hold focus groups with approximately 25% sample of intervention subjects from each site to best understand their barriers to participation and suggestions for future implementation. At each site, one group will consist of subjects who completed all of  the 12 week stroke self-management program and the other group will consist of subjects who completed less than the 12 week program.  The focus groups will be audio taped after participants have consented to be audio taped per VA and IU requirements.

**Patient self-management intervention**
5.a. Stroke Self-Management Program (SSMP) Overview: The stroke self-management program (SSMP) to be used in this trial includes core elements that have been shown effective in a primary care trial of veterans with musculoskeletal pain and depression conducted by our team as well as arthritis trials.  In addition, we have added stroke specific elements based upon our needs assessment of stroke survivors and input from clinical providers and family caregivers. Importantly, the SSMP is designed to assist veterans in identifying and improving self-management of a variety of common post-stroke symptoms and issues. Items listed below in the SSMP menu were derived from our focus group discussions.
As demonstrated in our pilot study, the SSMP will be delivered over 6 bi-weekly telephone or face to face sessions during the first 3 months and followed by 3

monthly reinforcement telephone sessions coupled with 3 monthly group sessions during months 4-6. The intervention subjects may choose to complete these sessions by phone or in person with the study care manager.  Additional telephone contacts will focus on reinforcing, monitoring, and adjusting the goals and self-management strategies (reinforcement calls). Support Group sessions and care manager telephone monthly call sessions during months 4-6 will promote maintenance. The first biweekly telephone or face to face session will take place after the baseline assessment is completed. The care manager will schedule subsequent sessions at a time convenient to the participant, every 2 weeks during months 1-3. During months 4-6, participants will receive 1 monthly call and will be expected to attend 1 support group meeting. Outcomes will be collected via interview at three, six, and twelve months post-discharge.
We have developed a detailed standardized program manual for all six self management sessions and included the following materials in the Appendices: 1) a detailed script for care manager which includes a summary of topics to be covered in the six sessions; 2) a patient standardized manual; and 3) a behavioral checklist for participant goal setting.

In subsequent telephone or face to face sessions, patients will receive individualized feedback about their progress. In addition, patients are encouraged to ask questions of their provider, participate in decisions about their healthcare, and to use positive talk and relaxation, two coping strategies that have been successful to manage negative affect. In subsequent sessions, patients may continue to work on the chosen behavior or may select a different behavior goal. Participants' chosen goals will be tracked by staff.
To promote self-efficacy, the program begins with patient education on the natural history of stroke and the rehabilitation process, emphasizing the potential outcome expectation for improvement over time.  This is designed to enhance patients' optimism for improved function and coping, but provide realistic expectations regarding disability.  Common diagnostic and treatment strategies will be discussed.  Post stroke symptoms and treatment strategies will be discussed as stroke survivors from the focus groups frequently mentioned that they did not recognize the symptoms of depression.  The instructor will promote behaviors based upon current evidence-based treatment recommendations found to have at least moderate support in the medical literature. In addition, patient education materials will show recommended exercises of stroke rehabilitation, including walking to improve mood and decrease fatigue. Patients are encouraged to adhere to their physicians' treatment recommendations, as well as to reduce their body weight (when appropriate). Another key issue identified from the focus group included adapting to a significant role change. Survivors and caregivers both reported a need to help the stroke survivor create a schedule or have something to do. We will incorporate the principles of behavior change to modify daily schedules of stroke survivors. To promote behavior change, the program includes goal setting and problem solving. Barriers to engaging in these behaviors are discussed.  During the planned meetings, patients will be educated on the benefits of physical activity for stroke and

depression management as well as the benefits of other strategies presented. Participants will be encouraged to develop an overall goal that they wish to achieve.

| Self-Efficacy Theoretical Concepts | Mapped Stroke Self-Management Strategies |
|---|---|
| 1. Verbal Persuasions | • Staff and lay leader explanations<br>• Promotion of physician and therapeutic recommendations |
| 2. Social Modeling/Vicarious Experiences | • Staff and lay leader demonstration of all strategies and new behaviors<br>• Peers practice behavior in group meetings and share vicarious experiences<br>• View material depicting stroke patients similar to them |
| 3. Past Achievements/Failures | • Set realistic, achievable behavioral goals<br>• Past failures may influence current level of effort so plan to overcome past failures.<br>• Gain an understanding of the course of stroke rehabilitation and realistic outcome expectations<br>• Negotiate the effort placed into cardiovascular risk factor modification |
| 4. Reinterpretation of Sensations/physical state | • Discuss symptoms and how to diminish<br>• Employ distraction methods – mental imagery<br>• Employ relaxation techniques |

Strategies to achieve these goals will be presented during the support group meetings. Patients will be encouraged to attempt incorporating strategies presented in group sessions or telephone meetings outside on their own. To increase self-efficacy, patients will set weekly, small behavioral goals that will eventually lead them to achieve their overall goal. The goals should be easy to accomplish and the patient should feel confident that she could achieve this goal over the next week. It is important for patients to succeed in obtaining their small goals (i.e., achieve mastery). This success builds self-efficacy and motivates future behavior performance. Patients will verbally commit to a goal each week, record this commitment on a behavior contract, attempt to achieve their goals in between class sessions, monitor and record behavior, and report back during the next session on their successes or barriers encountered. The support group will provide encouraging feedback and help patients with problem-solving to overcome their barriers. These methods improve self-efficacy by providing feedback and eliciting solutions regarding barriers from patients rather than the group leader. Patients learn to help themselves and understand the process of finding solutions in order to modify behavior long-term. In addition, sharing success stories provides patients with positive behavior models and vicarious experiences, thus enhancing self-efficacy.

According to Social Cognitive theory, increased patient self-efficacy to self-manage their stroke symptoms and to perform stroke self-management

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behaviors will empower the patient to engage in stroke self-management.
Increased stroke self-management therefore is proposed to improve patient
outcomes: functional status and stroke specific quality of life.

5.c  Telephone calls: the purposes of the telephone calls in the self-management
program are twofold. First, the 6 bi-weekly self-management intervention
sessions will be delivered by telephone during the first 3 months as we did in our
pilot study given that transportation and mobility barriers may hinder in-person
participation. Second, we will provide feedback and assist with goal setting
through bi-weekly telephone follow-up during months 1-3 and then monthly
during months 4-6. Calls will address the chosen behavior goal, self-
management strategies, and assess progress. We will help the patient problem-
solve and identify successes, and to modify goals and strategies appropriately.
At all calls we will ask patients to describe their current practice of chosen self-
management behaviors by type, frequency and duration. The staff will record
these practices and track in our database.

5.d. Quality Control. As we have previously done in prior studies, Dr. Damush will
observe a random sample of SSMP sessions by all instructors to insure the
fidelity of the program. We will utilize teleconferencing with the participant's
permission to have the call monitored during the session for quality control
purposes as we did in our pilot study. Dr. Damush will provide feedback to the
instructor as needed.

5.e  Support Group sessions: The SSMP sessions are based on Social-Cognitive
theory and focus on increasing self-efficacy and social support to self-manage
symptoms after stroke.  Participants will discuss goals and problem-solve to
sustain behavioral change.  Study staff will conduct the group SSMP sessions
using a standardized, written protocol. Since our focus group participants from a
prior research study comprised of stroke survivors stated that it was helpful to
hear from other stroke survivors, we will utilize the group sessions for stroke
survivors to share their successes and to help problem solve each others' issues
around stroke self-management and recovery. The Roudebush VA research staff
will provide the program for Wishard and Methodist participants as well given the
close proximity and their previous experience in doing so. Ms. Gloria Nicholas,
project coordinator and case manager, will train the Jesse Brown research staff
and provide monthly support as needed as she has previously done in our
previous research with staff located at external research sites. *Participants
enrolled in the intervention will be expected to participate at least one quarterly
support group session during months 4-6 months of their study participation.*  It is
anticipated each support group sessions will last 1 -1.5 hours.

After the completion of the 12 month assessment/interview, we will invite
intervention participants, who had attended at least 1 Stroke/TIA Support Group
while in the study, to attend the Stroke/TIA Support Group after they are finished
with the study. At the completion of the 12 month assessment/interview, we will
ask all participants in the intervention and control groups whether or not they are

interested in attending the Stroke/TIA Support group. Only those who say yes will then get invited for subsequent support group meetings.

5.f  Exit Focus Groups:  Focus groups are carefully planned group interviews guided by a facilitator to understand people's experiences on a given topic. They are ideal for understanding health care issues because group interaction produces insights that often do not surface in individual interviews.  The recommended method is to assemble people who have similar characteristics and experiences. Self-disclosure increases when participants can empathize with one another. In order to formally evaluate the process of implementation of the stroke self management program, we plan to conduct study focus groups during the last year in the study. The goal of these focus groups is a summative evaluation of participant barriers and facilitators.  The goal of this evaluation is to optimize implementation to improve potential for success. We will identify high and low stroke self-managers based upon program participation and our secondary outcomes and invite them to participate in an exit focus group.  We will query participants on their barriers and facilitators of participating in the program, perception of the components, identification of helpful and burdensome modules, and recommendation for improvements to the program. Data from the formative evaluation may lead to implementation improvement during the next phase of implementation, a regional, multi-site trial.

C. We estimate holding 6-9 focus groups of approximately 6-10 participants per group. At each site, one group will consist of subjects who completed all of  the 12 week stroke self-management program and the other group will consist of subjects who completed less than the 12 week program. Two groups will comprise of Jesse Brown VA Chicago participants, two groups will target Methodist participants, two groups will comprise of Wishard participants and the remaining two groups will comprise of participants from Indianapolis Roudebush VAMC.  Each focus group will meet once for up to two hours.  Sessions will be held in a conference room located at Jesse Brown VA, Roudebush VA, Wishard Hospital and Methodist Hospital, so that the location is easily accessible and familiar.  In the past, we have made transportation arrangements for participants and will do the same for participants in this study.  Participants will be reminded by telephone one week before, and again two days before the focus group.

At the beginning of each focus group, the moderator will explain the procedures and discuss patient confidentiality. Only first names will be used during the taped conversations to retain patient confidentiality. Dr. Damush, a trained qualitative researcher and moderator, will moderate the groups as she has done for her recent Veteran study.

5.g  Usual care:  Stroke and TIA survivors randomized to usual care will only receive written patient education materials on the stroke warning signs and pamphlets from the American Stroke Association on preventing secondary strokes. This is the current standard stroke/TIA education materials.  There are no current stroke self-management programs at Methodist, Wishard, Jesse Brown or Roudebush, so the potential for contamination is minimal. We will not

provide any telephone contact or self management materials during the intervention period to the usual care subjects except for contact to complete 3, 6 and 12 month assessments.  Usual care subjects will be contacted by phone, in person or in certain situations by mail by study staff to complete these assessments.

5.h  Adverse Events of the SSMP: If participants experience chest pain, shortness of breath, or dizziness, they will be instructed to cease activity and see their physician immediately if these symptoms persist or recur with further activity. The support group meetings will be held at the Roudebush and Jesse Brown VAMCs, Wishard Hospital and Methodist Hospital where access to emergency care is available 24 hours per day. All personnel will be trained in assessment and triage of symptoms post-stroke, and Ms. Nicholas has been successfully managing patients in this setting under the supervision of Drs. Williams and Damush during the past ten years. Per IRB protocol, all adverse events will be reported by the project coordinator/Care Manager to the IRB/VA R and D committee and VA research compliance officer.

5.i  Dose and success of the SSMP: We will track attendance at all group sessions and telephone calls completed using a computer database to record the received dose of the SSMP. We will also assess patient adherence to their chosen self-management behaviors.

6. Data Collection Protocol

Below we outline the data collection protocol, including the variables that will be measured, how and when they will be assessed. Each assessment will take approximately one hour (see Appendix ). Interviews for the self-management intervention component will be conducted by blinded staff.  As in our previous studies, we will complete the assessments in person at the hospital, by telephone, or by mail. For those, who are unable to travel to the hospital, our research staff will travel using a government issued vehicle to the patient home within a 2 hour limit to complete to insure adequate follow up rates. Often, stroke survivors are not able to drive in the immediate months after the stroke event. Based on our pilot study, we have extended the intervention period from 3 to 6 months. Indianapolis study team will access patients' medical records for all study sites including Jesse Brown VAMC, to pull data or abstract data on healthcare utilization, functional status, and stroke quality improvement processes at the time of the stroke/TIA event and during the study participation period of all enrolled patients from all study sites. If a participant withdraws we will record the reason provided and as listed in the informed consent, we will attempt to contact to complete the remaining assessments. Data will be analyzed on an intention to treat basis.

6.a. Measures: Primary Outcomes: Stroke specific, health-related, quality of life. Stroke specific quality of life will be assessed with the **SS-QOL.** This 62-item instrument assesses 12 domains relevant to stroke patients including energy, mobility, work, upper extremity function, ADLs, family roles, social roles, vision, language, thinking, mood, and personality. Our work has shown that the SS-QOL has good psychometric properties and that it provides a more meaningful assessment of overall post-stroke HRQOL than the SF-36. Our pilot data

demonstrated that 3 domains of the SSQOL were sensitive to change after the pilot intervention: family roles, social roles and work role functioning. In addition to the separate domains, an overall score can be calculated. We hypothesize that stroke survivors randomized to the intervention group will improve significantly on the domains of SSQOL and the overall score compared to those randomized to usual care.

Secondary Outcomes. Self-Efficacy; Stroke Risk Factor Self-Management Behaviors.  To evaluate the processes by which self-management programs affect health and quality of life, we included measurement of self-management behaviors promoted in the intervention program and self-efficacy to manage stroke symptoms and for carrying out self-management behaviors as developed by the Chronic Disease Self-Management Program.  Self-Management Behavior Frequency (e.g. minutes spent in aerobic, communicate with physician) will be assessed using validated scales designed to measure the frequency during the past week the patient engaged in the specific behaviors.   We have used these scales among patients with stroke and with chronic medical conditions.  Self-management behaviors (e.g., stretching exercises, progressive muscle relaxation) were assessed using questions adapted from a set of measures developed for intervention programs and previously published studies about the frequency of engaging in physical exercise, cognitive, and relaxation strategies that were promoted in the self-management program.  More specifically, respondents were queried about the total time spent during the past week spent doing stretching and strengthening exercises, walking and other aerobic exercise. Item responses ranged from none to more than 3 hours per week, which were converted to number of minutes per week of exercise ranging from 0 to 180 minutes. For cognitive strategies, we asked participants how often they practiced visualization or guided imagery, progressive muscle relaxation, positive thinking or positive self-talk when they were feeling pain or unpleasant symptoms. Response categories ranged from 0 ("never") to 5 ("always"). The mean of each item reflected the strategy score. We will also ask how many days a week is typically spent in strenuous exercise and for how many minutes. **Self-efficacy( i.e., confidence to perform specific behaviors)** will be measured using established scales designed to measure a patient's confidence level to manage stroke self symptoms, communicate with their providers, and engage in self-management behaviors (e.g. exercise regularly).  We have used these scales in our previous research where patient's rate their self-efficacy on a 1-10 scale where 10 denotes high self-efficacy. For example, in our pilot study, participants in the intervention reported a greater confidence to communicate with their physician and to exercise regularly at six months compared to the control group.

Functional Status

In addition to assessing self-reported function, we will conduct several performance measures to assess functional status. We will begin with the Six-

Minute Walk Test.  If subjects are able to complete the Six Minute Walk Test without stopping, they will be asked to complete a Dual Task Walk Test.

**Six-minute walk test** has been used extensively to demonstrate functional status across a wide range of patients with specific medical conditions and older adults. It has demonstrated reliability and validity. Participants are instructed to walk as fast as they can on a marked course over six minutes. Distance walked is the outcome. Our co-investigator, Dr. Schmid is currently using the six-minute walking test to evaluate functional status among stroke patients and has not experienced any adverse events during the testing. We will conduct this test at the hospital. Similar to Dr. Schmid's methodology, we will measure off the walkway and mark it with cones as we conduct the timed walk.

Stroke outcomes will be assessed by having patients rank themselves on the **modified Rankin scale**, a commonly used global stroke outcome measure that categorizes patients into five outcome groups from no symptoms at all to severely disabled.  In addition, our research staff is trained on assessing a retrospective **NIH Stroke Scale** for stroke patients using the patient medical record within 24 hours of admission.  Dr. Williams established the methodology and training module that our research staff has all been trained. This scale captures stroke deficits in several domains (consciousness, vision, extraocular movement, facial control, limb strength, ataxia, sensation, and speech and language) and is used as a measure of stroke severity.

Covariates. Site will be coded dichotomously to control for local effects. Demographics. Age, gender, race/ethnicity, education, marital status and household income will be assessed during the patient baseline interview. Household income will be assessed with a single item used in primary care interventions, "Do you have enough income to get by?" Depression symptoms are measured by the PHQ-9, a 9-item depression screener tool (derived from the first two items of the PHQ-9) that assesses DSM-IV symptoms of depression: depressed mood and anhedonia, and perform well as a depression screener in primary care and in post-stroke patients.  We will include to control for post stroke depression. Co morbidity - Patient co morbidity will be extracted from the medical record and evaluated using the Ambulatory Care Groups (ACG).  ACG is a reliable and valid evaluation that we have used in previous trials from this population as a covariate. Co morbidity will be used as a covariate in the analyses.
Screening for stroke risk factor management: We will examine CPRS records to determine the proportion of participants in goal of their stroke risk factors during the subsequent 6 months after the stroke event. The chart reviews will be conducted by the site research assistants. As we have previously done in our previous research, we have created a chart abstraction form that denotes all stroke risk factors and the targeted goals for stroke survivors and includes the following elements: cholesterol LDL < 100; Blood Pressure < 130/80; current smoking status; HgA1C levels if diabetic; INR if on anti-coagulation; weight/BMI; alcohol use.  We expect all patients to have fasting lipid profiles done during

hospitalization if not performed in the three months prior to stroke onset. We expect patients with diabetes to have hemoglobin A1c values checked if not performed in the three months prior to stroke onset and all patients to have fasting blood glucose to screen for diabetes. We expect hemoglobin A1c values to be checked if the patient does not have a diabetes diagnosis but has at least two fasting serum glucose values > 140mg/dl.

Lifestyle counseling/referral made. VISTA/CPRS (for veterans) and INPC (Methodist and Wishard patients) data will be pulled to search for evidence of lifestyle counseling and/or referrals made to appropriate specialists and existing facility programs in physical activity (e.g. use of rehabilitation facility to exercise), diet (e.g. nutrition clinic; dietitian), weight management (e.g. MOVE program), smoking cessation (e.g. classes), GRACE, Telehealth, and patient education during the study period including FY10 to FY18. Data will be scored dichotomously as yes/no. Raters (research study staff) in Indianapolis and Chicago will be trained to abstract these chart data and a random sample of charts will be dually-reviewed to assess ongoing inter-rater reliability as we have previously done. We expect the majority of stroke survivors to receive counseling and/or referrals to specialists in physical activity and diet, two modifiable stroke risk factors. For those who are overweight or smoke, we will calculate the proportion that received counseling/referral to program.

**In addition to pulling data from VISTA/CPRS and INPC for all enrolled study participants, data from FY10 to FY18 for the Veteran Affairs study participants would be pulled electronically from the Corporate Data Warehouse VINCI and Austin National VA data. These data include vital signs, orders, consults, labs, health factors, fee-basis data, inpatient and outpatient files and vital status.**

**We will use the Corporate Data Warehouse VINCI secure environment and the study folder on the Indianapolis VAMC HSR&D Research server, which is behind the VA firewall, for the abstracted data storage and analysis. The Indianapolis VAMC HSR&D Research server is behind the VA firewall and access is limited to approved individuals. Access to the server and study folder is controlled by VA username.**

**Provider-Based Outcomes.** Defining guideline-adherent treatment: We will determine medication management for stroke prevention treatment at the time of stroke discharge and at 3 and 6 months as a dichotomous yes/no variable using methodology developed in other VA studies and guided by a standard list of medications advocated in the stroke risk factor management program. The key stroke risk factors of interest are: 1) hypertension, 2) diabetes, 3) hypercholesterolemia. All of these outcomes will use the affected subgroup as the denominator and those on treatment as the numerator (e.g. subjects on treatment for hypertension/all subjects with a diagnosis of hypertension). Comparison will be by risk factor group. We expect all subjects to be discharged on either an antiplatelet (antithrombotics) or anticoagulant medication for stroke prevention, except in rare instances of contraindication (e.g. recent gastrointestinal or intracerebral hemorrhage, planned procedure in the next seven days) and so will assess this proportion treated out of all eligible patients. In addition, we will specifically examine the proportion of patients with atrial fibrillation and stroke who are appropriately

anticoagulated. In a similar method, the proportion of stroke survivors on statins, and antihypertensive medications will be assessed. In all treated patients, we will determine two key aspects of guideline adherence based on previously published methods in veterans:

- dosage adequacy (# of tablets x strength (mg) of tablet/# days of prescription);
- duration adequacy (# of days without medication/# days in the prescribing period after stroke) with inadequacy defined as > 21% of days without medication;

We will use PBM data from FY10 to FY18 to determine adherent stroke risk reduction treatment prescribed pre-stroke and post-stroke. This would include outpatient medications. PBM variables include: Dosing instructions; Days Supply of Medication; Fill/Refill/Partial Date; Generic Drug Name; New/Refill/Partial Indicator; Patient ID(SSN); Prescription Patient Status; Provider Class; Provider Service/Section; Provider Specialty; Provider Subspecialty; Release Date; Total Quantity Dispensed; VA Drug Class; VA Product Name. The following are the precise VA Drug class data from the PharmacyBenefits Management Services (PBM) that would be used or reviewed.

| Anti-hypertensives/ statins | |
|---|---|
| CV100 | Beta blockers/related |
| CV150 | Alpha blockers/related |
| CV200 CV250 | Calcium channel blockers Antianginals |
| CV300 | Antiarrhythmics |
| CV350 | Antilipemic agents |
| CV400 | Anti-hypertensive combinations |
| CV490 | Anti-hypertensives, other |
| CV800 | Ace inhibitors |
| CV805 | Angiotensin II inhibitor |
| CV806 | Direct renin inhibitor |
| CV900 | Cardiovascular agents, other |
| Diuretics | |
| CV700 | Diuretics |
| CV701 | Thiazides/related diuretics |
| CV702 | Loop diuretics |
| CV703 | Carbonic anhydrase inhibitor diuretics |
| CV704 | Potassium sparing/combinations diuretics |
| CV709 | Diuretics, other |
| Diabetic medications | |
| HS500 | Blood Glucose regulation agents |
| HS501 | Insulin |
| HS502 | Oral hypoglycemic agents, oral |
| HS503 | Antihypoglycemics |
| HS509 | Hypoglycemic agents, other |
| Thrombolytics | |
| | tPA, tissue plasminogen activator |
| | anticoagulants |
| | antiplatelets |
| Smoking Cessation Aides | |

**6.0    Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others**

Per IU IRB protocol, all adverse events will be reported by the project coordinator/Care Manager to the IRB, VA R and D committee and VA research compliance officer within the required reporting time frame in which to submit. Adverse Events or unanticipated problems involving risk to subjects or other will be reported at the time of DSMB reviews.

If participants experience chest pain, shortness of breath, or dizziness, while doing self management activities, they will be instructed to cease activity and see their physician immediately, if these symptoms persist or recur with further activity. The support and exit focus group meetings will be held at the Roudebush and Jesse Brown VAMCs, Wishard Hospital and/or Methodist Hospital, where access to emergency care is available 24 hours per day. All personnel will be trained in assessment and triage of symptoms post-stroke, and Ms. Nicholas has been successfully managing patients in this setting under the supervision of Drs. Williams and Damush during the past ten years.

**7.0    Study Withdrawal/Discontinuation**
Any participant is permitted to withdraw from the project at any time without adverse effects.  Participants from Wishard hospital, Methodist hospital and Roudebush VAMC may withdraw from the study by notifying any of the Indianapolis research study staff.  If a participant withdraws, we will complete a standardized form for detailing the reason.  At the time participants withdraw, they will be informed that data already collected on them prior to the withdrawal, may continue to be reviewed by the study team, but further data collection will not occur.

**8.0    Statistical Considerations**
 Planned Statistical Analyses
Baseline and Preliminary Analysis: In the randomized study, the preliminary phase of the analysis will consist of tabulating baseline characteristics of the participants who enrolled in the randomized study (from the survey and CPRS). The summary statistics will be compared between patients who were ineligible by provider review, eligible participants and eligible non-participants to see if the intervention reached a specific group of stroke survivors. We will use independent samples t-tests (for continuous measures) or chi-square tests (for categorical variables) to assess whether the randomization achieved balanced groups between sites. *Power Estimation: Our primary endpoint is 12 months measurement with a 6-month intervention. With almost double dose of intervention, we expect that the intervention effect at 6-month may be larger than the 3-month intervention for SSQoL (overall score, family, and social roles), self-management behavior frequency (minutes spent in aerobic, communication with*

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*physician), and self-efficacy (communication with physician). Taking into consideration of the imbalance baseline measurements between two groups in the pilot study, a two group comparison of change may not appropriately reflect the real intervention effect. <u>We therefore derive the change before and after the treatment in the intervention group from the pilot study and assume no change in control group as the basis of our sample size</u>. We assume conservatively that the continued improvement of each individual in the second half the proposed study is only ¼ of the change in the first half, i.e. the proposed intervention will have only 1.25 times the effect of that in the pilot study. We expect the intervention effect at 12 months will be similar to the effect at 6 months. We performed the power calculation for the primary outcome SSQoL (overall, family, and social role) and secondary outcomes: Self-Management Behavior Frequency (minutes spent in aerobic), Self-efficacy (communication with physician), and Six-minute walk test. All the sample size calculations assumed an 80% power and 5% Type I error.*

**9.0** **_SSQoL_**_: The primary hypothesis is participants randomly assigned to the intervention group will have a larger improvement of SSQoL overall score at the end of follow up (12 months) compared to those randomly assigned to the usual care group. Our pilot study demonstrated that overall SSQoL score in the intervention group increased by 0.2 with a SD<0.8. Assuming that in the stronger intervention of 6-month the improvement is 1.25 times of that of the pilot study and no change in the control group, the changes difference of overall SSQoL score will be 0.25. To achieve 80% power with 5% Type I error, we will need 162 subjects completing the 12 months follow up in each arm._

**10.0** *Our pilot study showed that SSQoL family role score in the intervention group increased 0.5 with a SD=1.2. Assuming a 1.25 times change, the change difference of SSQoL family role score will be 0.75. Forty-nine subjects completing the 12 months follow up are needed in each arm to achieve 80% power to detect an effect on family role functioning. For treatment effect of SSQoL social role at 12-month, if we have 162 subjects completing 12 months follow up in each arm, we will have 80% power detecting an effect size of 31% of one standard deviation. In our pilot study, the effect size based on intervention arm is 21.4%. The detectable effect size is as small as 1.5 times of the pilot study.*

**11.0** **_Self-Management Behavior Frequency:_** *Our pilot study showed that minutes spent in aerobics in the intervention group increased by 47.6 in the intervention group with a SD=126. Assuming 1.25 times of change in the stronger intervention, the change difference of minutes spent in aerobics will be 58.55. Seventy-four evaluable subjects completing the 12 months follow up are needed in each arm to achieve 80% power to detect an effect on minutes spent on aerobics.*

**12.0** **_Self-efficacy (communication with physician):_** *Our pilot study showed that communication with physician in the intervention group increased by 0.6 point in the intervention group with a SD=1.7. Assuming 1.25 times of change in the stronger intervention, the change difference of minutes*

*spent in aerobics will be 0.75. Eighty-two subjects completing 12 months follow up are needed in each arm to reach 80% power.*

**13.0** ***Six-minute walk test****: In a randomized trial (Marsden et al 2010) with a similar intervention, the intervention's group improvement at 3 months was a distance of 16.1 meters with 35.1standard deviation. Assuming a similar difference and standard deviation in improvement, we will need Seventy-six subjects per arm to reach 80% power. On the other hand, if we have 113 subjects in each arm completing the 12 months follow up, we will be able to detect of a difference of 13.5 meters in change of the walk test between the two arms with more than 80% power.*

**14.0** *The largest sample size needed for our primary and secondary outcomes is 162 subjects per arm for SSQol overall score. Assuming a conservative 25% dropout rate based on previous research, 216 subjects in each arm are needed at randomization. For the Six-minute walk, with 113 patients in each arm, we will be able to detect a difference of 30% standard deviation between the intervention and control group.*

**15.0** <u>Baseline analysis.</u> Site and patient characteristics including patient age, gender, and outcome measurements (e.g., NIH stroke scale score, SSQoL scores, Self-efficacy) will be compared between the control and intervention arm and among the three sites. For continuous outcome variables, two-sample t-tests will be used for comparison between arms and analysis of variance (ANOVA) model will be used for comparison among sites. Chi-square tests will be used for comparison of categorical variables at baseline. Appropriate transformation for continuous variable will be used if there is a normality assumption violation. Wilcoxon's rank sum test will be used if necessary. For all analysis, we will use Statistical Analysis Software (SAS, version 9.1, Cary NC).

**16.0** <u>Primary analysis:</u> Primary Aim 1. To determine the effect of a stroke self-management program on stroke specific functioning and quality of life at 3, 6, and 12 months.

**17.0** <u>Comparison: The primary outcome in this study is SSQoL scores</u>**.** The primary endpoints will be at 3, 6, and 12 months after randomization. We will first compare the 3-month, 6-month, 12-month, changes in overall SSQoL score between intervention and control groups using two-sample t test. We will also graphically examine the time course of the effects, testing the change from baseline for each time point.

**18.0** <u>Modeling</u>**:** We will fit linear mixed effect models for utilizing the repeated measurements of change of overall SSQoL score 3, 6, and, 12 months from baseline. Fixed and random effect covariates will be included. We will use time as a categorical predictor and include intervention and their interaction as factor. A positive significant interaction term indicates a larger improvement in the intervention group. Other fixed effects include: site, admission diagnosis (TIA/stroke), patients' age, gender, baseline overall SSQoL score, and PHQ9 depression score. A random intercept will be included to accommodate the correlation among repeated measurement of SSQoL from the same subject. We will use unstructured

covariance matrix to model the within subject correlation. The study is powered to test the difference of change of overall SSQoL score. Similarly, we will apply these analyses to the SSQoL domains. *We will add time since stroke event at baseline as a model covariate to control for this time effect*.

**19.0** *Missing Data: Patients baseline characteristics will be compared between those with and without missing outcome data. The primary analysis based on linear mixed model approach is used in many randomized clinical studies (e.g. SCAMP Trial by Dr. Kroenke, Bair, Damush et al: JAMA; 2009; 301(20):2099-2110) and is valid even with differential dropout rates as long as the missing-at-random assumption is not violated, i.e. the probability of missing is not dependent on the unobserved values. Although this assumption cannot be tested directly, we will first compare patients' baseline characteristics will be compared between those with and without missing outcome data to assess potential nonrandom dropouts. We will also fit a logistic regression model to compare intervention and control subjects with missing outcome data to determine if there is biased dropout. These will be followed by a number of sensitivity analyses. First, missing outcomes will be imputed using the last-observation-carried-forward (LOCF) method. Second, we will impute missing data using predicted values from linear models build on the observed data. Finally, multiple imputation techniques will be used to rerun the mixed model. If the various methods do not substantially change our findings on the main outcome, then the findings are robust. Otherwise, they will be interpreted with extreme caution.*

**20.0** Secondary analysis: Secondary Aim 2. To determine the effect of a stroke self-management program on self-management process factors: self-efficacy and self-management behaviors at 3, 6, and 12 months.

**21.0** The analytical technique in the primary outcome analysis will be similarly applied to our secondary outcomes which are continuous measurements including: the self-management behaviors and self-efficacy scores, and the Rankin scale. The change of six-minute walking distance from baseline to 3, 6, and 12-months will be compared using a two-sample t test.

**22.0** Summative Evaluation of Participants Barriers and Facilitators: Aim 3. To gather insights during the exit focus groups from those who participated in the intervention program. The method of analysis of exit focus group transcriptions is as follows:

At least two investigators will independently review and code transcripts by assigning labels and codes to data segments. Drs. Damush, Schmid and Williams have previously coded and analyzed transcripts together. We will permit emerging themes to be coded in a bottoms-up manner as we have done previously. We will use the session notes to catalog the principal themes that ensued and issues of both consensus and difference that transpired. The field notes and audiotapes will be transcribed into computerized text. The first step in the analysis will be to create a set of

agreed upon codes and a codebook that serve as a template for coding of the data. The investigators will use an iterative consensus building process to generate codes.  Each investigator, working independently will highlight sections of the field notes and transcripts that illustrate a theme. In the margin of the notes or transcript they will write down the name of the theme.  In a subsequent meeting the investigators will compare notes, note agreements and attempt to resolve disagreements.  Once agreement on the themes has been reached they will be arranged in terms of content and scope.  The codes will be arranged in a "hierarchical" structure where each major category of codes contains subcategories within it.  The codebook will allow us to convert the group conversations into a formal set of categories that will be systematically applied to each transcript.  Once the coding is complete, we will generate reports and frequency counts of key themes including how often and where they occur.  The key task in this stage of the analysis is to make comparisons among the different categories of participants in the full sample. The goal is to detect patterns within each dataset that characterize potentially meaningful differences or similarities between groups. When we are not identifying new themes across the group's text, we will have reached information saturation. Quotes will be grouped according to our major themes, including common and useful facilitators of stroke self-management behaviors, and barriers to such activity. Suggestions for improvements will be recorded. Frequency of themes will be analyzed first by identifying themes per question, then overall. We will construct a typology and describe findings using quotes to illustrate points. Analyses will include words, contexts, consistencies, frequencies, intensities, specificity, and finally, big overall barriers and facilitators of stroke risk factor management from the groups will be identified. Lifestyle and medication management needs and preferences will be identified. Moreover, we will solicit feedback on the delivery methods of the program and suggestions for improvement.


## 9.0    Privacy/Confidentiality Issues

To minimize risk of loss of confidentiality or privacy, our study team will implement several measures. The study research team in Indianapolis has extensive experience collecting and managing confidential research information. All study staff will be certified in human subject research training and will adhere to HIPAA and all VA standards for research study data privacy.  Study data will only be shared with approved study team members identified as having access to study data. Face to face interviews and self management sessions will be conducted in a private location at Methodist, Wishard, Jesse Brown VAMC, and Roudebush VAMC. Phone interviews and phone self management sessions will be completed at telephone number provided by the participant. Study staff will make these phone calls to participants from a private location within the study sites.  All subject interviews will be assigned a study ID number and all identifying information removed.   All paper files will be stored separately in locked file

cabinets only accessible to research staff and all electronic files will be placed on on a Roudebush VAMC server that is protected by the VA firewall. End of study subject focus groups will be audio recorded.  These audio recorded focus group sessions will be uploaded to a Roudebush VA study folder located on a secure server behind the VA firewall.  Uploaded audio recordings will then be immediately deleted from the recording device. The focus group audio recordings will be transcribed.  Transcribed and audio recorded data will be stored separately in locked file cabinets only accessible to research staff and/or on a computer that is password protected only accessible to research study staff at Roudebush VAMC.  Transcription will be performed using Microsoft Word by a VA approved/contracted service and stored on a password protected research servers that are protected by the VA firewall.  Participants will not be individually identified in any reports or manuscripts from the study data.

Data transfers:

Completed survey data for enrolled subjects will be sent via registered delivery service (i.e., UPS) from Jesse Brown VAMC in Chicago to Roudebush VAMC in Indianapolis, where the Indianapolis research staff will enter the data into the ACCESS database.

 Methodist and Wishard retrospective patient data will be extracted by data management from the Regenstrief Institute, Inc which is part of a hospital medical records system that is linked city-wide in Indianapolis excluding the Roudebush VAMC. Specifically, Regenstrief data managers will look for primary discharge diagnosis ICD-9 codes related to ischemic stroke and TIA of Methodist and Wishard patients. The data managers will extract data (patient name, SSN, date of discharge) and load this data onto a VA issued USB thumb drive. This thumb drive will be password protected and hand delivered to our project coordinator at Roudebush VAMC on a quarterly basis. Regenstrief data managers may also transfer Methodist hospital and Wishard hospital stroke/TIA patient data to Roudebush VAMC electronically to a secure VA network drive using "slashtemp". The Regenstrief retrospective data of Methodist and Wishard patients will be uploaded behind the Roudebush VA firewall and merged with the existing study data in a study file on a VA secure server, the "R" drive.

**10.0    Follow-up and Record Retention**

All data collected with identifiers will be stored at the Roudebush VAMC indefinitely or until RCS 10-1 signifies a destruction timeframe of research records.  At the time of identifiable data discard, paper will be shredded, files from computers and audio devices will be permanently deleted, and CDs will be deleted and destroyed.

5/11/2016