CLINICAL STUDY PROTOCOL

Observational Study of Individual or Group Template

Feasibility, Acceptability, and Barriers to Implementation of a Geriatrics Bundle in the ICU: a Pilot Study (ACE-ICU)

Protocol Number

2000029410

Protocol Version 4

4/7/2021

ClinicalTrials.gov Identifier

NCT 04652453

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Synopsis

Purpose

Despite the known benefits of geriatric care models among hospitalized older adults outside the intensive care unit (ICU), few studies have addressed the needs of older adults in the ICU; for example, sensory impairment, functional decline, and deprescribing of potentially inappropriate medications (PIMs) are rarely addressed in routine ICU practice. We have developed a geriatrics bundle for the ICU that implements evidence-based interventions from geriatric models of care (occupational therapy, assessment and treatment of hearing impairment, and deprescribing PIMs started in the ICU) and complements existing ICU best practices. This pilot study will evaluate the feasibility, acceptability, and barriers and facilitators to implementing these interventions in the ICU. This pilot work will provide invaluable preliminary data for a future hybrid effectiveness-implementation study of the geriatrics bundle in the ICU, with a long-term goal of adding the geriatrics bundle as the "G" component of the ABCDEF bundle (the existing standard of care) to facilitate widespread implementation across ICUs.

Primary Objective

The primary objective of this proposal is to evaluate the feasibility, acceptability, and barriers to implementing a "geriatrics bundle" in the ICU *as an addition* to the current bundle of ICU interventions (the "ABCDEF bundle").

Secondary Objective

The secondary objective of this study is to describe (as preliminary data) the in-hospital outcomes (such as incidence of delirium, mobility level, muscle strength at discharge, hospital length of stay) among patients who have received the geriatric bundle.

Study Design

This is a prospective pilot study that will draw participants aged 65 and older from the 36-bed medical intensive care unit (MICU) of the main campus of Yale-New Haven Hospital (YNHH). This study will use a pre-/post-intervention design; first, 30 control patients will be enrolled, and subsequently the geriatrics bundle will be implemented in 50 patients. A patient (or proxy) interview and medical record review will be performed at the time of enrollment by a research nurse. For patients in the intervention group, the research nurse will then orient the patient, proxy, and ICU nurse to the components of the geriatrics bundle. All patients in the intervention group will receive all 3 bundle components: occupational therapy (in addition to physical therapy delivered via our established early mobilization program, which the PI directs), a portable amplifying device to help with hearing, and a deprescribing intervention by the ICU pharmacist (in conjunction with the medical team) upon ICU-to-floor transfer.

Study Date Range and Duration

3 years (1 years for field activities, 2 years for data analysis and manuscript preparation)

Number of Study Sites

1 – the York Street campus MICU of YNHH

Primary Outcome Variables

The primary outcomes are all implementation outcomes; therefore, they will only be evaluated among participants and providers enrolled during the intervention phase of the

study. To evaluate the feasibility of bundle delivery in the ICU (*SA1*), we will assess the delivery of each bundle component separately. For the occupational therapy intervention (*Component 1*), we will review the electronic medical record (EMR) for OT notes from study enrollment through hospital discharge. In addition to gathering data on numbers of patients receiving OT, we will gather data about the frequency of and which OT interventions are performed. For the hearing impairment intervention (*Component 2*), we will perform a daily audit of use of the hearing amplifier (by speaking with the nurse, patient, and checking the bedside log). For the deprescribing intervention (*Component 3)*, we will review the chart for the ICU pharmacist's note. We will also gather data on the details of the deprescribing intervention (i.e. the number and type of medications that were changed or discontinued) as preliminary data for future studies.

To evaluate the acceptability of the geriatrics bundle among providers who are responsible for delivering and using the individual components (*SA2*), we will administer a survey with a 5-point Likert scale (range 1-5, where 5 indicates that the bundle is completely acceptable for use in its current form) to the providers who are responsible for delivering the intervention: occupational therapists (OT; *Component 1*), nurses (primarily, but also other ICU providers such as physicians and physical therapists; *Component 2*), and ICU pharmacists (*Component 3*).

To evaluate facilitators and barriers to implementation of the geriatrics bundle (*SA3*), we will use qualitative methods to allow for a more comprehensive understanding of barriers and facilitators encountered by the healthcare team (OT, nursing, and ICU pharmacy) during bundle delivery. We will approach all participating OT and Pharmacy providers and use purposive sampling for the nursing group (given the large number of ICU nurses). Focus groups will be recorded and professionally transcribed. Transcripts will be reviewed by the investigators with coding occurring according to the methods of Strauss and Corbin and analysis conducted using the constant comparative method.

Secondary and Exploratory Outcome Variables

From the intervention and control groups, we will gather data on in-hospital outcomes of importance to older adults, including but not limited to delirium, mobility level, muscle strength at discharge, functional status at discharge, and ICU/hospital lengths of stay. We will also ask patients about perceived benefit of the hearing impairment intervention.

Study Population

This is a prospective pilot study that will draw participants aged 65 and older from the 36-bed medical intensive care unit (MICU) of the main campus of Yale-New Haven Hospital (YNHH). All patients aged >=65 who are admitted to the MICU will be screened for enrollment. Nursing providers, occupational therapists, and ICU pharmacists delivering the bundle components will also be enrolled as study participants ("provider participants").

Number of Participants

We plan to enroll 80 patient participants (30 in the control group, 50 in the intervention group). Of the providers, we plan to enroll 75 nurses and all of the occupational therapists and ICU pharmacists (approximately 3-5 in each group) who deliver the interventions.

Study Schedule

Each patient participant will have 2 study visits that include assessments by the research team. Intervention participants will also have a brief daily audit asking about use of the portable amplifying device. The first visit will occur in the ICU and the second will occur on the hospital ward, prior to hospital discharge. Each interview/assessment will take approximately 45 minutes. Approximately one month after discharge, there will be one

follow-up phone call to ask about ongoing use of the portable amplifying device (in the intervention group) and to ask questions about functional recovery and health outcomes (in all participants).

The study schedule for provider participants will include a brief survey (5-10 minutes), and, for the subset that are recruited for and agree to participate in focus groups, one additional study visit for the focus group (lasting approximately 1 hour on a separate date).

Protocol Revision History

Version Date	Summary of Substantial Changes
1 11/5/2020	N/A – initial submission
2 11/25/2020	Addition of provider participants (nurses, occupational therapists, and ICU pharmacists delivering the bundle components) as study participants throughout the protocol.
3 1/6/2021	Addition of a control group (30 participants) and revision of the size of the intervention group to 50 participants (from 75)
4 4/7/2021	Clarification of triggers for proxy consent, removal of witness requirement for proxy consents given minimal risk, and addition (to the screening process, which currently only includes the JDAT screening report) of review of the MICU roster with an additional check to ensure that the participant has not opted out of research.

Statement of Compliance

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to the Common Rule at 45CFR46 (human subjects) and other applicable government regulations and Institutional research policies and procedures.

Abbreviations

EMR: electronic medical record

ICU: intensive care unit

MoCA: Montreal Cognitive Assessment

OT: occupational therapy

PIM: potentially inappropriate medication

PT: physical therapy

SOFA: Sequential Organ Failure Assessment

CLINICAL STUDY PROTOCOL

Observational Study of Individual or Group Template

1 Background/Literature Review and 2 Rationale/Study Significance

1.1 Background/Rationale and 2.1 Study Significance

Millions of older adults are admitted to an intensive care unit (ICU) every year, and this number is only expected to increase as the population ages.[1] By 2050, the number of older adults in the U.S. is expected to exceed 90 million. Advances in critical care medicine have concurrently resulted in increasing numbers of patients surviving a critical illness.[2-5] The majority of ICU survivors experience new impairments in long-term physical function, cognitive function, or mental health.[6-8] Indeed, a high-impact editorial noted that "survivorship will be the defining challenge of critical care in the 21st century."[9]

Older adults are more likely to present to the ICU with multifactorial health conditions that confer increased vulnerability to adverse outcomes. Older adults with pre-ICU vulnerability factors (e.g. frailty, cognitive impairment) are at greater risk of poor outcomes when exposed to a high acuity insult such as a critical illness, compounded with insults from the ICU environment (e.g. immobility and polypharmacy). Our work has demonstrated the importance of frailty, cognitive impairment, and their interaction on post-ICU disability among older adults,[10-12] established the strong association of an older person's pre-ICU functional trajectory with post-ICU disability,[13] and shown that hearing and vision impairment were the factors most strongly associated with (a lack of) functional recovery after an ICU hospitalization.[14] Despite the importance of these multifactorial health conditions on the post-ICU outcomes of older adults, these health conditions are not routinely assessed or addressed in the ICU.

In the fast-paced ICU environment, the consistent delivery of high-quality care has been improved through the use of bundles and checklists.[15] Over the past decade, the "ABCDEF bundle" ((A)ssess/manage pain, (B)oth spontaneous awakening and spontaneous breathing trials, (C)hoice of analgesia/sedation, (D)elirium assessment, prevention, and management, (E)arly Mobilization, (F)amily engagement) has become a core part of ICU practice, with each bundle component supported by a strong evidence base.[16-18] Likewise, checklists are a cornerstone of ICU practice, and have had the capacity to transform ICU care.[19] By running through a checklist at the end of rounds, providers ensure that quality care, including the ABCDEF bundle, is delivered to every ICU patient.[20]

Despite the increasing number of older adults admitted to the ICU, there has been no effort to target any bundle or checklist components to the needs of older ICU patients. To address the needs of critically ill older adults, the PI has developed an evidence-based (G)eriatrics bundle, with a long-term goal of adding this bundle as the "G" component of the ABCDEF bundle. The bundle includes occupational therapy evaluation and treatment (in addition to physical therapy already being delivered through early mobilization), the assessment and treatment of hearing impairment, and a deprescribing intervention of potentially inappropriate medications (PIMs) started in the ICU upon the ICU-to-floor transition.

The evidence base for this bundle is strong. Early mobilization, usually delivered by physical therapy, is already part of ICU practice through the ABCDEF bundle. We will add occupational therapy, a skilled service that focuses on daily functional tasks, and one that has previously shown benefit in improving functional outcomes among hospitalized older adults[21] and in the ICU population,[22] to existing early mobilization protocols. Prior work among older adults has demonstrated the importance of assessing and treating sensory impairment,[23,24] and our own work has demonstrated the association of sensory impairment with post-ICU functional outcomes.[14] Finally, the continuation of potentially inappropriate medications (PIMs) initiated in the ICU is common,[25] with prior studies demonstrating that pharmacist intervention may be effective in reducing PIM continuation.[26] The proposed work will evaluate the feasibility of the healthcare team to deliver the geriatrics bundle to older

patients in the ICU (*Specific Aim 1*) and assess the bundle's acceptability among providers who are responsible for delivering and using the individual components (nurses, physicians, occupational therapists, and ICU pharmacists; *Specific Aim 2*). We will also evaluate facilitators and barriers to implementation of the geriatrics bundle in the ICU setting (*Specific Aim 3*). The results of this pilot proposal will provide preliminary data for an R01 application evaluating the bundle's effectiveness in improving in-hospital and post-ICU outcomes (primary aim) while also evaluating implementation outcomes (secondary aim).

Prior Experience (if applicable)

Dr. Ferrante has extensive experience conducting patient-oriented outcomes research in the intensive care unit. Other active protocols enrolling in the ICU include the PREDICT study (PI: Ferrante, protocol #2000026657) and the VALIANT study (mPI: Cohen, Ferrante, Hajduk, protocol #2000028175).

2.2 Purpose of Study/Potential Impact

Despite the strong evidence base for several of the geriatrics bundle components in hospitalized older adults, most of these components have never been studied or implemented in the ICU environment. This study leverages strategies (bundles and checklists) that have been known to work in the ICU to build on existing evidence-based interventions (the ABCDEF bundle) to improve outcomes for older ICU patients.

This pilot study will generate invaluable preliminary data about feasibility, acceptability, facilitators, and barriers to implementation that will be used to support a hybrid effectiveness-implementation R01 of the geriatrics bundle in the ICU setting. Long-term, the overarching goal is to leverage the existing ABCDEF bundle by adding the geriatrics bundle as the "G" component to facilitate its widespread implementation.

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

The risk associated with this study is minimal, since our study leverages three interventions that already exist in ICU practice, but are underutilized. Occupational therapy has been part of the STEPS-ICU program (a YNHH quality improvement program) since its inception in March of 2015. This study does not change anything about the OT or STEPS-ICU program itself; the study only ensures that all patients age 65 and older (in the intervention group) are prescribed OT (since most physicians only remember to order PT, but forget about OT). Of note, Dr. Ferrante has been the physician lead of YNHH's early mobilization program in the MICU (the "STEPS-ICU" program) since its inception in 2015, and has worked closely with partners in Rehab Services throughout the duration of the program. In terms of the hearing impairment intervention, portable amplifying devices have been available in the hospital for years, so the minimal risk is that the patient may find the headphones bothersome. We will provide a laminated instruction sheet at each patient's bedside so that the nurse and patient have a resource for use of the device. In terms of the deprescribing intervention, there is a small risk of a patient having a home medication discontinued, but this risk will be minimized by having ICU pharmacists deliver the deprescribing intervention, so that they ensure that only medications started in the MICU (that are now inappropriate) are discontinued. As with any study, there is a small risk of breach of confidentiality, but we will minimize this risk through our use of secure data practices.

There are no risks to the provider participants in this study, other than the inconvenience associated with the 5-10 minute survey and/or the 1-hour focus group.

2.3.2 Potential Benefits

The patient participants in the intervention group are likely to benefit from receipt of the geriatrics bundle. First, ensuring the default receipt of occupational therapy (OT) is likely to identify impairments in activities of daily living (ADLs) and instrumental activities of daily living (IADLs) that may not have been observed without an OT evaluation. Second, the receipt of a portable amplifying device for hearing-impaired patients is likely to benefit their ability to hear in the short-term (and potentially the long-term, if they continue to use a portable amplifier after discharge). Provision of the device may also benefit patients who do not report hearing impairment, as they may have objective hearing impairment (but not subjective hearing impairment) and may still benefit from use of the device and realize the benefit once they have tried it. Third, the deprescribing component will actually prevent potential harm from reaching the patient, because it is discontinuing medications started in the MICU that are no longer appropriate for the patient. There are no benefits to the patient participants in the control group. However, if the bundle is (eventually) successfully implemented into clinical practice, there will be potential benefit to future patients.

There is potential benefit to the nursing and occupational therapy provider participants, as provision of the portable amplifying device to the patient may help improve their ability to communicate with a hearing-impaired older patient. There is no potential benefit to the ICU pharmacy providers, though the knowledge gained in this study may improve ICU pharmacy practice in the future.

3 Study Purpose and Objectives

3.1 Hypothesis

We hypothesize that the geriatrics bundle will be feasible to implement among older patients in the medical intensive care unit (MICU), and that the bundle will be acceptable to the providers responsible for its implementation. We hypothesize that the qualitative aim will uncover additional barriers and facilitators to the bundle's implementation that were not identified in the first two aims.

3.2 Primary Objective

The primary objective of this proposal is to evaluate the feasibility, acceptability, and barriers to implementing a "geriatrics bundle" in the ICU *as an addition* to the standard of care (the "ABCDEF" bundle).

3.3 Secondary Objective (if applicable)

The secondary objective of this study is to describe (as preliminary data) the in-hospital outcomes (such as delirium, mobility level, muscle strength at discharge, ICU/hospital length of stay) among patients who have received the geriatric bundle, as well as their 30-day functional outcomes and health outcomes (i.e. readmissions). An additional secondary objective is to describe the ongoing use of the portable amplifying device after hospital discharge among the intervention group participants.

4 Study Design

4.1.1 General Design Description

This is a prospective pilot study that will draw participants aged 65 and older from the 36-bed medical intensive care unit (MICU) of the main campus of Yale-New Haven Hospital (YNHH). The study uses a pre-/post-intervention design. First, 30 consecutive patients will be recruited for the control group (during the "control phase" of the study). The geriatrics bundle will then be implemented, and then 50 intervention group participants will be enrolled (during the "intervention phase" of the study). For all study participants, a patient (or proxy)

interview and medical record review will be performed at the time of enrollment by a research nurse. All participants will undergo another interview and assessment prior to hospital discharge, and will receive a brief follow-up phone assessment at approximately 30 days after discharge.

For participants in the intervention group, the research nurse will orient the patient, proxy, and ICU nurse to the components of the geriatrics bundle during the baseline interview in the ICU. All intervention group participants will receive all 3 bundle components: occupational therapy (in addition to physical therapy delivered via our established early mobilization program, which the PI directs), a portable amplifying device to help with hearing, and a deprescribing intervention by the ICU pharmacist (in conjunction with the medical team) upon ICU-to-floor transfer. Providers who are delivering the bundle components (nurses, occupational therapists, and ICU pharmacists) will also be enrolled as study participants, hereafter referred to as "provider participants." Participants enrolled during the intervention phase will also undergo brief "check-in" assessments between enrollment and hospital discharge to gather feedback and acceptability data about the interventions.

4.1.2 Study Date Range and Duration

3 years (1 year for field activities, 2 years for data analysis and manuscript preparation)

4.1.3 Number of Study Sites

1 – the York Street campus MICU of YNHH

4.2 Outcome Variables

4.2.1 Primary Outcome Variables

The primary outcomes are all implementation outcomes; therefore, they will only be evaluated among participants and providers enrolled during the intervention phase of the study. To evaluate the feasibility of bundle delivery in the ICU (*SA1*), we will assess the delivery of each bundle component separately. For the occupational therapy intervention (*Component 1*), we will review the electronic medical record (EMR) for OT notes from study enrollment through hospital discharge. In addition to gathering data on numbers of patients receiving OT, we will gather data about the frequency of and which OT interventions are performed. For the hearing impairment intervention (*Component 2*), we will perform a daily audit of use of the portable amplifying device. The daily audit will include asking the participant and nurse about use of the device, as well as checking a daily bedside log where use of the device is recorded. For the deprescribing intervention (*Component 3)*, we will review the chart for the ICU pharmacist's note. We will also gather data on the details of the deprescribing intervention (i.e. the number and type of medications that were changed or discontinued) as preliminary data for future studies.

To evaluate the acceptability of the geriatrics bundle among providers who are responsible for delivering and using the individual components (*SA2*), we will administer a survey with a 5-point Likert scale (range 1-5, where 5 indicates that the bundle is completely acceptable for use in its current form) to the providers who are responsible for delivering the intervention: occupational therapists (OT; *Component 1*), nurses (primarily, but also other ICU providers such as physicians and physical therapists; *Component 2*), and ICU pharmacists (*Component 3*).

To evaluate facilitators and barriers to implementation of the geriatrics bundle (*SA3*), we will use qualitative methods to allow for a more comprehensive understanding of barriers and

facilitators encountered by the healthcare team (OT, nursing, and ICU pharmacy) during bundle delivery. We will approach all participating OT and Pharmacy providers and use purposive sampling for the nursing group (given the large number of ICU nurses). Focus groups will be recorded and professionally transcribed. Transcripts will be reviewed by the investigators with coding occurring according to the methods of Strauss and Corbin and analysis conducted using the constant comparative method.

4.2.2 Secondary and Exploratory Outcome Variables (if applicable)

From the intervention and control groups, we will gather data on in-hospital outcomes of importance to older adults, including but not limited to delirium, mobility level, muscle strength at discharge, functional status at discharge, and ICU/hospital lengths of stay. We aill also submit a JDAT request for deidentified, aggregate historical data from the York Street MICU on the same in-hospital outcomes.

From the intervention and control groups, at approximately 30 days after hospital discharge, we will also gather data on functional outcomes, cognitive outcomes, and health outcomes (including, but not limited to, readmissions). From the intervention group only, we will gather feedback and data about ongoing use of the portable amplifying device since hospital discharge.

4.3 Study Population

This is a prospective pilot study that will draw participants aged 65 and older from the 36-bed medical intensive care unit (MICU) of the main campus of Yale-New Haven Hospital (YNHH). All patients aged >=65 who are admitted to the MICU will be screened for enrollment.

Nursing providers, occupational therapists, and ICU pharmacists delivering the bundle components will also be enrolled as study participants (“provider participants”).

4.3.1 Number of Participants

We plan to enroll 80 patient participants (30 in the control group, and 50 in the intervention group). Of the providers, we plan to enroll 75 nurses and all of the occupational therapists and ICU pharmacists (approximately 3-5 in each group) who deliver the interventions.

4.3.2 Eligibility Criteria/Vulnerable Populations

This is a prospective pilot study that will draw participants from the 36-bed medical intensive care unit (MICU) of the main campus of Yale-New Haven Hospital (YNHH), where approximately half of the 2900 annual admissions are among patients age 65 and older. All patients age 65 and older who are admitted to the YNHH MICU will be screened for enrollment. Inclusion and exclusion criteria for the patient participants are outlined in the table below.

For the provider participants, all nurses, occupational therapists, and ICU pharmacists delivering the bundle components will be eligible for inclusion. The only exclusion criterion for the nurses is if the nurse encountered by the research team is not the patient’s primary nurse (such as if the nurse is covering for the primary nurse’s lunch break).

Table 1. Inclusion and Exclusion Criteria	
Inclusion Criteria	Exclusion Criteria
1. Age $\geq$ 65 years	1. Unable to provide informed consent and no proxy available

2. Hospitalized in the Medical Intensive Care Unit (MICU) on the York Street campus of Yale-New Haven Hospital. 3. Has not opted out of research	2. Advance directive of "comfort measures only" (CMO) or change to CMO anticipated during this hospital admission 3. Planned discharge to hospice 4. Primary language other than English 5. Tracheostomy with long-term ventilator dependence 6. Patients with non-family conservators (e.g. a lawyer serving as the conservator for the patient) 7. Unable to participate in the OT and hearing impairment interventions due to cognitive status (e.g. advanced dementia, anoxic brain injury, vegetative state, etc) or the need for deep sedation (e.g. if treatment of the critical illness requires deep sedation and neuromuscular blockade, such as in severe ARDS [the acute respiratory distress syndrome]) 8. COVID-19 positive 9. Already receiving OT in the ICU

5 Study Methods/Procedures

5.1 Study Procedures

Screening and enrollment of patients

The Yale-New Haven Hospital (YNHH) Joint Data Analytics Team (JDAT) will provide a list of medical intensive care unit (MICU) patients age 65 and older who have not opted out of research. Study personnel will review this list on a daily basis to screen for eligible patients. For screened patients, basic demographic information will be captured in a REDCap screening form as this is a feasibility study and we will need to provide descriptive statistics for the patients screened and enrolled. Study personnel will apply the inclusion and exclusion criteria from Table 1 (above in section 4.3.2) and identify eligible patients.

Once an eligible patient is identified, a research nurse or research assistant will assess the patient for his/her ability to consent and participate in the study interventions by first assessing mental status via the Richmond Agitation-Sedation Scale (RASS). For patients who are too deeply sedated (RASS -2 to -5) or agitated (+2 to +5), as often occurs in the ICU due to severity of illness or the need for mechanical ventilation, a proxy will be approached for consent. Patients with an acceptable RASS score (-1, 0, or +1) will undergo an assessment of delirium using the Confusion Assessment Method for ICU (CAM-ICU). For patients who are delirious according to the CAM-ICU, as often occurs in the ICU due to severity of illness, a proxy will be approached for consent. Patients who have acceptable RASS scores and a negative CAM-ICU will be approached for enrollment. If study personnel have any concerns about the patient's capacity to consent once they begin speaking to the patient, they will administer the University of California San Diego Brief Assessment of Capacity to Consent (UBACC). If the patient is found to lack decisional capacity, a proxy will be approached for consent.

Participants will be provided with a copy of the consent form. Proxies who sign the consent form in person will also be provided with a copy of the consent form. In light of hospital visitation restrictions due to COVID-19, and considering that many proxies will not want to visit the hospital during the COVID-19 pandemic, we will allow for verbal consent by proxy. If verbal consent by proxy is obtained, we will log this in the REDCap database and mail the proxy a key information sheet. The consent form will be signed by research personnel and scanned into REDCap. The research nurse will be required to check the following attestation in REDCap: "I verbally explained the purpose, procedures, risks, benefits, confidentiality, and voluntary nature of the ACE-ICU study. The proxy was given time to ask any questions and agreed to have the participant take part in the study."

Baseline interview and provision of portable amplifying device (45 minutes of participant contact)

After consent is obtained, the research nurse will perform a baseline interview that includes an assessment of geriatric factors, demographics, and in-hospital factors that have been found to be important in prior research. This interview is expected to take approximately 45 minutes. Data will be collected about demographics, health conditions, pre-ICU functional status, healthcare utilization, frailty, falls, social support, living situation, depressive symptoms, cognitive function, hearing impairment, and vision impairment. Hearing impairment will be assessed with the single-item hearing question in the National Health and Nutrition Assessment Survey (NHANES), which asks the participant or proxy to best describe the participant's hearing without a hearing aid or other listening device.

For participants enrolled during the intervention phase of the study, research personnel will then orient the participant and the nurse to the portable amplifying device and help set up the amplifier for the patient. A bedside laminated sheet with instructions on how to use the device will be provided and left at the bedside so that the participant and nurse have a resource for reference. Due to COVID-19 restrictions, every study participant will be provided with their own portable amplifying device which will be theirs to take home. Study personnel will then notify the physician team and occupational therapist of the participant's enrollment in the study, so that an OT order is placed in the EMR. The ICU pharmacy team will also be notified of the participant's enrollment.

Daily in-hospital audit (5 minutes of participant contact/day)

For participants enrolled during the intervention phase of the study, study personnel will perform a daily audit of use of the portable amplifying device. Participants will be asked a short series of questions about their device use. Study personnel will also ask the nurse about use of the device and will check the bedside log of device use.

Occupational therapy

For participants enrolled during the intervention phase of the study, the occupational therapist will assess the patient's need for OT and develop a treatment plan as they normally would in clinical practice. This study does not alter any aspect of the OT assessment or treatment plan; the study only ensures that OT is ordered as a default for all enrolled participants.

Deprescribing of potentially inappropriate medications (PIMs) started in the ICU

When a participant in the intervention arm is ready for transfer to the floor (as indicated by the primary MICU team placing a transfer order or indicating that they will place a transfer order that day), the ICU pharmacy team will review the active medication list for PIMs that were started in the ICU and are now potentially inappropriate. Common examples include atypical antipsychotics (often inappropriately started for ICU delirium) and acid suppressants (which are indicated for stress ulcer prophylaxis during mechanical ventilation, but are no longer indicated after discharge unless they are a home medication). The ICU pharmacist

will review the patient's home medication list to ensure that PIMs flagged for discontinuation were started in the ICU. The ICU pharmacist will then write a brief note in the EMR documenting which PIMs were discontinued and why.

Hospital discharge interview (45 minutes of participant contact)

Prior to hospital discharge, all participants will undergo an assessment of functional status, cognitive status (with the Montreal Cognitive Assessment), and 3 objective assessments: manual muscle testing according to the 6-point Medical Research Council (MRC) system,[27] hand grip dynamometry, and a short walk test. We will also ask participants in the intervention arm about perceived benefit of the portable amplifying device, their comfort with the device, and acceptability of the device.

- Manual muscle testing via the 6-point MRC system: Strength in each of 12 muscle groups is assessed via a 6-point system, in which a score of 0=no contraction, 1=flicker of a contraction, 2=active movement with gravity eliminated, 3=active movement against gravity, 4=active movement against gravity and resistance, 5= normal power.

30-day interview (15 minutes of participant contact)

At approximately 30 days after hospital discharge, we will call all participants (or their proxies) to ask about functional status, cognitive status, and health events (such as, but not limited to, readmissions). We will also ask participants in the intervention arm about ongoing use of the portable amplifying device since discharge.

Medical record abstraction

Study personnel will review the EMRs of all participants to gather data about the patient's demographics, health conditions, and clinical course in the hospital including, but not limited to, medications, ICU and hospital diagnoses, hospital length of stay, delirium, physical therapy treatments, SOFA score (a measure of severity of illness), as well as ICU treatments and complications (e.g. mechanical ventilation, tethering devices (e.g. lines, tubes, and restraints), and the need for dialysis). After the follow-up phone interview (or, if the patient cannot be reached, after the window for that follow-up interview has closed), study personnel will again review the EMR to capture data on health outcomes such as readmissions and mortality.

Payment for study participation

All participants will be given a $50 gift card at the conclusion of study activities to thank them for participation in the study. In most cases, the gift card will be mailed to the participant after completion of the follow-up interview. If there are any concerns about the participant's ability to reliably receive the gift card after discharge (such as if the participant is being discharged to a short-term rehab facility), we will provide the gift card prior to hospital discharge.

Screening and enrollment of provider participants

Occupational therapy providers

At least one occupational therapist (OT) is assigned to the Medical Intensive Care Unit (MICU) as part of the quarterly rotation for rehab personnel who staff the MICU's STEPS-ICU early mobilization program. Research personnel will identify the occupational therapist(s) rotating through the MICU during the study period and approach them for inclusion in the survey and focus groups. The appropriate information sheet (survey only or survey and focus group) will be provided. We estimate that up to 5 occupational therapists will be enrolled in this study.

ICU pharmacist providers

There are three ICU pharmacists who are dedicated to the MICU. Research personnel will approach the three ICU pharmacists for inclusion in the survey and focus groups. The appropriate information sheet will be provided.

Nursing providers

Research personnel will identify the patient's primary nurse by reviewing the electronic medical record, including the patient's primary team in Mobile Heartbeat. Nurses in the ICU or who are caring for the patient on the ward (after ICU transfer) may be approached for inclusion in the survey and focus groups. The appropriate information sheet will be provided.

Payment for study participation

Focus group participants will be provided with a $50 gift card at the conclusion of study activities to thank them for their participation. Survey respondents will not be compensated.

5.1.1 Data Collection

Location of data storage

The majority of the research data will be entered directly into a data management software program (REDCap), using either an on-site computer or an iPad on the Yale secure network. Paper collection materials (such as parts of the MoCA) will be scanned into REDCap and then stored in locked file cabinets. Data coordination, data management and database design will occur within the Yale School of Medicine's Program on Aging (POA). All data will be collected and maintained electronically. Data management procedures will ensure accurate and efficient data collection and analysis; confidentiality and real-time, on-demand study monitoring reports. Patient identifiers will be collected to facilitate gathering of complete data from the electronic medical record (EMR), but all participants will be assigned a unique REDCap study ID for identification in the study. Data will be maintained in accordance with HIPAA guidelines for participant confidentiality and privacy. All data will reside on secure, HIPAA-compliant database and file-sharing resources managed by the Data Management and Informatics Core (DMIC) of the POA and by Yale ITS. Access to data resources will be strictly limited to research staff and investigators.

Data collection and data elements

The data elements and method of collection during the study visits and for the EMR abstraction are outlined above in Section 5.1; therefore, in this section we will add these details for data elements related to the primary outcomes. To evaluate the feasibility of bundle delivery in the ICU (*SA1*), we will assess the delivery of each bundle component separately. For the occupational therapy intervention (*Component 1*), we will review the electronic medical record (EMR) for OT notes/flowsheet data from study enrollment through hospital discharge. In addition to gathering data on numbers of patients receiving OT, we will gather data about the frequency of and which OT interventions are performed. For the hearing impairment intervention (*Component 2*), we will sum data from the daily audit. Of note, if the patient is deeply sedated or unconscious due to critical illness, that day would not count as an eligible day of hearing amplifier use. For the deprescribing intervention (*Component 3)*, we will review the chart for the ICU pharmacist's note. We will also gather data on the details of the deprescribing intervention (i.e. the number and type of medications that were changed or discontinued) as preliminary data for future studies.

To evaluate the acceptability of the geriatrics bundle among providers who are responsible for delivering and using the individual components (occupational therapists, nurses, physicians, and ICU pharmacists), we will administer a survey with a 5-point Likert scale (range 1-5, where 5 indicates that the bundle is completely acceptable for use in its current form) to the providers who are responsible for

delivering the intervention: occupational therapists (OT; *Component 1*), nurses (primarily, but also other ICU providers such as physicians and physical therapists; *Component 2*), and ICU pharmacists (*Component 3*). The survey will include questions about whether the device improved workflow (e.g. For PT, did it help facilitate early mobilization?) and ask for feedback that may help adapt the intervention to improve its utility. For the deprescribing component, we will administer the survey to the ICU pharmacist after they have performed the intervention. The acceptability survey will be developed during the study to allow the investigator team to observe implementation of the geriatrics bundle and ensure that the survey is assessing all important workflow elements.

To evaluate facilitators and barriers to implementation of the geriatrics bundle using a qualitative approach, we will use qualitative methods to allow for a more comprehensive understanding of barriers and facilitators encountered by the healthcare team (OT, nursing, and ICU pharmacy) during bundle delivery. This aim of the study will be conducted in collaboration with Dr. Cohen, a qualitative and mixed-methods expert. We will select participants for focus groups organized by discipline. Because the goal of qualitative research is to obtain a broad representation of experiences and perceptions, we will use purposive sampling to identify nursing participants with diverse viewpoints regarding the acceptability of the intervention, as indicated by the survey in Aim 2. (Purposive sampling will be needed for the nursing group because the YNHH MICU employs well over 100 nurses.) For the OT and ICU pharmacy focus groups, all providers who implemented the bundle will be included. During the first 3 months of the study, we will develop and pilot test an interview guide that includes probes for elaboration. We will ask the participants in each focus group to first elaborate on their role caring for older adults in the MICU, and how implementation of the geriatrics bundle changed (or did not change) their workflow. We will then ask more specific questions about bundle implementation, including: whether/how other care processes were affected, perceived effects on workload, perceived benefit to the patient, ease/difficulty of using any new technology (e.g. the portable amplifying devices), whether/how the bundle components interacted with each other, and suggestions for improvement. At the end of the study, Dr. Cohen will conduct the focus groups by discipline. As the OT and ICU pharmacy groups are fairly small, we anticipate that only 1 focus group will be needed for each of these disciplines. We anticipate that 3-4 focus groups (of 4-6 people) will be needed for nursing. Focus groups will be recorded and professionally transcribed. Transcripts will be reviewed by Drs. Ferrante, Cohen, and Pisani, with coding occurring according to the methods of Strauss and Corbin and analysis conducted using the constant comparative method.[33] The investigators will meet again to discuss the themes and what facilitators and barriers have been identified. These themes will provide invaluable data to help us refine and improve the geriatrics bundle for a future hybrid effectiveness-implementation study.

5.1.2 Adverse Events Definition and Reporting

a. Attribution of Adverse Events:

Adverse events will be monitored for each subject participating in the study and attributed to the study procedures / design by the principal investigator (Dr. Ferrante) according to the following categories:

a.) Definite: Adverse event is clearly related to investigational procedures(s)/agent(s).

b.) Probable: Adverse event is likely related to investigational procedures(s)/agent(s).

c.) Possible: Adverse event may be related to investigational procedures(s)/agent(s).

d.) Unlikely: Adverse event is likely not to be related to the investigational procedures(s)/agent(s).

e.) Unrelated: Adverse event is clearly not related to investigational procedures(s)/agent(s).

b. Plan for Grading Adverse Events:

The following scale will be used in grading the severity of adverse events:

1. Mild adverse event
2. Moderate adverse event
3. Severe

c. Plan for Determining Seriousness of Adverse Events:

Serious Adverse Events:

In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it results in any of the following outcomes:

1. Death;
2. A life-threatening experience in-patient hospitalization or prolongation of existing hospitalization;
3. A persistent or significant disability or incapacity;
4. A congenital anomaly or birth defect; OR
5. Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its "seriousness" when determining whether reporting to the IRB is necessary.

d. Plan for reporting UPIRSOs (including Adverse Events) to the IRB

The principal investigator will report the following types of events to the IRB:

Any incident, experience or outcome that meets ALL 3 of the following criteria:

Is unexpected (in terms of nature, specificity, severity, or frequency) given (a) the research procedures described in the protocol-related documents, such as the IRB-approved protocol and informed consent document and (b) the characteristics of the subject population being studied; AND

Is related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND

Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, legal, or social harm) than was previously known or recognized.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) may be medical or non-medical in nature, and include – but are not limited to – *serious, unexpected, and*

related adverse events and *unanticipated adverse device effects*. ***Please note*** that adverse events are reportable to the IRB as UPIRSOs **only** if they meet all 3 criteria listed above.

5.2 Study Schedule

All patient participants will have two 45-minute study visits that include assessments by the research team. The first visit will occur in the ICU and the second will occur on the hospital ward, prior to hospital discharge. All patient participants will also receive a brief follow-up phone call at approximately 30 days after hospital discharge. For participants in the intervention arm, study personnel will also perform a daily 5-minute audit of hearing amplifier device use and gather data about acceptability from the participant and nurse (when available).

The study schedule for provider participants will include a brief survey (5-10 minutes), and, for the subset that agree to participate in focus groups, one additional study visit for the focus group (lasting approximately 1 hour on a separate date).

5.3 Informed Consent

For patient participation in the study, we will obtain informed consent. The patient and/or their proxy will be approached in the ICU by study personnel. All patient rooms in the ICU are private rooms. The patient's ability to make an informed decision will be assessed through multiple methods, including (1) speaking with the care team to ensure that there are no concerns about capacity, (2) assessing the potential participant's mental status (for coma or agitation) via the Richmond Agitation Sedation Scale (RASS), and (3) performing a CAM-ICU to ensure that the patient is not delirious. If the patient is able to provide informed consent, study personnel will leave a copy of the signed consent form with the patient. If the patient is not able to make an informed decision the proxy will be approached for consent. As noted above, if consent is obtained from the proxy via telephone, we will mail the proxy an information sheet which serves as a copy of the consent.

Because this is a feasibility study that is gathering preliminary data, we need to gather basic data on the patients who are screened for this study; therefore, we are requesting a waiver of HIPAA authorization for screening/recruitment purposes only. A waiver of HIPAA authorization 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.

For provider participation in this study, we will provide the appropriate information sheet (survey only, or survey and focus group) as this part of the study meets criteria for a waiver of documentation of consent. Research personnel will review the information sheet with the potential participant and answer any questions about the study.

5.3.1 Screening

The Yale-New Haven Hospital (YNHH) Joint Data Analytics Team (JDAT) will provide a list of medical intensive care unit (MICU) patients at the York Street campus who are age 65 and older and who have not opted out of research. Study personnel will review this list on a daily basis, as well as the MICU list with an extra check to ensure that the patient has not opted out of research, to screen for eligible patients. As noted in the prior section, because this is a feasibility study that is gathering preliminary data, we need to gather basic data on the patients who are screened for this study; therefore, we are requesting a waiver of HIPAA authorization for screening/recruitment purposes only. Study personnel will record basic demographic information and basic identifying information about the screened participants. The basic identifying information is necessary because we need to know if participants are screened more than once for this study, which is likely to happen since readmissions to the ICU are common.

A waiver of HIPAA authorization 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.

5.3.2 Recruitment, Enrollment and Retention

Study personnel will review the JDAT-provided screening report and MICU roster (with an additional check to ensure that the patient has not opted out of research) each day and review the list for eligible patients by applying the inclusion and exclusion criteria detailed above in section 4.3.2. As outlined above in the Study Procedures (section 5.1), once an eligible patient is identified, a research nurse or research assistant will assess the patient for his/her ability to consent and participate in the study interventions by first assessing mental status via the Richmond Agitation-Sedation Scale (RASS). For patients who are too deeply sedated (RASS -2 to -5) or agitated (+2 to +5), as often occurs in the ICU due to severity of illness or the need for mechanical ventilation, a proxy will be approached for consent. Patients with an acceptable RASS score (-1, 0, or +1) will undergo an assessment of delirium using the Confusion Assessment Method for ICU (CAM-ICU). For patients who are delirious according to the CAM-ICU, as often occurs in the ICU due to severity of illness, a proxy will be approached for consent. Patients who have acceptable RASS scores and a negative CAM-ICU will be approached for enrollment. If study personnel have any concerns about the patient's capacity to consent once they begin speaking to the patient, they will administer the University of California San Diego Brief Assessment of Capacity to Consent (UBACC). If the patient is found to lack decisional capacity, a proxy will be approached for consent. Because we are studying a critically ill population, it is essential that we allow for consent by proxy because many of the participants may be too sick to consent themselves or participate in the baseline interview themselves.

All participants and/or proxies will be provided with a copy of the consent. In light of hospital visitation restrictions due to COVID-19, and considering that many proxies will not want to visit the hospital during the COVID-19 pandemic, we will allow for verbal consent by proxy. If verbal consent by proxy is obtained, we will log this in the REDCap database and mail the proxy an information sheet. If in-person consent is obtained, a copy of the consent will be provided at that time.

5.3.3 Study Visits

The study visits have been described in detail in section 5.1; as such, in this section we are providing the bulleted list of visits only. The estimated time for participant contact is listed next to each visit.

Patient participant study visits

- Baseline interview and provision of the portable amplifying device: 45 minutes
- Daily audit: 5 minutes/day.
- Hospital discharge interview: 45 minutes
- Follow-up phone interview approximately 30 days after discharge: 15 minutes

Provider participant study visits

- One 5-10 minute survey
- If the provider is recruited for and agrees to participate in a focus group, one additional study visit for the focus group: 1 hour on a separate date

5.4 Statistical Methods

5.4.1 Statistical Design, 5.4.2 Sample Size Considerations, and 5.4.3 Planned Analyses

SA1 Statistical Analysis: First, we will compile the data for each bundle component into an implementation report card. We will report the proportion of eligible patients receiving each

component, as well as the number of “doses” (for OT) and usage (for the hearing component) as outlined above. As a secondary analysis, we will evaluate delivery of the overall bundle. A feasibility threshold of 70% will be used for the individual bundle components, as well as the combined bundle (all 3 components).

The null hypothesis will be that <70% of patients will have received the bundle, with the alternative hypothesis that >= 70% of the patients will have received the bundle. Analysis consists of a simple comparison of the post-delivery proportion of patients who have received the bundle. Using PASS 15 statistical software for a one-sided exact test based on normal approximation per the method of Fleiss, Levin and Palk (2003) with a one-sided alpha of 5%, we will have 100% power to detect a minimal proportion of 70%. To show robustness, if we lower power to 80%, with a sample of 65 we are powered to detect a proportion of 75% and with a sample of 55 we are powered to detect a minimal proportion of 78%. This implies our sample of 75 is more than adequate to detect meaningful rates at or above 70%.

SA2 Statistical Analysis: For each bundle component, we will define acceptability as a minimum average score of 7/10 on the Likert Scale (i.e., the minimum average over all Likert measurements for that component). As described in the grant, the pharmacists will rate acceptability at one timepoint (since the deprescribing intervention occurs once), whereas the nurses and occupational therapists will rate acceptability at multiple timepoints. For the latter two groups, we will calculate the overall mean count (i.e. the mean Likert score) over time, again using a minimum average of 7 as the smallest level of permissible acceptability.

The null hypothesis will be a mean less than 7 and the one-sided alternative a mean greater than or equal to 7. Using PASS 15 statistical software for a non-parametric test of a single mean, based on the methods of Machin, Campbell, Fayers and Pinol (1997) and Zar (1984), and assuming a one-sided alpha of 5% and a null mean of 7, with a sample of 75 we will have 90% power to detect mean counts of 7.3 or greater. To show robustness, if we lower power to 80%, with a sample of 55 we are powered to detect a minimal mean of 7.4. This implies our sample of 75 is more than adequate to detect mean outcomes at or above 7.

SA3, Statistical Analysis: Focus groups will be recorded and professionally transcribed. Transcripts will be reviewed by Drs. Ferrante, Cohen, and Pisani, with coding occurring according to the methods of Strauss and Corbin and analysis conducted using the constant comparative method.[28] The investigators will meet again to discuss the themes and what facilitators and barriers have been identified. These themes will provide invaluable data to help us refine and improve the geriatrics bundle for a future hybrid effectiveness-implementation study.

5.4.4 Analysis of Subject Characteristics (if applicable)

Analyses for this prospective cohort study will follow best practices for analyzing and accounting for limitations of observational data. Variables will be examined univariately using descriptive techniques to analyze distributions and missingness. Standard bivariate and multi-variable adjusted methods will be used to investigate hypotheses, including but not limited to t-tests/analyses of variance for continuous variables, Wilcoxon/Kruskal-Wallis tests for ordered/non-normally distributed variables, chi-squared tests for non-ordered categorical variables, and regression methods (e.g., linear, logistic) for multivariable-adjusted analyses.

5.4.5 Interim Analysis – N/A

5.4.6 Handling of Missing Data

In cases of variables with >5% missing data, multiple imputation will be employed.

6 Trial Administration

6.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

Consent forms will be Institutional Review Board (IRB)-approved and the participant or legally authorized representative (LAR) will be asked to read and review the document. The study personnel will explain the research study to the participant and answer any questions that may arise.

Participants/LAR will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants/LAR should have the opportunity to discuss the study with their family or surrogates, or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants/LAR must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants/LAR for their records.

As part of the consent process, trained research staff will review all the required elements of informed consent and HIPAA authorization, including the purpose, study procedures, risks, benefits, confidentiality of records, and voluntary nature of the study. The principal investigator will be available to answer any questions.

Specific plans for the decisionally impaired: We recognize that among older hospitalized patients, there may be a proportion of eligible patients who are decisionally impaired (i.e., who have a compromised capacity to understand information and make a reasoned decision about participation in research) and therefore require additional protections. We also recognize that the purpose of identifying eligible patients who may be decisionally impaired is not necessarily to exclude them from research, but to seek ways to enable their participation in an ethically appropriate manner that is also compliant with regulatory requirements. Therefore, at the time of approaching any potential participant for consent, our plans are as follows:

A) **Use standardized criteria to determine if the potential participant is capable of providing consent.** Members of the study team who are responsible for participant recruitment and consent are all highly trained and experienced in obtaining informed consent. They will receive training in the process for determining capacity to consent in aging populations. Ability to provide informed consent will be assessed using the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC), a brief instrument designed to assess decision-making capacity for research participation according to NIH standards. Factors to be considered include the ability to articulate a choice regarding study participation, its purpose, and understanding that participation does not constitute medical treatment.

B) **Follow up with identified proxies when decisional impairment is identified**. Proxies will be approached for consent because the risks of this study are minimal and the potential benefits of developing generalizable knowledge that will benefit elderly hospitalized patients nationwide is significant. All potential participants deemed decisionally impaired will be notified of that determination before permission is sought from their legally authorized surrogate to enroll in the study. Because many proxies will not be available in person due to COVID-19 visitor restrictions, we will allow for verbal consent by proxy and will then mail a copy of the consent/information sheet.

C) **Seek assent for potential participants who are decisionally impaired**. If permission is given by the surrogate to enroll in the study, the potential participant will be notified and their verbal assent will be obtained (i.e., their active affirmation of a desire to participate). In all cases in which assent is sought, the assent discussion will include the following: (1) a simplified description of the purpose of the research, including risks and

benefits; (2) a description of the study procedures to which the participant will be exposed; (3) a statement explaining that participation in this study is voluntary; and (4) a question and answer period in which the participant will be encouraged to ask questions about his or her participation in the study.

6.2 Institutional Review Board (IRB) Review

This is a prospective study that is being conducted in a clinical setting (the intensive care unit) and includes interviews and standard assessments used in geriatrics research. The protocol will be submitted to the IRB for review and approval. Approval of the protocol must be obtained before initiating any research activity. Any change to the protocol or study team will require an approved IRB amendment before implementation. The IRB will determine whether informed consent and HIPAA authorization are required. A study closure report will be submitted to the IRB after all research activities have been completed.

6.3 Subject Confidentiality

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No data will be released to any unauthorized third party without prior written approval of the sponsor. All research activities will be conducted in as private a setting as possible.

The study monitor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical 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, or, if applicable, sponsor requirements.

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 (POA).

Patient identifiers will be stored within REDCap for research purposes, but upon entry into the REDCap system, each study participant will be assigned a unique Study ID that does not include identifiers. REDCap includes features for HIPAA compliance including real-time data entry validation (e.g. for data types and range checks), a full audit trail, user-based privileges, de-identified data export mechanism to statistical packages (SPSS, SAS, Stata and R), and integration with the institutional Active Directory. Access to study data in REDCap will be restricted to the members of the study team with authentication through University NetID credentials. The REDCap@Yale database and web server are housed on secure platforms that are backed up daily. REDCap@Yale meets the security standards for use with high risk data as set forth by the Yale Information Security Office. All of these measures minimize risks to subjects and decrease the likelihood of potential breaches of confidentiality. At the end of the study, all study databases will be de-identified and archived in REDCap at the Yale Program on Aging.

6.4 Deviations/Unanticipated Problems

A protocol deviation is any noncompliance with the study protocol. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the site investigator to identify and report deviations within 14 working days of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the study sponsor, and the reviewing Institutional Review Board (IRB) per their policies.

Unanticipated problems involving risks to participants or others include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the study sponsor. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and study sponsor, if applicable within 5 days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and study sponsor within 14 days of the investigator becoming aware of the problem.

6.5 Data Quality Assurance

In addition to required training for research staff at Yale, all research personnel have undergone additional training at the Yale Program on Aging to ensure that data are collected in a standardized and reliable way. This includes training in geriatric assessments. The risk of harm from routine physical assessments performed will be minimized by using Program on Aging (POA) field staff who follow standardized procedures outlined in a manual of operations. For example, as part of the walk test, research nurses will monitor for stability, assess for contraindications, use assistive devices, and will not attempt to complete walk test if there is a risk of fall. It is routine practice for POA research nurses to be trained in safe mobilization techniques and fall prevention for older adults. Participants will be encouraged to walk at a comfortable pace during the test, using assistive devices as needed.

Participants will have the right to refuse the physical assessments at any time. In the unlikely circumstance of a fall or other event, the research coordinator will follow the protocol for adverse events outlined in Section 6.4.

6.6 Study Records

Study records include (1) case report forms, (2) electronic health records, (3) the log of portable amplifying device use, (4) consent forms, (5) surveys, and (6) all regulatory documents, including the protocol.

6.7 Access to Source Data

Source data will be maintained per Medical Records policy in REDCap, a password protected, secure, Health Insurance Portability and Accountability Act (HIPAA) compliant, web-based electronic database with a built-in audit trail.
Only Institutional Review Board (IRB) approved research team members who have current HIPAA and Collaborative Institutional Training Initiative (CITI) Good Clinical Practice (GCP) and human subjects protection training will be authorized to access records.

6.8 Data or Specimen Storage/Security

All study staff will follow Yale's guidelines for data protection, which include storing all programs, data and documents on Yale-managed central file shares. No files or documents will be permitted on unencrypted portable media or on local hard drives, or on file shares other than those maintained by ITS specifically for the study. Remote access to central file shares will be permitted only by remote desktop connection from computers that are encrypted and secured according to Yale policy for managed workstations (http://its.yale.edu/services/software-computers-mobile-devices/software-delivery-configuration/managed-workstation-program).

Study data at Yale will be managed according Yale University Information Technology Services (ITS) policies for "3 lock data" (http://its.yale.edu/secure-computing/security-standards-and-guidance). Primary research data across sites will be managed using REDCap. REDCap is a secure, web application designed to support data capture for research studies. It includes features for HIPAA compliance including real-time data entry validation (e.g. for data types and range checks), a full audit trail, user-based privileges, de-identified data export mechanism to statistical packages (SPSS, SAS, Stata and R), and integration with the institutional Active Directory. Access to study data in REDCap will be restricted to the members of the study team with authentication through University NetID credentials.

All study staff will be trained in HIPAA and Human Subject Protection and will follow local institutional guidelines and policies for data protection. No files or documents will be permitted on unencrypted portable media or on local hard drives, or on file shares other than those securely maintained by ITS specifically for the study. Any paper records will be maintained in locked file cabinets within locked offices.

6.9 Retention of Records

The NIH requires that records must be retained for a minimum of 3 years after completion of the research. However, since we plan to use the data generated from this study as preliminary data for future studies, thereby inviting additional scrutiny, we will plan to store the data for 10 years (the more conservative time frame used by the FDA) after study

completion in the secure REDCap server. At this point in time, the master list linking the unique subject number to the research data will be destroyed.

6.10 Study Monitoring

This pilot study presents minimal risks to participants, and adverse events are not anticipated. In the unlikely event that serious adverse events do occur (for instance, breach of confidentiality of data), they will be reported within 7 days by the Principal Investigator (PI) to the IRB, all co-investigators, and any appropriate funding and regulatory agencies. The investigator team will specify whether the serious adverse event is considered related to the study.
The PI will be responsible for all scientific, organizational, and implementation decisions, including assuring that study participants are not exposed to risks and that the study is conducted according to high scientific and ethical standards.

6.11 Study Modification

All study modifications will be submitted to the IRB as a protocol modification. The change will be implemented into the study after IRB approval of the modification.

6.12 Study Completion

The NIH requires that records must be retained for a minimum of 3 years after completion of the research. However, since we plan to use the data generated from this study as preliminary data for future studies, thereby inviting additional scrutiny, we will plan to store the data for 10 years (the more conservative time frame used by the FDA) after study completion.

6.13 Funding Source

This study is funded by the Pilot/Exploratory Studies Core of the Yale Claude D. Pepper Older Americans Independence Center (P30 AG021342).

6.14 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, 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.

At the present time, no investigators or study personnel have any conflicts of interest with regard to this study. Dr. Ferrante, the principal investigator, is an attending physician in the MICU. It is possible that a subject enrolled in this study may have been a MICU patient of Dr. Ferrante's. To avoid any perceived conflicts of interest, Dr. Ferrante will not be involved in the direct recruitment of any potential subjects with whom she had a clinical relationship (i.e., she will ensure that she is not the study team member approaching the patient).

6.15 Publication Plan

The data arising from this study will be published in peer-reviewed journals and submitted for presentation at national meetings, including (but not limited to) the American Thoracic Society (ATS) meeting and the American Geriatrics Society (AGS) meeting. The PI holds primary responsibility for publishing the study results.

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