SPONSOR PROTOCOL

FY19_Pilot2_Hwang:
Pathway to Detection & Differentiation of Delirium & Dementia
in the Emergency Department (PD4ED)

Protocol Version
6/28/2021
Version 2.3

Clinical Trials Registration Number (NCT04846322)

Synopsis

Purpose

This is a pilot study that will lead to a pragmatic clinical trial. It will evaluate the implementation of an embedded pragmatic, clinical intervention. The intervention will assess older adults (age 65+) in the Emergency Department (ED) for delirium and risk for undiagnosed cognitive impairment and dementia (UCID), refer patients who are found to be at risk for UCID for outpatient evaluation and primary care follow-up.

Objectives

The primary objective of this pilot project is to evaluate the feasibility of incorporating and implementing a delirium and dementia assessment and referral protocol to assess for UCID in ED patients age 65 and older. This will lead to a future multicenter, pragmatic clinical trial.

The secondary objective is to determine optimal workflow for integration of cognitive impairment screening, referral assessment, and cognitive health follow-up in a pilot sample of patients and to analyze rates of screening, referral, and diagnosis of cognitive impairment or dementia.

Study Population

All community dwelling ED patients 65 years of age or older seen in the Yale New Haven Health System (YNHHS) St. Raphael's Campus (SRC) ED or Northwestern Memorial Hospital (NMH) ED.

Number of Participants

A total of 100 subjects (50 from each site) will be included to gather retrospective observational data via telephone follow-up and chart review. These data will provide estimates in rates of screening and referral for a pilot sample of ED patients to ascertain the feasibility. Additionally, we will compare differences in processes, utilization, and outcome endpoints across the two sites. The number of subjects will provide the needed information to inform a future pragmatic clinical trial proposal.

Study Design

The study is observational consisting of telephone interviews and medical record review.

Study Duration

The study period is January 2021 – December 2022. Subject participation will take place over approximately 3 months and will occur January 2021 - December 2021.

Outcome Variables

Primary outcome: ED screening and detection rates of delirium, vs. suspect dementia, vs. no cognitive deficits.

Secondary outcomes:

- Rate of screened patients who are referred to outpatient cognitive evaluation
- Rate of screened patients who have outpatient cognitive evaluation
- Rate of screened patients with outpatient evaluation that test positive for dementia

For patients identified as at risk for dementia:

- Referral for additional services
- Rate of primary care follow-up referral
- Rate of cognitive brain health plan, including changes in medications
- New diagnosis of Alzheimer's Disease and Related Dementias

Locations/Facilities

- The Yale New Haven Hospital (YNHH) York Street and St. Raphael's Campuses and the YNHHS Adler Center for Geriatric Comprehensive Assessment
- Northwestern Memorial Hospital (NMH) ED and Northwestern Medicine Geriatrics Outpatient Clinic

Abbreviations

Abbreviation	Explanation
AEs	Adverse events
ED	Emergency Department
MCI	Mild Cognitive Impairment
NIA	National Institute of Aging
NMH	Northwestern Memorial Hospital
Redcap	Research Electronic Data Capture
UCID	Undiagnosed Cognitive Impairment and Dementia
YNHH	Yale New Haven Hospital

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Protocol Revision History

Version Date	Summary of Substantial Changes
12/11/2020	IRB submission
6/28/2021	Update protocol to allow for calling potential participants in 1-6 weeks post-ED visit

1 Background

1.1 Background

Many older adults live with unrecognized cognitive impairment and dementia (UCID). Cognitive impairment, which increases with age and multimorbidity, often goes undetected and persons may not even realize they have impairment. These persons may be at greatest risk of poor health outcomes. Detecting UCID in the ED has important public health implications, as it can guide treatment and improve health outcomes for affected persons. Identification of patients who may have dementia in the ED would expedite diagnosis and effective management, identify essential patient and caregiver resources, and likely improve safety outcomes. UCID may be a cause of increased ED use as it has been shown that patients with dementia diagnoses have a higher rates of ED visits[1, 2] and return ED visits within 30-days of discharge.[3] Though assessment for dementia is not traditionally performed in the ED, many patients in the ED are at high risk for it and detection at this point of contact may provide a pathway for improved care delivery and outcomes.

2 Rationale/Significance

2.1 Rationale and Study Significance

Limitations in standard emergency care and the ED environment can make detection of patients UCID complex. Emergency clinicians must deal with acute and urgent medical issues including delirium which can be difficult to differentiate or may co-occur with cognitive impairment for persons living with dementia. Identifying patients with UCID in the ED will impact clinical decision making, patient care, and patient outcomes. Before such programs can come into existence, however, it needs to be determined if integrating cognitive assessments in the ED (by incorporating into clinical care with training and electronic screening tools) is feasible. Implementation will require changes to workflow, determining the rates of ED screening of patients presenting with UCID, and rates of referral of patients and families for additional evaluation after ED care.

The goal of this proposal is to evaluate the feasibility of implementing a pragmatic intervention to improve identification of patients at risk for unrecognized cognitive impairment and dementia.

2.2 Risks

This protocol presents minimal risks to participants, as it is an observational, data collection study. The probability and magnitude of harm or discomfort anticipated in the research are no greater than those ordinarily encountered in daily life or during the performance of routine health, memory, and thinking examinations or tests. The primary risks associated with this study are those seen in ordinary life including: responding to health-related interviews, performing health assessments, and sharing health-related information.

2.3 Anticipated Benefits

The potential benefits to study participants include the opportunity for clinical assessments affirming or clearing risk of suspected dementia or related diseases, the coordination and communication about these results with your primary care provider, and receipt of brain health plans if deemed necessary. The benefit to society is the generation of knowledge to improve the care and outcomes of older persons presenting to the ED. As an observational study with no therapeutic intent, the only alternative is for patients to choose not to participate. Therefore, all patients will receive standard clinical care as determined by their physician irrespective of study participation.

3 Study Purpose and Objectives

3.1 Purpose

This is an observational study of the pragmatic implementation of an ED screening, outpatient referral, and care coordination process for older ED patients who may have UCID. Results from the study will inform plans for a future proposed pragmatic clinical trial. It will evaluate the implementation of an embedded pragmatic, clinical intervention. The intervention will establish a new clinical protocol to assess older adults (age 65+) in the ED for delirium and risk for UCID and refer patients who are found to be at risk for UCID for outpatient evaluation.

3.2 Hypothesis

We are evaluating the feasibility of implementing a quality improvement initiative of ED screening, referral, and care coordination process of older ED patients with UCID. We hypothesize this will be feasible.

3.3 Objectives

The primary objective of this pilot project is to evaluate the feasibility of implementing into routine clinical care the assessment for UCID in older ED patients. This will lead to a future multicenter, pragmatic clinical trial proposal.

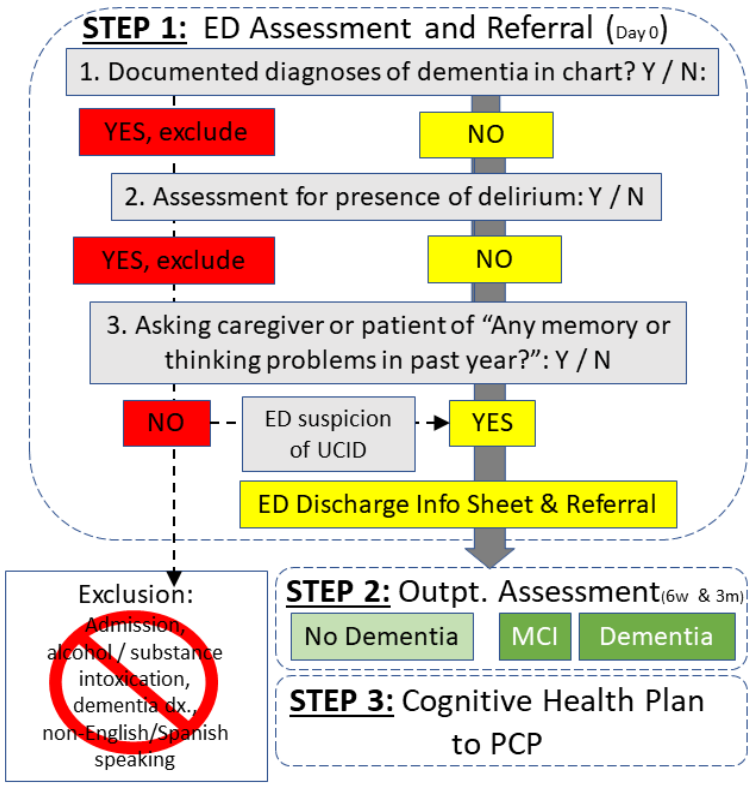
The secondary objective is to determine optimal workflow for integration of cognitive impairment screening, referral assessment, and cognitive health follow-up in a pilot sample of patients and to analyze rates of screening, referral, and diagnosis of UCID.

4 Study Design

This is a multicenter, single-protocol observational pilot pragmatic intervention study that consists of both retrospective and prospective data collection.

The pragmatic intervention that will be evaluated consists of 3-steps: 1. ED assessment for cognitive impairment and outpatient referral, 2. Outpatient assessment and evaluation, and 3. Cognitive Brain Health Planning. For a schematic of the pragmatic intervention, see Figure 1.

Figure 1. Proposed PD4ED Intervention Structure:



4.1 Study Duration

This study will last for 2 years. The expected duration of subject participation will be approximately 3 months, starting from the date of initial ED evaluation. We anticipate 6 months of subject enrollment and follow-up and then 18 months of data collection, preparation, and analysis.

4.2 Outcome Variables/Endpoints

As this is a feasibility study, we are not testing hypotheses. Observational results gathered from this study will inform effect sizes needed to propose a future full-scale, pragmatic, multicenter study.

4.2.1 Primary Outcome Variables/Endpoints

The variables use to assess the primary objective include rates of routine ED screening and detection of delirium, suspected UCID, or no cognitive deficits noted in all older (age 65+ years) ED patients, and rates of successful outpatient referral of patients found to be at risk for UCID.

4.2.2 Secondary and Exploratory Outcome Variables/Endpoints (if applicable)

The variables use to assess the secondary objectives include healthcare utilization, rates of outpatient evaluation, confirmation of outpatient assessment, new diagnoses of dementia or mild cognitive impairment (MCI), and changes in outpatient primary care.

5 Study Participants

5.1 Study Population

The study will include all ED patients 65+ years in age seen in the YNHH and Northwestern Memorial Hospital EDs that receive an outpatient clinic referral for a cognitive assessment evaluation over January 2021 – December 2021.

5.2 Number of Participants

All patients 65+ years in age seen in both EDs during the study period will be screened in the ED using clinical screening for UCID.

A convenience sample of 100 hundred subjects (50 from each site) will be included for retrospective and prospective observational data via chart review and interview to evaluate rate of UCID detection in the ED, rates of referral for outpatient evaluation, rates of confirmed cognitive impairment or dementia by the outpatient evaluation, and differences across the two sites with processes, utilization, and outcome endpoints.

5.3 Eligibility Criteria

In order to be eligible for inclusion in the study, an individual must meet all of the following criteria:

- Adults age 65 or older
- Discharged from the adult ED at YNHH or the ED at NMH

Any individual who meets any of the following criteria will be excluded from participation in this study:

- Documented or known history of dementia
- Alcohol/substance intoxication while in the ED
- Non-English or Non-Spanish speaking

5.4 Recruitment Procedures

Potential study participants will receive an informational sheet about the study stating that they are eligible to participate, either at discharge from the ED or by letter(paper or electronic through my chart). If given informational sheet while in the ED, research staff will ask for permission to contact by phone. The sheet will notify them that research staff may call them to participate but that they have the right to refuse to participate. They will also be provided with a mechanism to opt-out prior to receiving a call soliciting participation. Research staff will receive daily lists of potential study subjects.

Potential study participants will be identified at each site based on the site recruitment policy. They will be consented by study staff over the telephone and provided the required information about the study and allowed to ask questions before, during and after assent. They will be made aware that they can stop participating at any time and that such a choice will not impact their ability to seek care at the study site. Verbal consent time, date and initials of the research assistant collecting verbal consent will be documented in a case report form.

It is possible that the study PI's (Hwang and Dresden) may be providing or have a history of providing care for study participants, given their role as attendings in the ED. As assent to participate will be provided after ED discharge, no undue influence is expected to impact the choice to participate in the study.

5.5 Consent/Assent Procedures/HIPAA Authorization

A partial waiver of HIPPA Authorization and waiver of written informed consent will be sought for recruitment and screening of patients in the ED. purposes A convenience sample of total of 100 eligible subjects will be contacted by telephone for follow-up and informed telephone assent with a waiver of written consent to participate in telephone surveys and medical record review. We will screen for basic inclusion and exclusion criteria via the electronic medical record (EMR). These waivers of HIPAA authorization and written informed consent for recruitment/screening purposes will lessen burden on patients and families (since we only intend to enroll patients who meet basic inclusion criteria), and still allow us to accurately report the number and characteristics of screened patients.

A full waiver of HIPPA Authorization is being sought for all the ED patient (EMR)records over 65 years of age during the study time period to compare with the enrolled population.

These waivers are being sought as the study is of minimal risk and for restrictions in place because of COVID.

Trained research staff will contact eligible participants by telephone approximately at 1-6 weeks and again at 3 months after their ED visit. The study will be explained to the potential participant, and any questions will be discussed. If the study personnel have concerns over the patient's capacity for informed decision making, the patient's capacity to consent will be assessed through performance of the University of California San Diego Brief Assessment of Capacity to Consent. If the patient is determined, based on a score of <10 on the capacity of assessment, to not able to make an informed decision, a proxy or legally authorized representative will be sought for consent. If the patient regains decision-making capacity during the course of the study (for example, if delirium was present at enrollment but subsequently resolves), then consent will be obtained from the patient. If the patient then refuses to consent or withdraws consent given by the proxy, the patient will be disenrolled from the study.

We will enroll Spanish-speaking subjects in addition to English-speaking subjects. We have research personnel with years of experience in patient recruitment and enrollment who are fluent in Spanish. Only these personnel will contact Spanish-speaking patients for enrollment and consent. The translated consent form and recruitment letters will be submitted to the IRB for approval prior to use.

6 Study Methods/Procedures

6.1 Study Procedures

Clinical ED Practice Intervention.

As part of routine ED care, clinicians conduct delirium screening at bedside to evaluate presence of cognitive impairment in ED who are 65 years and older. The intervention will augment this process to include questions assessing for documented history of dementia or asking the patient, or caregivers present, in the ED if the patient has had any memory or thinking problems in the past year. If clinicians suspect the patient may have cognitive impairment, regardless of the response from patient or caregiver, and the patient has no documented history of dementia, the physicians may refer these patients to available outpatient cognitive evaluation. Referral will occur using EMR outpatient consult requests or by emailing outpatient clinics for available appointments as part of routine patient care referral processes.

Standard Care for Outpatient Cognitive Assessment Referral

The outpatient clinics receiving the ED referrals will reach out to patients to establish and schedule an outpatient evaluation after discharge from the ED.

As part of routine care, the outpatient assessments may include brief neuropsychological tests of cognition memory, language, executive function and attention that may include the Montreal Cognitive Assessment (MoCA), a cognitive screening test to aid in detecting cognitive impairment and evaluations to assess competency in completing instrumental activities of daily living such management of money, behavioral deficiencies and others for standardized consensus evaluation for diagnosis of dementia, cognitive impairment or normal with subtype of impairment. The outpatient evaluations will allow for clinical diagnosis and validation of ED assessment for the presence of dementia or mild cognitive impairment.

In addition, following the evaluation, the outpatient centers will document cognitive impairment diagnoses (if present) and notify patients, caregivers and their primary care providers of results. The centers will utilize available resources to connect patients to their primary care provider with feedback and recommendations for brain health care and management.

6.1.1 Data Collection

As this is a pilot study, we will gather a convenience sample of 100 participants who are eligible to be referred for outpatient cognitive assessment (50 from each site) will be evaluated. Data will be collected by telephone interview follow-up and chart review for observational characterize subjects, sites, processes, utilization, and outcome endpoints.

Research staff at both sites will contact by telephone the selected participants to conduct two focused interviews at 1-6 weeks and 3 months post-ED visit. The survey will assess the participants experiences through the process, findings of the assessment and the participants follow-up care plan. A retrospective chart review will be conducted on these participants. Trained research staff at each site will conduct chart review in the Electronic Medical Record to determine rates of:

- Healthcare utilization by the patients during the subsequent 30 days in addition to the requested outpatient cognitive assessment, inpatient hospitalizations, and/or ED revisits up to 6 months prior to the current ED visit

- Referral and completion of outpatient cognitive assessment
- New outpatient diagnoses of Alzheimer's Diseases or Related Dementia diagnoses or mild cognitive impairment
- Documentation of Outpatient Cognitive Assessment communication with the patients' primary care providers or other consults of results and recommendations for brain health treatment and management.

Trained research assistants will review the medical records of potentially eligible participants seen in the ED during the study period to assess clinician compliance and acceptance of screening intervention.

Data for this study will be collected, recorded and stored using Redcap (Research Electronic Data Capture). Redcap is a secure, web application designed to support data capture for research studies. Data from any paper study forms will be entered into Redcap and then stored in locked file cabinets restricted to the study team. Data coordination, data management, and database design will occur within the Yale School of Medicine's Program on Aging. See Table 1 for data points that will be collected.

Retrospective chart review will be conducted on a subset of 100 patients as part of study enrollment: We will collect data on a subset of patients meeting inclusion criteria (50 from each site, for a total of 100 subjects).

Assessment	*Screening: Visit (Day 0)*	*Enrollment: Telephone follow-up #1 (Day 1-45)*	*Telephone follow-up #2 (Month 3)*	*Chart Review*
ESI level	X			X
ED chief complaint				X
Demographics	X			X
Comorbidities	X			
Disposition from ED (discharged or admitted)	X			X
Discharge to community	X			X
Delirium Screen	X			X
Memory or thinking problem in prior year	X			X
ED referral for outpatient cognitive evaluation requested	X			X
Outpatient appointment scheduled		X	X	X
Outpatient appointment completed		X	X	X
Outpatient cognitive assessment batteries		X	X	X
New Outpatient Cognitive Impairment Diagnoses		X	X	X
Primary Care Brain Health Communication Coordination		X	X	X
Healthcare Utilization		X	X	X
Adverse Events		X	X	X

6.2 Method of Assignment/Randomization (if applicable)

N/A

6.3 Adverse Events Definition and Reporting

This is an observational study with minimal risk, we do not anticipate any untoward events occurring in association with the study.

Adverse events (AEs) will be evaluated retrospectively via chart review. If AEs are identified, they will be reported to the Principal Investigator and PI will notify the IMPACT Collaboratory. Subsequently IMPACT Collaboratory will notify the National Institute of Aging, the Data and Safety Monitoring Board and the Advarra IRB within 48 hours of AE notification. If an adverse event is unexpected, the PI will determine if the event places the participant or others at greater risk of physical or psychological harm than previously known. The PI will report any potential harm to IMPACT Collaboratory who will then report this to the NIA and the IRB within 2 weeks of the event.

6.4 Reaction Management

N/A

6.5 Withdrawal Procedures

Study participant's consent to participate will be verified during every encounter with research staff. Participants can verbally report their withdrawal from the study.

6.6 Locations/Facilities

Locations include the Yale New Haven Hospital (YNHH) York Street and St. Raphael's Campuses and the YNHHS Adler Center for Geriatric Comprehensive Assessment, and the Northwestern Memorial Hospital (NMH) ED and Northwestern Medicine Geriatrics Outpatient Clinic.

7 Statistical Design

This is an observational pilot study and descriptive statistics will be completed comparing demographic and clinical characteristics of all patients 65+ discharged from the ED (denominator) versus those referred from the ED for outpatient cognitive impairment assessment. Student's t-test will be used for continuous variables (if normally distributed (e.g. age)) or the Wilcoxon rank-sum test (if not normally distributed (e.g., length of stay)), and the Chi-square test or Fisher's exact test for binary/categorical variables. All tests will be 2-sided at a significance level of 5%.

7.1 Sample Size Considerations

This is a feasibility study. Results gathered here will inform future sample, effect, and power calculations.

7.2 Planned Analyses

This is an observational study that will evaluate the feasibility of implementing a brief training and assessment protocol to assess for undiagnosed cognitive impairment and dementia in ED patients and refer those at risk for outpatient evaluation. The ED assessment protocol, referral process, and outpatient evaluation will be integrated into clinical care. Researchers will gather observational data about these processes to measure the proportion of patients who are at risk in the emergency department, number of patients who are referred to the outpatient setting up to 3 months post-discharge and number of patients who evaluated who are diagnosed with cognitive impairment. These sample sizes will provide estimates needed for future larger scale pragmatic evaluation of such clinical care and its impact on patient and caregiver outcomes.

7.2.1 Interim Analysis (if applicable)

An interim analysis will be conducted at 2-months from the start of data collection. This will be done for the purposes of safety and efficacy monitoring.

7.3 Data Relevance

Data analyses will consist of descriptive statistics comparing overall eligible subjects at both sites and of the subset of 100 patients for which chart review will be completed.

A valid analysis of the intervention effect between gender and racial/ethnic subgroups will be completed to identify differences between the subgroups and their characteristics.

7.4 Data Coding

Data will be coded by unique study ID for each participant.

7.5 Data Analysis Tools

Software use to analyze the data will include SAS, SPSS, and Stata.

7.6 Data Monitoring

See Data Safety Monitoring Board in Section 8 Below

7.7 Handling of Missing Data

As this is an observational study to guide future study design, missing data will be informative in this study. Missing data will be used to identify unexpected problems likely to occur in a future study.

8 Data/Specimen Handling and Record Keeping

8.1 Subject Data Confidentiality

Participant confidentiality and privacy is strictly held in confidence by the participating investigators, their staff, and the sponsor(s)/funding agency. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence.

All research activities will be conducted in as private a setting as possible.

Representatives of the Institutional Review Board (IRB), regulatory agencies or study sponsor/funding agency may inspect all documents and records required to be maintained by the investigator for the participants in this study. The study site will permit access to such records.

The study participant's contact information and data will be securely stored at each study site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, regulatory, or sponsor/funding agency requirements.

8.2 Data Quality Assurance

All research staff will be required to complete institutional research ethics and compliance training. This will occur online. Research staff will also be required to complete all institutional trainings. The PI and project manager will conduct an in-person training for the research staff that will include key topics essential to conducting clinical research in the emergency department. The training will also include a thorough review of the EMR chart review processes, and the requirement of replicating five gold standard abstractions of identified patients.

8.3 Data or Specimen Storage/Security

The data be collected by the research assistant and stored on the hospital’s encrypted secured servers. Participants will be assigned unique participant identification codes. Only assigned custodians who are part of the protocol will have access to the logs and passwords. The log will also include a tracker to document patients who participate in the outpatient assessments. Assigned custodians will have to be on hospital grounds or must connect using Virtual Private Network (VPN) with two-factor authentication to access the hospital servers.

8.4 Access to Source

For identification of eligible participants for recruitment and enrollment, research staff will maintain a password protected screening log to track patients who are referred from the ED

for outpatient cognitive assessment. Participants enrolled will be assigned generated participant identification codes to facilitate the de-identification process.

Data will be collected and merged from clinical and administrative reports and chart review by trained research staff into a single Redcap database.

As this use of administrative and retrospective clinical data and chart review are only minimal risk a waiver of signed consent will be requested.

Source data are all information, original records of clinical findings, observations, or other necessary activities in a research study. Source data are contained in source documents. Research staff at the local site will access the following source documents to extract data for medical record abstraction including: ED records, inpatient records, readmission records, consultations, outpatient records (clinical and office charts), medication administration records and other reports.

8.5 Retention of Records

In compliance with NIH guidance, it is the PI's responsibility to retain study essential documents for 3 years from the date of submission of Yale's federal financial report (FFR) to NIH.

8.6 Data and Safety Monitoring Plan

The study has a Safety Officer and a Data Safety Monitoring Board. See attached Data Safety Monitoring Plan for additional details.

The Safety Officer is:

Brian Patterson MD, Assistant Professor, BerbeeWalsh Department of Emergency Medicine, University of Wisconsin School of Medicine and Public Health
Email: bpatter@medicine.wisc.edu
Phone: 312.636.6957 (cell), 608.265.6043 (office)
Address:
800 University Bay Drive
Suite 310, Mailcode 9123
Madison, WI 53705

The Data and Safety Monitoring Board includes:

Mary Ersek, PhD, RN, FPCN
Professor of Palliative Care, Department of Biobehavioral Health Science
Dr. Ersek has decades of experience as a health services researcher in the field of clinical geriatrics and gerontological nursing. She has expertise in the fields of dementia, geriatrics clinical research, end of life care and clinical trials and has served as PI on NIH as well as Veterans Administration health services research studies.

Kenneth E. Covinsky, MD, MPH
Professor of Medicine; University of California, San Francisco School of Medicine
Dr. Covinsky is a senior geriatrician researcher and investigator in both the VA and the University of California, San Francisco health care systems. He has been a member of numerous NIH review committees, DSMBs and advisory committees. He has extensive experience doing research focused on older persons with advanced illness in end of life care policies and has led numerous clinical research studies focused on this population.

Kenneth P. Kleinman, Sc.D. Associate Professor, University of Massachusetts
Dr. Kleinman is a senior statistician who specializes in large cluster randomized clinical trials. He was the senior statistician on national studies of infection control supported by the

NIH Common Fund initiative on Pragmatic Clinical Trials and thus has the perfect credentials to review pilot studies being done in preparation for being launched as full blown embedded pragmatic clinical trials.

9 Study Considerations

9.1 Institutional Review Board (IRB) Review

The study will use Advarra as the IRB of record as required by the sponsor.

9.2 Research Personnel Training

All research staff will be required to complete research ethics and compliance training as prescribed by their home institution. The PI and project manager will conduct an in-person training for the research coordinator that will include key topics essential to conducting clinical research in the emergency department. The training will also include a thorough review of the EMR chart review processes, and the requirement of replicating five gold standard abstractions of identified patients

9.3 Study Monitoring

The PI will review monthly the data quality collected by the research assistant, and administrative and clinical data reports generated of aggregate monthly ED patient metrics. A Safety Officer and Data Safety Monitoring Board will review this study quarterly with online meetings reviewing study progress. Since this is an observational study with minimal risk, we do not anticipate any risk of severe adverse events occurring in association with the study.

9.4 Unanticipated Problems and Protocol Deviations

This protocol will be conducted in accordance with Good Clinical Practice of the International Council of Harmonization (ICH GCP) and will safeguard the rights and well-being of the study participants. A protocol deviation will be defined as divergence from the procedures outline in the protocol. An unanticipated problem may include events like subject or caregiver complaints related to safety, welfare, or rights of the patient or caregivers. The PI and project manager will review cases on a weekly basis and utilize a decision tree to guide the identification of protocol deviations. If the PI and project manager determine a protocol deviation has occurred, they will proceed to classify deviation and determine if it could impact the patients' well-being or the reliability of the study data. Deviations will be reported to the IRB for review and they will be documented in a deviation summary log.

9.5 Study Discontinuation

Patients may discontinue clinical care at any time. Withdrawal will not impact delivery of their remaining medical care. The clinicians may discontinue patient care if adverse events are observed. Patients who discontinue care will not be replaced.

9.6 Study Completion

We expect this study to complete recruiting by 12/31/21. Calendar year 2022 will be used for analysis, manuscript development, publications and closeout reports.

9.7 Conflict of Interest Management Plan

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. The study leadership in conjunction with the appropriate conflict of interest review committee has established policies and

procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

All investigators will follow the applicable conflict of interest policies.

9.8 Funding Source

National Institute of Aging through the IMPACT Collaborative

9.9 Publication Plan

Publication of the results of this trial will be governed by the policies and procedures developed by the IMPACT Collaboratory. Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NIA prior to submission.

10 References

1. LaMantia MA, Stump TE, Messina FC, Miller DK, Callahan CM. Emergency department use among older adults with dementia. *Alzheimers Dementia.* 2016;30(1):35-40
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4. Jeste DV, Palmer BW, Appelbaum PS, Golshan S, Glorioso D, Dunn LB, Kim K, Meeks T, Kraemer HC. A new brief instrument for assessing decisional capacity for clinical research. Arch Gen Psychiatry. 2007 Aug;64(8):966-74. doi: 10.1001/archpsyc.64.8.966. PMID: 17679641.