Educational Video to Improve Nursing Home Care in End-Stage Dementia (EVINCE)
Statistical Analysis Plan
for the
Final Report

PROTOCOL NUMBER: 12-013

PROTOCOL TITLE: EVINCE (Educational Video to Improve Nursing Home Care in End-Stage Dementia)

CO-PRINCIPAL INVESTIGATORS: Susan L. Mitchell, MD, MPH
Angelo E. Volandes, MD, MPH

FUNDING AGENCIES: National Institutes of Health (R01 AG 043440)

PREPARED BY: Michele L. Shaffer, PhD

RELEASE DATE: Version 1.0: 9 July 2013
Version 1.1: 11 July 2014
Version 1.2: 24 September 2014
Version 1.3: 12 December 2014
Version 1.4: 15 April 2015
Version 1.5: 15 February 2016
Version 1.6: 18 March 2016
Version 1.7: 17 August 2016

Version Number	Revision(s) and Reason(s) for Amendment	Release Date
1.0		9 July 2013

1.1	• *Section 1.6 updated to correct a minor grammatical error.*
	• *Based on discussion at the EVINCE investigators meeting on June 20, 2014 regarding the handling of deaths during the course of the study, Section 3.5 updated to reflect*
	  ○ *clarification of the cumulative definition of each outcome by the time point of interest or death*
	  ○ *using a survival analysis approach to estimate cumulative incidence for comparison of the intervention and control for sub-Aim 2 which allows for censoring due to death or dropout.*
		11 July 2014

1.2	• *The decision was made to drop special care dementia unit (SCU) from on-going nursing home (NH) matching in EVINCE due to changes in Massachusetts legislation regarding the definition of SCU mid study. While matched NH pairs 1-19 were matched on both SCU and for-profit status; thereafter, homes are matched solely on for-profit status.*
	  ○ *Sections 1.6 has been updated to provide the original matching criteria and to note the change in matching criteria as well as the rationale.*
	  ○ *Section 3.5 has been updated to reflect how matching is incorporated in the original analyses and how this change will impact the analyses of primary and secondary outcomes including planned sensitivity analyses.*
	• *Section 3.5 was updated to reflect that matching and clustering at the NH level will be taken into account for the analysis of sub-Aim 2 consistent with the analyses of the remaining aims.*
	• *Section 3.5 was updated to explain that cumulative outcomes defined for Aim 2 will only be based on time points following baseline because the baseline patient data are collected before the baseline proxy interview (i.e., before the proxy has seen the video in the intervention arm or heard options verbally in the control arm).*
		24 September 2014

1.3	• *A typo has been corrected in the power table in Section 1.6. The power was described appropriately in the text so that only the table is impacted.* • *The decision was made to pre-specify unmatched analyses for all aims of the study. Section 3.5 has been updated to reflect an unmatched analysis for all primary and secondary outcomes based on a lack of existing evidence of the relationship between matching*	12 December 2014

	criteria (later criterion) and the primary outcome as well as to provide greater analytic flexibility in accounting for covariate imbalances and allowing for direct estimation of the intraclass correlation coefficient (ICC) for future studies.	

1.4	• *Aim 3 and Hypothesis 3 have been reworded to reflect that we will analyze a rate, rather than a proportion, to make use of all available data.*
	• *The primary analysis for Aim 3 has been updated to*
	  ○ *use count regression methods, including hurdle models, to make use of all available data;*
	  ○ *provide only descriptive analysis for feeding tube;*
	  ○ *remove feeding tube from the definition of composite variables;*
	  ○ *add hospice referral as an outcome to be analyzed as time to first hospice referral.*
		15 April 2015

1.5	• *The following terminology is introduced to distinguish between baseline interview assessments: B-1: pre-video, B-2: post-video. For the control group, only a B-1 assessment is obtained.* • *Language has been added throughout as needed to distinguish between baseline data assessed by interview and by chart review.* • *The primary analysis for Aim 1 has been updated to use a cumulative definition of goals of care (comfort care vs. other) which includes baseline interview data (B-1 for control group, B-2 for intervention group).*	15 February 2016
1.6	• *The statement of sub-Aims 1 and 2 has been edited to reflect that the time point of interest is 12 months.* • *The examination of new hospice enrollment is now specifically listed as a fourth aim.*	18 March 2016
1.7	• *In Section 3.5, the wording of the composite outcome in the analysis of Aim 3 has been updated to include new feeding tube to be consistent with the statement of Aim 3 in Section 1.2.* • *A sensitivity analysis has been added for the primary outcome. The sensitivity analysis will be a subset analysis, limiting patients to those of white race.*	17 August 2016

PREFACE

The Statistical Analysis Plan (SAP) as outlined in this document will be finalized prior to the completion of the study and analysis of final study data. The SAP contains all modifications and updates to the planned analyses that were outlined in the original study protocol. This plan details all a priori specified analyses that will be performed upon study completion and database lock, with specifications for tables, figures, and statistical models. Tables and figures that are to be included in interim reporting are indicted with an (*) for overall or (**) for by intervention group (partially blinded) after the title.

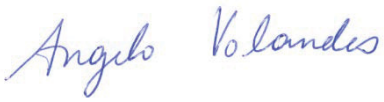
SIGNATURE PAGE

Analysis plan approved by:

July 9, 2013

Susan L. Mitchell, MD, MPH
Co-Principal Investigator

Date



July 9, 2013

Angelo E. Volandes, MD, MPH
Co-Principal Investigator

Date

July 9, 2013

Michele L. Shaffer, PhD
Biostatistician

Date

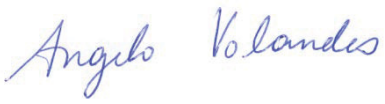
SIGNATURE PAGE

Analysis plan Version 1.1 approved by:

June 27, 2014

Susan L. Mitchell, MD, MPH
Co-Principal Investigator

Date



July 1, 2014

Angelo E. Volandes, MD, MPH
Co-Principal Investigator

Date

26 June 2014

Michele L. Shaffer, PhD
Biostatistician

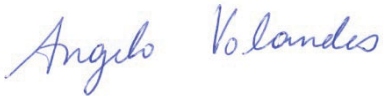
Date

SIGNATURE PAGE

Analysis plan Version 1.2 approved by:

September 19, 2014

Susan L. Mitchell, MD, MPH
Co-Principal Investigator — Date



September 19, 2014

Angelo E. Volandes, MD, MPH
Co-Principal Investigator — Date

September 17, 2014

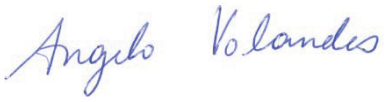
Michele L. Shaffer, PhD
Biostatistician — Date

SIGNATURE PAGE

Analysis plan Version 1.3 approved by:

Dec 10, 2014

Susan L. Mitchell, MD, MPH — Date
Co-Principal Investigator



Dec 10, 2014

Angelo E. Volandes, MD, MPH — Date
Co-Principal Investigator

December 11, 2014

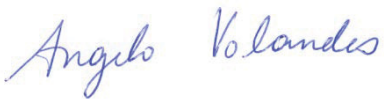
Michele L. Shaffer, PhD — Date
Biostatistician

Analysis plan Version 1.4 approved by:

April 3, 2015

Susan L. Mitchell, MD, MPH
Co-Principal Investigator

Date



April 3, 2015

Angelo E. Volandes, MD, MPH
Co-Principal Investigator

Date

March 18, 2015

Michele L. Shaffer, PhD
Biostatistician

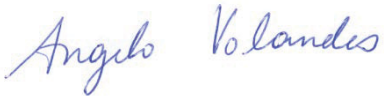
Date

Analysis plan Version 1.5 approved by:

February 6, 2016

Susan L. Mitchell, MD, MPH
Co-Principal Investigator

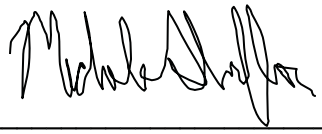
Date



February 6, 2016

Angelo E. Volandes, MD, MPH
Co-Principal Investigator

Date



February 9, 2016

Michele L. Shaffer, PhD
Biostatistician

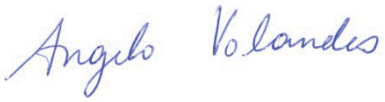
Date

Analysis plan Version 1.6 approved by:

March 17, 2016

Susan L. Mitchell, MD, MPH
Co-Principal Investigator

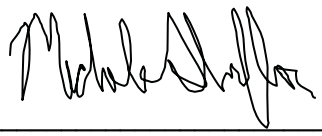
Date



March 17, 2016

Angelo E. Volandes, MD, MPH
Co-Principal Investigator

Date



March 17, 2016

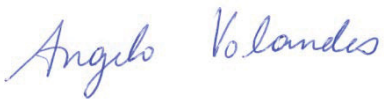
Michele L. Shaffer, PhD
Biostatistician

Date

Analysis plan Version 1.7 approved by:

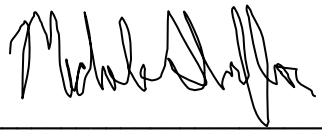
Aug 12, 2016

Susan L. Mitchell, MD, MPH — Date
Co-Principal Investigator



Aug 12, 2016

Angelo E. Volandes, MD, MPH — Date
Co-Principal Investigator



August 10, 2016

Michele L. Shaffer, PhD — Date
Biostatistician

1 Overview

1.1 Study Rationale and Design

Alzheimer's disease afflicts over 5 million Americans and is the 6th leading cause of death in the U.S. To date, advanced dementia research has largely focused on describing the end-of-life experience of patients with this disease. Designing and testing interventions targeting those opportunities is the current research priority for this field. Advance care planning (ACP) is the most consistent modifiable factor associated with better palliative care outcomes in advanced dementia.

The opportunity for ACP is exceptional in advanced dementia but often inadequate. Thus, advanced dementia patients often get aggressive interventions that may be inconsistent with preferences and of little clinical benefit. Recent work has particularly underscored the need to avoid unwanted and unnecessary hospitalizations among these patients. Traditional ACP primarily relies on ad hoc verbal descriptions of hypothetical health states and treatments. This approach is limited because complex scenarios are difficult to envision, information from providers is inconsistent, and verbal explanations are hindered by literacy and language barriers.

To address these shortcomings, the co-PIs have developed video decision support tools for ACP and shown their efficacy in several randomized controlled trials (RCTs) in out-patient settings. The overriding goal of the EVINCE (Educational Video to Improve Nursing home Care in End-stage dementia) study is to conduct a cluster RCT of an ACP intervention vs. control among 360 nursing home (NH) residents with advanced dementia (N=180/arm) in 20 matched NHs (10 intervention/10 control).

1.2 Objectives and Outcomes

The overriding goal of the EVINCE (Educational Video to Improve Nursing home Care in End-stage dementia) study is to conduct a cluster RCT of a video ACP intervention. The specific aims and hypotheses are:

Aim 1: To conduct a cluster RCT of an ACP intervention vs. control among 360 NH residents with advanced dementia (N=180/arm) in 20 matched NHs (10 intervention/10 control), and to compare their proxies' preferences for their level of care. Levels of care options are: comfort care (i.e., no hospital transfers except if needed for comfort, e.g. hip fracture), basic care (i.e., hospital transfers but no resuscitation, intubation, or intensive treatments (i.e., hospitalization, resuscitation, intubation, tube feeding, ICU care), or uncertain. Preferences will be ascertained from proxies at baseline [pre (B-1) (control and intervention group) and 10-minutes post video (B-2)(intervention group only) and 3, 6, 9, and 12 months. At baseline, proxies in the intervention NHs will view a video ACP decision support tool. Their preferred level of care ascertained ~ 10 minutes after viewing the video will be communicated to the primary care team. Proxies in the control NHs will experience the usual ACP practices in those NHs.

H1: A higher % of proxies in the intervention vs. control NHs will choose comfort care at baseline (~ 10 minutes after viewing video in intervention arm), and 3, 6, 9, and 12 months follow-up.

Sub Aim 1: To compare the % of residents who acquire a preference of comfort care among those that did not have this preference at baseline in the intervention vs. control NHs by 12 months

Aim 2: To compare the % of residents with advance care planning (ACP) in the intervention vs. control NHs at 3, 6, 9, and 12 months as measured by documented: 1. Explicit decisions to forego hospitalization; 2. Explicit decisions to forego other treatments (tube-feeding, parenteral therapy); and 3. Goal of care discussions between proxies and providers.

H2a: A higher proportion of residents in the intervention (vs. control) NHs will have documented decisions to forego hospitalization at 3, 6 (primary study outcome), 9, and 12 months.

H2b: A higher proportion of residents in the intervention (vs. control) NHs will have documented decisions to forego other treatments, and goals of care discussions at 3, 6, 9, and 12 months.

Sub-Aim 2: To compare the % of residents who acquire documentation of an explicit decision to forego hospitalization among those that did not have such a decision at baseline in the intervention vs. control NHs by 12 months.

H2c: A higher proportion of residents in the intervention (vs. control) NHs who do not have documentation of a decision to forgo hospitalization at baseline will acquire new documentation of a decision to forego hospitalization at 3, 6 (sub-primary study outcome), 9, and 12 months.

Aim 3: To compare the rate of hospital transfers (admission or emergency department visits) and other burdensome treatments (tube-feeding, parenteral therapy) over 12 months in intervention vs. control NHs.

H3: There will be a lower rate of hospital transfers or other use of other burdensome treatments (new feeding tube insertion or use of parenteral therapy) among residents in the intervention (vs. control) NHs over the entire follow-up period (up to 12 months).

Aim 4: To compare the rate of new hospice enrollment for those not on hospice at baseline over 12 months in intervention vs. control NHs.

H4: There will be a higher rate of new hospice enrollment among residents in the intervention (vs. control) NHs over the entire follow-up period (up to 12 months).

1.3 Inclusion and Exclusion Criteria

Resident eligibility criteria are: 1) Age ≥ 65 at the time of screening, 2) A diagnosis of dementia (any type), 3) Global Deterioration Scale (GDS) score of 7, 4) NH length of stay > 30 days, 5) proxy is available who can speak in English, and 6) proxy must either live within a 60 mile radius of Boston or be available to come to the resident's NH within two weeks of recruitment in order to conduct the in-person baseline interview. Features of GDS stage 7 include: profound memory deficits (cannot recognize family), total functional dependence, speech < 5 words, incontinence, and inability to ambulate. Only proxies who can speak English will be included because data collection instruments have not been translated into other languages. As in our prior studies, we will enroll proxies who are formally designated to make medical decisions for the patient as noted in the NH chart (i.e., durable power of attorney for health care). However, if there is no such formal designation, we will enroll the informally designated health care decision-maker for the resident (i.e., next-of-kin) as indicated in the NH record.

Residents with cognitive impairment due to causes other than dementia (e.g., head trauma) and in short-term, sub-acute SNFs will be excluded.

1.4 Duration of Participation and Duration of Study

Residents and proxies will be followed for 12 months. The study will be completed over five years.

1.5 Interim Data Safety Advisory Committee Reviews

Safety monitoring will be the responsibility of a Data and Safety Advisory Committee (DSAC) composed of voting and non-voting members. The non-voting members include: the co-Principal Investigators (Mitchell, Volandes), the study biostatistician (Shaffer), the data analyst, and project director. The voting members include: two experienced clinical dementia investigators and one experienced biostatistician from outside the Harvard/Hebrew SeniorLife

system. One voting member will be designated as chair. The NIH Project Officer responsible for EVINCE will also be invited to attend DSAC meetings but will be a non-voting member.

DSAC meetings will occur every 6 months via conference call. At least two weeks prior to each DSAC meeting, the study analyst will compile two reports with oversight from Dr. Shaffer, one with data to be reviewed by all members and the other with data to be reviewed only by the voting members. Each meeting will consist of an open and a closed session. The open session will be attended by all of the DSAC members. Issues discussed during the open session will include aggregated (two study arms combined) reports of the following: resident/proxy dyad and facility recruitment rates, dropout rates, deaths, protocol deviations, SAEs, and unanticipated problems. The closed session will immediately follow the open session and will be attended only by voting DSAC members. Data reviewed in the closed session will include all items presented in the open-session (resident/proxy dyad and facility recruitment, dropout rates, death, protocol deviations, serious adverse events and unanticipated problems) stratified by the two study arms in a partially blinded fashion (i.e., intervention groups denoted by 1 and 2). The DSAC will be free to determine the need to stop the protocol based on examination of serious adverse events and can request interim analysis of study outcomes. Within a week after the DSAC meeting, the Project Director will send a summary of the open-ended meeting to all DSAC members, and the DSAC chair will send a summary of the closed session to the voting members. Pre and post meeting reports will also be sent to the NIH Project Officer at her request.

It will be the responsibility of the co-PIs and the DSAC chair to submit the post-meeting reports from the DSAC to HSL IRB within a week of the meeting. The IRB chair will be informed of any SAEs or DSAC decision to stop the study for any reason within 48 hours.

1.6 Rationale for Number of Dyads

The sample size of 360 dyads from 20 matched NHs (180 dyads/10 NHs per treatment arm) will provide sufficient power to detect clinically meaningful differences between the intervention and control NHs for our primary outcome: a decision to forego hospital transfer by 6 months. We are able to make realistic estimates of outcomes in the control group based on our extensive prior studies. Additional power calculations are provided for selected secondary outcomes for Aims 1 and 3. All calculations use two-sided testing and a 5% type I error rate. Power calculations are adjusted for potential dependence of observations within NHs using an intraclass correlation of 0.05 and assuming 18 residents per NH. Based on our estimates, we will have 96% power to detect an absolute difference of 25% for the primary outcome (Aim 2) and 82% power to detect a 20% difference. For secondary outcomes, power to detect a 25% difference is excellent for baseline preferences (post video in intervention arm) (Aim 1), and good for a 20% difference. Power to detect a 15% difference in hospital transfers (Aim 3) is very good, but limited for smaller differences

Table 3. Power estimates

Hyp	Outcomes	Control (%)	Detectable difference (%)	Power (%)
H1	Preference for comfort at baseline (post-video in intervention arm) (2^o)	70	25;20	94;80
H2a	Decision to forego hospital transfer by 6 months (1^o)	48	25;20	96;82
H3	Hospital transfer by 12 months (2^o)	20	15;10	89;50

NHs were originally randomized using a paired approach matched for for-profit status and whether or not the NH had a special care dementia unit (SCU). In March 2014, the state of Massachusetts changed legislation defining an SCU. Many of the changes focused on specifics of staff training. As a result, SCUs in several participating facilities did not meet the new criteria and lost this official designation, although the actual clinical structure of the existing units did not change. Nonetheless, we opted to maintain the initial matching criteria of the first 19 NHs which included SCU based on the definition before the Massachusetts legislation change, but dropped this matching criterion after the legislation change. Thus, beginning with matched pair 20, NHs were matched solely on for-profit status.

For the sub-Aim 2, H2c analysis, the proportion of residents who begin the study with a decision to forego hospital transfer at the baseline is 0% in both groups. For the sub-primary outcome defined as acquisition of new documentation of a decision to forego hospitalization among those free at baseline by 6 months, we will have 80% power to detect a difference of 22% between groups with 18 dyads per 10 nursing homes per group or 360 total dyads if the control acquisition rate is 5%. We will have 80% power to detect a difference of 25% between groups with 18 dyads per 10 nursing homes per group or 360 total dyads if the control acquisition rate is 10%. To have 80% power to detect a difference of 20% between groups would require 18 dyads per 11 nursing homes per group or 396 total dyads if the control acquisition rate is 5%. To have 80% power to detect a difference of 20% between groups would require 18 dyads per 14 nursing homes per group or 504 total dyads if the control acquisition rate is 10%. Thus, while our target sample size is 360 dyads based on our primary outcome, we will endeavor to recruit closer to 400 dyads in order to achieve greater power towards the sub-primary aim.

2 Reporting

2.1 Data Flow

Data management and analysis for the study will take place at Hebrew SeniorLife (HSL).

Drs. Mitchell and Volandes will oversee the training of the field staff for four months prior to starting data collection. During the study, the co-PIs will perform unannounced reliability checks on a 5% sample of chart reviews and proxy interviews.

Five research Assistants (RAs) will be responsible for screening participants, obtaining informed consent, interviewing nurses and proxies, implementing the intervention, conducting chart reviews, and doing the brief baseline resident cognitive examination. RA1 will have sole responsibility for all the in-person baseline proxy interviews and implementing the video decision support tool and provider feedback in the intervention facilities. As such RA1 will not be blinded to the randomization scheme. RA2, RA3, and RA4 will be blinded to the randomization scheme to the extent possible, and will collect all the other outcome data through chart reviews and follow-up proxy interviews. RA5 is primarily responsible for proxy recruitment and obtaining consent from proxies. She will not be blinded to the study assignment.

All data will be collected and entered electronically by the RAs using laptop computers or tablets in the field. State-of-the-art electronic data capture software and programming (REDCap) will be used for these purposes. Once entered, the data will be downloaded and entered into the computer systems at HSL IFAR for cleaning, programming, and analyses.

All procedures will be conducted using good computing practices for the handling and analysis of data for clinical trials.

2.2 Report Generation

The final statistical report will describe and justify any deviations from the original statistical plan described herein. If necessary, such deviations will be treated as a protocol amendment.

The final statistical report will be accompanied by a description of the data cleaning process and will provide summaries of key findings. All programs used to produce the statistical reports will be documented, tested, and archived.

2.3 Definitions of Analysis Populations

Intent-to-Treat (ITT) Population:

All eligible resident/proxy dyads recruited into the study will be included in the ITT population. The ITT population will be the primary analysis population for all primary and secondary outcomes.

Safety Population:
As randomization is at the level of NH, the safety population will be coincidental with the ITT population for this study.

No documented decision to forego hospitalization baseline subgroup population for sub-Aim 2:
An a priori subgroup of interest is defined as residents who begin the study without a documented decision to forego hospitalization.

3 Overview of Planned Analyses

3.1 Recruitment and Participant Status

Total dyad recruitment over time will be summarized overall and by intervention group. Study visit completion will be summarized overall for both residents and proxies. The number of resident/proxy dyads screened, recruited, withdrawn, and completing the study will be summarized overall and by intervention group. Reasons for screen failure and dropout will be summarized overall and by intervention group.

The corresponding descriptive summaries are outlined in Appendix A, Section A.1.

3.2 Resident and Proxy Demographics and Baseline Characteristics

Demographic and clinical characteristics of residents and proxies at baseline will be summarized by intervention arm. Resident characteristics will include measures of demographic information, health status, cognitive status, functional status, and advance care planning. Proxy variables will include measures of demographic data, relationship to the patient, and preferences for the resident's care.

The corresponding descriptive summaries are outlined in Appendix A, Section A.2.

3.3 Adverse Events

The study has been granted a low-risk status by the NIH. Given this, SAEs (serious adverse events) are not expected. The potential adverse events that could occur during this study involve negative responses of proxies for the recruited nursing home residents to viewing the intervention video. The following represents the two expected potential adverse events:

1. The trained Research Assistant witnessed what they assess to be severe proxy distress while watching the video or during the interview. (Due to the sensitive nature of the material, tearing up by the proxy can be expected and is not deemed to be a reflection of distress.)
2. The proxy asks for the video or discussion to be stopped, or leaves the room during the video or discussion, due to related distress.

Adverse events will be compared between intervention groups using chi-square tests or Fisher's exact tests as appropriate. The corresponding descriptive summaries are outlined in Appendix A, Section A.3.

3.4 Protocol Deviations and Unanticipated Problems

Any protocol deviations or unanticipated problems will be listed by intervention group and summary statistics such as frequencies and percentages will be included if appropriate. The corresponding listings and descriptive summaries are outlined in Appendix A, Section A.4.

3.5 Primary and Secondary Outcomes

All analyses will be performed unmatched. The rationale for breaking the matches for the analyses includes 1) no existing evidence (prior to the conduct of this study) of a strong relationship between the matching criteria and the primary outcome, 2) the matching criteria changed during the course of the trial , 3) matched analyses lack the flexibility to directly estimate the intraclass correlation (ICC) that may be useful in planning future studies, and 4) allowing greater flexibility in accounting for individual-level covariates if baseline imbalances exist. The matching variable for-profit status will be included in the pool of potential covariates.

Aim 1: To compare the preferred level of care of proxies in the intervention (vs. control) nursing homes (NHs). The percent (%) of proxies choosing each of the following levels of care at baseline [prior to (B-1) and ~10 minutes after viewing the video (B-2) in intervention group], 3, 6, 9, and 12 months will be calculated: intensive treatments, basic care, comfort care, or uncertain. For Hypothesis 1 (H1), the outcome will be dichotomized as comfort care vs. other. The proportion of proxies who have chosen comfort care will be considered cumulatively at each assessment. These cumulative outcomes will include baseline interview assessment data (B-1 for control group, B-2 for intervention group) as the goals of care are collected immediately at the assessment. The proportion of proxies choosing comfort care will be compared between the intervention and control groups using an extension of logistic regression based on general estimating equations (GEE) to account for clustering at the NH level at each time period. The focus of H1 will be on comparing preferences obtained from proxies ~10 minutes after viewing the video in the intervention arm and at baseline in the control arm. Analyses at follow-up periods will inform the stability of preferences and intervention effect over time. Analyses will be at the level of the proxy. While the NHs are randomized, any baseline imbalances identified between key proxy or resident characteristics will be added to the final model using the change-in-effect method.

For sub-Aim 1, we will examine the acquisition of comfort care in the subset of residents for whom the proxy had not chosen comfort care as the preferred level of care at baseline. The modified ITT population will be the subgroup of residents who begin the study without comfort care as the preferred level of care and survive to the 3 month assessment. Only residents who survive to the 3 month assessment are included as there is no proxy interview conducted after death, therefore only baseline proxy interviews would be available. The outcome will be acquisition of comfort care by 12 months. The analysis will utilize Cox proportional hazards regression with a robust estimate of variance to account for clustering at the NH level. Results will be summarized using a hazard ratio and associated 95% confidence interval as well as plots of the cumulative incidence by group. Sensitivity analysis will be conducted to examine if the potential competing risk of death impacts the estimates of cumulative incidence.

Aim 2: To compare advance care planning (ACP) between residents in the intervention vs. control NHs: The initial approach will be to describe the % of residents in both arms with the following ACP outcomes by 3, 6, 9, and 12 months determined from documentation in the resident's chart: 1. Decisions to forego hospitalization; 2. Decisions to forego tube-feeding, 3. Decisions to forego parenteral therapy, and 4. Goal of care discussions. The proportion of residents with this outcome will be considered cumulatively at 6 months, including those who died; i.e., a composite of the percent of residents alive at six months who had a decision not to hospitalize and those who died before six months with this outcome prior to death. These cumulative outcomes will only be based on time points following baseline. No baseline data will be included in these analyses as the baseline chart review data are collected before the baseline proxy interview (i.e., before the proxy has seen the video in the intervention arm or heard options verbally in the control arm). For Hypotheses 2a and 2b, the proportion of residents with each ACP outcome will be compared between the intervention and control groups at 3, 6, 9, and 12 months using an extension of logistic regression based on GEE to account for clustering at the NH level. The % of residents with a documented explicit decision to forego hospital transfers by 6-months follow-up will be the primary outcome of this randomized clinical trial.

For sub-Aim 2, the modified ITT population will be the subgroup of residents who begin the study without a documented decision to forego hospitalization, and the outcome will be acquisition of a documented decision to forego hospitalization by 12months. The analysis will utilize Cox proportional hazards regression with a robust estimate of variance to account for clustering at the NH level. Results will be summarized using a hazard ratio and associated 95% confidence interval as well as plots of the cumulative incidence by group. Sensitivity analysis will be conducted to examine if the potential competing risk of death impacts the estimates of cumulative incidence. Similar analyses will be conducted to examine acquisition of documented decisions to withhold other treatments and goals of care discussions.

Aim 3: To compare hospital transfers and other treatments in intervention vs. control NHs. The rate of each of following outcomes over the entire follow-up period (up to 12 months) expressed per 1000 resident-days will be calculated: i. hospital admissions, ii. emergency department (ED) visits (without admission), iii. new tube-feeding, iv. parenteral therapy, and the composite outcome comprising any hospitalization, ED visit, new feeding tube, or parenteral therapy. Analyses for H3 will focus on two outcomes: i. the rate of hospitalization or ED visit over the entire follow-up period and ii. the rate of residents experiencing any hospitalization, ED visit, new feeding tube, or parenteral therapy over the entire follow-up period. The outcomes will be compared between the intervention and control groups using hurdle models, modifications of count regression (Poisson or negative binomial regression) models, and a robust variance estimate to account for clustering at the NH level. Length of follow-up (time to death, dropout, or completion of the study) will be included as an offset. Analyses will be at the level of the resident. Odds and rate ratios and 95% confidence intervals will be generated from these analyses. Should the observed outcomes be too sparse, we will consider simplified analyses using an extension of logistic regression based on GEE to look at the binary outcome of any occurrence of the outcome of interest (e.g., any hospital admission or ED visit) over the entire follow-up period.

Aim 4: An additional secondary outcome is a new hospice referral. Residents who were on hospice at baseline will be excluded. Time to first hospice referral will be compared between the intervention and control arms using Cox proportional hazards modeling with a robust variance estimate to account for clustering at the nursing home level. Hazard ratios and 95% confidence intervals will be generated from these analyses.

As the matching criteria used for randomization were relaxed after matched NH pair number 19, all analyses of primary and secondary outcomes will incorporate a dichotomous phase variable to account for this change.

3.6 Sensitivity Analyses

A planned sensitivity analysis for each aim and sub-aim will include performing a matched analysis.

A planned sensitivity analysis for the primary study outcome will be conducted, subsetting to include only patients of white race.

Appendix A: Tables and Figures

Specifications for planned tables and figures are provided below. Cosmetic changes in style and formatting may be made as needed for presentation and publication requirements.

A.1 Recruitment and Participant Status

Table A.1.1. Overall Overview of Dyad Enrollment over Time*

Table A.1.2. Event Completion for All Participants

Study Event	Residents	Proxies
Baseline	31	31
Q1	5	1
Q2		
Q3		
Q4		
Death	0	0

Table A.1.3. Overview of Dyad Enrollment over Time by Intervention Group**

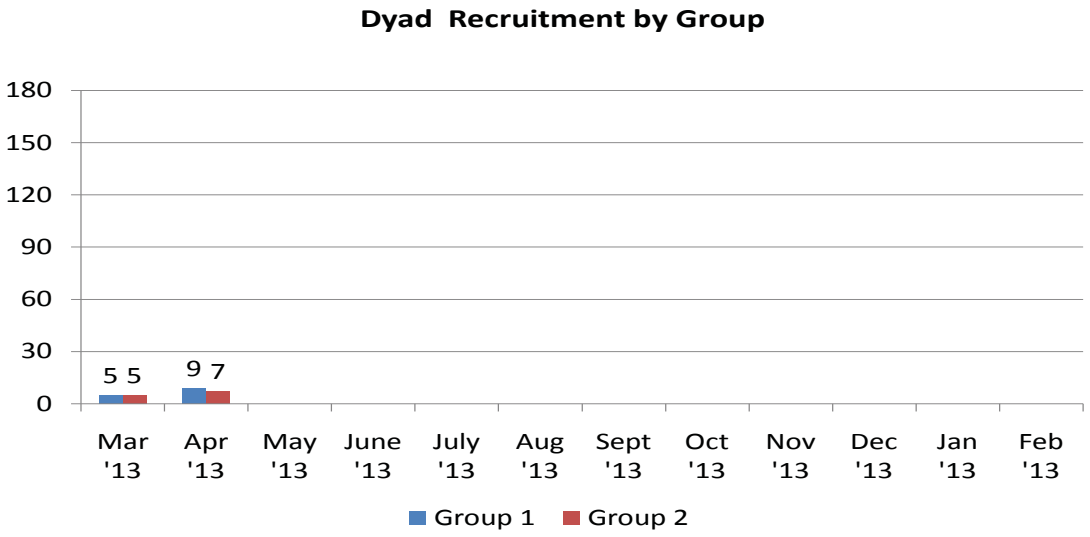


Figure A.1.1. Overall Dyad Status*

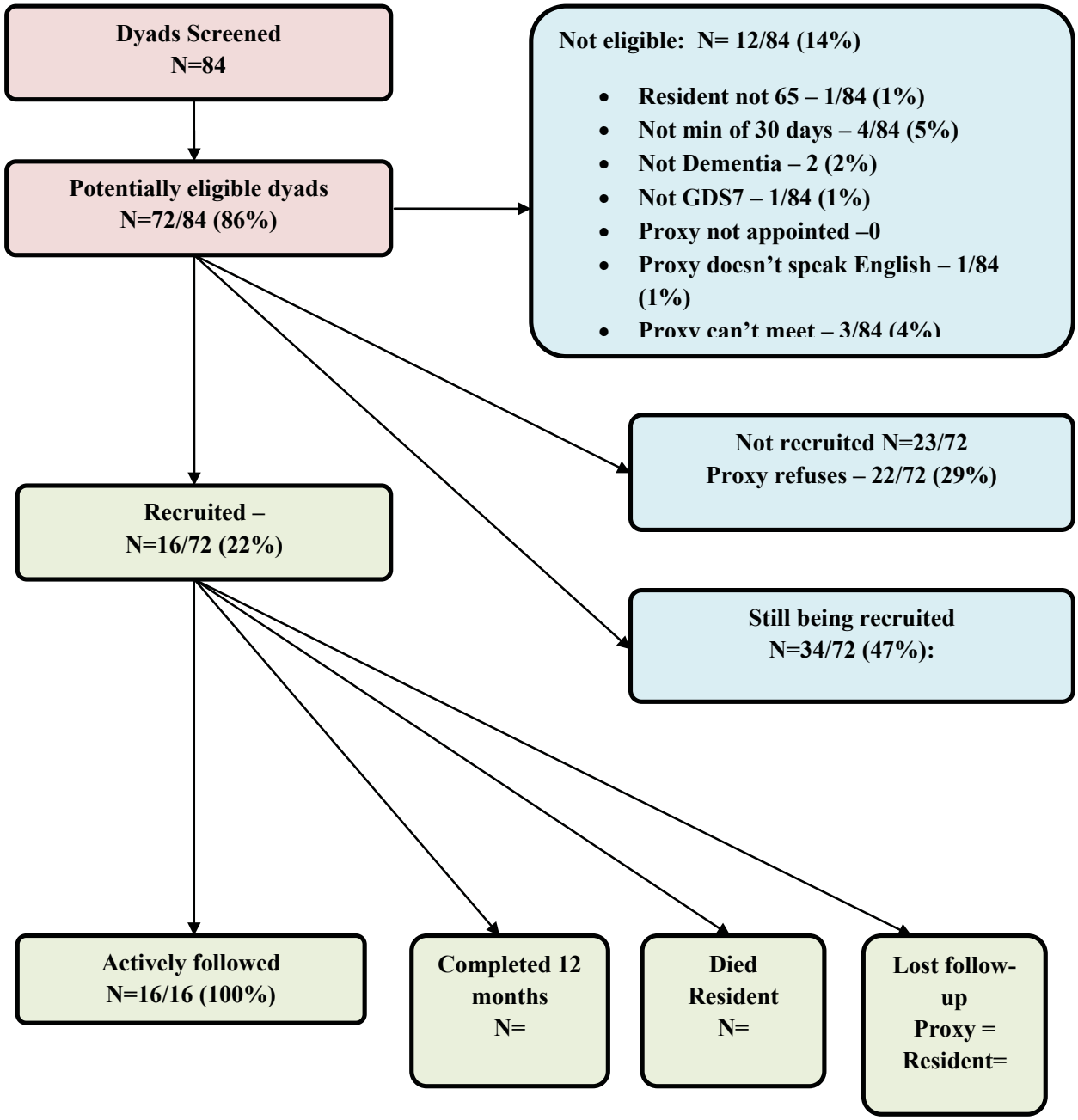
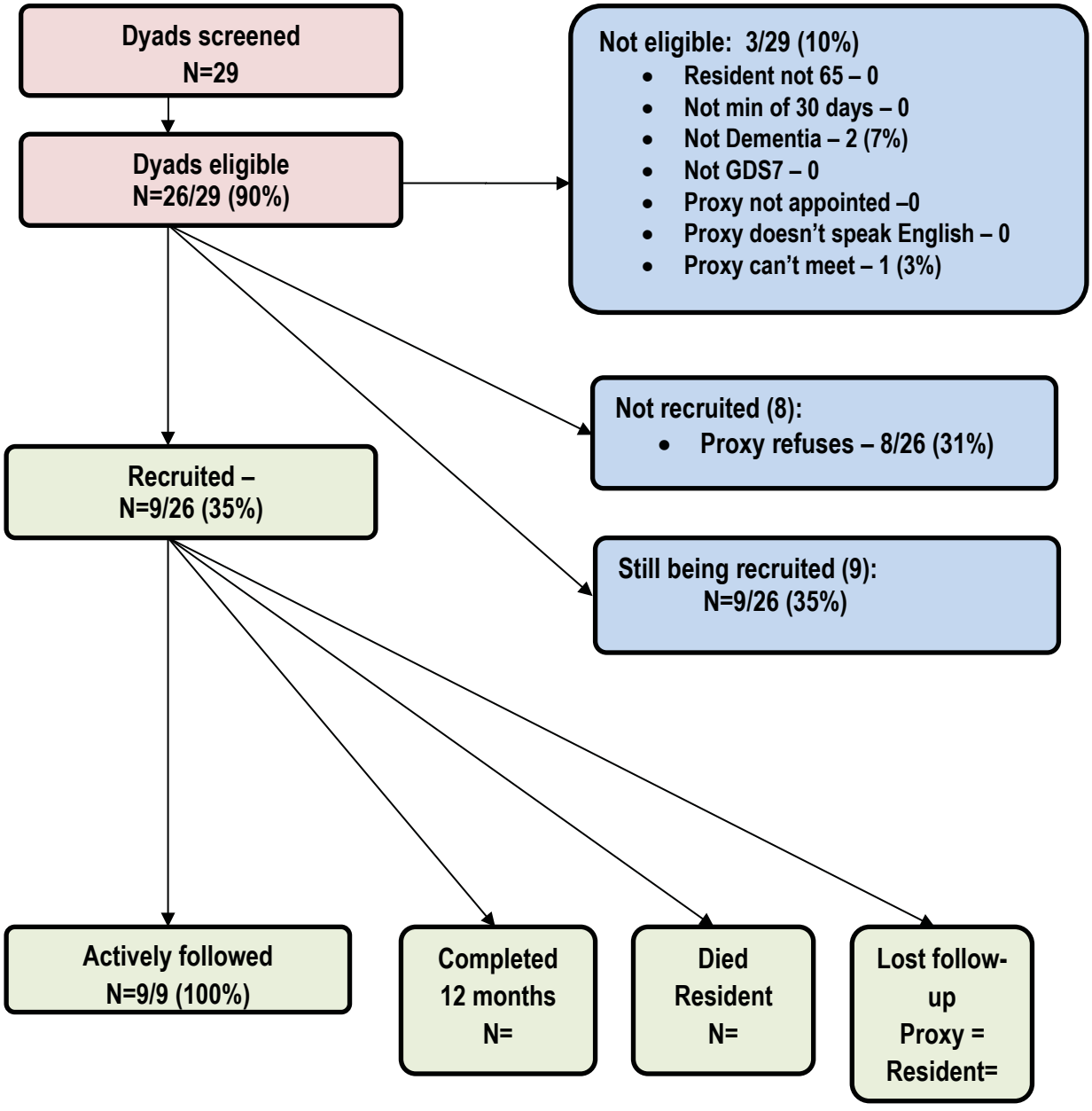
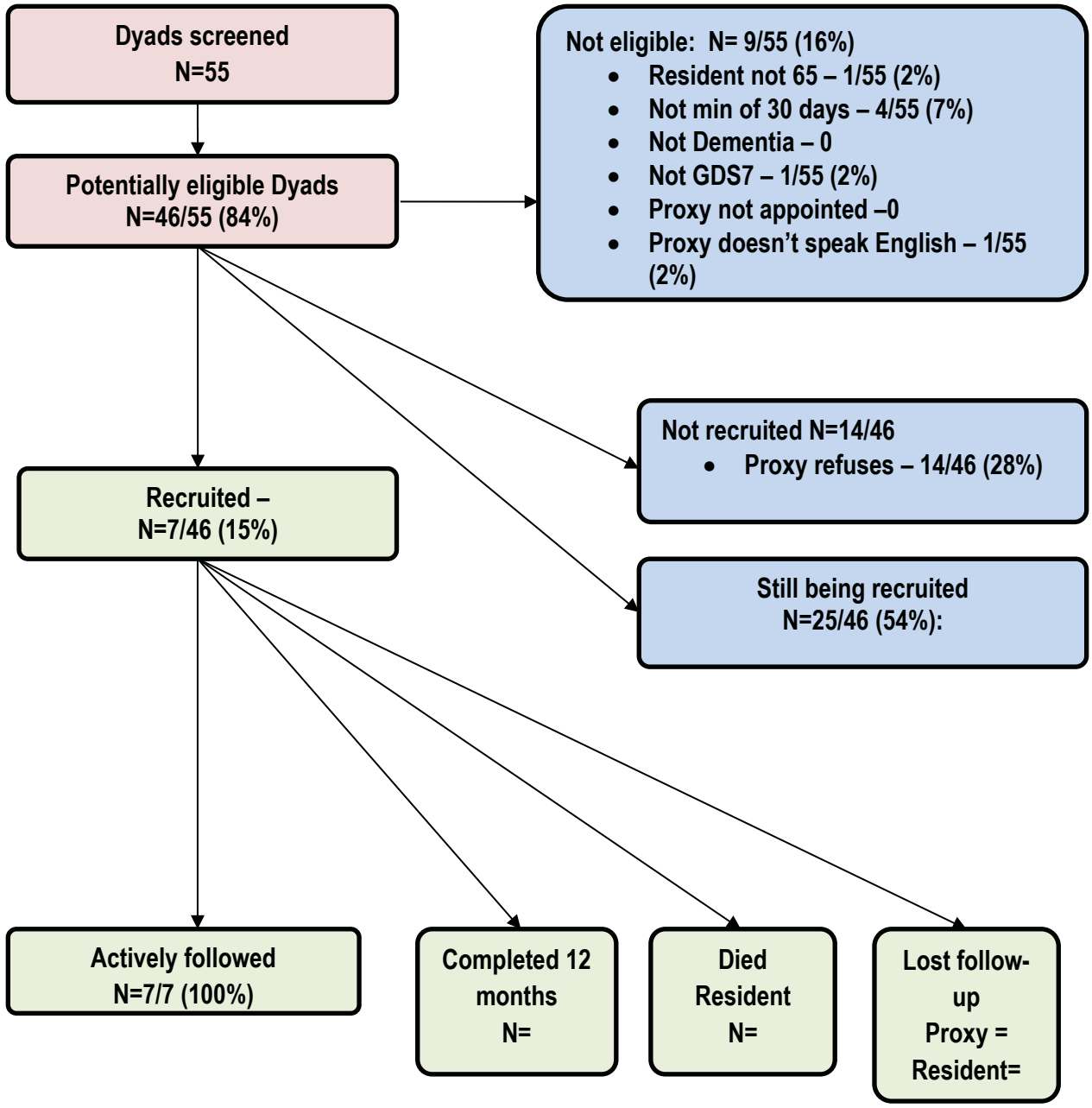


Figure A.1.2. Dyad Status by Intervention Group**

Panel A Group 1



Panel B Group 2



A.2 Resident and Proxy Demographics and Baseline Characteristics

Table A.2.1. Demographics and Baseline Characteristics of Residents and Proxies Overall and by Intervention Group

	Total in Study	Intervention	Control	Non-participants
Resident	33	17 (52%)	16 (48%)	30
Age				
Mean (Median)	85.8 (6.6%)			
Gender	33			
Male	5 (15%)			
Female	28 (85%)			
Ethnicity	29			NA
Black	3 (10%)			
White	26 (90%)			
Other				
Race	29			NA
Hispanic				
Non-Hispanic	29 (100%)			
Other				
Health status				
Cognitive status				
Functional status				
Advance care planning				
Proxy				
Age				NA
Mean	61.2 (11%)			
Gender				
Male				
Female				
Race				NA
Black				
White				
Other				
Ethnicity				NA
Hispanic				
Non-Hispanic				
Other				
Relationship to patient				
Preferences for resident's care				

A.3 Adverse Events

Table A.3.1. Overall Listing and Summary of Adverse Events*

Date	Description of Adverse Event	Action Taken	*Outcome*
Total # of Adverse events			

Table A.3.2. Listing and Summary of Adverse Events by Intervention Group**

Number	Date	Description of Adverse Event	*Action Taken*	*Group*
1				
2				
3				
4				
5				
6				
Total # of Adverse events				
Total Withdrawn from study				

A.4 Protocol Deviations and Unanticipated Problems

Table A.4.1. Overall Listing and Summary of Protocol Deviations*

Number	Date	Protocol Deviation
1		
2		
3		
4		
5		
6		
Total # of Deviations		
Participants Enrolled		
Deviations per Participant		

Table A.4.2. Listing and Summary of Protocol Deviations by Intervention Group**

Number	Date	Protocol Deviation	Group
1			
2			
3			
4			
5			
6			
Total # of Deviations			
Participants Enrolled			
Deviations per Participant			

Table A.4.3. Overall Listing and Summary of Unanticipated Problems*

Number	Date	Unanticipated Problem
1		
2		
3		
4		
5		
6		
Total # of Problems		
Participants Enrolled		
Problems per Participant		

Table A.4.4. Listing and Summary of Unanticipated Problems by Intervention Group**

Number	Date	Unanticipated Problem	Group
1			
2			
3			
4			
5			
6			
Total # of Problems			
Participants Enrolled			
Problems per Participant			