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Design Considerations for Embedded Pragmatic Clinical Trials of Advance Care Planning Interventions for Persons Living with Dementia

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Abstract

Advance care planning (ACP) is an important part of comprehensive care for persons living with dementia (PLWD). While many trials have established the efficacy of ACP in improving end-of-life communication and documentation of care preferences, there remains a gap in clinical usage. Embedded pragmatic clinical trials (ePCTs) may facilitate the uptake of evidence-based care into existing healthcare by deploying efficacious ACP interventions into real-world settings. However rigorous conduct of ePCTs of ACP for PLWD presents several unique methodological considerations. Here we describe a framework for the construction of these research studies, with a focus on distinguishing between the target of study: the PLWD, their care partners, or both. We outline specific considerations at each step of the research study process including (1) participant identification/eligibility, (2) participant recruitment/enrollment, (3) intervention implementation, and (4) outcome selection/ascertainment. These considerations are weighed in further detail by describing the approaches from three published trials. Specifically, we consider how potential challenges were overcome by tradeoffs in study design. Finally, we offer directions for future growth to advance ePCTs for ACP among PLWD and catalyze future research.

INTRODUCTION

There are over 5 million persons living with dementia (PLWD) in the US, and this number is predicted to grow dramatically in the coming decades. PLWD often experience fragmented, poor quality care, particularly at the end of life.[1] The broader spectrum of serious illness communication plays a critical role in care of PLWD. As one part of this spectrum, advance

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care planning (ACP) aims to improve end-of-life care by enabling patients to express their values and wishes regarding medical care to others, particularly their care partners and clinicians.[2] Thus, ACP may help to align the care PLWD receive to their expressed preferences Traditional randomized clinical trials (RCTs) evaluating ACP interventions in PLWD[3–5] have shown improvement in many outcomes, including advance directive completion, end-of-life communication, and healthcare savings.[6] Yet, these interventions have not been adopted into routine clinical care. Unlike traditional efficacy RCTs, embedded pragmatic clinical trials (ePCTs) are designed to evaluate the effectiveness of interventions under real-world conditions. The relative paucity of ePCTs evaluating and demonstrating the effectiveness of ACP interventions in PWLD may be one factor hindering their adoption into clinical practice.

The Pragmatic-Explanatory Continuum Indicator Summary (PRECIS)-2 tool identifies nine domains of trial-design that can be modified to make a trial more or less pragmatic.[7] Because the PRECIS-2 draws trialists' attention to considerations such as eligibility, setting, flexibility of intervention delivery, and follow-up that are important to all ePCTs, the tool is broadly useful in evaluating design decisions. Within each of the PRECIS-2 domains, there are numerous smaller decisions for trialists' to make and considerations to be addressed; decisions and choices within one domain will often affect other domains.

For instance, PLWD are a vulnerable population because they have disabling cognitive impairments and are often dependent on others to make decisions and care for them. Therefore, ePCTs evaluating ACP programs for PLWD present unique ethical and clinical considerations—such as capacity, consent, and surrogate decision making—with critical design implications.[8] Investigators must decide whether the target of the ACP intervention is the PLWD, their care partner, or both. Each choice entails new challenges and tradeoffs. Consider that ePCTs frequently use existing electronic health records (EHR) or claims data to identify eligible participants and ascertain outcomes. While many ePCTs meet the criteria for a waiver of informed consent based on federal guidelines,[9] the ability of cognitively impaired PLWD to provide consent for research or engage in ACP or other research procedures may not be discernable in the EHR, and EHRs rarely provide care partners' names or their contact information. The content and delivery of the ACP intervention may differ depending on whether the investigator seeks to engage the PLWD or the care partner, given cognitive variability. For example, if only the CP is targeted, then less focus may be placed on choosing a surrogate decision maker. Finally, choosing a primary outcome for an ePCT of an ACP intervention is fraught with challenges, often involving compromises between what is pragmatically attainable and what is most meaningful for the PLWD and care partner.

In this article, we provide a framework highlighting the unique methodological, clinical, and regulatory challenges investigators must consider when designing ePCTs of ACP interventions for dementia care in each of these three target groups around four key design features: (1) participant identification/eligibility, (2) participant recruitment/enrollment, (3) intervention implementation, and (4) outcome selection/ascertainment. Options for each design element and the trade-offs entailed are described. Next, we use the framework to describe strategies used in three examples of ACP interventions for PLWD.[10–12] Finally,

we offer insights for future researchers, including novel approaches to be considered or developed to advance this challenging but important field.

FRAMEWORK AND APPROACH

Three general populations can be targeted in ePCTs of ACP interventions for PLWD: PLWD only, care partners only, or both PWLD and care partners. In this section, we consider each of these features in turn, noting advantages and disadvantages of targeting a particular population. Table 1 summarizes the framework. Notably, the setting in which the planned research will be conducted plays a critical role, informing all levels of the study design process. How the infrastructure available within a particular setting, (e.g. electronic health records (EHR) availability), and may be appropriately leveraged or conversely pose a barrier, should be carefully considered.

Participant Identification and Assessment of Eligibility

Commonly, ePCTs use existing EHR data to identify eligible participants efficiently; this approach may help reduce the need for additional research infrastructure. In prior ePCTs designed to target ACP interventions at PLWD, researchers have used several validated algorithms that identify PLWD from EHR data, often using ICD-10 codes and other captured data (e.g., receipt of prescriptions for dementia drugs).[13–16] One disadvantage of this approach is that most EHRs do not include standardized data describing the patient's stage of cognitive impairment or decision-making capacity. Thus, if understanding dementia stage is important to distinguish eligible PLWD, this information will need to be gleaned from a clinician, potentially undermining the pragmatic nature of the ePCT. In addition, EHRs do not always capture advance directives or health proxy data in a standardized way. This hinders the ability to base participant eligibility criteria on the PLWD's baseline advance directive status (e.g., exclude those on comfort care) or health care proxy activation.

A decision to target the ACP intervention towards only care partners enables enrollment of PLWD with more advanced cognitive impairment in the ePCT. Since the care partner represents both the PLWD and themselves, the PLWD would not be directly engaged. Unfortunately PLWD in early-stage disease may need to be excluded, and determining the stage of dementia may require clinician input. Also, ePCTs that include care partners as participants are hindered by the fact that in most health care systems, EHRs do not routinely capture or update care partners' names and contact information. Thus, ePCTs requiring a care partner participant may exclude many PWLDs when there is no documentation of a care partner or when they are unbefriended; this will limit generalizability and potentially introduce biases into the trial.

Finally, ePCTs designed to include both PLWD and care partners have the advantage that they can evaluate the effect of the ACP intervention for PLWD at all stages of dementia. However, for PLWD with capacity, engaging a care partner may not be clinically appropriate. Also, requiring a PLWD-care partner dyad for eligibility still faces the challenge of identifying care partners using the PLWD's EHR. Additionally, researchers might consider whether specific eligibility criteria apply to the PLWD and the care partner separately.

Participant Recruitment and Enrollment

Participants in ePCTs may be randomized at the individual or cluster (e.g., primary care practice or nursing home; an aspect of the study design which directly informs how participants are recruited and enrolled. For example, if the unit of randomization is a nursing home or provider practice group, it may be impracticable to obtain consent on each individual participant. Thus, the issue of consent in ePCTs of ACP interventions for PLWD is particularly complex.[8]

As ACP is a part of usual clinical care, engaging in ACP does not require research consent itself. Notably, the cognitive ability needed to engage in ACP is generally lower than the level of cognition and capacity needed to consent to research.[17] Whether a PLWD can engage in ACP may not be explicitly determinable using existing data sources such as medical claims or EHR, thus requiring clinician involvement for determination. Assessing whether a PLWD has the cognitive ability to engage in ACP and express their preferences in an informed and consistent matter is beyond the scope of this paper.

In general, obtaining a waiver of informed consent for research is advantageous, as the process of obtaining consent may be antithetical to the pragmatic nature of the trial. Previous authors have discussed these conditions in detail, including specific considerations for PLWD.[8,9] If individual informed consent for research is *not* waived and PLWD are target participants, their capacity to engage in research must be assessed. This will require the research team to engage the PWLD during the recruitment process, as cognitive tests obtained in usual clinical care should not substitute for assessing capacity to consent to research. Moreover, requiring consent directly from the PLWD may limit generalizability by excluding those with more advanced dementia who lack the requisite decision-making abilities. While targeting PLWD is facilitated by availability in EHR data, cognition may limit their ability to actively respond to recruitment efforts (e.g., calling the phone number on a flyer).

If the ePCT targets only care partners, they may be more responsive to enrollment efforts. If individual consent is required, the care partner will typically be able to consent to their own research participation, and so do not raise the same concerns of capacity assessment relevant to PLWD. Biases may be introduced if the care partner's contact information is not available in the EHR to enable recruitment efforts, if clinician input is needed to identify care partners who should be approached for participation, or if the PLWD is unbefriended. Finally, there remains the possibility that neither the PLWD nor their care partner is aware of the dementia diagnosis, even though it is documented in the EHR.[18] Thus, investigators must thoughtfully design recruitment materials to avoid inadvertently disclosing a diagnosis not previously communicated by a clinician.

Those ePCTs designed to include both PLWD and care partners have increased potential for successful enrollment. If individual consent for research is not waived, one may need to seek consent from both the PLWD and the care partner. In some cases, the care partner may provide informed permission for the PLWD's research participation. There may, however, be situations where the care partner is not the PLWD's legally authorized representative and thus cannot make decisions on the PLWD's behalf. Further, laws regarding research

consent vary from state to state; investigators should familiarize themselves with local laws and regulations. If a care partner provides informed permission, investigators should still seek the assent (or respect the dissent) of the PLWD, as even people with severe dementia can evince preferences about research participation. As noted above, clinician input may be needed to determine which care partners to contact, which may introduce bias.

Intervention Design and Implementation

When PLWD are the target participants, a potential advantage is a possibility of using existing health care system infrastructure to efficiently deliver program materials and engage directly with the PLWD (e.g., patient portals). However, cognitive impairment may limit the PLWD's ability to adhere to the ACP intervention and protocols (e.g. completing written materials). Moreover, the content and implementation of the ACP intervention need to be appropriate for the unique considerations of PLWD, for example, artificial nutrition or antibiotic use for aspiration pneumonia. In an ePCT, the intervention is generally not delivered by research staff. If the intervention is to be deployed by existing clinical staff, the investigator may need to consider additional training or resources for care providers to implement the ACP intervention.

Targeting the care partner as the main ePCT participant may improve adherence to intervention protocols and reflect how ACP is typically approached for PLWD with more advanced cognitive impairment. In this situation, however, ACP will rely on the surrogate's perceptions of the PLWD's preferences which is a limitation because PLWD may not necessarily agree with their care partners, and there is no way to assess dyad discordance. It should be acknowledged that the surrogate decision-making process can be extremely challenging, and that surrogates sometimes may make decisions that oppose previously expressed preferences.[19–21]

Those ePCTs designed to include both PLWD and care partners have the advantage that they can evaluate the effect of the ACP intervention for PLWD at all stages of dementia. While the PLWD may be a primary decision-maker for those with early disease, the care partner is often more involved for those with advanced disease. Designing the intervention to engage both the participant and care partner, as appropriate, allows one to most closely approximate actual clinical care encompassing a spectrum of disease severity. Furthermore, the care partner can be relied upon when the PLWD lacks the cognitive capacity, potentially enhancing protocol adherence. Despite these advantages, this option complicates the research protocol, necessitating processes to determine whether the intervention should be delivered to the PLWD, care partner, or both. Two different sets of intervention materials and delivery strategies may be needed—one directed at the PLWD and another at the care partner.

Outcome Selection and Ascertainment

Outcomes should be carefully selected to be meaningful for the PLWD-care partner dyad yet obtainable pragmatically. Common data sources for outcome ascertainment in ePCTs include the EHR and Medicare Claims data, which are typically easily linked to the PLWD and similarly measurable in both intervention and control groups without needing primary

data collection. Yet, important outcomes reflecting effective ACP are often recorded in non-standardized fashions or entirely absent from these sources. Of particular concern, EHR data rarely captures the nuances of goals of care discussions or patient-centered outcomes, such as whether hopes and expectations were discussed or prognosis communication. Thus, adjudicating whether the PLWD received goal-concordant care, the holy grail of successful ACP,[22–24] is very challenging using an ePCT design and generally will require resource-intensive primary data abstraction and/or primary data collection.

Targeting the ACP intervention toward care partners raises similar challenges. Specific care partner-related outcomes, such as satisfaction with end-of-life care, bereavement, or caregiver stress, may be of particular interest to researchers. However, ascertaining care partner-specific outcomes of an ACP intervention, such as whether the care partner believes the PLWD received goal-concordant care or decisional conflict, is typically not documented in the EHR and therefore challenging to obtain in a pragmatic fashion. If the researchers want to measure health care outcomes for the PLWD, whether based in the EHR or otherwise, it may be necessary to obtain consent from the PLWD, separate from that provided by the care partner. Finally, if the PLWD dies, the ability to contact the care partner through the health care system may be lost.

Designing ePCTs to include both PLWD and care partners has strengths and limitations for measuring the outcomes of ACP interventions. Including the dyad best approximates real-world experiences. This includes the possibility of progression of a PLWD's disease, over the course of the study, necessitating care partner involvement. Additionally, including both offers the opportunity to measure dyadic concordance related to preferences and alignment of care with goals. The same challenges for outcome ascertainment arise for dyads as for either the PLWD or the care partner alone. Further, suppose a dyad member is not consistently available. In that case, there may be a need to account for discrepancies in outcome measurement between decisions made by the PLWD only, care partner only, or both.[25]

Examples of ePCTs of Advance Care Planning Interventions Among PLWD—

Here, we provide descriptions of three embedded RCTs evaluating the effectiveness of ACP in PLWD. Although not all have published results in entirety, these have been selected for the range of possibilities and challenges faced by investigators. Table 2 describes how the investigators navigated the challenges identified within the framework.

First, the PROVEN study was a cluster ePCT of an ACP video program for older adults with advanced illnesses, including dementia, living in nursing homes.[11] A total of 360 nursing homes were randomized to either control or intervention arms. All eligible participants in nursing homes were enrolled, with no exclusion criteria for individual participants. The institutional review board (IRB) granted a waiver of informed consent for the study, allowing for maximum generalizability with no restrictions, thus including those with severe dementia. Although nursing home administrators could opt out of the program, they were not informed that facilities were involved in a research trial. Each nursing home had an ACP video program "champion" who identified participants and families and showed them the ACP video. The intervention delivery was done by the clinical staff and thus

very pragmatic. The primary outcome, hospital transfers, was obtained from Medicare claims data, thus highly pragmatic but not particularly patient-centered. Advance directives were not recorded in a standardized fashion across facilities, and goal concordance could not be ascertained. Ongoing pragmatic trials of ACP interventions in real-world settings offer promising opportunities to establish sustainable programs for PLWD. For example, APPROACHES is an ePCT evaluating a staff led ACP champion intervention in partnership with nursing home corporations, which shares many design features with the PROVEN trial.[26]

The second study by Gabbard et al.,[27] evaluated a nurse navigator ACP pathway RCT for older adults with multimorbidity and cognitive or functional impairment in outpatient primary care clinics. The patients were the target of the intervention; thus, persons with moderate or severe cognitive impairment were excluded based on Short Portable Mental Status Questionnaire scores administered by trained clinical staff (nurse navigators). A Zelen design was used to randomize subjects in a 1:1 fashion. Only subjects randomized to the intervention arm were approached for phone consent to the ACP intervention by nurse navigators and had a written copy of the information sheet mailed to them.[28] Of those that were randomized to the intervention, only roughly half consented; however of those the vast majority (139/146) completed the intervention. The intervention involved a pre-visit ACP telephone consultation with the nurse navigator, followed by an ACP-focused visit with their primary care professional that included standardized ACP EHR documentation and billing procedures. The primary outcome was new documentation of an ACP discussion in the EHR, ascertained via manual abstraction by the research team, and thus not very pragmatic. However, more pragmatic measures were collected as secondary outcomes, including ACP billing codes, health care use, and ACP documentation extracted from the EHR.

Finally, our group is currently conducting the Bluestone ACP ePCT, testing the effectiveness of an ACP intervention among PLWD residing in assisted living settings. By partnering with an affiliated primary care provider group, EHR data was available for participant screening. All PLWD living in assisted living facilities with a diagnosis of dementia at any stage based on EHR diagnoses were eligible, although cognitive screening was not incorporated. The study enrolled residents without a Do-Not-Resuscitate (DNR) order. The Bluestone team created a new field in the EHR to document DNR status before the start of the trial. Target participants were the PLWD or care partner. The IRB granted a waiver of informed consent. Assisted living facilities were randomized to either the intervention or usual care. The intervention provided information about ACP to either the PLWD delivered directly to the ALC or the care partner electronically or via mail, adding complexity to the implementation protocol in determining who (i.e., PLWD or care partner) would receive study materials and how (i.e., mailing versus the electronic patient portal). To approximate clinical care and best integrate the intervention into existing clinical workflows, two sets of ACP information materials, one for PLWD and one for care partners, were created. The decision of which materials to send and by what modality was left to the discretion of the clinical staff. The primary outcome was proportion of residents with DNR orders ascertained from the EHR. Secondary outcomes included proportion of residents with DNH orders ascertained from the HER and Medicare billing codes for ACP conversations.

DISCUSSION

Conducting ePCTs of ACP interventions for PLWD addresses a critical need to evaluate their effectiveness as they would be used in clinical practice. Nevertheless, because the research occurs at the intersection of ACP, dementia, and ePCTs, these trials involve complex methodological challenges. The presented framework is intended to offer guidance to researchers designing ePCTs evaluating ACP interventions for PLWD within health care systems, highlight key design options, and present the advantages and disadvantages.

In general, including both PLWD and care partners most closely approximates clinical care and thus from a pragmatic perspective, may be the most desirable. In particular for ePCTs, ACP intervention design must consider whether to be relatively simple (e.g., nudges) and easier to implement but potentially too light a touch or, in contrast, more complex, harder to implement with fidelity but potentially more effective. Yet, even seemingly simple interventions like the ACP videos in the PROVEN trial were challenging to embed into clinical care with fidelity, as ultimately only roughly 1 in 5 of targeted residents receiving the intervention as per protocol and considerable adherence variability between facilities. Upfront involvement of key stakeholders (e.g., providers, care partners, PWLD, front-line staff, and health system EHR experts) may help navigate the challenges associated with dyadic participation, including leveraging clinical decision making instead of capacity assessment. Structural barriers to ePCT success include the lack of inclusion of care partner information within EHRs and lack of standardized measures of cognition. Both of these can be remedied. In other specialties such as pediatrics, parent and guardian contact information is routinely and effectively captured in the EHR. The EHR could also be amended to facilitate collection of cognitive measures as part of clinical care for staging. It is also advantageous to use a waiver of individual consent for research to maximize generalizability whenever possible; it is useful to design a study that is both scientifically and methodologically robust and to see if a waiver is possible with no or minimal modifications. For example, despite using the Zelen method in the Gabbard study, the process of obtaining consent still reduced participation by nearly half among those randomized to intervention.

Lastly, tension between pragmatic and patient-centered outcomes for ACP interventions remains a challenging issue for ePCTs. While leveraging secondary data sources is the most pragmatic approach, these may not capture goal-concordant care. There are no systematic means of determining baseline goals, changes in goals, and whether these are aligned. Adjudicating stated goals with care received is likely to be labor and resource-intensive and may involve primary data collection.[22,30] For both clinical and research purposes, there is a need for standardized ACP documentation in common EHR systems, such as PointClickCare[31] or Epic,[32] and other standardized assessments, such as the Minimum Data Set. Such documentation should not be limited to advance directive orders (e.g., DNR) but also goals of care discussions, preferences, and health care proxy designation. Creative novel solutions include creating new fields in the EHR, using natural language processing to obtain goals of care discussion from unstructured fields, or using keyword searches.[33]

CONCLUSION

Many of the considerations presented in this report are broadly relevant to ePCTs, ACP interventions, and care for PLWD. Recently, some have questioned the role of ACP both in clinical care and as a research focus,[34,35] due to relatively disappointing results of several large trials.[4,36] Indeed, designing robust trials is challenging. ACP interventions may lead to inconclusive trial results,[37] but it is misleading to conclude that these interventions lack efficacy or effectiveness. Advances in intervention design and trial methodologies continue to evolve and adapt as new technology enables researchers to deliver interventions and measure outcomes more pragmatically. Ongoing considerations for how to best include care partners and creative methods for outcome ascertainment remain priority areas for future studies to explore.

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TABLE 1.

ACP for PLWD ePCT Design Framework

	Participant Identification/ Eligibility	Participant Recruitment/ Enrollment	Intervention Structure/ Implementation	Outcome Selection/ Ascertainment
Participants (PLWD) Only	*Advantages* • Can identify PLWD in EHR using algorithms *Challenges* • If ACP status part of eligibility criteria (e.g., power of attorney not yet activated, no prior advance directives), this information may not be captured in EHR • If screening by cognitive status (e.g excluding severe dementia), may not be captured accurately in EHR • May require clinician input to restrict eligibility to only PLWD who have decision-making capacity for ACP thus limiting trial's generalizability	*Advantages* • PLWD contact information easily attainable in EHR, which facilitates Information about ACP intervention *Challenges* • Cognitive status may undermine PLWD's ability to ability to act on Information about ACP program (e.g., engagement with participants portals, letters) • PLWD decision making capacity for consent will need to be assess prior to enrollment	*Advantages* • Engaging in ACP directly with PLWD • PLWD contact information easily attainable in EHR, which facilitates direct delivery of ACP program materials *Challenges* • ACP materials need to be designed specifically for PLWD • If using existing clinical staff, may need to provide additional ACP training • Cognitive status may undermine PLWD's ability to receive intervention and adhere to implementation protocols	*Advantages* • Outcomes from EHR or claims easily linked to participants *Challenges* • Measures readily available in EHR or claims-based measures may not be the most important ACP outcomes • EHR may not capture ACP processes or advance directives in a standardized manner
Care Partner Only	*Advantages* • Can enroll PLWD who lack decision-making capacity *Challenges* • Care partner contact information may not exist, be listed or current in EHR • May need to restrict eligibility to care partners of PLWD who no longer have decision-making ability; will require clinician input for determination and limit trial's generalizability	*Advantages* • May be more responsive to program participation invitations • Care partners can provide individual consent for their own participation without consideration of PLWD's capacity *Challenges* • Care partner contact information may not be listed in EHR • Clinician input may be needed to determine if care partner 'okay' to approach for participation, potential for selection bias	*Advantages* • Care partners may be more likely to engage in intervention, improving protocol adherence *Challenges* • Reliant on care partner perceptions of PLWD preferences for ACP, which may not be concordant	Same as for PLWD only *plus* *Advantages* • May be able to assess unique care partner outcomes *Challenges* • Care partner-specific outcomes hard to obtain pragmatically in EHR, in especially control arms • If PLWD dies, may lose ability to contact care partners • PLWD with decision-making ability may need to consent for ascertainment of outcomes from their EHR separately
PLWD with Care Partner	*Advantages* • Can include PLWDs with and without decision-making capacity for ACP (i.e., can include all dementia stages) *Challenges* • If PLWD-care partner dyad cooperation necessary, may exclude PLWD without readily identifiable care partners and limit generalizability	*Advantages* • Can reach out / invite both care partner and PLWDs, increasing potential for engagement. • Care partners can provide individual consent for participation of the dyad if the PLWD cannot consent *Challenges* • Clinician triage likely needed to determine who to contact for enrollment (whether to contact PLWD or care partner) • Care partner contact information may not be listed in EHR • May need to obtain consent from both PLWD and care partner • Rules may vary by	*Advantages* • Engaging in ACP with options of PLWD and care partner closely approximates 'real' clinical care • If PLWD does not have capacity to participate in ACP, care partner can be relied upon to receive materials and improve protocol adherence *Challenges* • Protocol complicated by needing to determine whether to create materials, send materials to and have ACP discussions with PLWD, care partner or both	Same as above, *plus* *Advantages* • Potential to measure care partner and PWLD concordance • Both PLWD and care partner may self-report outcomes • Potential to assess goal concordant care from both PLWD and care partner perspective *Challenges* • If each member of the dyad is not consistently available for follow-up, may need to account for discrepancy between PLWD only vs care partner only vs dyad decisions • Care partner may need to

	Participant Identification/ Eligibility	Participant Recruitment/ Enrollment	Intervention Structure/ Implementation	Outcome Selection/ Ascertainment
		state complicating protocol development		consent for ascertainment of their outcomes separately

Note: This framework assumes that individual consent for research is waived; additional considerations if waiver of consent is not obtained are highlighted in gray.

Abbreviations: ACP – Advance Care Planning, DNI – Do Not Intubate, DNR – Do Not Resuscitate, EHR – Electronic Health Record

Table 2.

Examples of Pragmatic ACP studies and Specific Design Considerations

Title	Setting and unit of randomization	Participant Identification/ Eligibility	Participant Recruitment/ Enrollment	Intervention Structure/ Implementation	Outcome Selection/ Ascertainment
PROVEN JAMA-Internal Medicine 2020	• 360 Nursing homes • Randomized at nursing home level (241 in control, 119 in intervention arm)	• Who: All Participants in nursing home • Source: Electronic health records (EHR) • Exclusion: No exclusion based on cognitive status or prior code status	• Facility: Administrators notified they were assigned to ACP program, with option to opt out • Participants: All eligible Participants in the nursing home enrolled • Consent: Waiver of individual consent	• Target: Participants or their care partners, decided by clinical staff • Administered by: Nursing home staff • Intervention: Informational ACP video • Additional Infrastructure: Report added to EMR to record when video offered	• Source: Participants only. Medicare Claims and EHR • Primary Outcome: Hospital transfers • Secondary Outcomes: Burdensome treatments (eg. tube feeding, ICU admission), hospice enrollment
Hickman Clinical Trials 2022	• 137 Nursing Homes • Randomized at the nursing home level (68 intervention, 69 control)	• Who: All participants in nursing home • Source: Minimum Data Set • Exclusion: Hospice enrollment	• Facility: ACP Specialist to be identified within the nursing home • Participants: All eligible Participants in the nursing home enrolled • Consent: Waiver of individual consent	• Target: Participants or their care partners, decided by clinical staff • Administered by: Nursing home staff • Intervention: ACP Specialists to engage residents in ACP • Additional Infrastructure: Training and salary support for ACP specialist Program	• Source: Participants only. Medicare Claims and EHR • Primary Outcome: Hospital transfers • Secondary Outcomes: ACP Preference Documentation (Orders), hospice enrollment, location of death
Gabbard JAMA-Internal Medicine 2021	8 primary care practice in an accountable care organization • Randomized at the Participant level	• Who: 65 or older, with multimorbidity, cognitive or physical impairment (by ICD codes), or frailty (electronic FI) • Source: EHR • Exclusion: Moderate to severe cognitive impairment, moderate to severe hearing loss	• Facility: Primary Care clinics • Participants: Participants with care partner involvement invited, but not required • Consent: Verbal consent from participants only (not controls). Consent not obtained from care partner	• Target: Participants with option of their care partners • Administered by: Nurse navigators • Intervention: Called participants inviting to ACP visit. If participants agreed, scheduled dyad for ACP visit with PCP • Additional Infrastructure: EHR ACP interface to standardize ACP, integrated into clinical workflow	• Source: Participants only. Medicare claims and EHR • Primary Outcome: New documentation of ACP discussion in EHR identified through manual review • Secondary outcomes: Completion of ACP legal forms, ACP billing codes
Bluestone project	160 Assisted living facilities • Randomized at ALF level to two arms: control (usual care) vs information	• Who: Residents with dementia, full code or missing code status, being cared for by a Bluestone provider • Source: EHR • Exclusion: No Exclusion based on cognitive status	• Facility: Assisted Living Facilities (with affiliated Primary Care Provider group) • Participants: All eligible participants enrolled, with provider discretion for participant participation • Consent: Waiver of informed consent	• Target: PLWD or care partner • Administered by: Clinical/Primary Care Group staff • Intervention: ACP information sent Participants/care partners plus physician ACP training • Additional Infrastructure: Advance directive fields built into EHR	• Source: Participants only. Medicare claims and EHR • Primary outcome: proportion of residents with DNR order at end of 4-month follow up • Secondary Outcome: Proportion of residents with DNH order at end of 4-month follow up, Billing codes for ACP conversations

Note: Abbreviations: ACP – Advance Care Planning, DNI – Do Not Intubate, DNR – Do Not Resuscitate, EHR – Electronic Health Record