Data Analysis Plan

Project Number: IIR 17-068

Project Title: Hearing Impairment, Strategies and Outcomes in VA Emergency Departments

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Site: 630 – New York Harbor Healthcare System

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Rationale for the study sample size

We anticipate 12 months (one year) of subject recruitment over the eighteen-month study period. We base our enrollment on several conservative assumptions. 3600 Veterans who are 65 years and older and have an ESI criterion of 4 or 5 or otherwise likely to be discharged home and currently use the Manhattan and Brooklyn VA EDs per year. We anticipate the opportunity to screen 50% of all Veterans who meet these criteria or 1800 per year (5400 total). A conservative prevalence estimate for hearing loss is 35%. Using a cut point of 24, prior studies indicate a sensitivity of 0.33 and a specificity of 0.98 with ranges of 0.24 to 0.42 and 0.88 to 0.98, respectively. Based on VA pilot data from a QI initiative, we have lowered the cut point to 10 (a traditional cut point indicative of some hearing loss) because no Veterans in our pilot work scored >24 and over 50% of those > 10 agreed and used a hearing assistance device in clinic with subjective improvement. Of the group of 1800 using the ED, we estimate that 230 Veterans (based on the HHIE-S test characteristics) would score above the HHIE-S cut point of 10 and be eligible for recruitment and consent for this study. We assume that we will be able to screen at least 70% of these 230 Veterans coming to the ED, which would yield 160 Veterans with scores > 10. If 50% of these Veterans are consented (n=80) and 95% are discharged, we have 76 Veterans per year that can complete this study. Anticipating 10% attrition before survey

completion, 68 Veterans per year will complete this study. These highly conservative estimates ensure that we will achieve our desired minimum sample size of 180 Veterans if we continue the study beyond one year of recruitment. Our minimum goal for 12 months is 68 Veterans and maximum goal is 120.

We used simulation methods to estimate power and sample size requirements. We generated data from literature-based assumptions in each iteration for a specific sample size and an assumed effect size for each outcome. For each iteration, we conducted two t-tests in accordance with the multiple testing corrections and recorded whether one or both null hypotheses were rejected. For each sample size/effect size combination, we ran 1500 iterations; we calculated power as the proportion of iterations in which both null hypotheses were rejected. We evaluated total study (both arms) sample sizes ranging from 70 to 150.

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Specific description of how data will be collected

We will collect data from four primary sources: the VA CPRS, RA observations, a RA-administered 10-minute patient survey, and brief qualitative follow-up interviews with patients, nurses, and physicians. A fifth source will be follow-up phone calls to identify three-day and 30-day ED revisits that have occurred outside of the VA healthcare system. Survey data will be electronically linked to CPRS data using a subject-level linking code stored separate from these data. Brief qualitative interviews will be audio recorded, transcribed without identifiers, and electronically linked to survey data. The RA will enter de-identified survey data from each in-person survey (using tablets) into a VA security-compliant electronic REDCap database hosted by VA Informatics Computing Infrastructure (VINCI). VINCI will build a virtual environment to house all study data as well as the necessary statistical tools for data analysis. We will capture data from qualitative interviews by notes and audio recordings that will be transcribed for analysis.

Follow-up interviews with intervention Veterans who are willing to speak more extensively after discharge from their ED visit will be used to obtain a more detailed understanding of patients' ED experience of barriers and facilitators of HAD use and anticipated future use of a hearing device in medical and other settings. Brief semi-structured interviews with ED nurses and physicians (providers) around the time of patient discharge will be used to assess providers' experiences interacting with hearing-impaired patients with and without HADs to evaluate, from the provider's view, the benefits and feasibility of use of the PockeTalkerTM in the ED. Although almost all providers in the Harbor ED system are primary English speakers, we will also inquire as to provider dominant language at each encounter until we have a complete provider inventory for dominant language. We will use an explanatory sequential mixed methods design to develop semi-structured interviews for nurses and physicians in order to address additional areas of inquiry raised by the quantitative findings and/or discrepancies between qualitative and

quantitative data collected during the ED visit. Patient and provider interviews will be audio recorded, transcribed, and coded for themes.

Using administrative and CPRS data, we will abstract demographic data, the presenting complaint, all diagnoses (including cognitive diagnoses) prior to and during the ED stay, medications at ED admission and discharge, and discharge diagnoses and plans. Included in Veteran surveys, we will inquire about primary spoken language, prior non-VA ED experience, years of education, mood (using the Patient Heath Questionaire-9). We will code whether the Veteran came to the ED alone or with others and whether they live with others or alone. We will also use CPRS to calculate the distance between the VA ED and their residence and whether they have additional health insurance. We will determine whether patients have had an ED revisit within three and 30 days through CPRS review as well as a brief follow-up phone call four and 35 days after ED discharge. Some Veterans may not use the VA system for a revisit, although this is likely to be infrequent. Telephone follow-up may capture ED use that would otherwise be missed. To enhance reproducibility, published reports will profile subject socio-demographics and comorbidities, with key outcomes reported for the whole sample and stratified by amount of HAD use. We will report mean and variation in noise level in our NY VA Harbor ED environments, measured in decibels. Fitting protocols will be described in detail.

We will use Grounded Theory, a systematic and rigorous set of principles for text interpretation developed by Strauss and Corbin to interpret qualitative data from semi- structured interviews. Audio-recorded qualitative data will be transcribed verbatim. Dr. Nehrig and a research assistant will analyze the data using an inductive thematic text analysis approach, involving a rigorous review of the transcripts to identify key concepts and patterns. We will use ATLAS, a qualitative data analysis management software program to facilitate our multi-step iterative coding and analysis. Initially, meaningful statements that convey discrete concepts and ideas will be identified and allocated a code that maintains the meaning of the original expression as closely as possible. The coders will independently read and analyze a sample of interview transcripts to identify preliminary codes and sub-themes. The constant comparative method of analysis will be used to continually refine the interview and coding procedure. This method involves an iterative process of making comparisons at each level of analysis (data with data, data with codes, codes with categories, etc.) throughout data collection and analysis. This process allows investigators to continuously modify and refine coding and create categories as data is being collected and analyzed. After the initial round of coding, we will recode all interviews to ensure that the final codes are applied equally to all interviews. We will develop a coding manual using this iterative process. All transcripts will then be independently coded by the two reviewers to establish inter-rater reliability. We will group the codes into higher-level categories to be distilled into the main research themes. Over the course of the process, we will maintain a record of the process of idea generation, analyses, questions, and hypothesized understandings. In the final analysis stage, will integrate qualitative and quantitative data to describe the mechanism of HAD effectiveness.

Method of randomization

After consent, we will randomize subjects to receipt of a HAD or control. Randomization will be stratified by site to ensure a balance of intervention and control subjects at each site. The RA will provide subjects given HADs with instructions and will fit and test the devices to ensure

proper function. These subjects will be encouraged to use the HAD during any encounters with ED staff and others (for example, family). All consenting subjects will understand that consent includes: (1) completion of a post ED-care 10- minute survey and brief telephone follow-up four days after discharge, (2) abstraction of their medical records, and (3) awareness of the risks and benefits of participation. All consenting subjects will receive $20 cash and be able to keep the HAD when leaving the ED if they have found it to be helpful. If randomization is successful, the two groups should vary only in receipt of the HAD, which we hypothesize will affect downstream outcomes.

Plan for and specification of the purpose of any interim analysis of the data

Before addressing the specific aims, the data will be summarized numerically using descriptive statistics. Comparison of the baseline characteristics between the two treatment groups will be performed using chi-square tests for categorical data and t-tests or nonparametric tests for ordinal or continuous data.

We will compare intervention and control subjects with respect to baseline sociodemographic characteristics (age, gender, race, and education), comorbid medical conditions, and the Charlson comorbidity index and other potential co-variable measures. We will assess whether any adjustments need to be made in the final statistical models if we determine the differences are clinically meaningful. Besides the primary analyses described below, we will conduct exploratory mediation analyses with the goal of developing a better understanding of the mechanisms of the intervention. We will use R 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) for all analyses.

Methods for handling missing data points and subject dropouts

Missing data: We anticipate less than 5% loss to follow-up, as a majority of data is collected during one ED visit. If missingness is higher, multiple imputation will be used to estimate the group differences and the uncertainty due to missingness, under the assumption of missingness at random (MAR).

Definitions of Covariates

Data sources will include (1) patient responses to survey questions about their use of the hearing assistance device, the quality of their hearing and understanding in the ED, the quality of their preparation for discharge home, and the accuracy of their understanding of their discharge instructions (see Appendix 2 for specific items). A second source of data will be (2) clinical information from the patient's VA electronic medical record – Computerized Patient Record System (CPRS), including ED use in the past year, days since last ED visit, Charlson comorbidity index, medications at time of ED admission and discharge, all diagnoses prior to and during ED stay, and discharge instructions/plans. We will also determine whether patients have had an ED revisit within three days and 30 days through CPRS review as well as through a brief follow-up phone call four days and five weeks after ED discharge. The baseline CPRS data will be used to characterize the sample and may be used for covariate balance in multivariable analysis, if the treatment and control groups vary significantly. The follow-up (72-hour and 30-day revisit) data will be used to explore the relationship between providing a HAD

during an ED visit and the likelihood of revisit. A third source of data will be (3) observational data to determine the amount of HAD use when subjects (randomized to receive a HAD) are interacting with providers (physicians and nurses). A fourth of source of data will be (4) semi-structured interviews with patients, nurses, and physicians to identify barriers and facilitators of Veterans' willingness to be screened for hearing disability, and understand factors contributing to use (and non-use) of the hearing assistance device, as well as to qualitatively determine if the device improves the quality of hearing and understanding.

With regard to semi-structured interviews with staff (nurses and physicians), all staff will be informed about the study procedures in terms of 1) knowing that this this is a study about hearing impairment; 2) that we are interested in understanding the utility of using HADs during an ED visit and that we will match staff characteristics (gender and spoken language) with each patient that is an enrolled subject. Staff will also know that a research assistant may approach them for a brief conversation about their experience with specific patients and about HAD use, in general. They will understand that they are free to participate or refuse participation and their decision will not be known to their supervisor and will not impact their employment in any way. They will be asked permission for the RA to audio record their conversation and they will know that as soon as that conversation is transcribed (and without identifiers), that tape recording will be erased. They will also know that we will attempt to survey all nurses and physicians at least once who are working during those times that patients are participating in HearVA-ED.

Methods for Dealing with Data Transformations

Missing – Missing data will be removed by multiple imputation or by being re-coded into a "missing" category.

Distribution of Data – The distribution of the data will be determined. Non-normally distributed data will be transformed using log transformation.

Definitions of Analytical Sets

Intent-to-treat – Analysis will be conducted with patients included in their randomly assigned group (opt in versus opt out), regardless of the treatment received.

Complete-case – Analysis conducted including only participants who have no incomplete data regarding their treatment.

<u>Adverse and Serious Adverse Events</u>

Standard IRB-approved and HIPAA compliant measures will be used to maintain Veteran confidentiality, privacy, and data security that adhere to the standards of the VA privacy officer, Information Security Officer, and Chief Information Officer. All study personnel have already taken or will take the mandatory VA HIPAA training to ensure that they are aware of the importance of Veteran confidentiality and all appropriate laws regarding the protection against Veteran privacy breaches. Procedures will be in place to ensure that all files containing Veteran information will be kept in VA-encrypted, locked databases on VA computers. There will also be

a system in place for breaches in Veteran privacy or other adverse events to be reported to the Principal Investigator, so that he may take the appropriate steps to ensure that they are documented and there is minimal risk that it could happen again. We will obtain approvals from the VA New York Harbor Healthcare System human subjects committee. Adverse events will be reported to the study IRB and will include any medical event regardless of its relationship to the study intervention.

SAE/EA Response and Reporting Procedure

1. Research staff become aware of AE/SAE (via scheduled survey, spontaneous report from participant, or other means)
2. Research staff notify PI immediately if the event is an SAE or if immediate psychiatric or medical intervention is required, and within 7 days if the event is an AE.
3. PI makes determination for 3 key indices if suspected to be study related:
    a. Severity: Mild, Moderate, Severe
    b. Expectedness: Expected, Unexpected
    c. Study Related: Definitely, Probably, Possibly, Remotely, Not Study-Related
4. Project Director documents SAE/AE and PI determination in study database.
5. Project Director prepares a report for the local IRB as per local, state, and federal reporting requirements.
6. PI and Project Director plan measures to prevent future occurrences, if any warranted.
7. PI and Project Director make changes to protocol and/or consent form if needed

Data and Safety Monitoring Plan

As this is a minimal risk, single site study, – (Brooklyn and Manhattan campuses are both part of VANYHHS). A DSMB is not required.

Data and Safety Monitoring Plan (DSMP): Our study team will monitor all adverse events through weekly meetings to review enrollment progress and identify any adverse events. We will evaluate any adverse events related to recruitment, enrollment, hearing assistance device use, and the interview process. Adverse events will be reported to the study IRB and will include any medical event regardless of its relationship to the study intervention. All such events will be recorded and blinded (where possible) except for the IRB, who will be unblinded and notified immediately of any serious and unexpected event. In such instances, the IRB will determine appropriate action with respect to reporting and additional steps. For more urgent situations, the study interviewer will notify ED staff and any of the physician investigators on the team.