

Indiana University Dementia Screening Trial

The IU CHOICE Study

Study Protocol

Version 6

March 28, 2013

CHOICE Study Team

Malaz A. Boustani, MD, MPH

Principal Investigator
IDND Network Director
Regenstrief Institute, Inc. Scientist
IU Center for Aging Research
Email: mboustan@iupui.edu

Chris Callahan, MD

Co-Investigator
IU Center for Aging Research Dir
Regenstrief Institute, Inc. Scientist
IU Center for Aging Research

Greg Sachs, MD

Co-Investigator
Chief of Div of Gen Internal Med & Geriatrics
Regenstrief Institute, Inc. Scientist
IU Center for Aging Research

Paul Dexter, MD

Co-Investigator
Chief Med Information Officer WHS
Regenstrief Institute, Inc. Scientist
Biomedical Informatics

Amie Frame, MPH

Research Manager
Regenstrief Institute, Inc.
IU Center for Aging Research
410 West 10th Street, Suite 2000
Indianapolis, IN 46202-3012
Phone: (317) 423-5910
Fax: (317) 423-5653
Email: amiframe@iupui.edu

Table of Contents

A. Rationale and Study Specific Aims	3
B. Innovation	5
C. Background.....	8
D. Preliminary Studies.....	10
E. CHOICE Trial.....	20
F. Inclusion/Exclusion Criteria	35
G. Enrollment/Randomization	35
H. Data Collection	39
I. Statistical Plan	43
J. Limitations	47
K. Timeline	48
L. Protection of Human Subjects.....	49
M. Reporting of Unanticipated Problems & Adverse Events	54

A. Rationale and Study Specific Aims

A fundamental tenet of any screening program is that it should “reduce individual and societal burden from specific disorders”.^{1,2} Screening is, by definition, applied to individuals without symptoms. Thus, a physician completing a cognitive assessment on a patient presenting with complaints of memory problems is engaged in case-finding or diagnosis.^{1,2} Assessment of symptomatic individuals is not screening and is not the subject of this trial. Screening for some conditions among some populations has resulted in magnificent improvements in individual and societal burdens of diseases (e.g. colon cancer and cardiovascular disease, among others). However, screening can also cause harm, excess costs, and considerable societal controversy (e.g. mammography for some patient groups and prostate specific antigen testing, among others). Furthermore, not all screening is advisable at an individual level or at a societal level. In some conditions (e.g. depression), screening is not recommended unless a health care system has in place the resources and expertise needed to appropriately diagnose and treat positively-screened patients.^{3,4} According to the US Preventive Services Task Force, we do not have sufficient evidence of the benefits and harms of screening to recommend routine screening for dementia in primary care.⁵

In the context of insufficient data on harms and benefits, providers already have wide availability of dementia screening instruments,^{6,7} advocacy for and against routine screening^{2,5,8-12} and a downstream list of potential follow-up diagnostic testing including routine blood test such as thyroid stimulating hormone, as well as neuroimaging.^{13,14} Providers also have widespread availability of psychopharmacologic agents (ranging from anti-dementia drugs to antidepressants and antipsychotics) that are highly controversial in dementia care and associated with important adverse effects.¹⁵⁻²⁰ Clinical trials, such as our own collaborative care trial, require significant practice redesign to implement and many of these redesign elements are not reimbursable by the Center for Medicare and Medicaid Services (CMS). Finally,

Alzheimer's disease and related dementia are dreaded conditions and people are seeking answers. Even though no cure is in sight, patients and families seek help in managing behavioral symptoms and health care decision-making.²¹⁻²⁴ It is of little wonder that primary care physicians find themselves in a situation of therapeutic nihilism, cynicism, low levels of confidence, and frustration.²⁵⁻²⁷ Our prior explanatory trial demonstrated that primary care providers, given the proper resources, can improve behavioral and psychological symptoms associated with dementia, caregiver stress, and depression.

The objective of this proposal is to address the question of whether the benefits outweigh the harms of routine screening for dementia among older adults in primary care when the screening program is coupled with primary care practices prepared to provide care for those who screen positive. All subjects will complete a screening questionnaire that includes screening already recommended for older adults (e.g. smoking). A random sample of these subjects will have a cognitive screener embedded within this larger set of screening questions. Thus, the control condition (no screening) means no cognitive screener.

The proposed project will contribute important information to patient, families, providers, and policy-makers about the harms and benefits of routine screening for dementia. If this trial is successful, it will not only address the appropriateness of routine screening for dementia, it will also provide a template for the successful implementation of screening programs, coupled with diagnosis and treatment programs, that are practical for a broad range of health care systems. Finally, we will report data on cost and cost effectiveness.

The specific aim of the study is to conduct a pragmatic randomized clinical trial assessing the harms and benefits of screening for dementia, compared to no screening for dementia, among 4,000 typical, older adults, cared for in typical, primary care practices, prepared to deliver best practices dementia care.

Primary Specific Aim 1: Test the impact of dementia screening on health-related quality of life of the patient at baseline and at 1, 6, and 12 months.

(We hypothesis that screened subjects, compared with non-screened subjects, will have a higher health-related quality of life as measured by the Health Utility Index (HUI) at 12 months post-screening.)

Primary Specific Aim 2: Test the impact of dementia screening on the mood and anxiety symptoms of patient at baseline and 1, 6, and 12 months (i.e., primary potential harms).

(We hypothesize that screened subjects will not have higher depression or anxiety at one month post-screening (as measured by the Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder (GAD-7) scales)

Secondary Aims: Estimate the cost effectiveness of dementia screening.

(We hypothesize that screened subjects will have an Incremental Cost Effectiveness Ratio (ICER) below the maximum acceptable threshold of \$100,000 per quality adjusted life year saved at 12 months.)

B. Innovation

Pragmatic

Previous studies by our team and others have demonstrated that routine feedback of dementia screening scores, continuing medical education for dementia, and other passive educational interventions can improve rates of diagnosis, but not patient outcomes.^{12,28-32} We have shown that patients and families perceive potential harms from screening and that dementia screening can result in important incremental health care costs.^{21-23,33} Conversely, we and others have also already demonstrated that collaborative care, focused on non-

pharmacologic approaches to behavioral disturbances, can improve patient outcomes under experimental conditions.^{34,35} The innovation of this trial is in moving the process upstream to asymptomatic, older adults, cared for in typical but prepared community-based practices, to document actual benefits and harms, including costs. “Asymptomatic”, in the case of cognitive impairment, is paradoxical in some respects, but we denote asymptomatic to mean that the cognitive impairment is not a presenting symptom of the patient (just as hypertension is asymptomatic but can be detected by screening, cognitive impairment can be detected through screening tests).

Academic Community Partnership

Moving from an explanatory trial to a pragmatic trial is much more complicated than simply a change in setting. Moving research to “the usual conditions in which it will be applied” requires an entirely different research approach.³⁶⁻⁴¹ We are not new to this area. Through prior work, we have a running start in terms of a program (screening, diagnosis, treatment, and longitudinal assessment tools) and in understanding the process of adapting an intervention to local micro-environments.^{42,43} Through funding from the NIMH, we not only have experience in conducting implementation research in community settings, we also have experience in conducting pragmatic mental health services research. One hallmark of a true community-based participatory research is that the community partners have meaningful input into the study design and interpretation. A partnership is more than a venue change.

Integrated Health Information Technology

We have access to a regional health information exchange (RHIO) which we have used in prior research.⁴⁴⁻⁷¹ Additionally, we have already initiated the building of research partnerships with the targeted community-based health care systems through prior research

projects.^{1,34,42,43,72,73} Thus, we have a track record of successful human subject recruitment at these sites as well as co-management of the projects.

Primary Care Focus

Most older adults are cared for in primary care and primary care is the most likely site for early identification and treatment of dementia. However, the typical primary care physician with a panel of ~2,000 patients would care for only about two dozen older adults with dementia, at least half of whom would be undiagnosed. Among the 300 other patients aged 65 years and older in this practice, 150 would suffer from at least three chronic conditions, 200 would report pain, 100 feeling anxious, and 63 patients would require hospitalization.⁷⁴ This primary care provider needs an estimated 10 hours per working day to deliver all of the recommended care for patients with chronic conditions and an additional seven hours per day to provide preventive services.⁷⁵ Patients with dementia in the primary care system also suffer from numerous chronic medical conditions, receive multiple prescriptions including psychotropic drugs, display a wide range of behavioral and psychological symptoms, and extensively utilize the health care system.^{46,47,76-78} Organizational and procedural changes in this care environment, that continue to place new demands on providers, are not only difficult, but they may have unintended consequences. We recognize the complexity of the primary care environment and have established the relationships needed to conduct research in this arena.

The key innovation of this proposal is our inter-related capacity to conduct a **pragmatic** trial within an **academic-community partnership** served by **health information technology** and to focus the study in the site of care where the intervention is most likely to be applied: overburdened **primary care** practices.

C. Background

There were an estimated 5 million cases of dementia in the U.S. in 2000 and this number may grow to 18.5 million by the year 2050.^{79,80} According to the Global Burden of Disease estimates for the 2003 World Health Report, dementia contributed to 11% of years lived with disability in people aged 60 years and older; more than cancer, stroke and cardiovascular disease.^{81,82} Currently, Medicare beneficiaries with dementia account for 34% of Medicare spending, even though they constitute only 13% of the beneficiaries aged 65 and older. By 2050, Medicare will be spending over \$1 trillion on beneficiaries with this syndrome.^{81,83,84} Most older adults with dementia receive their medical care in primary care settings, yet most primary care physicians care for less than two dozen older adults with dementia.^{33,74,78,85} Researchers and policy-makers consistently document suboptimal quality and poor outcomes among older adults with dementia receiving the usual care of generalist physicians.^{33,48,86,87} Beginning in January 2011, CMS started covering the costs of an annual wellness visit for Medicare beneficiaries that included detection of cognitive impairment.⁸⁸ Yet, the US Preventive Services Task Force could not identify sufficient data to recommend for or against routine screening for dementia;⁵ patients and caregivers report concerns about potential harms from screening;²¹⁻²⁴ and most primary care practices are not prepared to follow-up positive screening with appropriate diagnosis, education, and management strategies.^{26-31,89,90} In the top quartile of research priorities in 2010, the Institute of Medicine recommended research to “Compare the effectiveness and costs of alternative detection and management strategies for dementia in community-dwelling individuals.”⁹¹

Patients, families, policymakers, and researchers are understandably seeking a cure for Alzheimer’s disease and related dementias. In 2011, President Obama signed legislation approving the National Alzheimer’s Project Act to increase funding for research on prevention and treatment strategies. Multiple agencies within the Department of Health and Human

Services, including CMS and the NIH, have identified Alzheimer's disease and related dementias as a top priority for research. While seeking a cure is the ultimate goal, we must also recognize that millions of Americans already have dementia and many more will develop dementia over the coming decades even if new prevention strategies are identified.⁷⁹ Experts agree that we must prepare the health care system to provide hands-on care for millions of older Americans with dementia. This proposal makes the assumption, backed by our research and that of others, that early recognition of dementia could improve patient and caregiver outcomes, even if there are no cures, and even if there is only minimally effective (and sometimes dangerous) pharmacologic options for treatment of symptoms. This is true because randomized controlled trials have shown that nonpharmacologic approaches, either alone or in combination with pharmacologic approaches, can improve patient and caregiver outcomes, alter use of nursing home care, or reduce the use of harmful medications. Thus, a contention that screening for dementia is not useful because providers have nothing to offer, is not supported by the existing literature.^{34,35} What remains highly controversial is the value, including harms and benefits, of screening populations of asymptomatic, older adults for dementia in an attempt to identify the disease at its earliest manifestations. Data clearly shows that early recognition of treatment of vascular risk factors, even in their asymptomatic manifestation, improves patient outcomes. Such data is not available for dementia.

The proposed project will contribute important information to patient, families, providers, and policy-makers about the harms and benefits of routine screening for dementia. If this trial is successful, it will not only address the appropriateness of routine screening for dementia, it will also provide a template for the successful implementation of screening programs, coupled with diagnosis and treatment programs, that are practical for a broad range of health care systems. Finally, we will report data on cost and cost effectiveness.

D. Preliminary Studies

We have a longstanding commitment to improving the care of older adults with dementia in primary care. This preliminary studies section describes (a) our experience in conducting clinical trials among older adults with dementia; (b) responsible use of data in the RHIO; (c) our initial work in understanding the benefits and harms of dementia screening from the patient's and caregiver's perspective; (d) estimates of potential cost savings with more effective management of dementia; and (e) initial efforts to adopt new models of care to real-world practices and demonstrate their financial sustainability.

Primary Care Clinical Trial Experience

In the early 1990s, our study team completed an extensive screening program of 4,000 older adults who were approached during their regularly scheduled primary care appointments. The program was designed to assess the prevalence of cognitive impairment, depressive symptoms, suicidal ideation, and alcohol abuse.^{48,54-56,92} Less than 25% of patients with moderate-severe cognitive impairment had dementia recorded as a diagnosis; depression and problem drinking were similarly under-diagnosed. We coupled these screening data with clinical practice data from the Indiana Network for Dementia Care (INPC) (at that time known as the Regenstrief Medical Record System).^{49,60,61,66} We then followed this cohort of older adults for up to seven years to study the association between cognitive impairment and mortality.⁴⁵ Cognitive impairment, measured at baseline, was a significant predictor of early mortality, even when controlling for comorbid conditions. These early observational studies provided the foundation for later intervention clinical trials in primary care. More recently, we reported the mortality experience of this cohort at 15 years.⁴⁴

We were part of the design team and one of the clinical sites for the IMPACT trial of late life depression among primary care patients.^{93,94} Over two years, 1,800 older adults with major depression or dysthymia were recruited with 250 recruited from the Indiana site. Half of the

subjects were randomly assigned to a collaborative stepped care program where a depression clinical nurse specialist worked with the patient's regular primary care provider to treat depression using antidepressant medications and Problem Solving Treatment in Primary Care. The intervention was specifically designed to coordinate care for depression with the patient's regular primary care provider. Intervention patients were significantly more likely to receive guideline-level care, recover from depression, and to report improvement in physical function, health-related quality of life, and satisfaction with care.⁹³ We learned a great deal from the conduct of this study and used this experience to conceptualize a study of collaborative care for dementia in primary care.

In 2000, our research team designed a collaborative, primary care intervention based on published treatment guidelines for the recognition and treatment of Alzheimer's disease.³⁴ The program included a screening and diagnosis program and a randomized controlled clinical trial. Dementia was diagnosed according to ICD-10 criteria by an expert consensus panel using a process that mirrored the diagnostic scheme of the Alzheimer's Disease Cooperative Studies group.³³ We completed a controlled clinical trial of 153 older adults with Alzheimer disease and their caregivers who were randomized by physician to receive collaborative care versus augmented usual care.⁵ Both study groups completed a counseling visit with an advanced practice nurse who provided education about Alzheimer's disease and a referral to community resources. Over the following year, intervention patients received care management by an interdisciplinary team led by a nurse practitioner working with the patient's family caregiver.⁹⁵ In addition to consideration for treatment with cholinesterase inhibitors, the team used standard protocols to identify, monitor, and treat behavioral and psychological symptoms of dementia (BPSD). The guidelines stressed non-pharmacologic management. Outcome measures included the instruments of the Alzheimer's Disease Cooperative Studies group: Neuropsychiatric Inventory (NPI), Activities of Daily Living (ADL), and the Resource Use Scale. Study procedures assured that enrolled patients received an adequate dose and duration of the

treatment and we monitored the fidelity of the intervention, patient contacts, and patient outcomes using a web-based tracking system.

Initiated by caregivers' reports, 89% of intervention patients triggered at least one protocol for BPSD with a mean of four (4) per patient from a total of eight (8) possible. These results highlight the clinical observation that primary care patients with Alzheimer's disease are indeed highly symptomatic. Intervention patients were more likely to receive cholinesterase inhibitors (79.8% v. 55.1%, $p = 0.002$) and antidepressants (45.2% v. 27.5%, $p=0.03$). There were no group differences in prescriptions for antipsychotics or sedative-hypnotics. Intervention subjects were more likely to rate their primary care as very good or excellent (82.8% v. 55.9%, $p = 0.002$). Intervention patients had significantly fewer BPSD at 12 months (mean difference -5.6, $p = 0.011$) as measured by the NPI. Intervention caregivers also reported significant improvements in distress and depression at 12 months. These improvements in behavioral symptoms are among the largest reported in the literature. This explanatory trial establishes that, under experimental conditions, the care of patients with dementia can be improved with interventions that can be deployed in primary care given sufficient practice redesign and resources.

In 2007, we updated the USPSTF review with a focus on identifying practical and accurate dementia screeners suitable to the primary care systems. Among the 29 dementia screening instrument studies included, we found 12 instruments with promising performance and practical implementation (less than seven minutes of administration time).⁶ Rather than identifying one best instrument, our review suggested that the clinician's strategy should simply be to pick one tool based on the population they cared for, with an awareness of how educational level, race, and age affect scoring, and then consider adding one or two others for special situations as needed. In addition to the brief screeners, we found a number of comprehensive instruments that evaluated multiple domains of cognition, thus having the potential to increase accuracy at the cost of increased administration time. We also identified

screening tests that could be useful in special situations. For example, the Telephone Interview for Cognitive Status (TIC) and MIS-T (Memory Impairment Screen – telephone version) could be useful for brief telephone based screeners outside the pressured atmosphere of the primary care visit, a critical feature for ensuring screening can occur feasibly in a broad range of healthcare delivery settings. Based on this review, we selected the MIS-T as the instrument of choice to be used within the diverse primary care clinics of our recruitment sites.⁹⁶ The MIS-T is a quick test of recall ability (4 minutes to perform) and has a high accuracy for dementia diagnosis with a positive LR ranging from 11 to 33 (95%, CI 15 to 72) and negative LR of 0.08 (95%, CI 0.02 to 0.3).⁹⁷⁻⁹⁹

Responsible Use of Data from the Regional Health Information Exchange (RHIO)

The proposed pragmatic trial will rely heavily on data routinely collected and stored in “Indiana Network for Patient Care (INPC), the RHIO in central Indiana. A full review of our prior work using the INPC, and its predecessor, the Regenstrief Medical Record System, is beyond the scope of this review of preliminary work. Over the past 20 years, we have used these data to describe patterns and cost of care for older adults across the entire urban public health system⁵², described emergency department use⁶⁷, medication use⁶⁸, patterns of care for dementia, depression, alcohol abuse, and other geriatric syndromes.^{33,48,54,56,70,92} We have described mortality outcomes of older adults with cognitive impairment and depression^{44,45}, and explored treatment of older adults with advanced cancer.⁷¹ We have an excellent track record of using these epidemiologic data to design, implement, and test interventions to improve the care of older adults.

We have also combined data from the RHIO with Medicare claims data as well as Medicaid, MDS, and OASIS data.^{46,69} To our knowledge, this dataset represented the first time these databases, which span the continuum of care, have been combined. In an ongoing NIMH-funded study, we are using these data to describe the patterns of health services use over a 10-

year period among older adults with lifelong serious mental illness. In a recent paper, we used these data to map transitions in care over five years among a cohort of older adults with prevalence and incident dementia. Compared to subjects never diagnosed (n=2,674), older adults with prevalent (n=524) or incident dementia (n=999) had greater Medicare (11.4% v. 44.7% v. 44.8%, $p < .0001$) and Medicaid (1.4% v. 21.0% v. 16.8%, $p < .0001$) nursing facility use, greater hospital (51.2% v. 76.2% v. 86.0%, $p < .0001$) and home health use (27.3% v. 55.7% v. 65.2%, $p < .0001$), more transitions in care per person in year of follow-up (1.4 v. 2.6 v. 2.7, $p < .0001$), and more mean total transitions (3.8 v. 11.2 v. 9.2, $p < .0001$). Among the 1,523 subjects with dementia, 74.5% of transitions to nursing facilities were transfers from hospitals. Among transitions from nursing facilities, the conditional probability was 41.0% for a return home without home health care, 10.7% for home health care, and 39.8% for a hospital transfer. Among subjects with dementia with a ≤ 30 -day re-hospitalization, 45% had been discharged to nursing facilities from the index hospitalization. At time of death, 46% of subjects with dementia were at home, 35% in the hospital, and 19% in a nursing facility. Thus, we found that patients with dementia live and frequently die in community settings. Nursing facilities are part of a dynamic network of care characterized by frequent transitions. This study again demonstrates the fundamental role of primary care in the longitudinal care of older adults with dementia.

Understanding the Patient and Caregiver Perspective

Over the past six years, we used the Health Belief Model (*HBM*) as the theoretical framework for the development of an instrument to capture the public perceived benefits of dementia screening, the PRISM-PC questionnaire.^{21-23,100} We completed the PRISM-PC questionnaire on more than 500 **patients aged 65 years and older attending several primary care clinics in Indianapolis who had no documented history of dementia or other illness such as depression, schizophrenia, or bipolar disorder**. Approximately 13% of this group of older adults screened positive for the presence of cognitive impairment. The majority of subjects

had positive attitudes of dementia screening such as that 65% to 90% felt that dementia screening would provide them with the opportunity to plan their future finance and health care, advance directive, to participate in research, and motivate them to have a healthier life style. Few older adults perceived a negative impact of dementia screening on their emotional health or their independence. These findings suggest that the process of dementia screening may improve the quality of life not only for patients with unrecognized dementia but also for older adults with screen negative results, including at minimum the assurance of the absence of significant cognitive impairment. However, older adults did report concerns about potential harms including suffering from depression or anxiety, loss of driving privileges, difficulty obtaining long-term health insurance, and worries that people would treat them differently.²¹⁻

23,100

Estimating Economic Impact

To investigate the current and future economic impact of the collaborative dementia care management program in primary care settings, we developed a model to evaluate the net benefits for CMS of applying the collaborative dementia care program early via a routine screening in primary care. We used data from the collaborative dementia care trial, the dementia screening and diagnosis study, the USPSTF systematic review, and North Carolina public health impact of dementia forecasting study.^{1,33,34,79} We used cost terminology suggested by Gold et al.¹⁰¹ Direct formal costs included those costs in which a Medicare payment will be made for the services (e.g., physician visits, medications, hospital care, paid home care, and long-term care services); direct informal costs were the hourly wage of a worker who would need to be hired to provide the same care that an unpaid caregiver is providing; and finally cost estimates for different time periods were inflated by the Medical Care component of the Consumer Price Index (CPI). After estimating the per capita total annual costs, we generated aggregate estimates of dementia prevalence over the period 2010 - 2050. The per-patient costs

were multiplied by the national prevalence weight to extrapolate the sample costs to population size for calculation of the total direct aggregated healthcare cost.

The model predicts that total direct annual savings with the early implementation of the collaborative dementia care intervention among unrecognized dementia patients relative to usual care model are \$4 billion dollars in 2010, \$22 billion dollars in 2025, and \$29 billion dollars in 2050. We further developed modified projections based on three scenarios: The discovery of a medical therapeutic that would reduce dementia incidence rate by 50%; the discovery of an intervention that would delay institutionalization by 12 months; and the discovery of therapeutics that would lead to reduction in dementia incidence rate and delay institutionalization. Compared to the baseline projections, the projected saving ranged from \$24 billion in 2011 to \$50 billion in 2050 under any of the three scenarios. Our forecasting study demonstrated that at varying rates of effectiveness and in constant dollars, early implementation of the collaborative dementia care intervention via a routine screening in primary care, is cost effective for CMS with direct annual savings ranging from four billion dollars in 2010 to \$29 billion dollars in 2050.¹⁰²

Initial Efforts to Adopt New Models of Care to Real-World Practices

Through funding from the NIMH “Interventions and Practice: Research Infrastructure Program (IP-RISP R24), we have been building the infrastructure for an academic-community research partnership. The specific aims of the Indianapolis IP-RISP were to (1) *foster an academic community-provider partnership that supports a research culture focused on the practical implementation and evaluation of novel mental health services for older adults; and (2) conduct and evaluate mental health services and implementation science pilot projects that address the quality improvement priorities of the community partner and their patients.* Although the entire project is composed of eight different pilot projects, two are of particular interest to this proposal. The first was to create an integrated medical record to support clinical care for primary care patients who were also cared for in the local Community Mental Health Center. Records

had been previously kept in two different silos for these two different sites of care. The project is important to the current proposal because it taught us that technical barriers are often minor compared to cultural and legal barriers and resistance due to fear of change. The second project was to implement a collaborative care model for older adults with depression, cognitive impairment, or both and also integrate the care of cardiovascular disease. Manuscripts describing the success of this major implementation science project were published in *Aging and Mental Health* (2011).^{42,43} This second project is particularly important to the current proposal because we developed three infrastructure components to facilitate adoption of the collaborative care in primary care.

The first component is the Healthy Aging Brain Care (HABC) Monitor. Funded through a combination of the IP-RISP, the NIA IU Roybal Center, and industry, we developed a novel new caregiver “blood pressure cuff” for dementia, suitable for routine use in primary care.¹⁰³ This HABC Monitor will assist with one of the main tenets of chronic care which is longitudinal tracking of patient outcomes. The HABC Monitor has excellent psychometric properties and is a practical measure of behavioral and psychological symptoms of dementia.¹⁰³ The second component is the electronic medical record for aging brain care or eMR-ABC. In order to efficiently deliver the various components of the collaborative care model, we developed a web-based program management platform called eMR-ABC. The platform of the eMR-ABC includes a set of processes and software such as:

- Flexible and secure access to platform from multiple locations and by various clinical users;
- Manual, web-based, and optically scanned solutions to capture self/caregiver reported functional, behavioral, psychological, and cognitive symptoms;
- Decision support to deliver personalized, pharmacological and non-pharmacological care protocols;

- Tracking process of care coordination tasks delivered by the care coordinators;
- Monitor patients' and their caregivers' biopsychosocial needs;
- Monitor population-based outcomes to guide overall program performance;
- Integration capacity with other informatics tools such as the Indiana Network for Patient Care (INPC); and
- Easy interface to move data from the eMR-ABC to analyzable datasets and potential merging with other datasets.

The third component is a manual to assist practices in replicating the collaborative care management program. Through funding from the NIMH and other local and federal funding, we have developed the prototype for an implementation manual. The implementation or “replication manual” is based on a combination of the original collaborative care clinical trial and the field experience we gained through our initial local implementation efforts. We first adapted our original collaborative care model to improve its long-term adoptability by an urban public hospital.^{42,43} Capitalizing on the substantial interest in the US on the patient-centered medical home and reducing 30-day re-hospitalizations, we re-conceptualized our collaborative care model as the Aging Brain Care Medical Home. This new program was adapted to target older adults with dementia or depression who had been recently hospitalized by providing collaborative care in the home setting immediately following hospitalization discharge. In a recent publication, we described a structured set of activities that laid the foundation for a new partnership with the health care system and the lessons learned in implementing this new care model. We used the reflective adaptive process as a relationship building framework that recognizes primary care practices as complex adaptive systems.¹⁰⁴⁻¹⁰⁶ This framework allows for local adaptation of the protocols and procedures developed in the clinical trials. Tailored care for individual patients was facilitated through a care manager working in collaboration with a

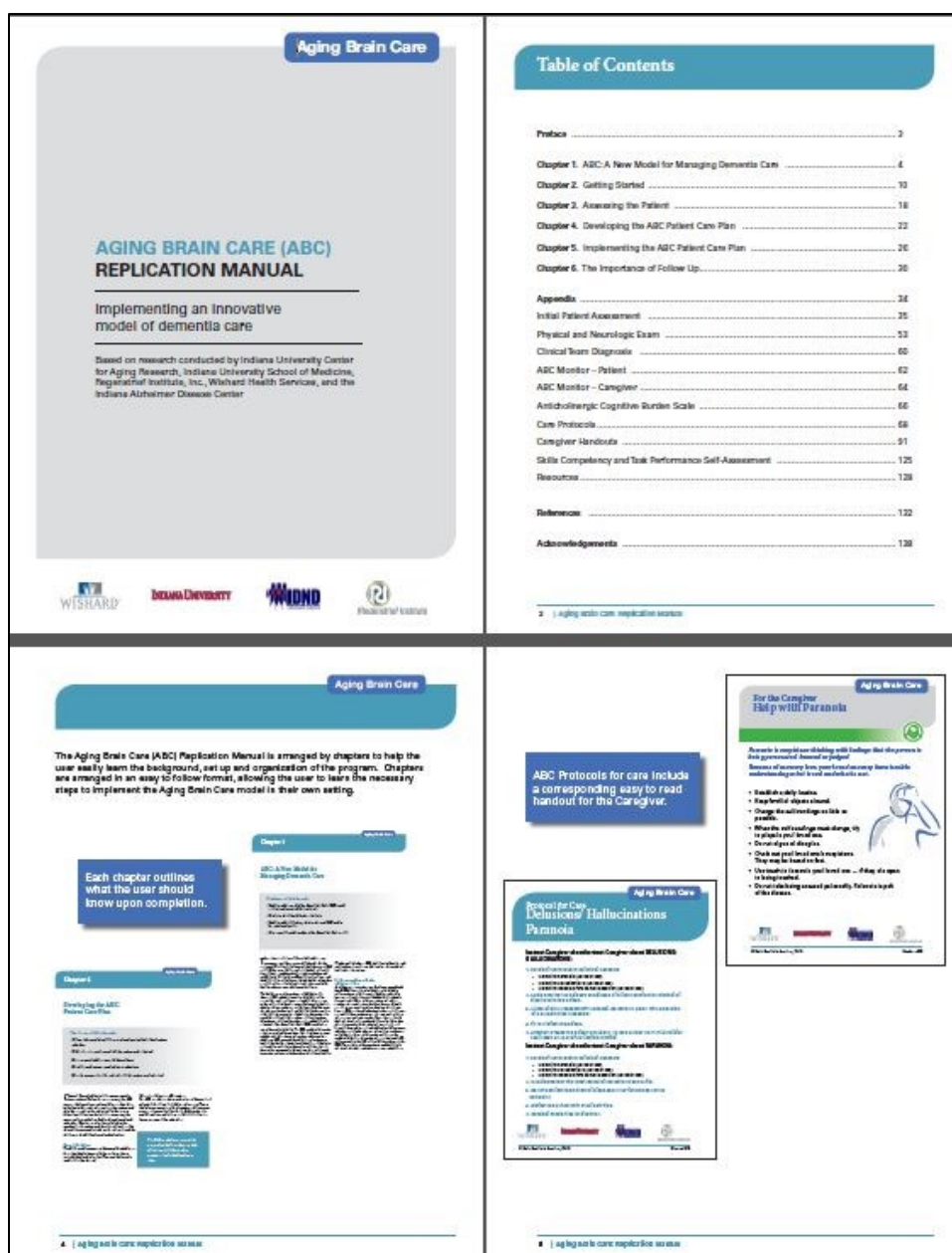
primary care physician and supported by specialists in a memory care clinic as well as by information technology resources.

Building on the success of this project, we received funding from the Regenstrief Institute to begin development of a replication manual to facilitate the wider dissemination of this care model. A few summary pages from this existing manual are depicted in the picture at right.

The manual provides information to primary care practices on how to set up a functional model of best practices for the care of older adults with dementia or depression. We emphasize that

any screening program would need to have in place the capacity to provide education, diagnosis, and care for screen positive patients and their family caregivers.

This replicable manual not only provides instructions that are consistent with treatment guidelines^{13,14}, it also provides

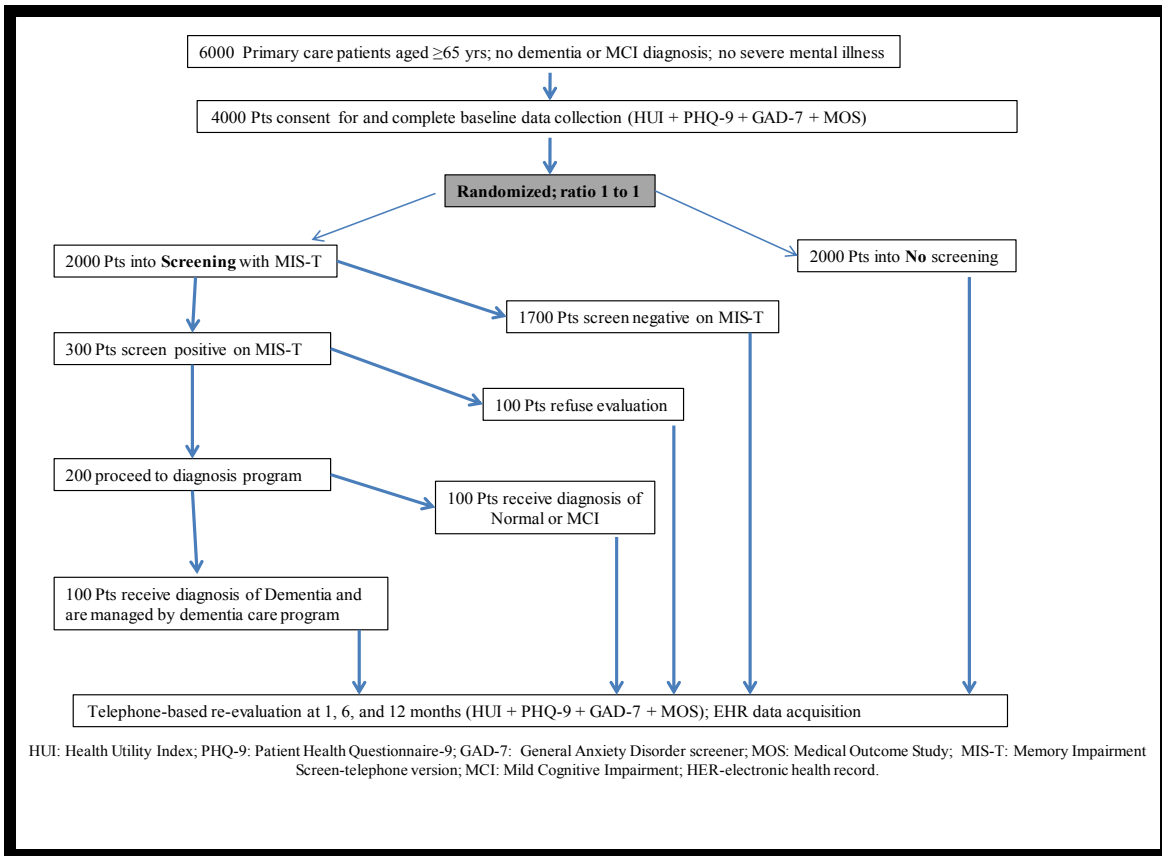


written materials to assist in caregiver education and support.

Through this summary of our preliminary studies we hope to establish our preparedness for the successful completion of this pragmatic clinical trial of dementia screening in primary care.

E. CHOICE Trial

We are proposing to enroll 4,000 adults, aged 65 and older, attending 10 primary care clinics in Indianapolis; these clinics are representative of two large health care systems: Wishard Health Services (WHS) and IU Health (IUH). We will randomize older adults at ratio of 1:1 into “no screening” or “screening” groups. Subjects randomized into the screening group who have a positive screening would be further referred into a dementia diagnostic assessment and counseling and management program. Our outcomes will be measured at baseline, 1, 6 and 12 months. Using data from our local Regional Health Information Exchange, the Indiana Network for Patient Care (INPC), we will collect health care utilization data of our samples; and monitor new diagnosis, diagnostic testing, and prescribed treatments and referrals. The flow diagram for the proposed study is depicted below.



Subject Recruitment

Established in 1999, the Indiana University Practice Based Research Network (IU-PBRN) consists of 17 primary care centers affiliated with Wishard Health Services and Indiana University Health.⁷³ These two systems serve a diverse population of insured and uninsured patients throughout Indianapolis. More than 110 primary-care physicians practice at these sites. These physicians treat approximately 100,000 patients per year in more than 300,000 visits annually. Using the INPC data repository, IU-PBRN effectively uses informatics tools to streamline patient recruitment and follow-up.⁷³ Since its inception, the IU-PBRN has screened more than 45,000 primary care patients, enrolling more than 17,000 subjects into more than 75 studies. The study team has been utilizing the IU-PBRN since its inception and the successful completion of these projects, described in the Preliminary Studies section, are a testament to

the effectiveness of the IU-PBRN. The IU-PBRN achieved this success through the following informatics innovations.

Centralized Electronic Data Management:

Before a study is operationalized, data managers extract from INPC a list of eligible patients based on the study's inclusion criteria (e.g. patients cared for in the targeted primary care practice, over the age of 65, and without a diagnosis of dementia). Once an eligible list of patients has been extracted, it is provided to the clinicians, who must authorize the study to approach their patients for potential participation. Letters are sent to those patients informing them of the study and the appointments records are queried to determine when the patients are next due for appointments. Lists of patients with upcoming appointments are then generated to develop a weekly list of the patients eligible for the study. This electronic list is accessed via the intranet by the IU-PBRN research assistants, who subsequently enter recruitment information into the database about all patients contacted. The data manager then merges the data into a master database that is used to generate future lists. IU-PBRN has established a study monitoring system that uses the above-mentioned master database to upload enrollment dates into the electronic medical record. The electronic medical records contain the dates of enrollment and discharge from the project for each patient. This allows the data managers to establish date ranges for clinical data among enrolled patients. It allows them to know when patients have completed or have been removed from a study as they may be available for recruitment into other studies.

Electronic Data Collection

At the start of a new study, an electronic data extraction is performed to generate a list of potential subjects from the INPC. Patients are then automatically excluded if they have previously indicated an unwillingness to participate in future trials. IU-PBRN generates a

customized list of patients for each physician. The treating physician indicates whether IU-PBRN should approach a patient for enrollment in the study. Eligible patients will be approached by research assistants (RAs) at their next scheduled appointment. The patient's preference and any initial screening information are recorded at this session using portable computers. Electronic data management ensures that patients' and physicians' preferences are stored, retrieved, and delivered to minimize inconvenience to both parties and to maximize the efficiency of the RAs. We will use the IU-PBRN experience and research recruitment infrastructure to identify older adults for RAs to approach for potential participation into our pragmatic dementia screening trial.

Not all inclusion and exclusion criteria can be reliably assessed through the INPC data available to the IU-PBRN. A final determination of the subject's eligibility is made during the face-to-face encounter in clinic with the IU-PBRN RA. We will exclude any subject who:

- are a permanent resident of a nursing facility;
- have a serious mental illness such as bipolar disorder or schizophrenia as determined by the presence of related ICD-9 codes indicative of such an illness; or
- have a pre-existing diagnosis of dementia or cognitive impairment

The list of inclusion and exclusion criteria will be given to the PBRN coordinator to arrange for subject contact during their next primary care visit. Based on our previous dementia related studies in the targeted primary care systems^{22,33,34,100,107}, we anticipate approaching 6,000 older adults to enroll 4,000. Rolling enrollment will take place over 30 months with an approximate monthly enrollment rate of 130 subjects. As outlined in the figure above, we anticipate that the dementia collaborative care program will manage 100 subjects with dementia. They will also counsel 100 subjects regarding the future impact and management of their diagnosis of mild cognitive impairment and assure them that their cognition is normal

despite their positive screening results. The entire 4,000 subjects will be followed for 12 months. Across the various primary care practices, we will have access to more than 12,000 adults aged 65 and older. From our prior screening studies, we know that the prevalence of screening positive for possible dementia is 13-15% and of these, 50% will have dementia on subsequent diagnostic assessments. Although we have designed this study as a pragmatic trial, we will be requesting that patients sign informed consent for participation in the project.

Telephone Recruitment:

We will also employ a telephone version of the informed consent process to allow for potential recruitment of previously identified eligible patients via the INPC that were not approached in clinic by the ResNet team due to time and prioritization restraints. We will obtain a list of the eligible participants that were not approached from the PBRN Program Manager on a regular basis. These participants will be contacted for participation by telephone by study research assistants. We will also utilize the same telephone consenting process to recruit subjects attending the IU Health Arnett primary care clinics. Eligible patients from the IU Health Arnett primary care clinics will be identified by the treating physician and a list generated for the study research team.

Screening Process

Both subjects who are randomized into the non-screening arm of the study and those who are randomized into the screening arm will complete a set of standardized questions about successful aging, preventive health measures, and lifestyle behaviors. This is to invest the patients randomized into the non-screening arm of the study in the project, minimize the potential excess focus on cognitive screening alone, and to remove any impressions among the “non-screened” group that they missed out on an important health screen. We have not pre-specified the content of this screener because it will be designed based on ongoing data collection in the two targeted health care systems. This is consistent with our approach to embed the project, whenever possible, into ongoing or emergent activities. Examples of

questions to include in this control questionnaire might include: smoking, physical activity, influenza vaccination, or seat belt use for example. At the time of this questionnaire, enrolled subjects will also complete the baseline study assessment described later in this proposal.

Through the systematic review described in the Preliminary Studies section, we have identified a screening instrument that meets the following criteria: 1) demonstrated validity in primary care settings; 2) requires less than five minutes to administer; and 3) has a positive likelihood ratio (LR) of 5 or higher. Based on our systematic evidence review for the literature that was published in *JAMA* in 2007⁷⁸, we selected the Memory Impairment Screen Telephone version (MIS-T)⁹⁶ as the screening instrument. The MIS-T takes only four minutes to complete with excellent inter-rater reliability, has been validated in multiple primary care and community samples, and has a positive LR of 33.^{6,96-99} The MIS-T has a total score from 0 point to 8 points. A cut-score < 5 has 86% sensitivity and 91% specificity for dementia with a positive predictive value of 72% and negative predictive value of 96% in a setting with a dementia prevalence of 15%.^{6,96-99} The MIS-T will be administered by the study research assistants after the subject consents to be enrolled in the study and randomized into the screening arm of the study.

Subjects who are randomized into the screening arm of the trial and score less than 5 points on the MIS-T will be referred to the collaborative dementia care program for a subsequent diagnostic assessment, counseling and management. We are not expecting the primary care practice to complete this next step. Among the 300 patients who will score less than 5 on the MIS-T (15% positive screening rate), we anticipate that approximately 100 (a refusal rate of 33%) will refuse follow-up diagnostic assessment, 100 subjects will not be diagnosed with dementia despite their positive screening results, and 100 subjects will be diagnosed with dementia.

Why not simply rely on the primary care practice to deliver the Collaborative Care Program?

Given that this is a pragmatic trial, reviewers might question whether the provision of the collaborative care program moves this project too close to an explanatory design. Our research team did

discuss this decision in assessing our design via the PRECIS tool. Three issues guided our decision-making. First, we know from prior research that simple provision of screening data or treatment guidelines has little impact on patient outcomes. Second, we know from prior research on depression screening that screening harms outweigh benefits if the clinical practice is not prepared to evaluate and treat the patients who screen positive. Third, we already know the collaborative care program is more effective than usual care under experimental conditions. The collaborative care program patients, referred to in the current proposal, are exemplary of the practical application of the collaborative care.^{34,42,43}

The Collaborative Dementia Care Program

The goal of the program is to assist primary care clinicians in achieving the recommended standard of care in the diagnosis and management of older patients with dementia. Much of the intervention, facilitated by an Advanced Practice Nurse as the care coordinator, is targeted to co-manage or support the practice behavior of primary care clinicians, enhance self-management skills of both the care-recipient and the informal caregiver, and maximize the coping behavior of the patient and the informal caregiver. By design, the program planned protocols lead to individualized and patient-centered profiles of actual interventions for individual patients and their informal caregivers. The program has four main phases: the initial assessment phase, the plan of care development phase, the second home visit phase, and the follow-up phase.

The initial assessment: The care coordinator conducts a demographic and medical information interview, reviews medication lists and discharge plans if the patient is currently hospitalized or is post-hospitalization, gathers and reviews any diagnostic testing and brain imaging results with the primary intention of identifying any reversible and co-morbid conditions, and schedules an initial home visit with the patient and the patient's informal caregiver. After completing a pre-

home visit interview, the care coordinator travels to and conducts a face-to-face initial assessment at the patient's and/or informal caregiver's residence or preferred location. At the patient's home, the care coordinator conducts a brief cognitive assessment; biopsychosocial needs assessment of patient and informal caregiver, and medication reconciliation. The program uses standardized assessment tools including: The Healthy Aging Brain Care Monitor (HABC-M).¹⁰⁸ If there is no available or identified caregiver, the care coordinator attempts to identify a caregiver and complete the caregiver questions at a later date either by phone or in person. The care coordinator documents the initial and follow up visits using care coordination software called the eMR-ABC.

The Plan of Care Development Phase: This phase is designed to facilitate the creation of an

individualized care plan with an emphasis on coordinating care with the patient's primary care provider. This phase begins after the first home visit and concludes with the second home visit by the care coordinator. After consultation and coordination with the program geriatrician and primary care physician, the care coordinator rules in or out the diagnosis of dementia and its subtypes, and finalizes the individualized care plan with the primary care physician.

Complex patients or patients with diseases that may benefit from specialty care, may be recommended for specialty evaluation and co-management. If necessary, the patient will be referred for a more extensive cognitive

and mental health evaluation at the local memory care practice. This decision would be jointly reached by the program geriatrician (Dr. Sachs) and the patient's primary care provider. Finally,

Program Services and Protocols

- Self-Management /Caregiver Skills Enhancement
- Support Group Participation
- Informal Telephone Support
- Problem Solving Training
- Reducing Anticholinergic Medications
- Prescribing FDA-Approved Medications
- Managing High Vascular Burden
- Monitoring and Supporting of Caregiver's Emotional and Physical Health
- Managing Transitional Care
- Managing Acute Care Problems
- Root-Cause Analysis of Re-Hospitalization or Re-Emergency Room Visit
- Care Prioritization

the care coordinator will schedule a second face-to-face home visit with the patient and the informal caregiver within 2-4 weeks of the initial home visit.

The Second Home Visit Phase: The care coordinator discusses the individualized care plan; explains the diagnosis, the natural history, and the prognosis of dementia; implements appropriate care protocols; reviews, explains, and distributes the corresponding educational handouts for both the patient and the informal caregiver; and connects patients and informal caregivers to in-home services and community resources as needed.

The Follow-Up Phase: It includes interaction with the patient or the caregiver via face-to-face home or clinic visit, phone contact, email, fax or mail. The minimum amount of contact during this time will be once monthly for the first three months and once every three months thereafter. During these interactions, the care coordinator will answer any questions generated from previous visits; collect patient and informal caregiver feedback; reconcile medications and review medication adherence; have the informal caregiver complete the HABC Monitor to trigger the use of specific care protocols; and facilitate the informal caregiver's participation in the Support Program. Throughout the duration of the follow-up phase, the team will continue to work with the patient, the informal caregiver, and the patient's primary care provider to monitor, implement, and adjust as necessary the individualized care plan. The program care services and protocols already developed and fields tested include:

1) Self-Management/Caregiver Skills Enhancement: Prior to this second home visit, the care coordinator prepares the various relevant materials to enhance patient self-management or caregiver skills. These materials (the Patient or Caregiver Care Manual) can include: information on legal and financial planning with referrals made to elder law specialists and legal services programs in the community; specific behavioral interventions techniques to help

manage, reduce or avoid patient problem behaviors; and/or coping strategies to ensure the caregivers' emotional and physical health remain intact. These materials are provided to the patient or the caregiver via various face-to-face or home counseling sessions. If the patient's or caregiver's needs are particularly complex, the counseling can take place over more than one face-to-face and/or telephone sessions.

2) Support Group Participation: In collaboration with the Central Indiana Alzheimer's Association, the program will organize a monthly support group, facilitated by the care coordinator, and located at the Indianapolis Senior Center. While support groups are available in the metropolitan area through the Alzheimer's Association (AA), the program support group will be specifically designed to give the dyads tailored information to meet their needs within WHS and IU Health systems. While mandatory participation is difficult to enforce, the team will encourage participation by stressing the importance of the support group for the overall health of both the patient and the caregiver. The support group meets on the fourth Friday of each month at the local senior center for two hours. In cases that the dyad cannot make the support group due to access and distance, the team will write a pro-active prescription to connect the dyad with their local AA that specifies the type of support needed from the local Alzheimer Association, such as belonging to a monthly support group, provision of particular educational materials, or case management. The team will obtain permission from the caregiver/patient to be proactively contacted by their local Alzheimer Association.

3) Informal Telephone Support: The dyads will have access to telephone consultation by the care team. The telephone contact can be initiated by the spouse or any other family member participating in the patient's care. Offering access to the care team empowers the informal caregiver to try different interventions more readily.

4) Problem Solving Process: Using data collected from the structured caregiver interview or during face-to-face visits, the care team, in coordination with the primary care provider, uses standardized problem solving protocols to manage any behavioral and psychological symptoms related to dementia. The care team educates the caregiver on implementing these protocols and monitors the success of such implementation via face-to-face or telephone follow-up interactions.

5) Reducing the Anticholinergic Cognitive Burden: Using the Anticholinergic Cognitive Burden Scale (ACBS), developed by our Aging Brain group, the care team reviews the over-the-counter and prescribed medications taken by the patient and coordinates with the primary care clinician to identify the presence of any anticholinergic medication in efforts to balance their benefits and harms.^{109,110}

6) Prescribing FDA-Approved Medications: The care team, in coordination with the primary care provider, prescribes and discusses the indications, benefits and expectations of using FDA-approved medications for dementia.

7) Managing High Vascular Burden: The care team will review the current vascular burden of the patient and work with the primary care provider on reducing such a burden using both pharmacological and non-pharmacological interventions.

8) Monitoring and Support of the Caregiver's Emotional and Physical Health: The care team will use the HABC Monitor to monitor the cognitive, functional, behavioral and psychological symptoms of patients and caregiver stress (see supportive tools below).

9) Managing Transitional Care: The care coordinator conducts a home visit within 72 hours of hospital discharge to reconcile discharge medications and counsel and support the dyad to carry out any post-hospital care plans.

10) Managing Acute Care Problems: There are times when a patient will call the ABC team with an acute care problem and seek direction. To avoid a potentially unnecessary ED visit, the care team may make a home visit, inform the primary care physician, and manage the problem accordingly.

11) Root-Cause Analysis of Re-Hospitalization or Re-Emergency Room Visit: Within one week of the re-admission event date, the care team will interview the patient, the caregiver, and the clinical team to determine the appropriateness of the re-admission and brainstorm about possible underlying causes for preventable re-admission. In addition, the team will review the medical records and try to identify a list of potential triggers for preventable re-admission failure. The team will review the failure case within a week of the event date.

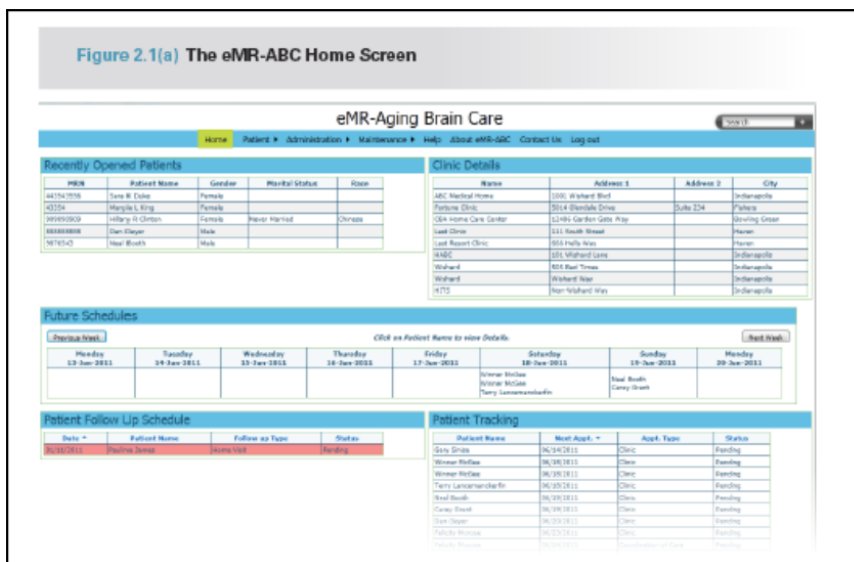
12) Care Prioritization: Under circumstances where patients have significant needs that exceed the capacity of the clinical program, the care team will utilize set guidelines to prioritize addressing these needs to ensure the most vulnerable patients (those who require a hospital or emergency department visit followed by those who require post-hospital or emergency department transitional care) receive timely care coordination by the care team including a home visit within 72 hours of discharge from a hospital or emergency department.

13) Discharge Criteria: The care team will discharge the patient and caregiver if they meet any of the following criteria: 1) patient expires; 2) patient and/or family/caregiver decline to continue in the program; 3) primary care provider requests patient discharge from the program; 4) patient

transitions to another health care system or move outside Marion County; or 5) patient’s living situation/environment becomes unsafe for patient and/or staff and therefore requires long-term skilled nursing home care.

The Support Tools of the Collaborative Dementia Care Program

1) The Mobile Office: The “Mobile Office” concept enhances the opportunity for the care team to see patients and caregivers in a variety of settings that are most conducive for their physical, emotional and psychological comfort, thus allowing for conducting a biopsychosocial needs assessment, care coordination, information gathering, or support for self-management education. The mobile office sites may include any of the primary care clinics; the patient’s home; the Center for Senior Health; any of the specialty clinics at Wishard or IU Health; or areas in the community, including the caregiver’s place of employment.



2) The Care Coordination Support Software: In order to efficiently deliver the various components of any collaborative coordination care model, we developed and implemented a web-based care coordination software called eMR-ABC. This software includes the following functions: 1) flexible and secure access to the platform from multiple locations and by various users; 2) manual, web-based, and optically scanned solutions to capture patient centered outcomes such as functional, behavioral, psychological, and cognitive symptoms; 3) decision support to deliver personalized pharmacological and non-pharmacological care protocols; 4) a

tracking process of care coordination tasks delivered by the care coordinator; 5) monitoring patients and caregiver responses to care protocols; 6) monitoring population-based outcomes to guide the overall program performance; 7) integration capacity with other informatics tools such as the local electronic medical record and regional health information exchange; and 8) an easy interface to move data from the eMR-ABC to analyzable datasets. The Advanced Practice Nurse will have access to the eMR-ABC via a laptop with wireless air card connection.

3) The Healthy Aging Brain Care (HABC) Monitor: The team will use the HABC Monitor to

monitor the cognitive, functional, behavioral and psychological symptoms of patients and the caregiver stress. The HABC

monitor is comprised of 32 items tapping the previous four

constructs.¹⁰³ While the total HABC Monitor score is helpful to measure change over time, each question

eMR-Aging Brain Center
 Home Patient Administration Maintenance Log out

Care Giver Monitor
 MRN No.: 263643-1
 Harry W. Harris (09/04/1940 : 70 : Male)
 2445 Quest Ave. Testing Yalestown Indiana
 Care Co-ordinator: Tiffany L Campbell

Legend: Not at all (green), Several days (yellow), More than half the days (cyan), Almost Daily (red)

	12/01/2009	12/08/2009	12/22/2009	01/07/2010	12/14/2009
Judgment or decision-making.					
Less interest or pleasure in doing things, hobbies, or activities.					
Repeating the same things over and over such as questions or stories.					
Learning how to use a tool, appliance, or gadget.					
Forgetting the correct month or year.					
Handling complicated financial affairs such as balancing checkbook, income taxes & paying bills.					
Remembering appointments.					
Thinking or memory.					
Planning, preparing or serving meals.					
Taking medications in the right dose at the right time.					
Walking or physical ambulation.					
Bathing.					
Shopping for personal items like groceries					
Housework or household chores.					
Leaving her/him alone					
Her/his Safety.					

Copyright © 2009 Mavensphere, Inc. All rights reserved.

also indicates a specific care area where help or coping strategies might be indicated. The HABC Monitor also includes questions on dangerous behaviors such as falls, home safety, and automobile driving. When these functional, cognitive, behavioral, psychological, or psychiatric conditions (for either the patient or the caregiver) are identified, the care team will work with the primary care clinician and other providers to begin initial pharmacological and non-pharmacological management. This may also include working with the caregiver's primary care provider. Consistent with current recommendations, protocols for patient management emphasize non-pharmacologic treatment at the outset.

A patient who screened positive for cognitive impairment but found to have no dementia by the subsequent assessment, will continue to be referred for an annual cognitive assessment with the local memory care practice at WHS or IU Health.

Assuring Adherence to our Intervention:

The director of the clinical core (Dr. Sachs) will meet with the Advanced Practice Nurse on a weekly basis to review the performance of the program, its fidelity and any complicated care using the electronic reports generated by the care coordination support software (eMR-ABC). The eMR-ABC will provide Dr. Sachs with a weekly report of the performance of the care coordinator in regards to the adherence of delivering specific protocols.

The Usual Care Control Groups:

The 2,000 subjects who would be randomized into the “no screening group” will continue to receive their usual care, including a referral to the local memory care practices if their primary care provider suspects the presence of a cognitive problem at any time during the study follow-up.

Overview of Data Sources		
Construct	Source of data	Specific variables/Instruments
Social, Demographic, Advance care planning	Study Survey	MOS, age, gender, race, education, income, living situation, marital status, and advance care planning
Health Related Quality of Life, Mood and Anxiety	Study Survey	HUI, PHQ-9, GAD-7
Health Care Utilization	Indiana Network for Patient Care records for the 4000 subjects	ER episode, location
		Hospital episode, location
		Inpatient diagnoses (ICD9 codes)
		Length of stay
Co-morbidity	Indiana Network for Patient Care records for the 4000 subjects	ICD-9 codes for the 10 common chronic diseases

Medication Use	Indiana Network for Patient Care records for the 4000 subjects	Psychotropics
Care Processes	eMR-ABC and INPC	Visits to memory care practice. Collaborative dementia care team visit. Visits with HABC monitor Protocols delivered by the care team

F. Inclusion/Exclusion Criteria

Inclusion criteria include:

- adults age 65 and older;
- at least one office visit to their primary care physician within the previous year;
- no previous diagnosis of dementia or memory problem as determined by ICD-9 codes or the presence of prescription for anti-dementia medications (cholinesterase inhibitors or memantine);
- ability to consent to participate in the study; and
- ability to communicate in English

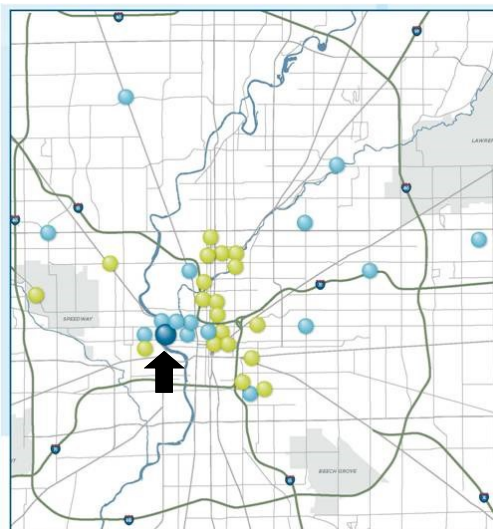
Exclusion criteria include:

- adults who are a permanent resident of a nursing facility;
- a serious mental illness such as bipolar disorder or schizophrenia as determined by the presence of related ICD-9 codes indicative of such an illness; or
- a pre-existing diagnosis of dementia or cognitive impairment

G. Enrollment/Randomization

Clinical Settings and Population

The proposed study will be conducted in multiple primary care clinics affiliated with Wishard Health Services and Indiana University Health in Indianapolis, IN that provide medical care for a diverse, urban population of older adults. We have a long-standing research partnership with WHS and a growing relationship with IU Health. It is only in the last year that IU Health came into existence through a new collaboration between the IU School of Medicine and a statewide health care system formerly known as Clarian Health.



Wishard Health Services (WHS) is responsible for the care of medically-indigent patients who live in Marion County, Indiana as well as those who are uninsured or under-insured. WHS provides care for about 20% of the population of Indianapolis. Fifty percent of its patients are African American and approximately 10% are Hispanic. Recognizing the importance of the community's access to care, WHS developed a network of community health centers throughout the Indianapolis area as shown in the figure to the right. Underscoring WHS's standing in the local community, Marion County voters approved a new WHS facility. This new \$750 million facility is on schedule and on budget and will be opened in less than two years. The new, modern and efficient \$1.2 million square-foot facility will equip the hospital with 327 inpatient beds, 17 operating rooms, four interventional labs, 12 labor and



delivery rooms, an emergency department with 90-treatment rooms, a 20-bed clinical decision unit, more than 200 exam rooms, one of two Adult Level I trauma centers in Indiana, and the region's only adult burn center. The outpatient care building, which links functionally and operationally to the hospital, will offer 110 exam rooms in a clinical setting and serve as the point of entry to the hospital for most visitors and non-emergency patients.

The partnership between WHS and faculty scientists in the IU Geriatrics Program and the Center for Aging Research has a history that spans more than 20 years. Within this 20-year history are multiple examples of repeated cycles of moving research to the bedside and bringing the bedside to research. Our programs have been inspired by, co-developed and evaluated by the clinicians providing care to older adults. In this regard, WHS has been the living laboratory for innovative, explanatory clinical trials for vulnerable elders with dementia, late life depression, delirium in need of end-of-life care, among others. In addition, WHS was our community partner in the academic-community research partnership development program, funded by the NIMH (IP-RISP R24), that focused on mental illness among older adults.

The newly formed "Indiana University Health" (IUH), is one of the largest health care systems in the United States and is Indiana's largest and most comprehensive healthcare system. It is comprised of three hospitals in Indianapolis and seventeen hospitals statewide. The system includes hospital-based physician practices, outpatient centers, and pharmacy and home care services. Through its new partnership with Indiana University School of Medicine (IUSOM), the nation's second largest medical school and a global leader in medical education and research, IU Health is uniquely positioned to participate in innovative pragmatic research trials. As an academic health center, IU Health and IUSOM work in partnership to train physicians, blending breakthrough research and treatments with the highest quality of patient care. Research conducted by IUSOM faculty gives IU Health physicians and patients access to the most cutting edge and comprehensive treatment options.

We view WHS as a longstanding partner in explanatory research who will now collaborate with us in pragmatic research; we also view IU Health as a potential statewide site of pragmatic research. WHS represents the nations many urban, public hospitals and associated community health centers while IU Health represents the growing number of very large integrated health care systems. Between the two health care systems, we have access to a broad range of diversity in older adult patients as well as a large population of dual-eligible (Medicare and Medicaid), older adults. WHS cares for a population of approximately 12,000 older adults (60% African-American) in nine primary care practices whereas IU Health cares for approximately 36,000 older adults (13% African-American) in 19 primary care practices. The Indiana Hispanic population is growing rapidly, but it is dominated by younger adults. Consequently, the population of Hispanic older adults in both health care systems is less than 2%.

As already mentioned, both of these health care systems are served by a regional health information exchange. In 1995, with support from the AHRQ, the National Library of Medicine, the National Cancer Institute, and the Regenstrief Institute, IU researchers created the first regional health information technology network called the Indiana Network for Patient Care (INPC).^{49,64-66} The INPC is a regional health information exchange that integrates clinical information from the five major health care systems in Indianapolis in support of medical care.⁴⁹ These five health care systems provide INPC with laboratory results, emergency department data, inpatient and outpatient encounter data, coded diagnoses and procedures, radiology reports, hospital discharge summaries, operative notes, pathology reports, medication records, and electrocardiogram reports, among many other data elements. These five participating systems operate fifteen hospitals and more than 100 clinics and day surgery facilities that account for over 95% of all beds, hospitalizations, and emergency department visits in the Indianapolis metropolitan area (which has a population of 1.5 million). Together, they have 165,878 inpatient admissions, 450,000 emergency visits, and 2.7 million outpatient visits per

year. INPC also carries data from the Marion County Health Department; the Indiana State Department of Health; Indiana Medicaid; and RxHub, a national consortium of pharmacy benefit managers.⁴⁹ The INPC's rich clinical repository is organized by patient and medical record data and segregated into separate files by institutional source, but the data about one patient from many institutions can be viewed as a single virtual medical record, and clinicians can review a patient's record in a variety of video screens and hard-copy formats.

With initial focus in support of quality improvement, INPC is also beginning to serve biomedical research. In a recent clinical trial,^{34,51} we used INPC data to track utilization across the five health care systems in support of analyses examining the impact of new models of care on older adults health care utilization. These data were made available after appropriate approvals from the INPC Privacy Board which includes representative from all five health care systems and the Regenstrief Institute. Our study team has a track record in the responsible use of these data and in their appropriate data management and analysis.

Randomization

We will use a central, computer generated, web-based, randomization scheme to assign individual patients rather than providers or clinics to treatment conditions to minimize the effects of unmeasured case mix differences and clinic-level clustering. We estimate that the risk for 'spillover' from having participating clinics treat both intervention and usual care patients is likely to be small.^{34,51,72} If anything, patient-based randomization will conservatively bias the results in favor of usual care.

H. Data Collection (We will use face-to-face or telephone interviews for our data collections)

Health Related Quality of Life (HRQOL)

The primary outcome measure will be the HRQOL measured at baseline, 1, 6 and 12 months among the entire 4,000 enrollees. We will use the 15-item **Health Utility Index (HUI)** to

determine the subject's HRQOL.¹¹¹ The HUI is a generic, utility-based HRQOL instrument applied in patients with a wide range of medical conditions.^{111,112} It has eight attributes: Vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. The individual health domain scores range from 0.00 (maximum impairment) to 1.00 (no impairment) and the multi-attribute (HUI index) scores, a multiplicative function of individual attribute levels, range from 0.36 to 1.00 with anchors 0.00 = dead and 1.00 = perfect health. Naglie et al found that test-retest reliability exceeded the standard for adequate reliability of 0.70 in those with mild dementia (ICC = 0.75).¹¹³ Dr. Barbara Vickrey recently published a paper that provides new evidence regarding the construct validity (including responsiveness) of the HUI in community-based subjects with dementia.¹¹² The mean HUI multi-attribute utility score for 408 primary care patients with dementia was 0.54 (SD = 0.23) and the mean one year change was -0.30 among 240 dementia patients who remained in their own home after one year of receiving dementia care program whereas the mean one year change was -0.76 among 29 dementia patients who moved into a skilled nursing home facility.¹¹²

Mood and Anxiety Outcomes

We will use the **Patient Health Questionnaire–9 (PHQ-9)**¹¹⁴⁻¹¹⁶ and **Generalized Anxiety Disorder Scale (GAD-7)**^{117,118} to determine the impact of screening on our subjects' mood and anxiety at baseline, 1,6, and 12 months. We have used both instruments in various primary care-based research studies including our dementia collaborative care trial.^{34,51,93,114-118} The PHQ-9 is a nine-item depression scale with a total score from 0 to 27 and the GAD-7 is a seven-item anxiety scale with a total score from 0 to 21. Both of these scales are derived from the Patient Health Questionnaire; have good internal consistency and test–retest reliability; as well as convergent, construct, criterion, procedural and factorial validity for the diagnosis of major depression and general anxiety disorder.¹¹⁴⁻¹¹⁸ In our previous primary care studies, the mean

PHQ-9 scores ranged from 3.8 (SD = 5.1) to 4.4 (SD = 5.6) and the mean GAD scores ranged from 2.7 (SD = 3.2) to 3.2 (SD= 3.5).^{34,114-118}

For any subject who expresses thoughts/tendencies of self-harm (a positive response of 1, 2, or 3 to question 9 on the PHQ-9), the Research Assistant will notify the Study Coordinator. The Study Coordinator will keep a detailed log of these events and will be responsible for notifying the subject's primary care provider immediately.

Health Care Utilization

We will obtain consent at enrollment from all subjects for permission to review their medical records. We will then use the Indiana Network for Patient Care (a fully operational Health Information Exchange) to identify any episode of ambulatory or acute care that occurred within the following 12 months of enrollment date. We will structure continuous variables that describe the number of ambulatory and/or acute care episodes. Furthermore, we will structure additional variables that describe a potentially preventable hospital admission (preventable hospitalization).⁷⁶ Preventable hospitalizations will include any hospitalization for an ICD-9 based disease that is considered an ambulatory care sensitive condition where the condition itself or its course can be mitigated through optimal outpatient management.

Other Data Collection

Social and Demographic

Patient age, gender, race, education, income, living situation, and marital status will be collected, along with social support as measured by the five-item Medical Outcome Study (MOS) social support instrument.¹¹⁹ The five-item MOS social support instrument was derived from the Medical Outcome Study (5 = worst to 25 = best). It has a minimum factor loading of 0.738 with Cronbach's alpha of 0.859.¹¹⁹ The five-item MOS instrument includes having

someone to confide in or talk to about problems, to get together with for relaxation, to help with daily chores if sick, to turn to for suggestions about how to manage personal problems, and to love and make feel wanted.^{119,120}

Common Chronic Conditions

Using the Indiana Network for Patient Care, we will evaluate all 4,000 subjects for the presence of ten common chronic diseases detected by ICD-9 codes in the year prior to enrollment: arthritis, congestive heart failure (CHF), coronary artery disease (CAD), cancer, chronic obstructive pulmonary disease (COPD), diabetes, stroke, hypertension, kidney disease, and liver disease. These conditions were chosen based on their high prevalence in our older adult population.^{33,47}

Medication Use

Prescription records for all patients enrolled in the study will be reviewed using the Indiana Network for Patient Care to evaluate the use of psychotropic medications such as anticholinergics, antidepressants, anxiolytics and antipsychotics. These psychotropic medications will be categorized based on the American Hospital Formulary Service system criteria into anti-dementia (including cholinesterase inhibitors or memantine), antipsychotics, antidepressants, and anxiolytics.¹²¹

Care Processes

We will use the web-based tracking system (eMR-ABC) and INPC to monitor multiple processes of dementia care measures for both the control and the intervention groups including all patient contacts by the local memory care or primary care practices, the referral to local Alzheimer disease support groups, the use of home health services, and assessment of the level of participation of patients and caregivers in the collaborative care intervention program.

Advanced Care Planning (ACP)

We will measure the subjects' advanced care planning including having power attorney for health care and/or financial affairs, having a living will, and having life and additional insurance policies at baseline and 12 months. Advocates for dementia screening, even in the absence of highly effective anti-dementia drugs, argue that screening would offer patients a window of opportunity to complete ACP while most still have the capacity to do so. We are unaware of any data documenting that participation in a screening program for dementia or any other serious illness is associated with greater participation in ACP.

Dementia Recognition

We will determine the recognition of dementia by searching the Indiana Network for Patient Care databases for any ICD-9 code indicative of dementia or Alzheimer disease at hospital admission, discharge, or during the 12-month period following enrollment into the study.

I. Statistical Plan

The outcome measures for this study are HRQOL (HUI multi-attribute utility score), mood (PHQ-9) and anxiety levels (GAD-7) obtained at baseline, 1, 6, and 12 months. To verify the comparability of the randomized groups, patients' baseline characteristics between the screened and no screening groups will be compared using *t*-tests for continuous variables and chi-square tests for categorical variables. We will carefully examine the distributions of continuous variable and use alternative approaches such as transformation or nonparametric methods in cases of violation to the normal distribution assumption. We will also examine the frequency distribution of all categorical variables and adopt exact inference procedures in cases of zero or small cell size. We will compare the baseline characteristics between subjects with missing outcomes due to death or refusal at 12 months to subjects who completed the follow-up

to detect potential violation to the missing at random assumption. Further sensitivity analyses will be performed using various methods of imputation or a full parametric likelihood approach assuming various patterns of missing data.¹²²

Primary Aim tests the hypothesis that subjects in the dementia screening group will have higher health-related quality of life compared those in the no screening group. We will compare mean measures of health-related quality of life levels in the “screening” group to the “no screening” group using analysis of covariance (ANCOVA) while including baseline measures as covariates. We will first conduct the ANCOVA models separately for outcomes obtained at 12 months while adjusting for baseline measures. We will then use the mixed effect models to examine whether the difference between the two groups changes over time using repeated HUI measures as the dependent variables, group, time, interaction between group and time as independent variables while controlling for other baseline covariates. All analyses will be conducted using SAS 9.3 (SAS Institute, Carey, North Carolina). For the patients who do not complete the 12 month surveys for health-related quality of life, they will be excluded from the analyses followed by sensitivity analyses on missing data described below.

Secondary Aim 1 compares depression and anxiety levels at 1 month post dementia screening between screened subjects and subjects in the no screening group. ANCOVA models will be used to compare PHQ-9 and GAD-7 obtained at 1 month between the screening and no screening groups adjusting for patients’ characteristics and baseline measures.

Secondary Aim 2 estimates the cost effectiveness of the dementia screening program in comparison to the “no screening”. This economic evaluation will be conducted from the societal and payer perspectives, including the direct medical care costs, caregiver and patient time and transportation costs, and the effect on quality of life for patients and caregivers.¹²³ Costs will be

divided into fixed and variable costs and by the screening, initial assessment phase and the follow-up phase of treatment. Total medical care utilization costs will be estimated for the control and screening groups from healthcare utilization and reimbursement data captured by the Indiana Network for Patient Care (INPC) during the trial. Prescription drug use will also be obtained from the INPC healthcare administrative database. The cost analysis will capture the extent to which screening, early diagnosis and coordinated care of patients with Alzheimer's disease affects medical care costs associated with dementia and co-morbid conditions such as diabetes, made worse by failure to manage dementia. Activity costing will be utilized to estimate the costs necessary to implement and operate the screening and collaborative dementia care management program and the usual care for dementia patients. Patient and caregiver time, staff time, fringe benefits, overhead costs, and materials will be logged by staff using the eMR-ABC software and assessed for the 12 month follow-up period. Included are waiting time, time with patients, time in meetings, lab services, telephone calls and mailings to participants. Excluded are costs associated with research. Transportation costs will be estimated from data on distance from home to clinic. Health care contacts will be dated and checked to avoid double counting via claims and activity costing methods.

Prescription drugs will be valued at the median wholesale price. A dispensing fee will be added for each 100 doses. Unit wage costs and fringe benefits will be standardized applying median values paid to personnel in the region; wage data collected from the health care system partners.

Costs will be accumulated during the trial based on the probability of survival each month times the monthly cost of care for survivors to address censoring.¹²⁴ Effects and costs will be discounted at a 3% annual rate for the two-year trial period. The incremental CE ratio (ICER), will compare the no screening and less resource intensive usual care treatment strategy (UC) with the screening coupled with the more intensive treatment intervention (the

collaborative dementia care program) using the following formulas for (1) dementia patients (AP) and (2) Dementia patients plus their caregivers (CG).

$$ICER_{AP} = [COST_{HABC} - COST_{UC}] \div [QALY_{HABC} - QALY_{UC}] \quad (1)$$

$$ICER_{AP+CG} = [COST_{HABC} - COST_{UC}] \div [QALY_{HABC} - QALY_{UC}] \quad (2)$$

Uncertainty in the cost-effectiveness ratios and 95 percent confidence intervals will be assessed with 1,000 bootstrap samples. The outcome of each sample will be expressed as a scatter plot of incremental costs and effects generated from the bootstrap samples, reflecting the uncertainty arising from the model parameters. Results will also be displayed using net benefit analysis and cost-effectiveness acceptability curves (CEAC).¹²⁵ There is controversy about the appropriate ceiling ratio for health benefits.¹²⁶ Garber et al have recommended that a value of twice the median annual per capita income will result in efficient resource allocation.¹²⁶ The effects on ICERs of alternative unit cost estimates for care-giver time value and overhead cost rate for the screening and coordinated care management will be examined in a series of one-way and multi-way sensitivity analyses. The ceiling ratio λ will be varied from \$30,000 to \$150,000 per QALY for the CEAC analysis. The cost-effectiveness hypothesis will be tested against the \$100,000 per QALY maximum willingness to pay norm.

Statistical Power, derived from sample size estimate, is used to test the primary hypothesis that subjects in the screening group will have higher health related quality of life than the no screening group. Previous randomized trials comparing collaborative care to usual care in demented patients have stated effect size of 0.4 being clinically significant.^{34,35} Considering that the majority of patients in the screening group or the no screening group are not demented, the observable effect size between these two groups will be a combined effect size measure in the non-demented subjects and in those demented subjects receiving the collaborative dementia care program.

Assuming 85% sensitivity of screening instrument and 15% prevalence of dementia in this patient population, to achieve 80% power to detect a significance effect size of 0.094 between the screening group and the no screening group at $\alpha=0.05$ level (two-sided), and allowing 10% of patients with missing follow-up outcomes at 12 months, we need to enroll at least 3951 patients into the study. The effect size of 0.094 between the screening group and the no screening group reflects a difference of 0.40 SD between demented patients in the collaborative dementia care program and demented patients who were not screened and a difference of 0.06 SD in the majority of patients who are not demented in either group. We demonstrate in the table below that our planned sample size of 4,000 will have sufficient power to detect significant differences between the “screen” group and the “no screen” group under various scenarios assuming varying degrees of efficacy measures for the collaborative dementia care program and for the screening only subjects.

Estimated power with a total sample size of 4,000 comparing primary outcome measures between the screening group and the no screening group (two-sided at $\alpha=0.05$) allowing 10% of patients with missing outcomes at 12 months.			
Effect size of collaborative care in demented subjects	Effect size In non-demented subjects	Observable Effect Size	Power Estimate
0.3	0.07	0.091	77.9
	0.08	0.100	85.1
0.4	0.07	0.102	86.4
	0.08	0.110	91.0

For the Secondary Aims, given the sample size of 4000, we will have greater than 95% power to test the equivalence levels in PHQ-9 and GAD-7 at 1 month assuming equivalence differences of 0.6 (SD=5.1) on PHQ-9 and 0.5 (SD=3.2) on GAD-7 based on our previous studies in primary care patients.^{34,51,93,114-118}

J. Limitations

The proposed study has some limitations. The major limitation is its short duration of four years including 30 months of recruitment and one year of follow-up. Dementia is a chronic condition that worsens over time. While one year of observation will provide time to monitor changes in the outcomes selected for this trial, it does not provide a long enough observation window for more distal outcomes such as nursing home placement or mortality. From prior studies, we know that one year of follow-up data is sufficient to detect the impact of the collaborative dementia care program on screened detected patients with dementia. In our clinical trial of the collaborative dementia care program, we were able to identify a clinically relevant effect within 12 months.

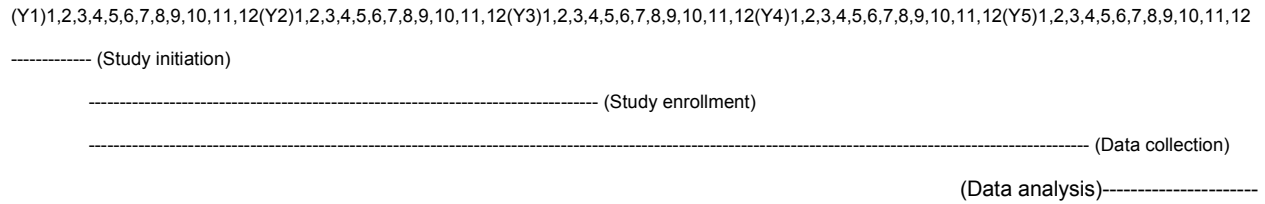
Perhaps the largest threat to the study as proposed is enrollment. The research infrastructures available for our study and the extensive experience of our investigators in enrolling similar large and vulnerable populations, greatly increases our likelihood of success in recruiting 4,000 subjects within 30 months. In addition, we have contingency plan to double our recruitment number by using additional Indiana University affiliated primary care clinics with access to more than 30,000 older adults aged 65 and older.

Finally, the generalizability of our collaborative care program and our urban and minority dominant population might be considered a limitation. However, we are testing our intervention in a very challenging patient population, so that if it is successful, it would only enhance one's confidence in the likelihood of success in health systems and settings that are not as resource constrained as our target WHS and IU Health.

K. Time Line

Following the study planning phase, we will spend additional 30 months recruiting our target sample size and 42 months to collect our 12 months outcomes. In the last six months we will analyze the data and start working on disseminating our study findings. The progress of our proposed project during this planning phase will be monitored by assuring the timing accomplishment of the following milestones:

1. Organize an annual meeting of the data safety and monitoring board for the trial within the first quarter of each year starting with the planning year.
2. Recruit a total of 1,660 subjects by the end of the second year.
3. Produce a report that describes the baseline characteristics of the first 1,000 subjects enrolled in the trial by the end of the first quarter of year 3.
4. Recruit a total of 3,220 subjects by the end of year 3.
5. Complete our target recruitment of 4,000 subjects by the end of second quarter of year 4.
6. Produce a report that describes the baseline characteristic of the entire cohort by the end of the fourth year.
7. Produce a report that describes the results of the analysis for the secondary aim (one month mod and anxiety symptoms) of the implementation phase by the end of first quarter of year five.
8. Produce a report that describes the results of the analysis for the primary aim (HRQOL at one year) and Secondary aim (Cost effectiveness) of the implementation phase by the end of third quarter of year five.
9. Disseminate the results of our study in a peer review journal, at a national meeting and on our own website by the end of year 5.



L. Protection of Human Subjects

Risks to the subjects

Human subjects’ involvement and characteristics: The target population will include community-dwelling individuals aged 65 and older who actively utilize their primary care providers with a minimum of one visit in the last 12 months. Most of these individuals have multiple comorbid conditions and approximately 6% of them will have dementia. The aims of our study require a face-to-face or telephone interview to assess the health-related quality of life, mood, anxiety, and cognition of this population. Data will also be collected from the subjects or the local INPC database. Elderly patients represent a vulnerable group. Our research specifically targets this group in an attempt to identify the benefit and harms of conducting a dementia screening, diagnosis, and management program and detect any potential harm that can be modified to improve the quality of care for these patients.

Sources of material: All material to be collected is data from interviews, questionnaires, and electronic data abstraction. Our interviews will include informed consent processes and up to four sets of questionnaires collected over four time points.

Potential risks: No experimental pharmacological intervention will be used in this study. On the contrary, the study aims to enhance recognition of dementia and provide collaborative dementia care management that is recommended to enhance dementia care. Although data will not be gathered from the patient without his or her consent, it is possible that some of the questions related to dementia screening and management asked of the respondents could cause anxiety.

The research personnel will be trained to recognize and minimize this discomfort and patients may discontinue participation at any time. If a respondent becomes anxious or upset, the principal investigator will be notified to intervene. Furthermore, patients who undergo the screening process and or the subsequent diagnostic assessment may end up with a dementia diagnosis. The impact of this diagnosis on their quality of life and care is not known and thus potential harms such as discrimination, loss of independence, or psychological burden may occur. On the other hand recognizing the presence of dementia would lead to receipt of appropriate and valuable treatment both pharmacologically and non-pharmacologically. Such a treatment may decrease the patient's disability resulting from unrecognized or unmanaged dementia and enhance the patients' adherence of medical management of other health conditions. Loss of confidentiality is also a risk in this type of data collection. Our data management and quality assurance technique has proven effective in past trials in maintaining confidentiality, and all study personnel have completed training in Human Subjects Research and HIPAA standards.

Should worrisome conditions such as depression, suicidality, or other concerning clinical conditions be apparent during a research interview, interviewers will follow a scripted protocol to notify the appropriate medical personnel and the PI so that appropriate notification and clinical follow-up is ensured. When such concerns occur for patients while in care management, this will be managed as any other clinical issue would be under usual circumstances through notification of the appropriate primary care provider or emergency personnel depending on the severity of the presentation. Again, the PI and other supporting staff are available to assist if and when this may occur.

Adequacy of protection against risks

Recruitment and informed consent: Our proposal will be approved by the Indiana University-Purdue University Indianapolis Institutional Review Board and the primary health centers where

the patients receive their care. Our study will require having informed consent from patients. The consent will be for the subject's involvement in the process of collecting data from HUI, PHQ-9, GAD-7, the MOS social support questionnaire, administrative data extraction in a de-identified manner and the possibility of undergoing dementia screening process if the subject is randomized into the screening arm of the study.

Consent procedure protection against risk: This study utilizes in person methods of recruitment and consent. Persons who are hearing impaired or too ill to answer questions will not be asked to participate in an interview. Subjects will not be asked to continue with the recruitment and enrollment processes who cannot understand the questions being asked of them, as indicated by either continued non-responsive answers or by asking the interviewer to repeat more than three questions three times each. In addition, we have employed usual methods of determining capacity to consent by asking the subject to repeat in their own words a description of the study and their rights as a research subject. Because we are recruiting only individuals without a diagnosis of dementia or some other form of diagnosed cognitive impairment, we have further limited the risk of soliciting from individuals who lack capacity, even though we recognize up to 6% of the sample may meet criteria for a dementia condition.

Moreover, should some individuals have mild to moderate dementia, we have evidence from prior studies that demonstrate that such individuals often have decision-making capacity and are able to recognize the risk-benefit profiles of various research study scenarios.^{127,128} Patients who refuse to participate in the study will not be approached again. The format and the procedure of data collection will be outlined in the consent form, the data will be extracted into a pre-designed database, and the research assistant will not collect any additional data without the consent of the patient and the university IRB. This process of approach and consent will adhere to all usual human subjects' policies and procedures. We will use the standard

procedures for addressing capacity that are employed by many institutions' human subjects review boards. The following questions will be employed:

I just went over what participating in this study entails. I am going to ask you a few questions just to make sure you understand the study before we begin.

1. What would you be doing if you agree to participate in this study?
(Examples of acceptable answers: "Take part in an interview/survey," or "Answer questions about my friend or relative.")
 Person is able to answer this Person is **not** able to answer this

2. What can you do or ask me to do if you are uncomfortable with a particular question in the survey?
(Examples of acceptable answers: "Ask to skip the question." "Ask you to read another question.")
 Person is able to answer this Person is **not** able to answer this

3. What can you do if you decide after we start that you do not want to participate in the study?
(Examples of acceptable answers: "Tell you that I do not want to answer any more questions.")
 Person is able to answer this Person is **not** able to answer this

For initial screening results, diagnostic determination will not be provided at that time except in instances where the subject asks and the results are considered normal. The interviewer will have a scripted response that indicates the test is not diagnostic and the results will be provided to the primary care provider (if the patient and/or proxy agree). They will be instructed that this can be discussed with that primary care provider.

For those subjects who screen positive and are determined to meet criteria for dementia, the team will disclose the finding of new information about the patient's health status (using carefully scripted protocols mindful of the potential harm that may result from disclosure of a stigmatizing condition) directly to the patient and the primary care physician. The principal investigator will be available to clarify any questions and offer any needed consultation.

We make the distinction between research-obtained data (through in-person and telephone interviews and electronically extracted data) and clinical data (obtained through

ongoing care management). The latter (clinical data) will be managed using all the protocols that one would normally use with respect to usual clinical care and information protection procedures. Confidentiality with respect to research-obtained data will be protected using a logbook containing each participant's unique identification number, name, and status. This logbook will be maintained at the data management center of the Indiana University Center for Aging Research. The unique identifier will be kept separate from subject identifiers and will be stored with a unique but otherwise meaningless identification number. All data will be double keyed by a data-entry professional. All telephone-acquired data gathered by computer-assisted telephone interviewing (CATI) will be automatically entered in a data secure method and double keying will not be necessary due to immediate and error free method of data entry. In addition, for those in care management the principal investigators will have the opportunity for feedback from the patient and the clinic staff to discuss any problems encountered during the data collection.

M. Reporting of Unanticipated Problems & Adverse Events

A data safety monitoring board (**DSMB**) will be established and will include Drs. Barbara Vickrey (a neurologist), Joshua Chodosh (a geriatrician), Soo Borson (a geriatric psychiatrist), and a biostatistician (TBN). The DSMB will be chaired by Dr. Vickrey. The committee will meet at the Indiana University Center for Aging Research prior to the first patient enrollment to determine the nature of the DSMB report, after enrollment of the first 1000 patients and every six months to evaluate safety measures including overall adverse effects related to the study (including the potential harms from screening such as anxiety, depression), serious adverse events, and death after enrollment into the study. In our study an adverse event will be defined as any untoward medical occurrence in a subject who received study intervention without regard to the possibility of a causal relationship. Adverse events will be collected after the subject has started to receive study intervention. If a subject experiences an adverse event after screening

for the study but prior to randomization, the event will be reported as not related to the study intervention. During the study, study personnel will note any change in the condition(s) and/or the occurrence and nature of any adverse events.

All adverse events occurring after entry into the study and until study completion will be recorded. An adverse event that later meets the criteria for a serious adverse event (SAE), between study enrollment and completion, will be reported to the local IRB as an SAE. All of the above safety data will be monitored throughout the course of the study in blinded fashion. If a death or clinical adverse event is deemed serious, unexpected, and possibly related to study intervention, the DSMB will be notified immediately to determine the appropriate action to take within the context of the event regarding blinding and reporting. Only the DSMB members will be unblinded in order to preserve the integrity of the data collected during this trial and minimize any potential for bias yet provide appropriate safety monitoring.

Potential benefits of the proposed research to the subjects and others

Although our study is collecting data to identify the benefits and harms of dementia screening among older adults attending primary care clinics, we anticipate some immediate benefit to participants at the stage of the research project following the screening results which may include assurance of a negative screening result or comprehensive assessment and management of positive screening results. Early recognition of dementia will lead to early enrollment in a multi-component dementia care management program that would improve the quality of care for dementia, reduce the burden of informal caregivers, and reduce acute care utilization.

Importance of the knowledge to be gained

In general, this study will add more information to the scant literature about the harms and benefits of dementia screening in addition to the benefits of enrolling patients with dementia into the collaborative dementia care program early in primary care settings. The data may lead to a national early detection and management program for dementia as an efficient and beneficial method of reducing the current and future burden of dementia. We are unaware of any similar studies that have been or will be conducted in a diverse primary care setting. Our study will provide some knowledge about the specific characteristics of the residents and their attitudes toward dementia screening. In addition, identifying the factors associated with the patients' acceptance of dementia screening, diagnosis and management program and its perceived harms will lead to the design of appropriate dementia screening programs that include individualized counseling that will decrease any potential harms of such program.