

PROVEN

PRagmatic Trial of Video Education in Nursing Homes

Protocol

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PRÉCIS

Study Title: PROVEN: PRagmatic trial Of Video Education in Nursing homes

Objective: To conduct a pragmatic cluster randomized control trial (RCT) of an Advance Care Planning (ACP) video support intervention for nursing home (NH) patients ≥ 65 cared for in 360 NHs (intervention, n=119; control, n=241) within two NH health care systems; Genesis HealthCare and PruittHealth.

Design and Outcomes: Aim 1 of this study is to implement all aspects of a pragmatic cluster RCT trial of an ACP video support intervention in two NH health care systems, including: 1. Recruitment of a sufficient number of NHs to achieve the sample size of patients needed to demonstrate a clinically meaningful difference in the primary outcome; 2. Facility staff training and implementation of the intervention; and 3. Outcome assessment using EMR records, the Minimum Data Set (MDS), and Medicare Claims.

In this stratified cluster RCT, the unit of random assignment is the facility but the unit of analysis is the patient, clustered within the facility. The intervention will be implemented facility-wide, thus all patients cared for in the NHs during the 24-month implementation period are subjects in this study ($N \simeq 152,160$). However, outcomes will be analyzed in targeted sub-populations with advanced comorbid conditions for whom the opportunity and need to improve ACP and goal-directed care are greatest. These subgroups include very disabled older patients with advanced dementia and advanced congestive heart failure (CHF) or chronic obstructive pulmonary disease (COPD) (i.e., cardiopulmonary disease).

Outcomes to be compared between patients in the intervention and control NHs include: advance directives orders (Do Not Resuscitate (DNR), Do Not Hospitalize (DNH), Do Not Intubate (DNI), and no tube-feeding), hospital transfers, use of other burdensome interventions (new feeding tube insertions, parenteral therapy, intubation, ICU care), hospice use, and Medicare ACP billing codes. The effectiveness of the intervention to improve these outcomes among those targeted sub-populations with advanced illness will be assessed among long-stay (≥ 90 days) NH residents > 65 (Aim 2) and new admissions to post-acute care (short-stay < 90 days) (Aim 3). Finally, we will evaluate the effects of the intervention by examining the aforementioned outcomes among long-stay NH patients and new admissions who do NOT have either of the pre-specified advanced illnesses (Aim 4).

The primary outcome for this pragmatic trial is hospital transfers (quantified as number of hospital transfers/person-days alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays over a 12-month follow-up period among long-stay residents with advanced dementia and/or advanced CHF/COPD. For all analyses involving this hospital transfer outcome, including the primary trial outcome, the main analyses will be restricted to Medicare Fee-for-Service patients because ascertainment of hospital transfers is most accurate from Medicare Claims data. Exploratory analyses will also be done on all patients, not just FFS, using the MDS as well as Medicare claims as the data sources. Secondary outcomes include advance directive orders, other burdensome treatments, and hospice use. An exploratory aim will be, among decedents, to compare the proportion of patients in the intervention and control facilities who had any of the following interventions in the last month of life: hospital transfer or other burdensome interventions (feeding tube insertion, parenteral therapy, intubation, ICU care).

Separate analyses will be done among decedents from the short and long-stay cohorts with advanced dementia, CHF or COPD, as well as those without advanced disease.

Interventions and Duration: The intervention consists of a suite of five videos designed to address common ACP decisions confronting NH patients and their families:

1. *Goals of Care for Any Patient*
2. *Goals of Care for Patients with Advanced Dementia*
3. *Decisions about Hospitalization*
4. *Decisions about Hospice*
5. *General Information about Advance Care Planning for Healthy Adults*

NHs randomized to the control arm of the study will use the usual ACP procedures already practiced in their facilities. The ACP Video Program will be implemented for 24 months in the intervention facilities. Individual patients in both arms who are in the NHs during the 24-month implementation period are eligible, and their outcomes will be assessed for up to 12 months in the long-stay cohort and 100 days in the short-stay cohort.

Sample Size and Population: The ACP video intervention will be implemented facility-wide in the NHs randomized to the intervention arm. Thus, ALL patients who are cared for during the 24-month implementation phase are potential participants in the trial and comprise the study population ($N \simeq 152,160$). However, the analyses described in Aims 2 and 3 will focus on target populations with advanced comorbid conditions that are cared for in the NHs during the 24-month implementation period. For Aim 2, the target sample is long-stay patients with advanced dementia or CHF/COPD ($N \simeq 14,760$). As the primary study trial outcome is hospital transfers in the long-stay patients, sample size estimates and power calculations are based on this target group. For Aim 3, the target sample is short-stay patients with advanced dementia or CHF/COPD. For Aim 4, the target sample is long-stay and short-stay NH patients who do NOT have either of the pre-specified advanced illnesses.

In this stratified cluster RCT, the unit of random assignment is the facility. Facilities will be randomized in the following strata in the following order: 1. Health care system (Genesis HealthCare and PruittHealth), and 2. Hospitalization rates in the 12 months prior to recruitment in target sub-populations (grouped as terciles). Outcomes analyses will not differ by strata.

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1. STUDY OBJECTIVES

Aim 1: To implement all aspects of a pragmatic cluster RCT trial of an ACP video support intervention in two NH health care systems, including: 1. Recruitment of a sufficient number of NHs to achieve the sample size of patients needed to demonstrate a clinically meaningful difference in the primary outcome; 2. Facility staff training and implementation of the intervention; and 3. Outcome assessment using EMR records, the Minimum Data Set (MDS), and Medicare Claims.

Aim 2: To evaluate the effectiveness of the ACP intervention by comparing the following outcomes over 12 months among long-stay NH residents ≥ 65 with advanced comorbid conditions (advanced dementia and/or advanced congestive heart failure (CHF) or chronic obstructive lung disease (COPD)) in the intervention vs. control NHs: 1. Advance directives to withhold specific treatments (DNH, DNR, DNI, and no tube-feeding), 2. Hospital transfers (# hospital transfers/person-days alive), 3. Other burdensome treatments (new feeding tube insertions, parenteral therapy, intubation, ICU care), 4. Hospice use, and 5. Medicare ACP billing codes.

H2a: A higher proportion of long-stay residents in the intervention (vs. control) NHs will have advance directive orders to withhold specific treatments over 12 months.

H2b: Over 12 months, hospital transfers (primary study outcome) and other burdensome interventions will be lower among long-stay residents in the intervention (vs. control) NHs.

H2c: A higher proportion of long-stay residents in the intervention (vs. control) NHs will be enrolled in hospice.

Aim 3: To evaluate the effectiveness of the ACP intervention by comparing the following outcomes in the intervention vs. control NHs among new admissions to post-acute care ≥ 65 with advanced comorbid conditions (as defined in Aim 2): 1. Advance directives to withhold specific treatments (DNH, DNR, DNI, no tube-feeding), 2. Hospital transfers within 100 days of the post-acute care admission (# hospital transfers/per-days alive), 3. Hospice enrollment within 100 days of the post-acute care admission, and 4. Medicare ACP billing codes within 100 days of the post-acute care admission.

H3a: A higher proportion of post-acute care patients in the intervention (vs. control) NHs will have advance directive orders to withhold specific treatments during their admission.

H3b: Hospital transfer rates will be lower among post-acute care patients in the intervention (vs. control) NHs.

H3c: A higher proportion of post-acute care in the intervention (vs. control) NHs will be enrolled in hospice.

Aim 4: To evaluate the effects of the ACP intervention by comparing outcomes (advance directive orders, hospital transfers, hospice use, and Medicare ACP billing codes) in the intervention vs. control NHs among long-stay residents and newly admitted post-acute care patients who do NOT have designated advanced illness (i.e., dementia, CHF, or COPD).

H4a: A higher proportion of NH patients without advanced dementia, COPD, or CHF in the intervention (vs. control) NHs will acquire advance directives to withhold specific treatments.

H4b: Hospital transfers will be lower among NH patients without advanced dementia, COPD, or CHF in the intervention (vs. control) arms.

H4c: A higher proportion of NH patients without advanced dementia, COPD, or CHF in the intervention (vs. control) NHs will be enrolled in hospice.

Exploratory Aim: Among decedents, to compare the proportion of patients in the intervention and control facilities who had any of the following interventions in the last month of life: hospital transfer or other burdensome interventions (feeding tube insertion, parenteral therapy, intubation, ICU care). Separate analyses will be done among decedents from the short and long-stay cohorts with advanced dementia, CHF or COPD, as well as those without advanced disease.

Cohort and outcomes specifications:

A. Hospital transfer outcome

1. For all analyses involving this outcome, including the primary trial outcome, the main analyses will be restricted to Medicare Fee-for-Service patients because ascertainment of hospital transfers is most accurate from Medicare Claims data. Exploratory analyses will also be done on all patients, not just FFS, using the MDS as well as Medicare claims as the data sources.
2. For the primary outcome and all relevant secondary outcomes, ‘hospitalizations’ was modified to ‘hospital transfers’ based on Medicare claims data, which include admissions, emergency department visits, and observation stays. This change was made so as to capture the main “decision” to send a patient from the nursing home to the hospital.

B. Advance directive outcome

1. For all aims, advance directives analyses will be limited to Genesis facilities in which >75% of patients have any advance directive because the remaining Genesis and Pruitt facilities do not have reliable sources for these data.
2. The proportion of residents in a facility whose last observed advance directive status during their observation period was DNR, DNH, DNI or feeding restrictions
 - i. The proportion of short-stay residents in a facility whose last observed advance directive status during their 100-day observation period was DNR, DNH, DNI or feeding restrictions
 - ii. The proportion of long-stay target residents in a facility whose last observed advance directive status during their 12-month observation period was DNR, DNH, DNI or feeding restrictions
 - iii. The proportion of long-stay non-target residents in a facility whose last observed advance directive status during their 12-month observation period was DNR, DNH, DNI or feeding restrictions
3. Among participants who are full code when they become part of the study (on admission to a NH), the average time to switching from full code to DNR, DNH, DNI or feeding restrictions during a 12-month observation period.

C. Burdensome interventions

1. For Aim 2.3, burdensome interventions will include: new feeding tube insertions (i.e., did not have a feeding tube at start of observation period), parenteral therapy (for hydration or medication delivery), intubation, or ICU care). The outcome will be analyzed as the proportion of long-stay target cohort residents that had any burdensome intervention during the 12-month observation period.

D. Hospice:

1. In the long-stay target cohort, the proportion of residents with any Medicare hospice claim in the 12-month observation period.
2. In the non-target long-stay cohort, the proportion of residents with any Medicare hospice claim in the 12-month observation period.
3. In the short-stay cohort without advanced comorbid conditions, the proportion of residents with any Medicare hospice claim in the 100-day observation period.
4. In the short-stay cohort with advanced comorbid conditions, the proportion of residents with any Medicare hospice claim in the 100-day observation period. For both long-stay and short-stay cohorts, residents on hospice at the start of the observation period will be excluded.

E. Medicare Advance Care Planning Billing

1. In long-stay target cohort, the proportion of residents with any Medicare ACP billing code in the 12-month observation period.
2. In non-target long-stay cohort, the proportion of residents with any Medicare ACP billing code in the 12-month observation period.
3. In short-stay cohort (with and without advanced comorbid conditions), the proportion of patients with any Medicare ACP billing code in the 100-day observation period.

2. BACKGROUND AND RATIONALE

2.1. Epidemiology: Nursing homes (NHs) care for approximately 3 million individuals annually, including 1.5 million frail older persons with advanced chronic disease requiring long-term care, and a growing proportion of seriously ill patients admitted for post-acute care.^{1,2} Approximately 11% of Americans over 85 years reside in NHs. In the past 3 decades, NHs have evolved into complex health care systems serving an increasingly sick and heterogeneous population. While NHs serve a growing number of patients recuperating from acute illnesses, they also are a common site of care for patients nearing the end-of-life. In 2009, 45% of U.S. Medicare beneficiaries who died were in a NH during the last 90 days of life, and 28% died in that setting.³ Taken together, NHs are often charged with guiding patients with complex medical problems and advanced illness through challenging decisions about the direction of their treatment.

2.2. Need to improve advance care planning (ACP) in NHs: Advance care planning (ACP) is a *process* of communication between providers and patients/families to identify anticipated medical decisions and clarify goal-directed treatment preferences. Ideally, ACP leads to completion of *advance directives that come into effect* if/when a patient becomes incapacitated. Advance directives include living wills, appointment of a health care proxy, and formal medical orders to withhold specific treatments, such as resuscitation. In observational studies, ACP is the strongest and most consistent modifiable factor associated with better palliative care outcomes in the NH setting.⁴⁻⁹ The lack of advance directives has been associated with greater use of feeding tubes,^{7, 10, 11} more terminal hospitalizations,^{5, 12-14} higher health care costs,⁹ worse family satisfaction and mental health outcomes,^{6, 10, 15, 16} and lower hospice use.^{10, 17}

The Patient Self-Determination Act (PSDA) of 1991 mandated that NHs ascertain and document patients' advance directives.¹⁸ Unfortunately, advance directive completion remains inadequate and does not always reflect the patient's goals of care.^{4, 6, 8, 18-24} The proportion of NH

patients with DNR orders increased from 31% in 1990 to 52%,¹⁹ but has remained relatively unchanged thereafter.²⁵ Other, perhaps more consequential directives for NH patients, were not influenced by the PSDA and continue to be low. In 2007, only 4% of U.S. NH patients had DNH orders and 11% had orders to withhold tube-feeding.²⁵ Not surprisingly, markers of the quality of end-of-life care, such as terminal hospitalizations, have also not improved.²⁵ Other serious concerns related to advance directives in the NH persist, most notably marked racial and regional disparities,^{8, 26-29} and very low completion rates in post-acute care, where only 32% and 2% of patients have DNR and DNH orders, respectively.²⁹

There have been some, albeit limited, efforts to design and evaluate approaches other than legislation to improve advance directives in NHs.³⁰ An RCT from the late 1990s of an advance directive program in 6 Ontario facilities resulted in more advance directive documentation, fewer hospitalizations, and lower expenditures, with no change in survival.³¹ A more recent initiative is the Physician Order for Life-Sustaining Treatment (POLST) program, which translates treatment preferences into medical orders that are documented on a form designed to be portable across care settings. POLST does not intervene on the process of counseling patients about how to make preference-based decisions. While many states have adopted POLST programs in NHs,³² its efficacy and effectiveness are under-studied. A retrospective cohort study from 90 NHs found that POLST resulted in care consistent directives and greater advance directive documentation.^{33, 34}

There is growing recognition that improving goal-directed care in NHs will require greater focus on improving the *process* of ACP (i.e., helping to prepare patients for medical decision-making), rather than just static advance directive completion.^{18, 35-37} In one of the few rigorous RCTs designed to improve this process, social workers were trained how to have structured ACP discussions with all newly admitted NH patients.³⁸ This approach reduced unwanted care and increased advance directive documentation, but was never adopted into practice perhaps because such complex interventions are resource intensive, require on-going staff training, and are difficult to replicate across facilities.

The proposed pragmatic RCT of the video decision support tools addresses many of the lessons learned, research gaps, and on-going concerns about ACP in NHs by rigorously evaluating the implementation of a standardized, practical intervention that targets the ACP process in two large NH systems.

2.3. Hospitalizations of NH patients are common, burdensome, costly, and often avoidable: An estimated 15% of NH patients are hospitalized in the last week of life.²⁵ Between one-third and one-fifth of patients in sub-acute skilled nursing facilities (SNFs) are re-hospitalized within 30 days.³⁹ Prior work reports that 23-60% of hospitalizations of NH patients are avoidable, either because hospital-level care is unnecessary or unwanted, and, if averted, could potentially save the U.S. health care system billions of dollars annually.⁴⁰⁻⁴⁴

This opportunity and need to reduce avoidable hospitalizations are greatest among patients with advanced chronic illnesses, for whom the burdens of hospitalization often outweigh the benefits. The decision to hospitalize patients should be guided by the primary goal of care (i.e., prolongation of life vs. comfort). The goal of care for many NH patients with advanced disease is comfort. With rare exceptions (e.g., hip fracture), hospitalization seldom promotes a goal of comfort. Hospitalization can be traumatic,^{45, 46} and often involves burdensome and costly treatments that may be of limited clinical benefit.⁴⁵⁻⁴⁸ For example, 68% of feeding tubes are placed in NH residents with advanced dementia during a hospitalization.⁴⁷ Care transitions also place NH residents at risk of medical errors and adverse drug events.^{49, 50} For those NH patients

whose goal of care remains life prolongation, many of the most common illnesses precipitating hospitalization (i.e., infections), can be usually treated with the same efficacy in the NH.⁵¹⁻⁵⁴

Better ACP is a key strategy to reduce avoidable hospitalizations.⁴⁴ A DNH order is the strongest factor associated with lower hospitalization rates.^{5, 12, 55, 56} NHs with higher rates of DNR orders, a marker of facility culture with better ACP, have lower hospitalization rates among dying patients.²⁵ A before and after study of an ACP-focused intervention in SNFs that targeted patients with > 3 hospitalizations in the prior 6 months reduced re-hospitalization rates by 20%.⁵⁷ The Interventions to Reduce Acute Care Transfers (INTERACT) program, of which ACP is a key component, has also been shown to reduce NH hospitalizations.⁵⁸

2.4. Video decision support tools improve ACP for multiple conditions: The traditional approach to ACP primarily relies on ad hoc verbal descriptions of hypothetical clinical states and interventions. This approach is limited because complex scenarios are difficult to envision, provider information is inconsistent, and verbal explanations are hampered by literacy and language barriers. Decision support tools have been used to overcome some of these barriers⁵⁹⁻⁶⁵ and are meant to supplement, not replace, provider counseling by providing standardized information about options and a framework for weighing options with preferences.

More than 700 decision support tools exist, including 50 that utilize videos.⁶³⁻⁶⁵ Video addresses some of the limitations of traditional verbal ACP by providing realistic visual images of complex medical scenarios. A growing body of work, including several RCTs, supports the effectiveness and feasibility of video decision support tools for ACP for various advanced illnesses (e.g., dementia, cancer, heart failure) and among patients in different settings (out-patient, hospital, short-term rehabilitation) (*see Section 3.C.i.c. Preliminary Studies*).⁶⁶⁻⁷⁵ These studies consistently find that subjects who view the video, when compared to those who listen to verbal information, have greater knowledge about their condition and treatment choices and are more likely to choose less aggressive interventions as their preferred care. Findings also show that the videos reduce the racial and health literacy disparities that typically characterize traditional verbal counseling.^{69, 76}

The promise of video for ACP is reflected by the widespread attention this work has received by the scientific community,⁷⁷⁻⁷⁹ media,^{80, 81} the U.S. Congress, and early adoption by major health care systems. Kaiser Permanente, Group Health Cooperative, and the Palo Alto Foundation are currently using the ACP videos in their out-patient and hospital practices. The state of Hawaii is using these tools across health care settings, including NHs (*see Section 3.C.i.d. Preliminary Studies*). However, none of these efforts involve formal research designs or evaluation. Thus, the proposed pragmatic trial is a logical next step towards understanding the real world application of a video ACP support tool for NH patients.

2.5. Electronic health records and secondary data sources are powerful tools for NH health systems research: Since 1998, when The Centers for Medicare & Medicaid Services required full electronic submission of Minimum Data Set (MDS) data, all licensed U.S. NHs have had rudimentary EMRs.^{82, 83} The MDS is a comprehensive, standardized resident assessment instrument federally mandated for use in all licensed U.S. NHs. The latest iteration, the MDS Version 3.0, was introduced in 2010. MDS assessments are completed on all NH patients upon admission, quarterly, annually, and whenever they have a significant status change. The uniformly collected MDS data have been used for care planning, fiscal, policy, and research purposes. Prior work has shown that MDS data are valid and reliable for these purposes as collected in the real world, not merely during field testing.⁸⁴⁻⁹⁰

Over the past 17 years, analyses of the MDS on its own and linked with other secondary data sources, most notably the Medicare and Medicaid claims, have made key contributions to our understanding of clinical outcomes and health care utilization in the NH setting. These merged datasets have been used extensively to address research questions in the areas of ACP and end-of-life care, including: tube-feeding in advanced dementia,^{7, 11, 91, 92} hospitalization,^{5, 8, 39, 93} hospice use,⁹⁴⁻⁹⁶ health care expenditures,⁵⁶ regional disparities,^{11, 92} and prognostication.^{11, 97} Much of this work has emanated from Brown University in efforts led by Dr. Mor and in collaboration with Dr. Mitchell (*See Section 3.C.i.a.2. Preliminary Studies*).

The introduction of the MDS stimulated the development of integrated EMR systems in NHs capable of filing MDS assessments, billing payers, and ultimately pharmacy management and physician ordering. One of our partner NH health care systems, Genesis HealthCare, uses PointClickCare™, one of the most sophisticated among these EMR systems.⁹⁸ PointClickCare™ integrates data from MDS assessments, physician order entry, health care utilizations (hospital transfer, hospice referral), and pharmacy prescriptions into patient care plans. Our second partner NH system, PruittHealth, uses American Health Tech,⁹⁹ which has capabilities and components that are very similar to PointClickCare™.

2.6. A pragmatic trial with a cluster randomized design is a well-suited approach to evaluate the effect of the ACP video intervention in NH health care systems: Over the past 15 years, cluster randomized controlled trial (RCT) designs have been increasingly used in health services research, including trials of NH interventions.^{52, 100-108} This work has contributed to more refined and standardized approaches to the unique biostatistical, implementation, and ethical considerations associated with clustered trial designs.^{103, 109-113} Several advantages of cluster RCTs for testing interventions in NHs are notable. Given that the facility is the unit of randomization, the contamination that can occur when randomizing individuals within NHs is avoided. Moreover, the types of interventions being tested will likely be implemented at the NH level. Finally, individual patient consent procedures are often unnecessary provided the study is of low risk.

While the increasing number of cluster RCTs conducted in NHs has established the feasibility of this approach, most were in a relatively small number of facilities and evaluated the effects of interventions under ideal circumstances (i.e., explanatory trials). Pragmatic trials, which intend to determine the effects of interventions under usual conditions, are a next critical translational step in NH research.¹¹⁴ A small but growing number of pragmatic trials of NH interventions have been conducted, all of which were outside the U.S.¹¹⁵⁻¹¹⁷ Based on the 10 domains outlined in the Pragmatic–Explanatory Continuum Indicator Summary Tool (PRECIS),¹¹⁸ the rationale for pragmatic trials in the NH setting is very compelling, particularly for an ACP intervention. NHs must engage all patients in ACP to maintain an expected standard of care and as a matter of federal legislation. However, NH providers include a variety of practitioners caring for a heterogeneous population. Thus, a pragmatic trial that involves facility-wide implementation of a standardized, feasible, but flexible, ACP intervention makes sense. Moreover, large networks of NHs across the U.S. are owned and operated by single corporations, such as Genesis HealthCare and PruittHealth. These NH systems are uniquely suited for pragmatic trials as they have efficient and established infrastructures for staff training and new program implementation. Moreover, they have integrated computerized clinical information systems (e.g., PointClickCare™) providing an easily accessible data source for patient characterization, intervention implementation, and outcomes measurement.

2.7. Summary of background and rationale based on the literature: The significance of the proposed pragmatic cluster RCT of an ACP video intervention in two NH health care systems is summarized in the following points: 1. NHs have evolved into complex health care systems serving an increasingly sick patient population with advanced comorbid conditions; 2. These NH patients often get aggressive and costly interventions that may be of little clinical benefit and inconsistent with their preferences; 3. There is an opportunity to promote more preference-based, higher quality, and cost-effective care among NH patients with advanced disease through better ACP; 4. An intervention comprised of a suite of ACP video decision support tools presents a promising, scalable, and efficacious approach to address that opportunity that can be implemented on a system-wide level in a flexible manner; and, 5. NH systems offer an ideal setting for a pragmatic cluster RCT. This design is enabled by system-wide infrastructures for staff training, program implementation, and existing electronic data capture. Taken together, this work has the potential to improve the quality of care provided to millions of older Americans in NHs and to enable future pragmatic trials in this increasingly important care setting.

3. STUDY DESIGN

This is pragmatic stratified cluster RCT that will evaluate an ACP video support intervention for patients ≥ 65 cared for in 360 NHs (intervention, n=119; control, n=241) within two NH health care systems, Genesis HealthCare and PruittHealth. Aim 1 of this study is to conduct all aspects of this pragmatic trial.

The intervention consists of a suite of five videos designed to assist NH patients with ACP decisions (*see Section 5*). The ACP video intervention will be implemented in NHs assigned to the intervention arm for 24 months. Data needed to assess outcomes will be derived from the NH EMR systems merged with MDS and Medicare files. NHs randomized to the control arm will use the usual ACP procedures practiced in their facilities.

In this stratified cluster RCT, the unit of random assignment is the facility but the unit of analysis is the patient, clustered within the facility (*See Section 4.4.2*). The intervention will be implemented facility-wide, thus all patients cared for in the NHs during the 24-month implementation period are subjects in this study ($N \approx 152,160$). However, our primary outcomes will be measured in targeted sub-populations with advanced comorbid conditions for whom the opportunity and need to improve ACP and goal-directed care are greatest. These subgroups (n~14,760) include very disabled older, long-stay patients with advanced dementia and those with advanced congestive heart failure (CHF) or chronic obstructive pulmonary disease (COPD) (i.e. cardiopulmonary disease).

Outcomes to be compared between patients in the intervention and control NHs include: advance directives orders (DNR, DNH, DNI, and no tube-feeding), hospital transfers, use of other burdensome interventions (new feeding tube insertions, parenteral therapy, intubation, ICU care), hospice use, and Medicare ACP billing codes. The effectiveness of the intervention to improve these outcomes among those targeted sub-populations with advanced illness will be assessed among long-stay (≥ 90 days) NH residents (Aim 2) and new admissions to post-acute care (short-stay < 90 days) (Aim 3). Finally, we will evaluate the effects of the intervention by examining the aforementioned outcomes among long-stay NH patients and new admissions who do NOT have either of the pre-specified advanced illnesses (Aim 4). The primary outcome for this pragmatic trial is hospital transfers (quantified as number of hospital transfers/person-day alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays over a 12-month follow-up period among long-stay residents with advanced dementia and/or advanced

CHF/COPD. Secondary outcomes for these patient groups include advance directive orders, other burdensome treatments, hospice use, and Medicare ACP billing codes.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1. Facility Inclusion Criteria

Facility eligibility criteria include:

Matched facility ID on Brown University's list of all Medicare/Medicaid-certified nursing facilities in the U.S.

Serve both short and long-stay patients

Have >50 beds

Have an EMR system

Have at least 20 admissions and 20 annual Minimum Data Set (MDS) assessments (regardless of whether patients were discharged alive)

We anticipated that a total of approximately 360 (297 Genesis HealthCare / 63 PruittHealth) facilities would be eligible for random assignment.

4.2. Patient Inclusion Criteria:

As the ACP video intervention will be implemented facility-wide, all patients in eligible NHs during the 24-month implementation period are eligible. There are no exclusions based on age, gender, race, ethnicity, or clinical features.

Although the ACP intervention will be implemented facility-wide, its effectiveness will be examined among targeted NH sub-populations for Aims 2, 3, and 4. Target populations for these Aims include patients ≥ 65 in the NHs during the 24-month implementation period who meet the following eligibility definitions based on MDS assessments. For all three aims, residents will be eligible for the target sub-populations if they meet these criteria either at the start (prevalent cases) or during (incident cases) the 24-month implementation phase. Incident cases include new admissions and long-stay residents who "convert" over the implementation phase by meeting eligibility criteria based upon changes in their repeated MDS assessments.

Aim 2: Patients ≥ 65 who are in nursing home ≥ 90 days (long-stay) who have EITHER of the following two conditions:

1. *Advanced Dementia:* must have all three criteria: a, b, and c
 - a. Alzheimer's disease or other dementia
 - b. Advanced cognitive impairment*
 - c. Extensive or total assistance needed for eating and transferring

*Advanced cognitive impairment is defined as a score of 3 or 4 on the Cognitive Function Scale based on variables from the MDS Version 3.0^{119, 120}

2. *Advanced COPD/CHF:* must have all three criteria: a, b, and c
 - a. CHF/COPD
 - b. Shortness of breath sitting or lying flat
 - c. Extensive or total assistance walking in room, transferring, walking in corridor, locomotion on/off unit, or dressing.

Aim 3: Patients ≥ 65 who are in nursing home < 90 days (short-stay) who have advanced dementia OR advanced CHF/COPD as defined above.

Aim 4: Long and short-stay patients ≥ 65 who do NOT have either advanced dementia OR advanced CHF/COPD as defined above.

4.3. Exclusion Criteria

Facilities with unstable organizational or regulatory issues (in transition or leadership problems or recent poor performance in regulatory surveys) such as those listed below will be excluded prior to randomization based on input from corporate leadership:

Recent turnover in NH Administrator or Director of Nursing
Recent bad state or federal quality assurance survey (e.g., restriction on admissions, levied large civil monetary penalty, etc.)
Current new initiatives/competing demands

There are no patient exclusion criteria other than those implied by eligibility criteria.

4.4. Study Enrollment Procedures

4.4.1. Facility Recruitment Procedures:

Facility recruitment will be conducted during months 1 and 2 of year 1. As a first step, eligible facilities among the Genesis HealthCare and PruittHealth NHs will be identified by the research team at Brown University using the most recent patient and organizational data available (at least 2014). Bed size will be determined using CMS's Provider of Service files. Case-mix (number of short and long stay patients) will be determined using the most recent aggregated nursing home resident assessment Minimum Data Set data available. Once candidate facilities are identified based on size and case-mix, final facility eligibility will be determined by corporate representatives based on the presence of EMR systems that include physician order sets and the absence of facility organizational instability or regulatory challenges since these will consume executive time and attention, possibly complicating participation in the implementation of the intervention.

Once eligible facilities are identified, they will be randomly assigned to either the control or intervention arm (*see Section 4.4.2. for randomization procedures*) by statisticians at Brown University. An information letter endorsed by senior corporate leaders will be mailed to the senior administrators of all NHs randomized to the intervention arm. The letter will explain what involvement the facility has been selected for the ACP Video Program. Facility leadership will be given the opportunity to opt out. While senior corporate leaders will strongly endorse the project, the final decision to participate in the intervention arm will be at the discretion of the individual facility's administrator. NHs randomized to the intervention whose administrators refuse to participate will not receive the intervention, but will be considered as intervention NHs in the intention-to-treat analyses (*see Section 9*). NHs randomized to the control arm will not be formally contacted and will not be aware that they are serving as control facilities.

The decision to randomly assign facilities prior to recruitment was based on the following reasons: 1. With strong corporate endorsement, we believe a very high recruitment rate in the intervention arm can be achieved (i.e., $> 90\%$), and 2. We feel it would be unfair to conditionally offer the ACP Video Program to all eligible NHs, and then rescind that possibility to the NHs

randomized to the control arm, and 3. Our partner health care systems strongly preferred post-randomization recruitment.

Once the intervention NHs are recruited, intervention training and implementation will be rolled out in a staggered fashion over the next 6 months (*see Section 5.2*), such that by month 8 of year 1, all intervention NHs will be up and running.

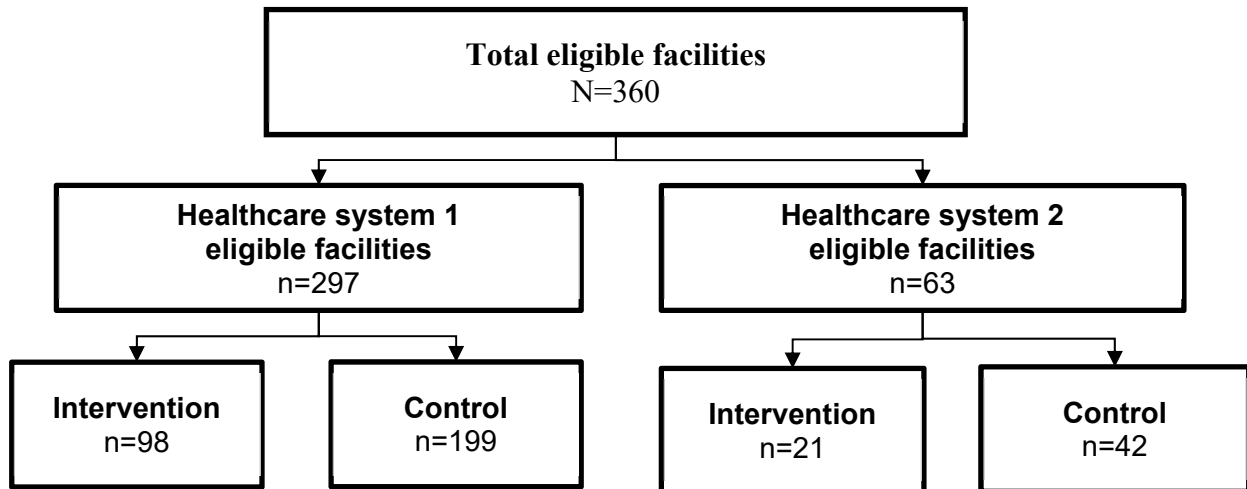
4.4.2. Facility Recruitment Estimates:

Based upon our sample size calculations, we require 103 facilities per arm (See section 9.2). To account for the fact that some (we estimated up to 10%) facilities randomized to the intervention arm would fail to participate fully in the intervention implementation (but will be included in our intention to treat analysis) we increased our facility recruitment targets by at least 10%, for a total of 119 facilities in the intervention study arm.

From the pool of eligible facilities, 119 will be randomly assigned to the intervention arm, and all the remaining eligible facilities (n=241) will be assigned to the control arm (approximate 2:1 control:intervention match). We will leave all non-intervention facilities in the control arm since there is no additional cost to do so and having the increased number of control facilities increased precision.

4.4.3. Facility Randomization and Stratification Procedures:

Facilities will be randomized using a stratified approach with two levels of stratification. The first stratum is the NH health care system (Genesis HealthCare and PruittHealth). Within each health system, the second stratum will be on the hospitalization rate as measured by # hospitalization/person-days alive for patients with advanced dementia or COPD/CHF in all NHs in each health care system in the prior 12 months based on MDS files available at Brown University. The rationale for this stratum is that hospitalization rates, the primary trial outcome, are known to vary considerably at the facility-level due to regional practice, market influences and underlying quality. Since inter-facility hospitalization rates vary quite broadly, facilities will be grouped into terciles to minimize the chance of misdistribution. After the second stratification level is applied, facilities will be randomly assigned to either the control or intervention arm by a statistician at Brown University. Immediately following random assignment, we will test the balance between the arms using all available facility and resident-level data.



4.4.4. Patient Participation and Consent

There are special informed consent considerations for individual patients in this pragmatic, cluster RCT (see Sections 6.2 and 11.2). The NH is the unit of randomization, the intervention is of relatively low risk, and it will be implemented facility-wide as part of the intervention facilities' standard operating procedures for ACP. In the control arm, usual care for ACP will be in place. In both study arms, all data will be ascertained from existing sources. NH administrators, who either agree or disagree to facility participation in the intervention arm, are serving as gatekeepers for the study. Thus, we will seek a waiver of individual informed consent as set forth by criteria found in HHS 45 CFR 46:116: (1) the research involves no more than minimal risk; (2) the waiver will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver; and (4) if appropriate, the subjects will be provided with additional pertinent information after participation.

5. STUDY INTERVENTIONS

5.1. Interventions, Administration, and Duration

The ACP Video Program will be implemented for 24 months in each intervention facility. The intervention consisted of five previously created videos that addressed common ACP decisions in NHs: 1. *Goals of Care for Any Patient*; 2. *Goals of Care for Patients with Advanced Dementia*, 3. *Decisions about Hospice*, 4. *Decisions about Hospitalization*, and 5. *General Information about Advance Care Planning for Healthy Adults*. The videos are in English and Spanish, 6-10 minutes in duration, and offered to patients, family members, or both as deemed appropriate by the providers.

The *Goals of Care for Any Patient* video outlines three broad levels of care: intensive medical care, basic medical care, and comfort care. A physician-moderator introduces the broad concept of ACP and the levels-of-care framework. The video continues with narrative explanations and visual images of typical treatments that align with each level. For example, for intensive medical care, a resuscitation being conducted on a simulated patient and an actual ventilated patient in an intensive care unit are shown. For basic medical care, a patient in a hospital bed getting intravenous treatment is shown. For comfort care, a patient lying comfortably getting oxygen via a face mask and an attendant assisting with self-care are shown. A similar rubric is used for the *Goals of Care for Patients with Advanced Dementia* video, but it is tailored to this specific condition and aimed at family members. The *Decisions about Hospitalization* and *Decisions about Hospice* videos focus on decision-making for these specific interventions. The *General Information about Advance Care Planning for Healthy Adults* video is designed for the relatively healthy patients admitted to a NH for post-acute care for a focused, time-limited medical issue, such for rehabilitation following an elective knee replacement. This is primarily an educational video that presents the basic concepts of ACP and advance directives in a manner that would be appropriate for any relatively healthy person to understand. Inclusion of this video was informed by our experience in the pilot study, during which NH staff felt they did not have the "right" video to show these relatively healthy post-acute care patients.

The videos are intended to supplement, not replace, existing ACP counseling practices. Thus, provider training included guidance on initiating ACP conversations, integrating videos into discussions, and debriefing with patients and families after the video.

5.2. Intervention Training, Implementation, and Adherence Monitoring

At each intervention facility, two senior staff members were designated as ACP Champions and were responsible for implementing all aspects of the ACP Video Program. Implementation involved two major components: 1. Use of the videos with individual patients and families, and 2. Integration of the ACP Video Program into the workflow of the NH. Our research team provided a standardized approach for both these components through our training program. However, in the spirit of a pragmatic trial, NH staff had the flexibility to tailor aspects of the implementation as dictated by local NH practices, workflow, and culture. Providers also individualized the timing, format, and intensity of ACP Video Program based on each patient's clinical needs.

Intervention training and implementation began in January 2015; approximately 30 intervention NHs were trained in each of 4 sequential waves. The implementation strategy was collaboratively designed by the research team and corporate leaders but executed almost exclusively by the healthcare systems. Each NH designated two ACP program champions, one of whom was a social worker, charged with leading implementation at their facility. Only corporate leaders were aware the intervention NHs were part of an RCT. ACP champions and NH providers were simply told the program was a new, corporate-led initiative.

In keeping with a pragmatic trial, healthcare systems and NHs had flexibility to tailor the implementation protocol to their specific environments. The protocol instructed NH staff to offer videos to patients or families at the following trigger events: 1. Within 7 days of admission or readmission, 2. Every 6 months for long-stay patients, 3. When decisions were being discussed for which there was a specific video (e.g., hospice), and 4. Special circumstances (e.g., out-of-town family visit, change in health status). Clinicians could choose which video(s) to show, with the goal-of-care video being the most widely applicable. Videos were pre-loaded onto tablet devices (two devices per facility) and available for out-of-town family members through a password-protected web link.

Training materials included two printed toolkits, webinar companions to the toolkits, and pocket-sized reference guides. One toolkit focused on protocols for providers showing the videos to patients and families; another focused on implementing the videos into the NH workflow. Training occurred during the month prior to the implementation for each wave and periodically thereafter. Monthly conference calls are held among ACP champions, corporate leaders, and researchers to review the progress of implementation and resolve difficulties.

To monitor adherence, a Video Status Report (VSR) was integrated into the electronic medical records of intervention NHs. Providers were instructed to complete the VSR each time a video was offered, even if it was not shown (e.g., patient refused). The VSR documented which video(s) was shown, who watched it (e.g., family, patient), and who showed it. The research team linked VSR with real-time MDS data to generate adherence reports which were sent to corporate leaders each month. The reports presented adherence measures for two primary indications for offering videos which were readily quantifiable; within 7 days of admission/readmission and every 6 months for long-stay patients. MDS data provided the denominator (e.g., number of admissions), and the VSR provided the numerator (e.g., VSRs completed for the new admissions). Both healthcare systems constructed similar internal reports, albeit primarily for admissions, every two weeks using their own data for more frequent monitoring.

All NHs are required by federal law to engage patients in ACP, which currently occurs in an ad hoc fashion. The intervention is intended to provide a standard framework for ACP to complement direct counseling by providers. Thus, the ACP Video Program will be integrated into

the workflow of each facility as part its standard operating procedures. The ACP Video Program will be rolled out at the facility-level in much the same way as other new system-wide clinical programs are introduced through existing NH corporate infrastructures and procedures with the exception that this roll-out will only occur in intervention facilities. Typically, these roll-outs are done on a regional basis under the direction of a senior corporate administrator responsible for NHs within specific regions. Our research team will work directly with these regional directors to facilitate the ACP Video Program roll-out and facility-level implementation.

The standardized approach for using the ACP videos with individual patients and families includes the following considerations: 1. When to offer the videos, 2. Who should offer the videos, 3. Which video to show which patients, 4. How to show the videos, and 5. How to integrate the videos into broader ACP discussions, and 6. Completion of a Video Status Report User Defined Assessment.

As per our protocol, NH staff will be instructed to offer videos to patients at the following clinical triggers:

- Within 7 days of a new admission or readmission
- Every 6 months for long-stay patients coinciding with regularly scheduled care planning meetings
- Whenever there is a significant change in clinical status
- When a treatment decision arises for which there is a specific video (e.g., hospice)
- Special circumstances when goals of care are being considered (e.g., family visiting from out-of-town)

The discipline of the NH staff member showing the videos can vary and should align with the person who is typically responsible for ACP in the facility (e.g., physician, social worker, nurse). The staff will have flexibility with respect to choosing which video (s) to show individual patients, with the general goals-of-care video being the most generic and widely applicable. The videos will be pre-loaded onto tablet devices provided to each NH (2 devices/facility). The videos are typically shown at the bedside. In addition, the videos will be available through password protected internet links for family members to access remotely.

5.2.2. Intervention training: The training materials and procedures described below have been developed and successfully tested in the 4 pilot facilities in the UH2 year. In the full trial, training procedures will be scaled up and conducted on a regional basis within each corporate chain using the existing infrastructures.

Training materials that have been developed specifically for this project include: i. an ACP Video Program toolkit, ii. a webinar companion to the toolkit, and iii. a laminated pocket sized quick reference guide. The toolkit presents detailed guidance and suggested protocols for: 1. using the videos with individual patients and families, and 2. integrating ACP Video Program into the workflow of the NH. The 30-minute webinar presents essentially the same material as the toolkit but in PowerPoint format narrated by Dr. Volandes. The pocket sized reference guide is intended for staff using the videos and serves as a reminder of key points (i.e., when to show a video, which video to show which patient, documentation to complete).

Training procedures involve several formats. As in the pilot study, members of our research team will travel to central locations to conduct regional trainings for staff representing multiple NHs within a corporate chain (i.e., regional directors, facility ACP Champions). We use a train-the-trainer approach such that these representatives will return to their facilities to train their own staff on-site. In addition, Webinars will be held on a regular basis via WebEx during the

implementation start up. The printed toolkit and pocket reference guide will be distributed to all NH staff involved in the ACP Video Program. SharePoint sites will be set up through both the Genesis HealthCare and PruittHealth intranets exclusively for the intervention NHs. The SharePoint sites will include all study related information including the training materials (toolkit, Webinar), dates of Webinars and other meetings, internet links to videos, and how to get help with the ACP Video Program. Webinars and regional trainings will continue periodically during the 24-month implementation period for new staff. Finally, we will hold at least bi-monthly check-in conference calls for each corporate chain during which NH staff will have the opportunity to problem solve any issues with the research team and share their experiences. As of June 2017, these group check-in conference calls have been cancelled and replaced with calls attended by members of the research team, healthcare system coordinators and ACP champions at each intervention site individually. These calls are dedicated to reviewing a list of long-term care patients at the facility and providing strategies for improving the show rates for these patients. A list of long-term care patients with names, numerical identifiers, and video offered/shown status is provided to the ACP Champions. Members of the research team are provided with the same list with numerical identifiers only. The following call is spent reviewing an update on the video shown status of each patient previously discussed and reviewing an updated list of long-term care patients. These calls occur every 2-3 months.

5.3. Concomitant Interventions

ACP is required by federal law in all NHs. Thus, intervention facilities will already have existing procedures or programs for ACP prior to this study. As this is a pragmatic trial, our research team will not interfere with ongoing ACP initiatives or dictate whether they should be replaced with the ACP Video Program. Rather, it will be left to the discretion of individual facilities to integrate the program into their existing ACP procedures.

5.4. Control

Participant NHs randomized to the control arm will use the usual ACP procedures practiced in their facilities. Control facilities will not be offered an alternative intervention for this pragmatic trial as this is not what happens in the “real world.” We recognize that control and intervention facilities may be using other programs intended to improve ACP and/or reduce hospitalizations that are continuously being introduced into health care setting (e.g., INTERACT,⁵⁸ POLST³²). This is what “usual” care reflects in a large pragmatic trial and experience suggests that these practices vary widely within and between NH systems.

5.5. Adherence Assessment

A user defined assessment record entitled a “Video Status Report” created and tested in the pilot study will be uploaded into the EMR of all the intervention facilities. Staff will complete this record each time they offer a video, which will capture: the date a video was offered, who offered it, the clinical trigger prompting the video, whether or not the video was shown, which video was shown, who viewed it (patient and/or family), if any serious negative reaction occurred, and if any clarifications were requested about the subject matter. Real-time MDS data, which will be obtained monthly from our partner health care systems for all intervention and control facilities, will provide the estimated number of patients who could have been shown a video within a specific time frame, (e.g., all new admissions) allowing us to calculate an estimate of the proportion of patients for whom a Video Status Report User Defined Assessment was completed and therefore the proportion of patients by type who watched a video. Adherence data

will allow the research team to measure intervention fidelity and to distribute reports to regional directors and ACP Champions that assess adherence to the video program so that they can make improvements as needed.

6. DATA SOURCES AND ELEMENTS

With the exception of the Video Status Report User Defined Assessment, all data are derived from existing data sources.

6.1 Data Sources

6.1.1. *Electronic Medical Record (EMR)*. Both NH systems have sophisticated EMR systems in their facilities. Genesis HealthCare uses PointClickCare™,⁹⁸ and PruittHealth uses American Health Tech.⁹⁹ Both EMRs integrate individual patient-level data such as MDS assessments and physician order entry. The EMR will be a source for MDS data, advance directives, and the Video Status Report User Defined Assessment (in intervention facilities only). The EMR will be used to ascertain health care utilization data (i.e., hospital transfers) for patients in Medicare Advantage programs, as Medicare claims will not have these data as they would for patients with traditional fee-for-service Medicare insurance.

6.1.2. *Minimum Data Set Standardized (MDS) Resident Assessment*: The MDS resident assessment instrument has nearly 400 data elements. The assessments are done for all patients admitted to Medicare- and Medicaid-certified NHs, including enrollees in both traditional Medicare and Medicare Advantage. Assessments are done upon admission and at least quarterly thereafter. NHs are required to submit their MDS data to CMS on a regular basis.^{82, 85, 121, 122} Repeated evaluations of the reliability of the MDS yielded adequate to good values on most data items and scales. Brown University investigators found that the “missingness” of elements is low.^{82, 85, 121, 122}

6.1.3. *Medicare Enrollment, Vital Status, and Claims data*: Medicare enrollment and vital status data will be used to obtain death dates and to identify patients enrolled in traditional fee-for-service Medicare or Medicare Advantage insurance programs. Medicare claims ascertain health care utilization data for fee-for-service Medicare beneficiaries, including hospital transfers (hospital admissions, emergency room visits, observation stays, etc.) and hospice enrollment.

6.1.4. *Online Survey Certification Automated Record (OSCAR)*: The OSCAR is a publicly available system of records based upon the Medicare/Medicaid certification and inspection process all NHs being reimbursed undergo. OSCAR data will be used to screen facilities for eligibility (i.e., size) and to describe characteristics of participant NHs (e.g., ownership, size, staffing, services, patient acuity and quality inspection results).^{123, 124}

6.2 Data Linkage and Management

Brown University investigators and database management staff already receive national MDS, Medicare, and OSCAR data semi-annually or quarterly under several CMS data use agreements (DUAs). There is a well-established data base management structure for linking these files. The only new activity for PROVEN is integration of the EMR data from experimental and control facilities with CMS Medicare enrollment records and Medicare claims. Both partner

NH systems have experience generating files for export for data warehousing. Using algorithms based on standard patient identifiers including Health Insurance Claim (HIC) numbers, date of birth, gender, and Social Security Numbers (SSNs), matching rates generally exceed 98%. In the UH2 pilot study, secure data transfer and linkage of EMR data from four facilities (two NHs/chain) to Brown University were successfully accomplished, and frequency distributions of the resulting data have been generated. During the full trial, EMR data for all eligible facilities will be transferred from participating health care system corporations' IT staff to Brown University on a monthly basis. These data will be transferred to a secure server at Brown University using an encrypted SFTP connection. Once the data are examined for completion, the health care system corporation IT staff will be notified that transfer was successful. The HIC and SSN identifiers will then be replaced by Brown University's system manager with an alphanumeric ID that will allow analysts to link these EMR records to Medicare datasets.

6.3 Data Elements

Data elements and sources are described below and in Table 2.

6.3.1. Facility-level data: Facility-level data are needed for facility recruitment, randomization, and descriptive purposes. Organizational data from OSCAR include: number of beds, for-profit status, and NH chain. Aggregated MDS data at Brown University provide information case-mix (% long-stay and post-acute care patients). MDS data are also used to calculate the hospitalization rate of each facility by estimating the number of patient days at risk of hospitalization from the nursing home and counting the number of actual hospital transfers to hospital per unit time. It is these hospital specific rates from the prior year which will be used to undertake the stratified randomization scheme (*see Section 4.4.2*). Medicare claims available at Brown University will be used to determine the facilities' hospitalization rates for the subset of patients with Medicare fee for service.

| Table 2: Data Element and Sources | | | | | |
|--|---|---------------|------------|-----------------|--------------|
| Data Element | Purpose | SOURCE | | | |
| | | EMR | MDS | Medicare | OSCAR |
| Facility-Level | | | | | |
| Organization | recruitment | | | | X |
| Case-mix | recruitment | | X | | |
| Prior Hospitalization rate | randomization | | X | | |
| | | | | | |
| Patient-Level | | | | | |
| Demographic | covariate | X | X | | |
| Long vs. short-stay | Cohort definition | | X | | |
| Functional status | target sub-population identification, covariate | | X | | |
| Cognitive status | target sub-population identification, covariate | | X | | |
| Medical condition | target sub-population identification, covariate | X | X | | |
| Insurance | covariate | | | X | |
| Advance directives | 2° outcome | X | | | |
| Health services use | 1° and 2° outcome | X | X | X | |
| Burdensome interventions | 2° outcome | X | X | X | |
| Death | description, competing risk | | X | X | |
| Intervention implementation | monitoring fidelity | X | | | |

6.3.2. Patient-level data:

6.3.2.a. Cohort description, identification of target sub-groups, and other independent variables

Demographic data: From MDS: Age, gender, race, ethnicity, religion, primary language, marital status, and length of NH stay.

Long-stay or new admission to post-acute care: From MDS.

Functional status: From MDS: Ability to perform specific activities of daily living ADLs (as required for cohort identification (i.e., feeding, transferring, ambulation) and validated ADL summary scale (range, 7-28).

Cognitive status: From MDS: Ability for daily decision-making and Brief Interview for Mental Status (BIMS).⁸⁷

Medical conditions: From MDS: Dementia, CHF, COPD and all other active medical diagnoses.

Insurance status: Medicare Enrollment file: Traditional Medicare Fee-for-Service or Medicare Advantage, Medicaid.

6.3.2.b. Outcomes

Advance directives: From EMR: DNR, do-not intubate (DNI), DNH, no feeding tubes, no artificial hydration.

Health services utilization: From Medicare claims and EMR/MDS (for patients not in traditional Medicare fee-for-service): i. hospital transfers, and ii. hospice.

Burdensome interventions: From Medicare claims and EMR/MDS: Feeding tube insertion, intubation, intravenous therapy.

Death: From Medicare Vital Status files: Date of death

Intervention implementation: EMR: Video Status Report User Defined Assessment.

7. SAFETY ASSESSMENTS

7.1. Minimal Risk Determination

We will seek a minimal risk determination for the PROVEN trial as per HHS 45 CFR 46.102: “*Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.*”

Justification for a minimal risk determination is based on several considerations. First, all NHs must engage patients and families in ACP as part of routine clinical practice. There is currently no standardized method by which NHs conduct ACP. PROVEN will compare a practice intervention (rolled out in intervention sites as standard operating procedures as directed by corporate leadership) that uses videos to enrich ongoing ACP practices. Prior studies evaluating the ACP videos by our group included several hundred subjects, including healthy older adults, NH patients, family members of patients with life-limiting illnesses and patients with advanced cancer and congestive heart failure.^{66, 67, 70-72, 125} The videos were also tested in our UH2 pilot study. Finally, the videos have been seen by thousands of patients in Hawaii as part of an on-going state-wide implementation program. In prior research, our pilot testing, and Hawaii initiative, there were no instances of untoward viewer distress and the videos never had to be stopped because of adverse viewer reactions. Thus, we believe the intervention does not incur any greater distress than usual ACP practices.

Second, data collection also conforms with the definition of minimal risk. No direct input from the resident or family member is needed to obtain any data for this study. All the data are already being collected as part of routine medical care (EMR, MDS, Medicare data). The only additional data being collected in the intervention NHs is the Video Status Report User Defined Assessment, which is being embedded into the EMR. The Video Status Report User Defined Assessment is needed to monitor intervention fidelity and will be incorporated into the intervention facility’s ACP protocol.

7.2. Serious Negative Reactions and Serious Adverse Events

The potential *serious negative reaction (SNR)* that could occur during this trial is serious distress by patients or family members in the intervention NHs while viewing an ACP video. As described in *Section 7.1.*, we anticipate that such SNRs will be exceedingly rare. Nonetheless, serious distress by may be manifested as a very negative emotional reaction while watching or after watching a video, asking for the video to be stopped, or leaving the room while a video is being shown. 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.

We do not believe that there are any potential consequences of this trial that meet the definition of *serious adverse events (SAEs)*.

(We do not believe death should be considered a SAE for the PROVEN trial for the following reasons. First, the study is being conducted in a frail NH population with advanced illnesses. Thus,

death is often not an unexpected event in their clinical course. Second, all NHs must engage patients and families in ACP as part of routine clinical practice. The videos are meant as an adjunct to facilitate ACP counseling. The underlying intent of all ACP, regardless of how it is done, is to help patients make informed treatment decisions so they receive care that is concordant with their preferences. For patients who prefer comfort or palliation as a main goal of care (vs. life prolongation), death is not an adverse outcome. Finally, it is not known whether more aggressive care (i.e., hospitalization) would result in greater mortality compared to less aggressive care (i.e., conservative or palliative treatment on-site in the NH). Therefore, while we hypothesize that there will be fewer hospitalizations among NH patients with advanced disease randomized to the intervention arm (vs. control), it is impossible to predict how this may impact mortality rates.)

7.3. Reporting Procedures

As part of NH staff training, instructions will be given to the facility ACP Champions and providers who will be showing the video (i.e., physician, nurse, social worker) about what constitutes an SNR, i.e., serious distress by a patient or family member during or immediately after a video. As described in *Section 7.1.*, we anticipate that such SNRs will be exceedingly rare. Nonetheless, staff will be instructed that if such an event occurs, then the video should be stopped. The provider should report the event to his/her immediate supervisor and ACP Champions as soon as possible, but not exceeding 4 hours after the event. Together, these health professionals will determine the severity of the event. If deemed to be a true SNR, the ACP Champion will complete an SNR Form created by our research team, which will be submitted to the research project directors via email or fax within 24 hours of the event. The ACP Champion will also inform the PROVEN project director within 24 hours of the event by telephone. The project director will report the SNR to all 3 co-PIs via email or telephone immediately upon becoming aware of the event and will also notify the Data Safety and Monitoring (DSMB) Chair in writing (email and hard copy) within 48 hours. It will ultimately be the co-PIs responsibility to ensure that the DSMB chair is informed in a timely manner. The Brown University IRB has indicated that SNRs do not need to be reported to them. This is because the video intervention itself is considered standard operating procedures in the nursing homes, and so it is not part of the human subjects research that the IRB is monitoring.

7.4. Follow-up for Serious Negative Reactions

The NH provider and ACP Champion will be instructed to check on the patient or family who experienced the distress at 6 and 24 hours after a SNR to see how he/she is managing. If deemed necessary, a patient should be referred for counseling with a NH social worker or other mental health professional. In the case of a family member, if deemed necessary, the NH provider may suggest to the proxy that he/she contact his/her own primary care provider. The research project director will contact the facility ACP Champion within 48 hours of the SNR to determine the status of the patient/family and whether further counseling was deemed necessary. The project director will in turn report the follow-up information to the co-PIs (by telephone) and to the DSMB (in writing) within 72 hours using an SNR Follow-up form.

7.5. Safety Monitoring

A DSMB for PROVEN will act in an advisory capacity to the National Institute on Aging (NIA) Director to monitor participant safety, data quality, and progress of the study. External DSMB members include: Christine S Ritchie, MD, MSPH (University of California San Francisco) (Chair), Cynthia J. Brown, MD, MSPH (University of Alabama at Birmingham), and

Michael E. Miller, PhD (Wake Forest University School of Medicine). Dr. Miller's membership was approved by Dr. Richard Hodes (NIA Director) on 6/9/2016 to replace Arthur V. Peterson, Jr., Ph.D. (Department of Biostatistics, University of Washington). Dr. Peterson served on the DSMB from 1/9/2015 to April 2016. Members of the PROVEN team who will participate in the open sessions of the DSMB include the 3 co-PIs (Mitchell, Mor, Volandes), the lead biostatistician (Gatsonis), and project director (Elaine Bergman). The NIA project officer for PROVEN, Dr. Marcel Salive, will attend DSMB meetings and serve as the liaison between the DSMB and NIA. A PROVEN DSMB Charter outlines its roles and responsibilities (*see Appendix 16.1*).

8. INTERVENTION DISCONTINUATION

The study may be discontinued at any time by the IRB, the NIA, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected. Individual NHs in the intervention arm may withdraw from study participation at any time at the discretion of their senior management or corporate supervisors. Individual patients and families, while not being asked to provide informed consent for this research, can refuse to watch a video offered to them as part of this new ACP video program being adopted into the clinical practice of participating intervention NHs. Such refusals are expected as part of this pragmatic trial.

9. STATISTICAL CONSIDERATIONS

9.1. General Design Issues

PROVEN is pragmatic cluster RCT of an ACP Video Program intervention for NH patients cared for in two NH health care systems: Genesis HealthCare and PruittHealth. Rationale for this choice of study design is provided in Section 2.6. The intervention will be implemented facility-wide; thus, all patients in the NHs during the 24-month implementation period comprise the study population. However, the analytic plan focuses on the effect of the ACP Video Program vs. control in the following targeted patient sub-groups:

- Long-stay residents (≥ 90 days) with advanced dementia or advanced CHF/COPD (Aim 2)
- Short-stay patients (< 90 days) with advanced dementia or advanced CHF/COPD (Aim 3)
- Long and short-stay patients without these advanced illnesses (Aim 4).

The primary trial outcome is hospital transfers (number of hospital transfers/person-days alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays over a 12-month follow-up period among Medicare fee-for-service long-stay residents with advanced dementia or advanced CHF/COPD. The primary hypothesis is that the rate of hospital transfers will be lower in the intervention group.

Secondary outcomes include hospital transfer rates in the sub-groups examined in Aims 3 and 4, and the following outcomes for all sub-groups in Aims 2, 3 and 4: advance directives, burdensome treatments, hospice use, and Medicare ACP billing codes.

Each long-stay resident will be followed for up to 12 months starting from the date they are first identified as meeting our target cohort definition during the 24-month intervention period and short-stay patients will be followed for 100 days from their NH admission date. The analytic approach to Aims 2, 3, and 4 are similar. Analyses begin with descriptions of all major variables using frequencies and means/medians with SDs/interquartile ranges, as appropriate. Outcomes will be compared between the control and intervention arms using a zero-inflated Poisson model

with random effects to account for clustering at the NH level. While we do not anticipate an effect on mortality, analyses will also examine the effects on mortality. Primary analyses will follow the intention to treat principle and will adjust for minor imbalances in patient characteristics, as needed.

9.2. Sample Size and Randomization

Sample size estimates are based on the primary trial outcome: # hospital transfers/person-days alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays over a 12-month follow-up period among Medicare fee-for-service long-stay residents with advanced dementia or advanced COPD/CHF. Based on data from our partners' NHs in 2012 and 2013, we estimate that hospital transfers per person-year alive in the control arm will be between 1.06 and 2.12. Based on prior research; we estimate the absolute reduction in hospital transfer rates in the intervention vs. control NHs will range from .200 to .275 points, representing approximately a 16% relative reduction.

| Initial Hospital Transfer Rates/Year | Effect Size | | | |
|--------------------------------------|-------------|-------|------|-------|
| | 0.20 | 0.225 | 0.25 | 0.275 |
| 1.06 | 81 | 63 | 50 | 41 |
| 1.51 | 165 | 129 | 103 | 84 |
| 2.12 | 351 | 275 | 220 | 180 |

Computations for sample size estimates were performed using the approach for the comparison of incidence rates discussed in Chapter 5 of Donner & Klar and in Hayes & Bennett (1999). The sample size computation is based on a simplifying assumption of a Poisson distribution for the numbers of hospital transfers, and it assumes equal number of facilities in each arm. To achieve power of at least 90% in testing for

a .25 point absolute reduction in the observed average hospital transfer rate of 1.51, we will require 103 facilities per study arm. This represents approximately a 16% relative reduction in the hospital transfer rate.

Although our sample size calculations indicate that we require 103 NHs/arm, to accommodate the anticipated 10% non-participation rate among NHs randomized to the intervention arm, we will recruit an additional 16 facilities in the intervention arm for a total of 119 intervention NHs. Moreover, because there is an available total pool of 360 eligible facilities in our partner health systems, we will choose to assign the remaining 241 facilities to the control arm (approximate 2:1 control:intervention match) since there is no additional cost to do so. While more control facilities only marginally increases power it allows for a more precise estimate of the outcome of interest in the control group.

Data for 2012-13 from our partners reveal that there are, on average, 42 people meeting advanced dementia and/or CHF/COPD target criteria per facility. Thus, we estimate that there will be approximately 4,326 target patients in the 103 control NHs in (103*42=4,326) required by our aforementioned power calculation. In the actual assigned facilities, we estimate there will be 4998 patients meeting these criteria in 119 intervention NHs and 10,122 patients in the 241 control NHs.

9.2.2. Treatment Assignment Procedures: Please refer to *section 4* for a detailed description of the treatment assignment procedures.

9.2.3. Blinding: Our partner health care systems will know which facilities are designated intervention facilities, but will not be aware of those in the control group. Only Brown University statistician and data management staff will know the identity of the control facilities. They will present aggregated post-random assignment comparisons of intervention and control facilities' baseline characteristics, but these preliminary analyses will be not generated at the individual facility level. As Dr. Volandes will be leading intervention training, he will be aware of the identity of the intervention NHs but will not be involved in data analyses activities. Drs. Mitchell and Mor will be blinded to the identity of both the control and intervention facilities. Facility assignment will be unblinded to the DSMB members at their request.

9.3. Interim Analyses and Stopping Rules

We are not including stopping rules in the PROVEN trial protocol for several related reasons. First, it is our contention that this is a minimal risk study for which serious negative reactions will be extremely rare (*see Section 7.1*). Second, a stopping rule would not be very feasible. The implementation period is only 24 months in each facility and the outcome observation period is 12 months for each target patient followed during that 24-month period. Final hospital transfer data may not be available for up to six months after the admission. Thus, differences in hospital transfer rates between the two study arms will not be known until the end of the 24-month study facility intervention period.

9.4. Outcomes

9.4.1. Primary outcome: The primary trial outcome is the hospital transfer rate (number of hospital transfers/person-day alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays) over a 12-month follow-up period among Medicare fee-for-service among long-stay residents with advanced dementia or advanced CHF/COPD over 12 months (Aim 2).

9.4.2. Secondary outcomes: Secondary outcomes include: i. hospital transfer rates in the sub-groups examined in Aims 3 (short-stay patients with advanced dementia or advanced CHF/COPD) and Aim 4 (short-and long stay patients who do NOT have advanced dementia or CHF/COPD), and ii. The following outcomes for target sub-groups defined in Aims 2, 3, and 4: advance directives, burdensome treatments (e.g., tube-feeding), receipt of hospice services, and Medicare ACP billing codes.

All outcomes in the long-stay patient populations are calculated over a 12-month follow-up period. For short-stay patients, advance directive completion rates will be calculated over the admission period, and hospital transfer rates, use of burdensome treatments, and hospice enrollment will be examined within 100-days after the NH admission date.

9.5. Data Analyses

Aim 1: To implement all aspects of a pragmatic cluster RCT: Assessment of Aim 1 will largely be experiential and based on meeting planned recruitment milestones. We will assess the implementation of the ACP Video Program by examining data from the new Video Status Report

User Defined Assessment record created in the EMR that documents the videos offered. Descriptive statistics will be generated describing the proportion of the general NH population and targeted sub-populations exposed to the video, which videos they saw, who saw them (patient and/or family members), who showed the videos (nurse, physician, social worker), and the timing of exposure (i.e., relative to admission, discharge care planning meetings).

Aim 2 To evaluate the effectiveness of the ACP intervention among long-stay NH residents with advanced comorbid conditions: The sample includes long-stay residents with advanced dementia and advanced CHF/COPD. The primary trial outcome is the hospital transfer rate (number transfers/person-days alive based on Medicare claims data), which include admissions, emergency department visits, and observation stays) over a 12-month follow-up period among Medicare fee-for-service) in this cohort. Secondary outcomes include: advance directives (DNR, DNH, DNI, no tube-feeding), burdensome treatments (new feeding tube insertion, intubation, parenteral therapy, ICU care), hospice admission, and Medicare ACP billing codes. All outcomes will be 12-month incidence measures starting from the date residents are first identified as meeting the criteria for definitions of having advanced dementia or CHF/COPD during the 24-month intervention period. While we do not anticipate the ACP intervention to affect mortality,³¹ our analyses will account for censoring during the 12-month observation period. We will formally test for a mortality differential between intervention and controls arms using a logistic regression random effects model, where clustering is performed by facility.

Using current MDS data from CMS, we observe that the distribution of the primary outcome, hospital transfers, is over-dispersed with many of the patients having no hospital transfer over the 12-month follow up period. In addition, we also observed that hospital transfer rates vary across facilities, even after adjusting for underlying patient risk. To account for these phenomena, we will utilize a zero-inflated Poisson distribution with facility random effects to test and estimate the effects of the ACP intervention. Zero-inflated Poisson models have been used in other public health settings.^{128, 129} Formally, let Y_{ij} be the number of hospital transfers for person i in facility j , N_{ij} is the number of person days alive for person i in facility j , and T_j is a treatment indicator that is equal to one if facility j is in the intervention group. Then where β_1 is the conditional increase in the log hospital transfer rate in facilities that receive treatment vs. those that do not, and α_1 is the conditional log odds ratio for being hospitalized vs. never being hospitalized in the intervention vs. the control arm. When both α_1 and β_1 are smaller than 0, the ACP video is effective in reducing the proportion of patients hospitalized and the number of times hospitalized. Using this model we will estimate the marginal average hospital transfer rate in each arm and calculate the difference between the two arms. We will use a two sided test to examine if the marginal average difference is significantly different than zero, and we will calculate the corresponding interval estimate. As a secondary analysis, we will use the likelihood ratio test to compare the null hypothesis, $H_0 : \alpha_1 = \beta_1 = 0$, to the alternative hypothesis $H_1 : \alpha_1 \neq 0$ or $\beta_1 \neq 0$.¹³⁰ Confidence intervals for α_1 and β_1 can be obtained by inverting the likelihood ratio test.¹³² This analysis will enable us to provide additional details as to whether the effectiveness of the intervention is to reduce the likelihood of one hospital transfer or the number of hospital transfers if transferred at least once.

The secondary outcomes are binary. Commonly used methods applied to the analysis of clustered RCT with binary outcomes are GEE and multilevel models.¹³¹ The former method provides a population “average” effect, while the latter results in a conditional cluster effect. For continuous Gaussian data, interpretation of the treatment coefficient

$$\begin{aligned}
 p(Y_{ij} = 0) &= \phi_{ij} + (1 - \phi_{ij}) \exp^{-\theta_{ij}} \\
 P(Y_{ij} = y) &= (1 - \phi_{ij}) \frac{\exp^{-\theta_{ij}} \theta_{ij}^y}{y!} \quad y = 1, 2, \dots \\
 \text{logit}(\phi_{ij}) &= \alpha_0 + \alpha_1 T_j + u_j \quad u_j \sim N(0, \sigma_u^2) \\
 \text{log}(\theta_{ij}) &= \beta_0 + \beta_1 T_j + \log(N_{ij}) + v_j \quad v_j \sim N(0, \sigma_v^2)
 \end{aligned}$$

is the same in conditional and marginal models; however, with binary data, the treatment coefficient from a marginal model is smaller than that from a conditional model and has a different interpretation.¹³² For binary outcomes, Bellamy et al¹³³ have shown that with few clusters GEE results were more likely to reject the null hypothesis, while conditional models resulted in more conservative estimates. Austin concluded that the power of GEE and multilevel models are very similar for studies, like ours, that include more than 30 clusters (facilities) with either variable or equal cluster size.¹³⁴ To estimate the effect of ACP on secondary outcomes we will use random effects logistic model. Formally, let S_{ij} one of the secondary outcomes for person i in facility j , and T_j is a treatment indicator that is equal to one if facility j is in the treated arm.

$$\begin{aligned}
 S_{ij} &\sim \text{Ber}(p_{ij}) \\
 \text{logit}(p_{ij}) &= \gamma_0 + \gamma_1 T_j + \zeta_j \\
 \zeta_j &\sim N(0, \sigma_\zeta^2)
 \end{aligned}$$

where γ_1 is the conditional log odds ratio for observing the secondary outcome in the treatment arm vs. the control arm. When γ_1 is smaller than 0, ACP is effective. As for the primary outcome we will use the likelihood ratio test the null hypothesis $H_0 : \gamma_1 = 0$, and by inverting this test we will obtain the corresponding confidence interval.

Aim 3. To evaluate the effectiveness of the ACP intervention among new admissions to post-acute care with the advanced comorbid conditions: Newly admitted NH patients to post-acute care with advanced dementia or advanced CHF/COPD disease will accrue throughout the 24-month intervention. Measured outcomes for this group will include: advance directives to withhold specific treatments (DNH, DNR, DNI, no tube-feeding) at any time during their post-acute care admission, hospital transfers, and hospice enrollment within 100 days following NH admission. Preliminary data found that 100-day hospital transfer rates among post-acute patients with advanced dementia and/or CHF/COPD was 37%, and that nearly 50% of advanced dementia and 30% of advanced CHF/COPD patients died within 6 months of NH admission. In light of the high mortality rate, we will adopt the hospital transfers per person-day alive approach described for Aim 2 to evaluate the effectiveness of the intervention.

Aim 4. To evaluate the effects of the ACP intervention among long-stay and new admissions to post-acute care WITHOUT advanced dementia or COPD/CHF: The intervention is being implemented facility-wide, thus all long-stay residents and post-acute care admissions will be exposed to it. Aim 4 tests the impact of the intervention on NH patients WITHOUT

$$p(Y_{ij} | X_{ij}) = \begin{cases} \pi_{ij} + (1 - \pi_{ij}) \exp(-\mu_{ij}) & Y_{ij} = 0 \\ (1 - \pi_{ij}) \frac{\exp(-\mu_{ij}) \mu_{ij}^{Y_{ij}}}{Y_{ij}} & Y_{ij} \geq 0 \end{cases}$$

advanced dementia or advanced CHF/COPD. Outcomes include: advance directives during their NH stay, the number of hospital transfers over 12-months for long-stay or over 100 days for short-stay; and hospice admission over 12 months for long-stay or over 100 days for short-stay. As hospital transfers and hospice enrollment among post-acute care patients are likely to occur after NH discharge, these outcomes can only be assessed among the fee-for-service Medicare beneficiaries using Medicare claims. The outcome, Y_{ij} , is a total count of hospital transfers. Many relatively healthy patients will have $Y_{ij}=0$ while others' hospital use depends on the number of days that they are alive. We will use a zero-inflated Poisson model^{135, 136} of the following form shown in the equation, where $\text{logit}(\pi_{ij}) = X_i\beta + \eta T_i + \delta_{ij}$, X_i are the covariates, η is the treatment effect, and $\varepsilon_{ij} \sim N(0, \sigma_\pi)$ is a random between facility effect. When η is larger than 0 and λ is smaller than 0, ACP video is effective. The same analytic approach described for Aim 2 will be used to evaluate the effectiveness of the intervention.

Sub-Group Analyses of Racial and Ethnic Group Differences in Intervention Effects: It is well-recognized that African-American NH patients with advanced illness are more likely than white patients to have outcomes reflecting more aggressive care, including higher hospitalization rates and lower advance directive documentation rates, even after controlling for patient and facility factors. Nonetheless, there is no evidence suggesting that African American patients respond differently to our ACP intervention than white residents. In fact, the videos have been specifically designed to be appropriate to viewers from all backgrounds

Based on existing data, we anticipate only 11% of the patients included in our analyses will be African-American, and even lower proportions will be of other non-white racial and ethnic groups. Thus, there will not be sufficient power to detect small differences in outcomes among non-white groups. Consequently, these sub-group analyses are necessarily exploratory. Nonetheless, we will conduct sub-group analyses for Aim #2 separately among African-American residents and other racial/ethnic groups (e.g., Hispanic) if numbers allow. Additionally, we will examine differences in video viewing rates among racial and ethnic groups.

9.6. Undertaking Supplemental “As Treated” Analyses

The primary analysis for the PROVEN trial is an “intention to treat” analysis in which the outcomes of target group long-stay nursing home residents of intervention facilities are compared to those of identically defined residents of control facilities. This approach assumes that most eligible subjects in the intervention facilities will be directly exposed to the intervention by watching one of the videos. While there may be an indirect effect on the facility culture related to the availability of the videos and increased discussions of “comfort care”, direct exposure by watching the video is assumed to be the more powerful and complete approach to delivering the intervention.

As part of the PROVEN trial, intervention staff are to record when patients are offered and subsequently shown a video at each facility. The total number of long-stay target residents who “should have been shown” the video and the total number of such patients who actually viewed the video at the facility are routinely calculated. Although some families and patients may have watched videos online, we are unable to identify this number precisely. Thus, the proportion of patients whom staff report as having watched the video is a reasonable proxy for the level of implementation of the intervention across intervention facilities. As of the end of February 2018, only 12.5% of the long stay residents in System 1 facilities and 31.4% in System 2 facilities were

reported as having been shown a video. However, there is substantial variation in the rates of target residents reported as having been shown the video, ranging from 0% to over 80%. This raises the question of whether it would be possible to compare the outcomes of patients exposed to the video who reside in nursing centers that embraced the video-assisted advance care planning intervention to similar control patients from similar facilities.

The principal stratification framework¹³⁸ has been proposed as a possible solution to address non-compliance in randomized trials and is appropriate in this instance because facilities can be classified on the basis of the extent to which they implemented the intervention. The basic principal stratification framework initially posits that patient i has two possible potential compliances: compliance under the intervention arm, $D_i(1)$, and compliance under the control arm $D_i(0)$. Using these potential states (outcomes), we can classify patients into different strata and calculate the average effect within each stratum. When patients can either comply with the intervention or not, there are four principal strata: compliers ($D_i(1) = 1, D_i(0)=0$); never takers ($D_i(1) = 0, D_i(0)=0$); always-takers ($D_i(1) = 1, D_i(0)=1$); and defiers ($D_i(1) = 0, D_i(0)=1$). For each patient, only one of these compliance outcomes is observed.

Studies, such as ours, in which patients in the control group cannot obtain the intervention are commonly referred to as one-sided non-compliance. There are three possible strata: (1) assigned to the intervention and did not take it – never-takers; (2) assigned to the intervention and receive it – compliers; (3) assigned to the control and received control – can be either never-takers or compliers. Thus, a statistical methodology that is aimed at identifying the effect among compliers needs to identify among the control group those that would have not refused the treatment were it to have been offered. Numerous studies have fruitfully employed the principal stratification framework to estimate the effects of an intervention on compliers.^{139, 140, 141, 142}

We will estimate the effect of the intervention on the compliers who reside in facilities that have adopted the video-assisted intervention by creating a hierarchy including compliance at the facility level and, within facility, adjusting for compliance status at the individual level. As noted, we find high variability between intervention facilities related to the likelihood that a patient would receive the intervention. Because the intervention is delivered almost entirely through the mechanism of facility staff, we assume that individual compliance is affected by the facility's and patient's characteristics. We can classify the treated facilities into compliance groups based on the reported show rates and/or based upon more qualitative assessment of research staff working to implement the intervention with participating facilities. Compliance groups can be constructed and facility-level characteristics that are predictive of the compliance status can be identified using the large amount of facility and aggregated resident data we have available. Preliminary analyses reveal that several facility-level characteristics are correlated with the video offer and show rates. We propose developing a Bayesian model to multiply impute the compliance groups of control facilities based upon these types of facility-level characteristics for which we have considerable data elements. The net result is a pool of high intervention implementers and a corresponding set of control facilities with similar predicted compliance.

Preliminary data suggest that facility-level characteristics are more correlated with facility offer rates than to facility show rates. This suggests that, although facility characteristics influence the offer rate, patient-level characteristics are also important determinants of actually watching the video. Thus, we will develop a modeling framework that identifies the compliance status for each patient within the hierarchy of the cluster randomized trial. This approach will first impute compliance status group for control facilities and then will impute patient-level

compliance status within each facility compliance group. This two-part imputation is performed using Bayesian models to predict compliance status for each facility, followed by a Bayesian model of patient-level compliance within facilities with similar predicted compliance status. Formally, let $Y_i(W)$ represent the potential outcomes for patient i under the intervention, $W=1$, or the control, $W=0$. In addition, let $L_j(1)$ be the average compliance of facility j if it would have been assigned to the intervention arm, and $M_i(1)$ be the compliance of patient i if s/he would have resided in a facility exposed to the intervention. We would estimate the following models:

1. $f(Y_i(1), Y_i(0) | L_j(1), M_i(1), X_i, W_i, Z_j)$ - The potential outcomes conditional on patient's and facility's compliance status, and patient- and facility-level covariates. These models would be hierarchical zero inflated Poisson models.
2. $f(M_i(1) | L_j(1), X_i, W_i, Z_j)$ - The compliances status of patients conditional on the compliance status of the associated facility and on patient- and facility-level covariates. This model would be a hierarchical logistic regression model.
3. $f(L_j(1) | Z_j, W_j)$ - Models the compliances status of facilities conditional on facility characteristics. This model would be a linear regression model (with possible transformation) where X are patient level characteristics and Z are facility level characteristics.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1. Data Collection

All data are derived from existing data sources with exception of the Video Status Report User Defined Assessment. Please see *Section 6* which details these sources.

10.2. Data Confidentiality

Brown University's Center for Gerontology and Health Care Research will receive EMR patient-level data from PruittHealth and Genesis HealthCare. Both NH systems have integrated sophisticated EMR systems in their facilities. Genesis HealthCare uses PointClickCare™,⁹⁸ and PruittHealth uses American Health Tech.⁹⁹ The NH networks already have experience extracting MDS from their EMR systems for purposes of submitting mandatory, regular MDS reports to CMS. To protect patient confidentiality, the two corporations will place their data in a SSH secure server and will provide login information to Brown University. Data transfer to Brown University secure servers will be via SFTP protocol with password protection. Once the files have been uploaded to Brown University's servers they will be stored, unmodified, in a secure file location specific to these uploads. They will then be read into SAS datasets, one per file type. Brown University will then notify the facilities that the data was successfully downloaded and extracted, at which point the facilities will remove the data from their servers. All data files will be accompanied by a manifest detailing the number of distinct persons and records expected in them. Brown University will connect to the corporation servers on a monthly basis. Identifiers such as HICs and SSNs, will be included in order to be able to merge these person-level data to the data received from CMS. Brown University's information systems manager will be in charge of the data transfer, and he will replace the HICs and SSNs fields with a Brown University-generated identification number (throughout our different data sources) to allow linkage of data for analytic purposes.

10.3. Data Management

Brown University's Center for Gerontology and Health Care Research will serve as the Data Management/Statistical Center for the PROVEN trial. The Center will be responsible for: 1. Receiving all data from CMS (Medicare, MDS), ii. Receiving all EMR data from PruittHealth and Genesis HealthCare Study facilities, iii. Linking all data sources, and iv. Creating an analytic file and conducting analyses. Brown University investigators and database management staff already receive national MDS, Medicare, and OSCAR data semi-annually or quarterly under several CMS DUAs. There is a well-established data base management structure to linking these files. The only new activity for PROVEN is integration of the EMR data from facilities with CMS Medicare claims and the MDS. The integration will be easily achieved thanks to the availability of HIC and SSN personal identifiers in both the EMR data from facilities and in the CMS Medicare claims and MDS data.

10.4. Data Use Agreements

The Brown University Center for Gerontology has an extensive history of working with ResDac to obtain DUAs to use CMS MDS and Medicare data for NIH funded projects, which will be obtained for this project. DUAs for the data sharing arrangement between Brown University and the two partner health care systems, Genesis HealthCare and PruittHealth have already been obtained. Our team will ensure all DUAs are compliant with NIH requirements.

10.5. Quality Assurance Metrics

For the primary outcome, hospital transfers, we will have a quality control metric which compares hospital transfers as derived from MDS assessments with hospital transfers obtained from Medicare Part A claims for patients who are in the traditional fee-for-service Medicare program.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1. Institutional Review Board (IRB) Review

The PROVEN protocol will be reviewed and approved by the Brown University IRB.

11.2. Informed Consent

There are special informed consent considerations for individual patients in this pragmatic, cluster RCT. The NH is the unit of randomization, the intervention is of relatively low risk, and it will be implemented facility-wide as part of the intervention facilities' standard operating procedures for ACP. In the control arm, usual care for ACP will be in place. In both study arms, all data will be ascertained from existing sources. NH administrators, who either agree or disagree to facility participation in the intervention arm are serving as gatekeepers for the study. Thus, we will seek a waiver of individual informed consent so as set forth by the four criteria found in HHS 45 CFR 46:116.¹³⁷

(1) The research involves no more than minimal risk: See *Section 7.1* for rationale for Minimal Risk Determination

(2) The waiver will not adversely affect the rights and welfare of the subjects: All NHs must engage patients and families in ACP as part of routine clinical practice. There is currently no standardized method by which NHs conduct ACP. The ACP Video Program is intended to

enrich ongoing ACP practices in the intervention NHs. Study randomization is at the level of the NH, not the patient. While the patients in the intervention arm are not informed of the study itself they *are* asked whether or not they want to be shown the video. They are free to decline as they are free to decline any type of ACP discussion. Patients in control NHs will be exposed to usual care. For NH residents in both study arms, we will be using data previously collected for non-research purposes (EMR and CMS data. These data will be obtained and managed in a confidential manner for study purposes (*see Sections 10.2*).

(3) The research could not practicably be carried out without the waiver: It would be impossible to conduct this *pragmatic trial* if it required ascertainment of individual informed consent for several reasons. Doing so would undermine the very intent of the pragmatic trial design: to test whether the videos are effective in a “real-world” application under usual conditions. ACP is part of usual NH care and is simply being augmented in the intervention facilities with the videos. Getting written informed consent is not ‘usual’ for everyday NH care. In that vein, members of the NH staff are offering the videos to the patients in the intervention facilities, not the research team. The ACP videos are being integrated into the NHs’ standard operating procedures and offered to ALL NHs residents as part of the facility’s daily work-flow. It would not be feasible for the NH staff to obtain informed consent from all residents being offered the videos, especially since the videos are being integrated into the standard of care in that NH. With regards to data acquisition, all the data used in the study, with the exception of the Video Status Report User Defined Assessment, are already being collected for non-research purposes in both the intervention and control NHs. If permission to use these data were required by way of informed consent, this would have to be done for ALL residents in all facilities by staff in BOTH the control and intervention NHs. It would be impossible and put undue burden on the NH staff and the residents themselves to collect individual consent for the use of their records. Such an approach would once again undermine the pragmatic intent of the study and also dramatically reduce both NH and patient participation to the extent the study would not be possible.

(4) If appropriate, the subjects will be provided with additional pertinent information after participation: We will provide the NH corporations, PruittHealth and Genesis HealthCare, with copies of the reports and manuscripts that result from this project. They are free to share the information with their NHs, and the NHs will be free to share the information with interested families and patients.

11.3. Participant Confidentiality

We request a HIPAA Waiver of Requirement for Authorization for Release of Protected Health Information for Research Purposes from the Brown University IRB to conduct this study. Please see Section 10.2 for procedures for data confidentiality.

11.4. Study Discontinuation

The study may be discontinued at any time by the IRB, the NIA, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected.

12. ETHICAL CONSIDERATIONS

Ethical consideration for the PROVEN trial will be in accordance with the Federal Policy for the Protection of Human Subjects (HHS Human Subjects Research 45 Code of Federal Regulations (CFR) 46).137

13. COMMITTEES

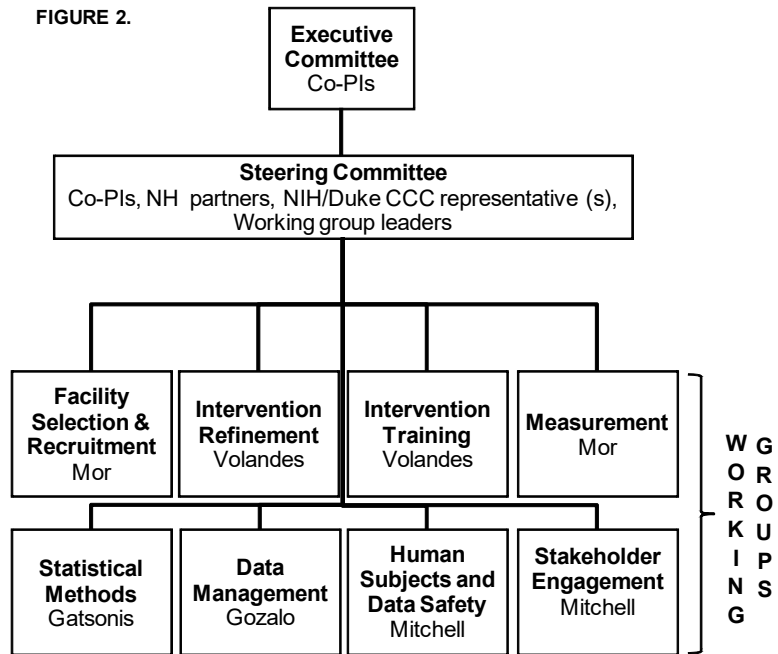
Figure 2 displays the organizational structure of the PROVEN team. The Executive Committee consisting of the 3 co-PIs will have ultimate responsibility for all aspects of the proven trial. As Brown University is the prime grant recipient, Dr. Mor will serve as the primary liaison for the trial to the NIH.

The project's Steering Committee has the following responsibilities: i. oversee overall project direction, ii. ensure close collaboration with HCS Research Collaboratory and NIH with timely submission of all requested project materials to these entities, iii. serve as the primary liaison between the project and the NH health care

systems, iv. coordinate tasks among individual working groups, v. ensure project milestones are met, and vi. review and approve all publications forthcoming from the PROVEN trial. The Steering Committee will ALSO serve as the primary vehicle for decision-making and help resolve conflicts or divergent approaches amongst investigators.

The functions of the individual working groups are to establish and coordinate all processes implicit in their titles.

FIGURE 2.



14. PUBLICATION OF RESEARCH FINDINGS

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

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16 APPENDICES

16.1. Data Safety and Monitoring Board Charter

16.1 Data Safety and Monitoring Board Charter

DSMB Charter

Title: PROVEN: Pragmatic Trial of Video Education in Nursing Homes,

Grant #: UH2AG049619

Principal Investigators: Vincent Mor, Susan Mitchell, and Angelo Volandes

Institution: Brown University

The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the National Institute on Aging (NIA) Director to monitor participant safety, data quality and progress of the study by the Principal Investigators Vincent Mor, PhD, Susan Mitchell, MD, and Angelo Volandes, MD for "PROVEN: Pragmatic Trial of Video Education in Nursing Homes" (grant UH2AG049619) and any successor grants funded by the National Institute on Aging.

DSMB Responsibilities

The DSMB responsibilities are to:

- review the research protocol, informed consent documents, and plans for data safety and monitoring;
- advise the NIA on the readiness of the study staff to initiate recruitment;
- evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
- review study performance, make recommendations, and assist in the resolution of problems reported by the Principal Investigator;
- protect the safety of the study participants;
- report to NIA on the safety and progress of the trial;
- make recommendations to the NIA, the Principal Investigator, and, if required, to regulatory authorities concerning continuation, termination, or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;

- ensure the confidentiality of the study data and the results of monitoring; and,
- assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection.

The DSMB will discharge itself from its duties when the study is complete.

Membership

Membership consists of persons completely independent of the investigators who have no financial, scientific, or other conflict of interest with the trial. Collaborators or associates of the PI are not eligible to serve on the DSMB. Written documentation attesting to absence of conflict of interest is required. This DSMB will consist of 3 members having been approved by the Director of NIA.

The DSMB includes experts in or representatives of the fields of:

- relevant clinical expertise,
- clinical trial methodology, and
- biostatistics.

Dr. Christine Ritchie, MD has been selected by NIA to serve as the Chairperson and is responsible for overseeing the meetings, reviewing the first draft of the meeting notes with the NIA Program Official, and any decision making in the case of a tie vote. The Chair and the NIA Program Officer are the contact people for the DSMB. Brown University shall provide logistical management and support for the DSMB.

The Chair will also serve as the safety officer. Any serious adverse events that might be related to the intervention will be reported to the Chair of the DSMB and the NIA Program Official by the PI within 24 hours of his learning of the event.

Board Process

The Principal Investigators will prepare the agenda to address the review of study materials, modifications to the study protocol and informed consent document, initiation of the trial, reporting of serious negative reactions, and statistical analysis plan for the first meeting. This will be in consultation with the DSMB Chairperson and NIA Program Official.

Meetings of the DSMB will be held at least two times a year or at the call of the Chairperson. The NIA Program Official or designee will be present at every meeting. An emergency meeting of the DSMB may be called at any time by the Chair or the NIA, should participant safety questions or other unanticipated problems arise.

Meetings shall be closed to the public because discussions may address confidential participant data. Meetings are attended by the Principal Investigators and members of their staff. These meetings are expected to be conducted via conference call, however an in-person meeting could be requested.

Meeting Format

DSMB meetings will consist of open and closed sessions. Discussion held in all sessions is confidential. The Principal Investigators and key members of the study team attend the **open sessions**. Open session discussion will focus on the conduct and progress of the study, including participant accrual, protocol compliance, and problems encountered. Unblinded data are not presented in the open session.

The **closed session** will be attended by the DSMB members and the NIA representative(s). The study statistician should be present to present the report. Any data by blinded study group and, as necessary, unblinded data, are presented during the closed session.

If necessary, an **executive session** will be attended by voting DSMB members and the NIA staff and their representatives. The executive session will be held to identify and discuss the DSMB's recommendations to the NIA. The study staff may be present, at the request of the DSMB, during the executive session.

Each meeting must include a recommendation to continue or to terminate the study made by a DSMB majority or unanimous vote. Should the DSMB decide to issue a termination recommendation, the full vote of the DSMB is required. In the event of a split vote, majority vote will rule and a minority report should be appended. The DSMB Chair provides the tiebreaking vote in the event of a 50-50 split vote.

A recommendation to terminate the study may be made by the DSMB at any time by majority vote. The Chair should provide such a recommendation to the NIA immediately by telephone and email. After the NIA Director makes a decision about whether to accept or decline the DSMB recommendation to terminate the study, the PI is immediately informed about the decision.

Meeting Materials

DSMB interim report templates will be prepared by the study staff, typically the statistician, to be reviewed by the DSMB members at the first meeting. Interim data reports generally consist of two parts:

- Part 1 - Open Session Report and
- Part 2 - Closed Session Report

Format and content of the reports for both the open and closed sessions and plans for interim analyses should be finalized and approved at the initial DSMB meeting, although changes throughout the trial may be requested by the Board.

The reports will list and summarize safety data and describe the status of the study. All meeting materials should be sent to the DSMB and the NIA at least 7 days prior to the meeting. The reports are numbered and provided in sealed envelopes within an express mailing package or by secure email as the DSMB prefers.

1. **Part 1 - Open Session Reports:** Open session reports will include administrative reports that describe participants screened, enrolled, completed, and discontinued, as well as baseline characteristics of the study population. Other general information on study status may also be presented. Listings of serious negative reactions and serious adverse events, as well as any other information requested by the DSMB, may also be in the open session

report, but none of the data will be presented in an unblinded manner. The DSMB may direct additions and other modifications to the reports on a one-time or continuing basis.

- 2. Part 2 – Closed Session Report:** Closed session reports will present the same information as presented in the open session but by blinded treatment group (e.g. A/B, etc.). The reports will contain data on safety measures. The closed session reports should be destroyed at the conclusion of the meeting. If meetings are held by telephone, printed copies of the closed reports should be destroyed immediately following the meeting.

Additional Reports

- 1. Mailings to the DSMB:** On a scheduled basis (as agreed upon by the DSMB) blinded safety data will be communicated to all DSMB members or to the designated Safety Officer. Secure email can be used for distribution.

- 2. Access to Interim Data:** Access to the accumulating endpoint data should be limited to as small a group as possible, such as the statistician. Limiting access to interim data to the DSMB members relieves the investigator of the burden of deciding whether it is ethical to continue to randomize individuals and helps protect the study from bias in recruitment and/or evaluation.

Reports from the DSMB

A report containing the recommendations for continuation or modifications of the study will be prepared by the NIA Project Officer. The draft report will be sent to the DSMB members not later than three weeks after the meeting. Once approved by the DSMB members, the Program Official will forward the DSMB recommendations to the Principal Investigator. It is the responsibility of the Principal Investigator to distribute the DSMB recommendation to all co-investigators and to ensure that copies are submitted to all the IRBs associated with the study.

As previously stated, the DSMB report must include a recommendation to continue or to terminate the study. This recommendation should be made by formal majority vote. A termination recommendation may be made by the DSMB at any time by majority vote. The NIA is responsible for notifying the Principal Investigator of a decision to terminate the study. In the event of a split vote in favor of continuation, a minority report should be contained within the regular DSMB report. The report will not include unblinded data or discussion of the unblinded data.

Confidentiality

All materials, discussions and proceedings of the DSMB are completely confidential. Members and other participants in DSMB meetings are expected to maintain confidentiality.